DEPARTMENT OF HEALTH & HUMAN SERVICES **Public Health Service**

Food and Drug Administration
Rockville, MD 20857

January 31, 2022

Kathryn Blankenberg
Paul J. Orfanedes
Judicial Watch, Inc.
425 Third Street SW
Suite 800
Washington, DC 20024

Sent via email: kblankenberg@judicialwatch.org
porfanedes@judicialwatch.org

Re: FDA FOIA Request 2021-4379; *Judicial Watch, Inc. v. U.S. Department of Health and Human Services,* 21-cv-2418

Dear Ms. Blankenberg and Mr. Orfanedes,

This is a partial response to the Freedom of Information Act (FOIA) request number **2021-4379** that is the subject of the Complaint filed in *Judicial Watch, Inc. v. U.S. Department of Health and Human Services*, 21-cv-2418, now pending in the U.S. District Court for the District of Columbia.

Enclosed are 663 pages of records, some of which contain redaction.

We have withheld portions of pages under Exemption (b)(4), 5 U.S.C. § 552(b)(4). That exemption permits the withholding of trade secrets and commercial or financial information that was obtained from a person outside the government and that is privileged or confidential.

In addition, we have withheld portions of pages under Exemption (b)(6), 5 U.S.C. § 552(b)(6). That exemption protects information from disclosure when its release would cause a clearly unwarranted invasion of personal privacy. FOIA Exemption 6 is available to protect information in personnel or medical files and similar files. This requires a balancing of the public's right to disclosure against the individual's right to privacy.

Please direct any questions regarding this response to Jonathan Silberman, Associate Chief Counsel, Food and Drug Administration, telephone number (240) 731-9982 or email Jonathan.Silberman@fda.hhs.gov.

Sincerely,

Beth Brockner Ryan
Chief, Access Litigation and Freedom of Information Branch
Division of Disclosure and Oversight Management
Office of Communication Outreach and Development
Center for Biologics Evaluation and Research

Enclosure(s)

(b) (4)

FINAL REPORT

Ad26 (b) (4): 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Test Article:
Ad26 (b) (4)

Sponsor:
Beth Israel Deaconess Medical Center
Division of Viral Pathogenesis
Research East Room 213
41 Avenue Louis Pasteur
Boston, Massachusetts 02115

Testing Facility:
(b) (4)

(b) (4)

Authors:
(b) (4), (b) (6)

Study Completion Date:
September 14, 2007

Document No.: (b) (4)

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COMPLIANCE STATEMENT

Ad26 (b) (4): 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

This study was conducted in compliance with current U.S. FDA Good Laboratory Practice (GLP) Regulations for Non-clinical Laboratory Studies (21 CFR Part 58) with the following exceptions:

- Stability analyses of the placebo/control article has not been provided by the Sponsor.
- Characterization of the test article was performed under GRP regulations.
- Characterization of the control article was performed under GMP regulations.

There were no deviations from the aforementioned regulations that affected the quality or integrity of the study or the interpretations of the results in this report.

Study Director:

(b) (4), (b) (6)

9-14-07
Date

QUALITY ASSURANCE STATEMENT

Ad26 (b) (4): 91-Day Intramuscular Single Dose
Biodistribution Study in New Zealand White Rabbits

This study was inspected/audited by Quality Assurance in accordance with (b) (4) (b) (4) Standard Operating Procedures, the protocol, and FDA Good Laboratory Practice regulations. All findings were reported to the Study Director and Testing Facility Management as indicated below.

		Date Reported	
Type of Audit	**Date(s) Audited**	**Study Director**	**Management**
Protocol Audit	January 30, 2007	January 31, 2007	January 31, 2007
Dose Administration	February 2, 2007	February 5, 2007	February 5, 2007
Draft Report and Raw Data	June 25-26, 2007	June 27, 2007	June 27, 2007
Final Report Post Audit	September 10, 2007	September 10, 2007	September 10, 2007

The Biodistribution analysis was conducted by (b) (4) under the purview of their QAU. (b) (4) Quality Assurance Statement is presented in Appendix No. 6.

Action has been taken in response to all items listed by Quality Assurance. It is concluded that the final report accurately reflects (b) (4) Standard Operating Procedures and the raw data for this study.

(b) (4), (b) (6)
Sr. Quality Assurance Auditor

14 Sept 2007
Date

SIGNATURE PAGE

Ad26 (b) (4): 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Authors:

(b) (4), (b) (6)

Study Director

9-14-07
Date

(b) (4), (b) (6)

Toxicology Associate

9/14/2007
Date

Peer Review:

(b) (4), (b) (6)

Senior Director of Toxicology

9/14/07
Date

SUMMARY

Ad26 (b) (4) 91-Day Intramuscular Single Dose
Biodistribution Study in New Zealand White Rabbits

The purpose of this study was to determine the biodistribution of an adenovector-based (b) (4) vaccine in New Zealand White rabbits during a 91-day study period when administered by a single intramuscular injection.

Forty eight rabbits were randomly assigned to one of two groups (9/sex in Group 1 and 15/sex in Group 2). Animals were administered placebo (Group 1) or Ad26 (b) (4) at 0.5 x 10^{11} virus particles (Group 2) via intramuscular injection on Study Day (SD) 1. Necropsies were performed on 3 animals/sex in Group 1 and 5 animals/sex in Group 2 on SD 11, 61, and 91 to collect tissues for biodistribution analysis. Parameters evaluated during the study included clinical and cageside observations, body weights, body weight changes, and biodistribution.

Treatment with Ad26 (b) (4) vaccine at a dose 0.5 x 10^{11} virus particles did not affect mortality, clinical observations or body weights.

Quantitative PCR (qPCR) analysis indicated that the vaccine was primarily localized in the spleen, iliac lymph node, and the muscle at the site of injection. By SD 61, the vaccine was no longer detected in the spleen. By SD 91, detection of the vector in the iliac lymph nodes and injection site muscle was noted in only 2 of 10 treated animals.

In conclusion, a single intramuscular injection of Ad26 (b) (4) vaccine (0.5 x 10^{11} virus particles) was well tolerated in male and female New Zealand White Rabbits. Biodistribution analysis indicated that Ad26 (b) (4) was cleared from most of the examined tissues by SD 91.

STUDY PERSONNEL AND TEST SITES

Study Director:	(b) (4), (b) (6)
Toxicology Associate:	(b) (4), (b) (6)
Report Associate:	(b) (4), (b) (6)
Technical Supervisor:	(b) (4), (b) (6)
Manager, Formulations:	(b) (4), (b) (6)
Supervisor, Necropsy:	(b) (4), (b) (6)
Director, Vivarium Operations:	(b) (4), (b) (6)
Director, Laboratory Animal Medicine:	(b) (4), (b) (6)
Sponsor:	Beth Israel Deaconess Medical Center Division of Viral Pathogenesis Research East Room 213 41 Avenue Louis Pasteur Boston, MA 02115
Sponsor's Representative:	(b) (4), (b) (6)
Laboratory Operations Animal Facility:	(b) (4)
Biodistribution Analysis:	(b) (4), (b) (6) (b) (4)
Archives Data:	(b) (4)
Preserved Specimens:	(b) (4)

STUDY TIMETABLE

Study Initiation Date:	January 8, 2007
Experimental Start Date/Receipt of Animals:	January 22, 2007
Randomization of Animals:	February 1, 2007
Dosing:	February 2, 2007
Necropsy	
Terminal (SD 11):	February 12, 2007
Recovery 1 (SD 61):	April 3, 2007
Recovery 2 (SD 91):	May 3, 2007
Experimental Completion Date:	July 6, 2007
Study Completion Date:	September 14, 2007

INTRODUCTION

The purpose of this study was to determine the biodistribution of an adenovector-based (b) (4) vaccine in New Zealand White rabbits during a 91-day study period when administered by a single intramuscular injection.

The rabbit was used for the study because of the FDA recommendation for assessing the biodistribution of adenovirus-vectored vaccines. The intramuscular route was selected since it is the intended route of human exposure. The dose for this study was selected based on the largest amount of vaccine that can be delivered into the rabbit muscle with one injection.

The protocol, amendments, and deviations are presented in Appendix 7.

METHODS AND MATERIALS

Test and Control Articles

Neat Materials

The neat test and control articles used on this study are described in Text Table 1.

Text Table 1: Neat Test and Control Articles

Name	Lot No.	Supplier	Purity	Description
Ad26 (b) (4) Placebo	06M05/01	Crucell Holland BV The Netherlands	Assumed 100%	Clear solution
Ad26 (b) (4)	06K02/01	Crucell Holland BV The Netherlands	Assumed 100%	Clear to slightly opalescence solution

The test article, Ad26 (b) (4) was received on dry ice and stored frozen at -75 ± 15°C upon receipt. The control article, Ad26 (b) (4) Placebo, was received on cool packs and stored refrigerated at 2 - 8 C upon receipt. The Certificates of Analysis are presented in Appendix 1.

No reserve samples were taken for this study because reserve samples of the same lot were taken in study (b) (4)

Any remaining test and control articles were returned to the Sponsor, and any empty containers were discarded on September 4, 2007.

Dose Formulations

No formulations were required because the control and test articles were supplied in ready-to-use form.

On the day of dosing, the appropriate number of control article vials were removed from the refrigerator and allowed to equilibrate to room temperature for approximately 30 minutes. The appropriate number of test article vials were removed from the freezer and allowed to thaw and equilibrate to room temperature for approximately 45 minutes.

Dosing materials, dispensed in pre-filled syringes, were maintained at room temperature before and during dosing and were used within 4 hours after thawing.

Stability analysis of the test article is presented in Appendix 1.

Test Animals and Husbandry

Animals

Animal information is provided in Text Table 2.

Text Table 2: Animal Information

	Males	Females
Species and Strain	New Zealand White rabbits (HsdOkd)	
Supplier	(b) (4)	
Number of Animals Received	26	26
Number Used on Study	24	24
Age at Receipt	11 – 16 weeks	11 – 16 weeks
Weight Range at Receipt	2276 – 2606 g	2100 – 2533 g
Disposition of Extra Animals	Extra animals were transferred to the training colony	

Animals were acclimated to laboratory conditions for at least 7 days prior to the first dose and released from acclimation by a staff veterinarian. During that time, animals were identified by a temporary number that was recorded on each cage label.

The Institutional Animal Care and Use Committee (IACUC) of (b) (4) approved this protocol and found it to be in accordance with provisions of the USDA Animal Welfare Act, the PHS Policy on Humane Care and Use of Laboratory Animals and the US Interagency Research Animal Committee Principles for the Utilization and Care of Research Animals.

Husbandry

Animal husbandry was provided as described in Text Table 3.

Text Table 3: Husbandry Information

Feed	Certified Global Harlan Teklad Laboratory Diet 2030
Water	Filtered tap water via an automatic watering system and/or water bottles
Housing	Individually housed in cages suspended on stainless steel racks
Temperature Range	16 to 22°C
Humidity Range	30 to 70%
Light Cycle	12-hour light/12-hour dark, interrupted as necessary for study related events
Air Changes	Minimum of 10 air changes per hour

Feed and water were provided *ad libitum*, unless otherwise noted. The feed was analyzed by the manufacturer for concentrations of specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates. The water is routinely analyzed for contaminants and specific microbes. No contaminants were known to be present in the feed or water at levels that might have interfered with achieving the objectives of the study.

Environmental controls were set to maintain animal room conditions as shown in Text Table 3. Actual temperature and relative humidity in the animal room or zone were monitored continuously by a computerized system. All environmental parameters were maintained within the protocol requirements with the exception of deviations noted in Appendix 7. The deviations had no effect on the health of the animals and/or the outcome of the study.

All animals were provided jingle balls for environmental enrichment.

Experimental Design

Group Assignment and Doses

Animals were initially accepted into the randomization pool based upon body weights and physical examinations. They were assigned to study groups using computer-generated random numbers. At randomization the mean body weight for each group was not statistically different ($p<0.05$) from the control mean. The animals were assigned to groups as shown in Text Table 4.

Text Table 4: Study Design

Group	Treatment	Dose Level (virus particles)	Dose Volume (mL)	Total Number of Animals	Scheduled Sacrifice Timepoint		
					SD 11	SD 61	SD 91
1	Placebo	0	0.5	9/sex	3/sex	3/sex	3/sex
2	Ad26 (b) (4)	0.5×10^{11}	0.5	15/sex	5/sex	5/sex	5/sex

After randomization, each study animal was assigned a unique number and identified by ear tag. Animal assignment is presented in Text Table 5.

Text Table 5: Animal Assignment

Group	SD 11 Necropsy		SD 61 Necropsy		SD 91 Necropsy	
	Males	Females	Males	Females	Males	Females
1	14530-14532	14539-14541	14533-14535	14542-14544	14536-14538	14545-14547
2	14548-14552	14563-14567	14553-14557	14568-14572	14558-14562	14573-14577

Dose Administration

Dosing information is presented in Text Table 6.

Text Table 6: Dose Administration Information

Route of Administration	Intramuscular
Frequency of Dosing	Once on SD 1
Dose Volume	0.5 mL
Dose Sites	Right hind thigh muscle
Equipment	1-cc insulin syringe with a 27-gauge 5/8-inch needle
Dosing Conditions	Formulations were kept at room temperature during dosing

Each dose site was shaved and marked prior to dosing and all formulations were dosed within 4 hours of thawing.

Observations

Animals were observed as shown in Text Table 7.

Text Table 7: Animal Observations/Measurements

Procedure	Frequency of Testing
Cageside Observations	≥ Twice daily
Clinical Observations	Prior to each dose, weekly thereafter, and at termination
Body Weight	Prior to each dose, weekly thereafter, and at termination

Cageside observations included observation for mortality, moribundity, general health and signs of toxicity. Clinical observations included evaluation of skin and fur characteristics, injection site, eye and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, and somatomotor and behavior patterns.

Termination, Necropsy and Tissue Collection

Blood Collection

Prior to termination, whole blood (≥ 0.6 mL) was collected into K_3 EDTA tubes via puncture of the medial auricular artery for biodistribution analysis. The tubes were inverted several times and the blood was transferred to cryovials, snap frozen in liquid nitrogen, and stored frozen at -75 ± 15°C.

Termination

On SD 11 (Terminal Kill), 61 (Recovery Kill 1), and 91 (Recovery Kill 2), three rabbits per sex from Group 1 and five rabbits per sex from Group 2 were euthanized by intravenous injection of sodium pentobarbital and exsanguinated.

Necropsy

Animals were necropsied as soon as possible after euthanasia. A gross necropsy, which included examination of the external surface of the body, injection site, all orifices, and the cranial, thoracic, and abdominal cavities and their contents, was performed.

Tissue Collection

Group 1 (control) animals were necropsied first, followed by Group 2 animals. The following tissues were collected: ovaries/testes, liver (left lateral), thymus, heart (apex), lung (right diaphragmatic lobe), kidney (hilar region), spleen (median region), mesenteric lymph nodes, iliac lymph nodes, skin and subcutis at injection site, thigh muscle at injection site, bone marrow from left femur, and brain. Paired organs were processed together. A fresh set of sterile instruments and a new pair of gloves were used for each organ of each animal. All tissues were snap frozen in liquid nitrogen and stored at -75 ± 15°C.

All specimens collected, including the whole blood, were shipped (on dry ice) to (b) (4) following each necropsy. All tissues collected on SD 11, 61, and 91 were processed and analyzed for the presence of the Ad26 (b) (4) using a qualified quantitative polymerase chain reaction (qPCR) method. The Biodistribution Report is presented in Appendix 6.

Data Collection and Statistical Analyses

Electronic data collection, including dosing, animal husbandry and environmental enrichment, clinical observations, body weight, and body weight change, was performed using Provantis™ NT 2000 (b) (4) (b) (4)

Body weights and body weight changes were analyzed using the Kolmogorov-Smirnov test for normality, the Levene Median test for equal variance, and by one-way Analysis of Variance (ANOVA). If either the normality or equal variance test failed, then the analysis was continued using the non-parametric Kruskal-Wallis ANOVA on rank-transformed data. For parametric data, if the ANOVA indicated statistical significance among experimental groups then the Dunnett's t-test was used to delineate which groups (if any) differed from the control. For non-parametric data, if the ANOVA indicated statistical significance among experimental groups then the Dunn's test was used to delineate which groups (if any) differed from the control. The probability value of less than 0.05 (two-tailed) was used as the critical level of significance for all tests.

Statistical analysis was conducted using SigmaStat™ Statistical Software, Version 1 (b) (4) (b) (4) The term "significant" is used throughout the text of the report to indicate statistical significance at $p<0.05$.

Record Retention

All study data, including but not limited to, animal data, formulations data, necropsy data, professional reports, study protocol (including amendments), final report and any communications concerning the conduct of the study will be retained in the archive of (b) (4) for a period of 5 years following completion of the final report. Due to a presumed limited stability, preserved tissues will be maintained for a 1-year period at (b) (4)

Following the 5-year period (or before at Sponsor's request), the Sponsor will be contacted to determine the disposition of these materials. All electronic data will be maintained at (b) (4) Records regarding disposition of data and specimens will be maintained at (b) (4) Study data generated by the Sponsor or sub-contractors will be archived by the Sponsor or sub-contractors, respectively.

RESULTS

Stability Analysis

As shown in the Stability Reports presented in Appendix 1, Ad26 (b) (4) is considered stable at room temperature for at least 4 hours, and at accelerated stability storage condition (2-8°C) for at least 6 months.

Animal Disposition and Observations

Data are presented in Table 1 (animal disposition and clinical observations) and Table 2 (cageside observations). Individual data are presented in Appendix 3.

A single intramuscular injection of Ad26 (b) (4) vaccine had no effect on mortality or clinical/cageside observations. All animals survived until the scheduled termination. The only incidental clinical observation noted was a urine stain for one Group 2 male on SD 91.

Body Weight and Body Weight Changes

Data are summarized in Table 3 (body weights) and Table 4 (body weight changes). Mean body weights are presented graphically in Figure 1 (males) and Figure 2 (females). Individual data are presented in Appendix 4 and Appendix 5, respectively.

Figure 1: Mean Body Weights – Males

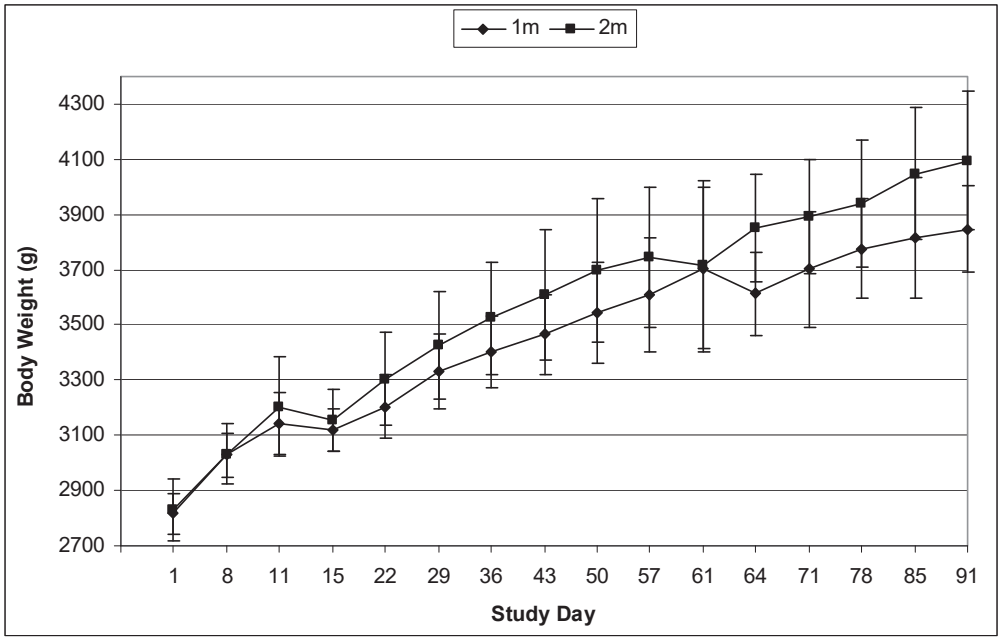
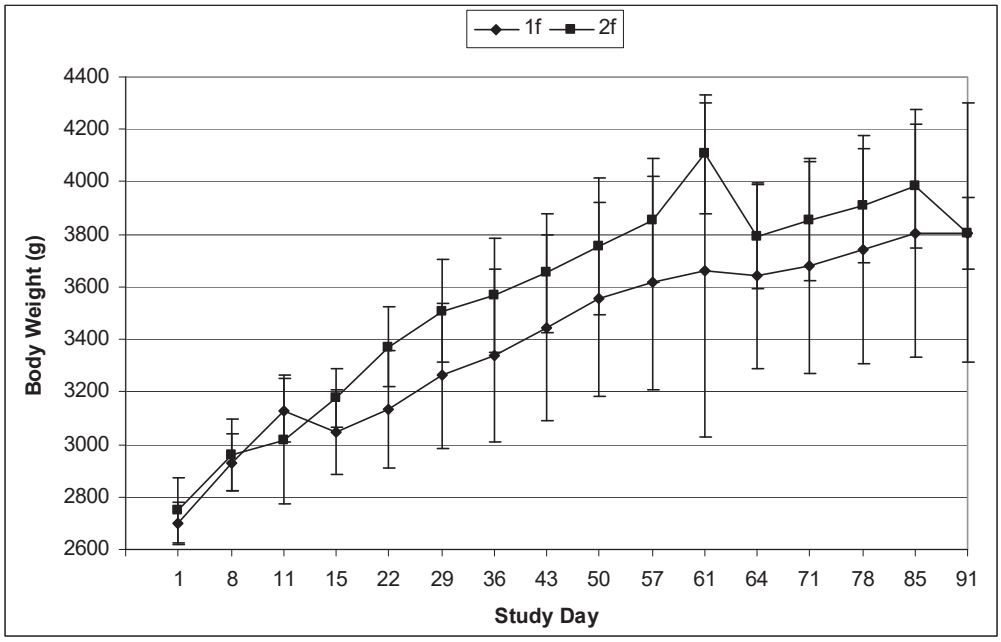


Figure 2: Mean Body Weights – Females



A single intramuscular injection of Ad26 (b) (4) vaccine had no effect on body weight or body weight changes. There were a few incidental, sporadic statistically significant differences noted in the body weight and body weight change data; the findings were not considered to be biologically or toxicologically significant.

Biodistribution Analysis

The Biodistribution Report is presented in Appendix 6.

Quantitative PCR (qPCR) analysis indicated that the vaccine was primarily localized in the spleen, iliac lymph nodes, and the muscle at the site of injection. By SD 61, the vaccine was no longer detected in the spleen. By SD 91, detection of the vector in the iliac lymph nodes and injection site muscle was limited to 2 of 10 treated animals.

CONCLUSION

A single intramuscular injection of Ad26 (b) (4) vaccine (0.5 x 10^{11} virus particles) was well tolerated in male and female New Zealand White rabbit. Biodistribution analysis indicated that Ad26 (b) (4) was cleared from almost all examined tissues by SD 91. Detection of the vector was limited to the iliac lymph nodes and injection site muscle in 2 of 10 treated animals.

ABBREVIATIONS

Not all abbreviations listed are used in this report.

↑	greater than control	**S.D.**	standard deviation
↓	less than control	**RSD**	relative standard deviation
>	greater than	**TK**	toxicokinetic
<	less than	**PK**	pharmacokinetic
≥	greater than or equal to	**AUC**	area under the curve
≤	less than or equal to	**C_{max}**	maximum concentration
~	approximately	**$t_{1/2}$**	half-life
°	degree	**SD**	study day
%	percent	**GD**	gestation day
C	Celsius	**PND**	post-natal day
F	Fahrenheit	**i.p.**	intraperitoneal
L	liter	**i.v.**	intravenous
mL	milliliter	**s.c.**	subcutaneous
µL	microliter	**i.m.**	intramuscular
g	gram	**EPA**	Environmental Protection Agency
kg	kilogram	**FDA**	Food and Drug Administration
mg	milligram	**GLP**	Good Laboratory Practices
µg	microgram	**GMP**	Good Manufacturing Practices
ng	nanogram	**IACUC**	Institutional Animal Care and Use Committee
pg	picogram	**ICH**	International Conference on Harmonization
cm	centimeter	**MHLW**	Ministry of Health, Labor and Welfare
mm	millimeter	**NIEHS**	National Institute of Environmental Health Sciences
µm	micrometer	**NTP**	National Toxicology Program
sec	second	**OECD**	Organisation for Economic Co-operation and Development
min	minute	**PHS**	Public Health Service
h	hour	**QA**	Quality Assurance
d	day	**QAU**	Quality Assurance Unit
wk	week	**SOP**	Standard Operating Procedures
rpm	revolutions per minute	**USDA**	United States Department of Agriculture
NBF	neutral buffered formalin	**LCA**	Laboratory Corporation of America
No.	number	**PAI**	Pathology Associates, A Charles River Company
NA	not applicable	**RACB**	reproductive assessment by continuous breeding
N	number		

Table 1
Summary of Animal Disposition and Clinical Observations
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Day Numbers Relative to Start Date

	Group 1	Group 2
Sex: Male		
Animal Disposition		
Terminal Kill		
Number of Observations	3	5
Number of Animals	3	5
Days from - to	11 11	11 11
Recovery Kill 1		
Number of Observations	3	5
Number of Animals	3	5
Days from - to	61 61	61 61
Recovery Kill 2		
Number of Observations	3	5
Number of Animals	3	5
Days from - to	91 91	91 91
Clinical Observations		
Urine stain		
Number of Observations	.	1
Number of Animals	.	1
Days from - to	.	91 91

. – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Table 1 (continued)
Summary of Animal Disposition and Clinical Observations
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Day Numbers Relative to Start Date

	Group 1	Group 2
Sex: Female		
Animal Disposition		
Terminal Kill		
Number of Observations	3	5
Number of Animals	3	5
Days from - to	11 11	11 11
Recovery Kill 1		
Number of Observations	3	5
Number of Animals	3	5
Days from - to	61 61	61 61
Recovery Kill 2		
Number of Observations	3	5
Number of Animals	3	5
Days from - to	91 91	91 91

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Table 2
Summary of Cageside Observations
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Cageside observations were performed twice daily. No abnormal cageside observations were noted.

Table 3
Summary of Body Weights (g)
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Group Sex		Day Numbers Relative to Start Date 1	8	11	15	22	29	36	43
1m	Mean	2815.8	3028.9	3141.3	3120.2	3204.5	3329.3	3402.2	3465.3
	S.D.	73.2	80.4	112.5	75.4	115.2	135.2	131.8	146.6
	N	9	9	3	6	6	6	6	6
2m	Mean	2831.8	3033.5	3202.8	3153.4	3303.5	3426.5	3525.6	3608.4
	S.D.	112.2	111.2	179.9	113.0	168.3	193.2	204.2	236.6
	N	15	15	5	10	10	10	10	10
1f	Mean	2699.6	2931.0	3128.3	3044.8	3133.2	3261.7	3340.3	3442.8
	S.D.	79.2	110.0	121.1	160.5	221.7	275.4	328.5	352.8
	N	9	9	3	6	6	6	6	6
2f	Mean	2747.6	2960.3	3018.8	3175.3	3372.1*	3507.7	3569.6	3652.5
	S.D.	123.5	133.9	247.2	111.9	150.9	194.3	215.6	225.6
	N	15	15	5	10	10	10	10	10

m – Male f – Female * – Significantly different from the control value, $p<0.05$

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Table 3 (continued)
Summary of Body Weights (g)
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Group Sex		Day Numbers Relative to Start Date 50	57	61	64	71	78	85	91
1m	Mean	3542.0	3609.7	3705.7	3612.3	3702.7	3776.0	3815.0	3847.0
	S.D.	183.0	206.8	293.5	149.8	209.8	181.1	216.5	157.6
	N	6	6	3	3	3	3	3	3
2m	Mean	3697.7	3745.5	3712.6	3851.2	3892.4	3941.2	4046.2	4096.2
	S.D.	260.6	251.7	308.2	196.1	204.6	229.0	239.2	249.3
	N	10	10	5	5	5	5	5	5
1f	Mean	3552.8	3616.2	3664.3	3645.0	3680.3	3743.7	3804.0	3806.0
	S.D.	366.9	406.5	634.3	353.5	412.2	434.0	470.7	493.9
	N	6	6	3	3	3	3	3	3
2f	Mean	3754.8	3853.3	4105.6	3792.2	3851.6	3910.0	3983.6	3802.2
	S.D.	259.7	234.3	225.4	198.0	224.7	217.6	236.8	136.5
	N	10	10	5	5	5	5	5	5

m – Male f - Female

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5 x 10^{11} virus particles

Table 4
Summary of Body Weight Changes (g)
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Day Numbers Relative to Start Date

Group Sex	Base Weight Day 1	From: To:	1 8	8 11	Absolute Change 1 11	Percent Change 1 11	8 15	15 22	22 29	29 36	36 43	43 50	50 57
1m	2815.8	Mean	213.1	90.0	319.3	11.3	102.5	84.3	124.8	72.8	63.2	76.7	67.7
	73.16	S.D.	23.75	14.73	36.83	1.15	18.40	70.03	22.91	27.32	30.32	64.95	48.69
	9	N	9	3	3	3	6	6	6	6	6	6	6
2m	2831.8	Mean	201.7	116.2	299.0	10.3	146.5	150.1	123.0	99.1	82.8	89.3	47.8
	112.18	S.D.	63.71	47.11	65.68	1.98	61.91	68.37	38.32	41.69	47.03	42.10	63.58
	15	N	15	5	5	5	10	10	10	10	10	10	10
1f	2699.6	Mean	231.4	147.7	368.3	13.3	138.7	88.3	128.5	78.7	102.5	110.0	63.3
	79.22	S.D.	58.58	76.25	115.52	4.15	68.76	73.54	58.02	57.40	33.60	26.24	40.18
	9	N	9	3	3	3	6	6	6	6	6	6	6
2f	2747.6	Mean	212.7	146.4	323.8	11.9	171.0	196.8*	135.6	61.9	82.9	102.3	98.5
	123.48	S.D.	56.37	97.70	131.47	4.59	84.33	57.13	54.05	74.11	45.69	53.88	33.39
	15	N	15	5	5	5	10	10	10	10	10	10	10

m – Male f – Female * – Significantly different from the control value, $p < 0.05$

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Table 4 (continued)
Summary of Body Weight Changes (g)
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Day Numbers Relative to Start Date

Group Sex	Base Weight Day 1	From: To:	57 61	Absolute Change 1 61	Percent Change 1 61	57 64	64 71	71 78	78 85	85 91	Absolute Change 1 91	Percent Change 1 91
1m	2815.8	Mean	54.7	909.3	32.5	44.0	90.3	73.3	39.0	32.0	1018.0	36.0
	73.16	S.D.	14.84	286.85	10.17	35.34	62.32	56.86	46.29	76.62	89.77	2.88
	9	N	3	3	3	3	3	3	3	3	3	3
2m	2831.8	Mean	9.0	892.6	31.5	63.8	41.2	48.8	105.0*	50.0	1324.6	47.8
	112.18	S.D.	38.37	230.01	7.34	29.66	23.34	55.30	16.54	24.73	248.09	9.33
	15	N	5	5	5	5	5	5	5	5	5	5
1f	2699.6	Mean	41.7	1011.0	37.7	35.3	35.3	63.3	60.3	2.0	1120.7	41.5
	79.22	S.D.	100.92	546.41	19.09	22.19	60.93	22.90	44.86	104.89	428.37	14.84
	9	N	3	3	3	3	3	3	3	3	3	3
2f	2747.6	Mean	108.8	1283.2	45.6	82.4	59.4	58.4	73.6	-181.4	1076.8	39.5
	123.48	S.D.	25.17	212.44	7.90	53.10	53.10	45.74	37.24	112.81	125.97	4.80
	15	N	5	5	5	5	5	5	5	5	5	5

m – Male f – Female * – Significantly different from the control value, $p < 0.05$

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Appendix 1
Certificates of Analysis
Ad26 (b) (4) 91-Day Intramuscular Single Dose
Biodistribution Study in New Zealand White Rabbits

Crucell

Certificate of Analysis

Ad26 (b) (4) Placebo
(b) (4)

[redacted]

Crucell

Certificate of Analysis

Ad26 (b) (4) **Placebo**

(b) (4), (b) (6)

(b) (4)

Cobra Biologics

Certificate of Analysis

Ad26 (b) (4) **Drug Product for toxicity studies**

(b) (4)

Crucell

Certificate of Analysis

Ad26 (b) (4) **Drug Product for toxicity studies**

(b) (4), (b) (6)

(b) (4)

Appendix 2
Stability Reports
Ad26 (b) (4) 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Crucell

Crucell

DATA REPORT (*in vitro* study)

TITLE: **Stability study of Ad26 (b) (4) Drug Product stored at room temperature**

(b) (4), (b) (6)

Crucell

(b) (4)

Crucell

(b) (4), (b) (6)

Crucell

(b) (4)

Crucell

(b) (4)

Crucell

(b) (4)

Crucell

(b) (4)

Crucell

(b) (4)

Crucell

(b) (4)

Crucell

(b) (4)

Crucell

Attachment 3: SPSS syntax

Syntax used for SPSS statistical analysis:

```
COMPUTE start_dat = LAG(data) .
EXECUTE .

COMPUTE dif = data-start_dat .
EXECUTE .

USE ALL.
COMPUTE filter_$=(tijd = 4).
VARIABLE LABEL filter_$ 'tijd = 4 (FILTER)'.
VALUE LABELS filter_$  0 'Not Selected' 1 'Selected'.
FORMAT filter_$ (f1.0).
FILTER BY filter_$.
EXECUTE .

T-TEST
 /TESTVAL = 0
 /MISSING = ANALYSIS
 /VARIABLES = dif
 /CRITERIA = CI(.95) .
```

Crucell

(b) (4), (b) (6)

Crucell

(b) (4)

Crucell

(b) (4)

Crucell

(b) (4)

2 Scientific Review

Responsible Scientist:

Name: (b) (6) Sign: (b) (6) Date: 12 June 07

Peer Reviewer:

Name: (b) (6) Sign: (b) (6) Date: 12 Jun 07

Qualified Person:

Name: (b) (6) Sign: (b) (6) Date: 12 June 07

Crucell

(b) (4)

Crucell

(b) (4)

Crucell

(b) (4)

Crucell

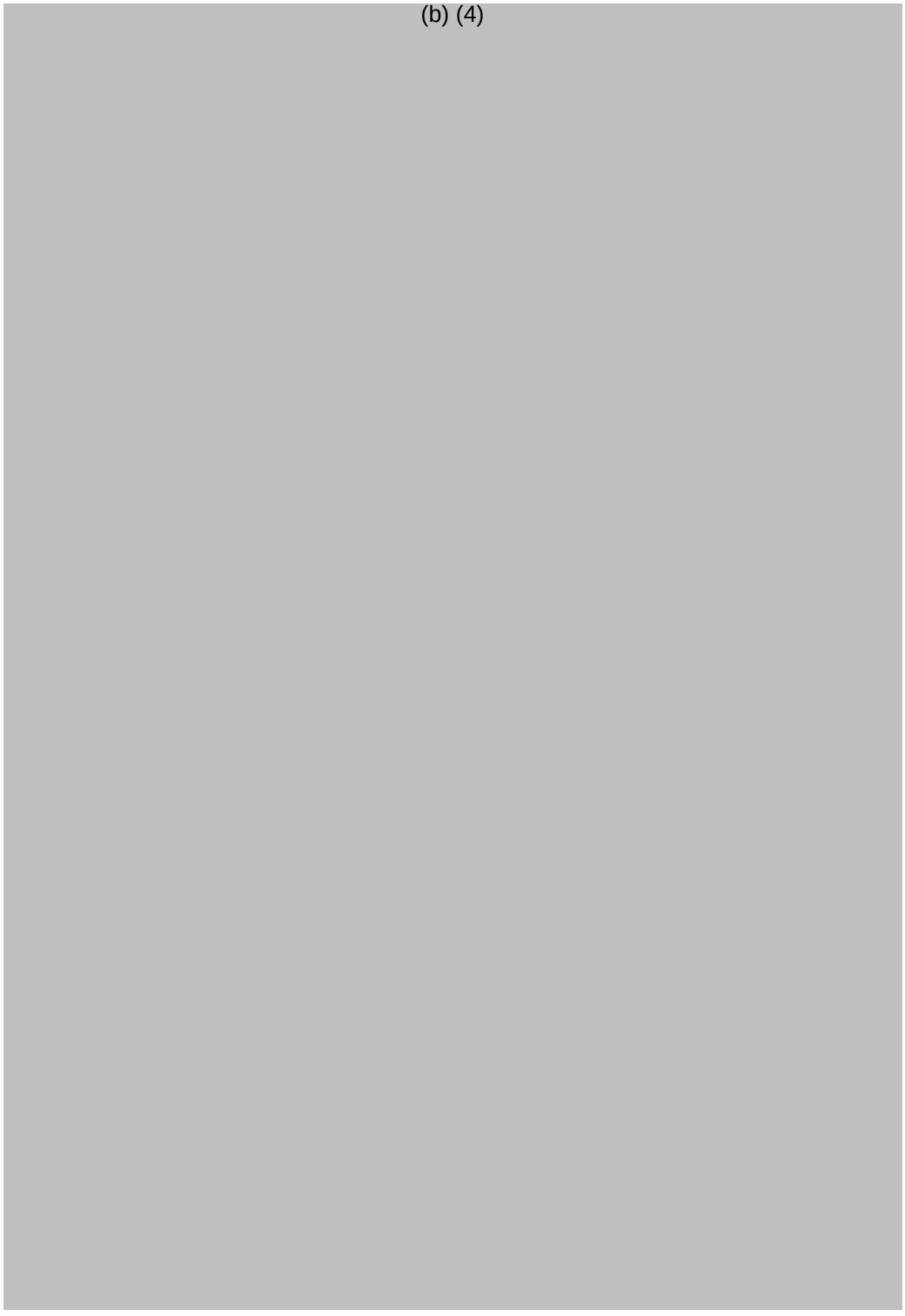
(b) (4)

Crucell

(b) (4)

Crucell

(b) (4)



Crucell

(b) (4)

Crucell

(b) (4)

7 Attachments

7.1. Certificate of Analysis (b) (4)

Appendix 3
Individual Animal Disposition and Clinical Observations
Ad26 (b) (4) 91-Day Intramuscular Single Dose
Biodistribution Study in New Zealand White Rabbits

Appendix 3
Individual Animal Disposition and Clinical Observations
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Day Numbers Relative to Start Date

Group Sex	Animal Number	Clinical Sign	1	8	11	15	22	29	36	43	50	57	61	64	71	78	85	91
1m	14530	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14531	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14532	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14533	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14534	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14535	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14536	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14537	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14538	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

m – Male X – Present . – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Appendix 3 (continued)
Individual Animal Disposition and Clinical Observations
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Group Sex	Animal Number	Clinical Sign	Day Numbers Relative to Start Date: 1	8	11	15	22	29	36	43	50	57	61	64	71	78	85	91
2m	14548	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14549	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14550	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14551	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14552	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14553	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14554	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14555	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14556	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14557	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14558	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14559	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	.
		Urine stain	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14560	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14561	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14562	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

m – Male X – Present . – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Appendix 3 (continued)
Individual Animal Disposition and Clinical Observations
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Group Sex	Animal Number	Clinical Sign	Day Numbers Relative to Start Date: 1	8	11	15	22	29	36	43	50	57	61	64	71	78	85	91
1f	14539	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14540	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14541	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14542	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14543	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14544	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14545	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14546	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14547	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

f – Female X – Present . – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Appendix 3 (continued)
Individual Animal Disposition and Clinical Observations
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Day Numbers Relative to Start Date

Group Sex	Animal Number	Clinical Sign	1	8	11	15	22	29	36	43	50	57	61	64	71	78	85	91
2f	14563	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14564	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14565	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14566	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14567	No Abnormalities Detected	X	X	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Terminal Kill	.	.	X	.	.	.	.	.	.	.	.	.	.	.	.	.
	14568	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14569	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14570	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14571	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14572	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	X	.	.	.	.	.
		Recovery Kill 1	.	.	.	.	.	.	.	.	.	.	X	.	.	.	.	.
	14573	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14574	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14575	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14576	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X
	14577	No Abnormalities Detected	X	X	.	X	X	X	X	X	X	X	.	X	X	X	X	X
		Recovery Kill 2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	X

f – Female X – Present . – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Appendix 4
Individual Body Weights
Ad26 (b) (4) 91-Day Intramuscular Single Dose
Biodistribution Study in New Zealand White Rabbits

Appendix 4
Individual Body Weights (g)
Ad26 (b) (4): 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Group Sex	Animal Number	Day Numbers Relative to Start Date 1	8	11	15	22	29	36	43	50	57	61	64	71	78	85	91
1m	14530	2803	3010	3083	.	.	.	.	.	.	.	.	.	.	.	.	.
	14531	2745	2971	3070	.	.	.	.	.	.	.	.	.	.	.	.	.
	14532	2918	3173	3271	.	.	.	.	.	.	.	.	.	.	.	.	.
	14533	2734	2943	.	3062	3170	3305	3415	3495	3618	3653	3704	.	.	.	.	.
	14534	2839	3070	.	3181	3371	3512	3557	3619	3798	3929	4000	.	.	.	.	.
	14535	2816	2985	.	3054	3033	3117	3198	3246	3301	3371	3413	.	.	.	.	.
	14536	2855	3059	.	3175	3243	3370	3438	3550	3546	3668	.	3739	3895	3905	3938	3975
	14537	2720	2937	.	3041	3148	3263	3303	3326	3365	3390	.	3447	3479	3569	3565	3671
	14538	2912	3112	.	3208	3262	3409	3502	3556	3624	3647	.	3651	3734	3854	3942	3895
2m	14548	2890	3158	3226	.	.	.	.	.	.	.	.	.	.	.	.	.
	14549	2688	2864	2936	.	.	.	.	.	.	.	.	.	.	.	.	.
	14550	3050	3293	3443	.	.	.	.	.	.	.	.	.	.	.	.	.
	14551	2964	3023	3198	.	.	.	.	.	.	.	.	.	.	.	.	.
	14552	2927	3095	3211	.	.	.	.	.	.	.	.	.	.	.	.	.
	14553	2704	2908	.	2981	3032	3164	3264	3322	3376	3453	3516	.	.	.	.	.
	14554	2948	3107	.	3241	3353	3497	3584	3687	3839	3944	3978	.	.	.	.	.
	14555	2749	2935	.	3049	3129	3206	3291	3339	3371	3469	3450	.	.	.	.	.
	14556	2887	3080	.	3310	3566	3739	3866	4010	4152	4117	4112	.	.	.	.	.
	14557	2812	2953	.	3059	3167	3251	3327	3422	3490	3535	3507	.	.	.	.	.
	14558	2797	3085	.	3179	3354	3422	3499	3565	3634	3544	.	3653	3677	3768	3876	3918
	14559	2718	3024	.	3125	3236	3358	3421	3430	3529	3582	.	3633	3667	3632	3713	3750
	14560	2696	2957	.	3169	3412	3531	3717	3769	3880	3939	.	3967	4046	4150	4258	4331
	14561	2773	2945	.	3099	3279	3408	3551	3637	3760	3868	.	3937	3984	4038	4165	4243
	14562	2874	3075	.	3322	3507	3689	3736	3903	3946	4004	.	4066	4088	4118	4219	4239

m – Male . – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5 x 10^{11} virus particles

Appendix 4 (continued)
Individual Body Weights (g)
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Group Sex	Animal Number	Day Numbers Relative to Start Date 1	8	11	15	22	29	36	43	50	57	61	64	71	78	85	91
1f	14539	2771	3039	3256	.	.	.	.	.	.	.	.	.	.	.	.	.
	14540	2761	2949	3015	.	.	.	.	.	.	.	.	.	.	.	.	.
	14541	2748	2954	3114	.	.	.	.	.	.	.	.	.	.	.	.	.
	14542	2766	3105	.	3256	3471	3671	3822	3970	4118	4242	4359	.	.	.	.	.
	14543	2587	2793	.	2943	3030	3112	3203	3267	3390	3437	3518	.	.	.	.	.
	14544	2607	2752	.	2856	2911	2974	2992	3058	3173	3189	3116	.	.	.	.	.
	14545	2626	2898	.	3047	3065	3225	3299	3429	3534	3608	.	3640	3695	3751	3843	3726
	14546	2654	2917	.	2951	2980	3067	3076	3180	3249	3279	.	3294	3261	3306	3315	3357
	14547	2776	2972	.	3216	3342	3521	3650	3753	3853	3942	.	4001	4085	4174	4254	4335
2f	14563	2494	2629	2717	.	.	.	.	.	.	.	.	.	.	.	.	.
	14564	2704	2842	2858	.	.	.	.	.	.	.	.	.	.	.	.	.
	14565	2606	2841	3037	.	.	.	.	.	.	.	.	.	.	.	.	.
	14566	2768	2959	3122	.	.	.	.	.	.	.	.	.	.	.	.	.
	14567	2903	3091	3360	.	.	.	.	.	.	.	.	.	.	.	.	.
	14568	2979	3179	.	3409	3667	3851	4007	4111	4259	4327	4438	.	.	.	.	.
	14569	2708	2907	.	3187	3353	3459	3608	3672	3759	3860	3954	.	.	.	.	.
	14570	2924	3136	.	3218	3383	3533	3527	3583	3712	3776	3857	.	.	.	.	.
	14571	2764	2989	.	3253	3468	3666	3588	3793	4006	4045	4193	.	.	.	.	.
	14572	2737	2925	.	3209	3499	3701	3753	3808	3881	3976	4086	.	.	.	.	.
	14573	2725	2938	.	3032	3128	3231	3283	3345	3402	3531	.	3526	3533	3621	3644	3639
	14574	2660	3037	.	3126	3376	3477	3560	3623	3759	3865	.	3978	3985	4108	4155	3898
	14575	2802	2994	.	3140	3317	3441	3573	3637	3727	3844	.	3916	4037	4049	4162	3951
	14576	2679	2920	.	3019	3208	3236	3242	3333	3384	3535	.	3638	3696	3734	3824	3680
	14577	2761	3018	.	3160	3322	3482	3555	3620	3659	3774	.	3903	4007	4038	4133	3843

f – Female . – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Appendix 5
Individual Body Weight Changes
Ad26 (b) (4) 91-Day Intramuscular Single Dose
Biodistribution Study in New Zealand White Rabbits

Appendix 5
Individual Body Weight Changes (g)
Ad26 (b) (4): 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

				Day Numbers Relative to Start Date										
		Base Weight				Absolute Change	Percent Change							
Group	Animal	Day	From:	1	8	1	1	8	15	22	29	36	43	50
Sex	Number	1	To:	8	11	11	11	15	22	29	36	43	50	57
1m	14530	2803		207	73	280	9.989	.	.	.	.	.	.	.
	14531	2745		226	99	325	11.840	.	.	.	.	.	.	.
	14532	2918		255	98	353	12.097	.	.	.	.	.	.	.
	14533	2734		209	.	.	.	119	108	135	110	80	123	35
	14534	2839		231	.	.	.	111	190	141	45	62	179	131
	14535	2816		169	.	.	.	69	-21	84	81	48	55	70
	14536	2855		204	.	.	.	116	68	127	68	112	-4	122
	14537	2720		217	.	.	.	104	107	115	40	23	39	25
	14538	2912		200	.	.	.	96	54	147	93	54	68	23
2m	14548	2890		268	68	336	11.626	.	.	.	.	.	.	.
	14549	2688		176	72	248	9.226	.	.	.	.	.	.	.
	14550	3050		243	150	393	12.885	.	.	.	.	.	.	.
	14551	2964		59	175	234	7.895	.	.	.	.	.	.	.
	14552	2927		168	116	284	9.703	.	.	.	.	.	.	.
	14553	2704		204	.	.	.	73	51	132	100	58	54	77
	14554	2948		159	.	.	.	134	112	144	87	103	152	105
	14555	2749		186	.	.	.	114	80	77	85	48	32	98
	14556	2887		193	.	.	.	230	256	173	127	144	142	-35
	14557	2812		141	.	.	.	106	108	84	76	95	68	45
	14558	2797		288	.	.	.	94	175	68	77	66	69	-90
	14559	2718		306	.	.	.	101	111	122	63	9	99	53
	14560	2696		261	.	.	.	212	243	119	186	52	111	59
	14561	2773		172	.	.	.	154	180	129	143	86	123	108
	14562	2874		201	.	.	.	247	185	182	47	167	43	58

m – Male . – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Appendix 5 (continued)
Individual Body Weight Changes (g)
Ad26 (b) (4): 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Group Sex	Animal Number	Base Weight Day 1	Day Numbers Relative to Start Date From:	57	Absolute Change 1	Percent Change 1	57	64	71	78	85	Absolute Change 1	Percent Change 1
			To:	61	61	61	64	71	78	85	91	91	91
1m	14530	2803		.	.	.	.	.	.	.	.	.	.
	14531	2745		.	.	.	.	.	.	.	.	.	.
	14532	2918		.	.	.	.	.	.	.	.	.	.
	14533	2734		51	970	35.479	.	.	.	.	.	.	.
	14534	2839		71	1161	40.895	.	.	.	.	.	.	.
	14535	2816		42	597	21.200	.	.	.	.	.	.	.
	14536	2855		.	.	.	71	156	10	33	37	1120	39.229
	14537	2720		.	.	.	57	32	90	-4	106	951	34.963
	14538	2912		.	.	.	4	83	120	88	-47	983	33.757
2m	14548	2890		.	.	.	.	.	.	.	.	.	.
	14549	2688		.	.	.	.	.	.	.	.	.	.
	14550	3050		.	.	.	.	.	.	.	.	.	.
	14551	2964		.	.	.	.	.	.	.	.	.	.
	14552	2927		.	.	.	.	.	.	.	.	.	.
	14553	2704		63	812	30.030	.	.	.	.	.	.	.
	14554	2948		34	1030	34.939	.	.	.	.	.	.	.
	14555	2749		-19	701	25.500	.	.	.	.	.	.	.
	14556	2887		-5	1225	42.432	.	.	.	.	.	.	.
	14557	2812		-28	695	24.716	.	.	.	.	.	.	.
	14558	2797		.	.	.	109	24	91	108	42	1121	40.079
	14559	2718		.	.	.	51	34	-35	81	37	1032	37.969
	14560	2696		.	.	.	28	79	104	108	73	1635	60.645
	14561	2773		.	.	.	69	47	54	127	78	1470	53.011
	14562	2874		.	.	.	62	22	30	101	20	1365	47.495

m – Male . – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Appendix 5 (continued)
Individual Body Weight Changes (g)
Ad26 (b) (4): 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

			Day Numbers Relative to Start Date										
		Base				Absolute	Percent							
		Weight				Change	Change							
Group	Animal	Day	From:	1	8	1	1	8	15	22	29	36	43	50
Sex	Number	1	To:	8	11	11	11	15	22	29	36	43	50	57
1f	14539	2771		268	217	485	17.503	.	.	.	.	.	.	.
	14540	2761		188	66	254	9.200	.	.	.	.	.	.	.
	14541	2748		206	160	366	13.319	.	.	.	.	.	.	.
	14542	2766		339	.	.	.	151	215	200	151	148	148	124
	14543	2587		206	.	.	.	150	87	82	91	64	123	47
	14544	2607		145	.	.	.	104	55	63	18	66	115	16
	14545	2626		272	.	.	.	149	18	160	74	130	105	74
	14546	2654		263	.	.	.	34	29	87	9	104	69	30
	14547	2776		196	.	.	.	244	126	179	129	103	100	89
2f	14563	2494		135	88	223	8.941	.	.	.	.	.	.	.
	14564	2704		138	16	154	5.695	.	.	.	.	.	.	.
	14565	2606		235	196	431	16.539	.	.	.	.	.	.	.
	14566	2768		191	163	354	12.789	.	.	.	.	.	.	.
	14567	2903		188	269	457	15.742	.	.	.	.	.	.	.
	14568	2979		200	.	.	.	230	258	184	156	104	148	68
	14569	2708		199	.	.	.	280	166	106	149	64	87	101
	14570	2924		212	.	.	.	82	165	150	-6	56	129	64
	14571	2764		225	.	.	.	264	215	198	-78	205	213	39
	14572	2737		188	.	.	.	284	290	202	52	55	73	95
	14573	2725		213	.	.	.	94	96	103	52	62	57	129
	14574	2660		377	.	.	.	89	250	101	83	63	136	106
	14575	2802		192	.	.	.	146	177	124	132	64	90	117
	14576	2679		241	.	.	.	99	189	28	6	91	51	151
	14577	2761		257	.	.	.	142	162	160	73	65	39	115

f – Female . – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Appendix 5 (continued)
Individual Body Weight Changes (g)
Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

Group Sex	Animal Number	Base Weight Day 1	Day Numbers Relative to Start Date From:	57	Absolute Change 1	Percent Change 1	57	64	71	78	85	Absolute Change 1	Percent Change 1
			To:	61	61	61	64	71	78	85	91	91	91
1f	14539	2771		.	.	.	.	.	.	.	.	.	.
	14540	2761		.	.	.	.	.	.	.	.	.	.
	14541	2748		.	.	.	.	.	.	.	.	.	.
	14542	2766		117	1593	57.592	.	.	.	.	.	.	.
	14543	2587		81	931	35.988	.	.	.	.	.	.	.
	14544	2607		-73	509	19.524	.	.	.	.	.	.	.
	14545	2626		.	.	.	32	55	56	92	-117	1100	41.889
	14546	2654		.	.	.	15	-33	45	9	42	703	26.488
	14547	2776		.	.	.	59	84	89	80	81	1559	56.160
2f	14563	2494		.	.	.	.	.	.	.	.	.	.
	14564	2704		.	.	.	.	.	.	.	.	.	.
	14565	2606		.	.	.	.	.	.	.	.	.	.
	14566	2768		.	.	.	.	.	.	.	.	.	.
	14567	2903		.	.	.	.	.	.	.	.	.	.
	14568	2979		111	1459	48.976	.	.	.	.	.	.	.
	14569	2708		94	1246	46.012	.	.	.	.	.	.	.
	14570	2924		81	933	31.908	.	.	.	.	.	.	.
	14571	2764		148	1429	51.700	.	.	.	.	.	.	.
	14572	2737		110	1349	49.288	.	.	.	.	.	.	.
	14573	2725		.	.	.	-5	7	88	23	-5	914	33.541
	14574	2660		.	.	.	113	7	123	47	-257	1238	46.541
	14575	2802		.	.	.	72	121	12	113	-211	1149	41.006
	14576	2679		.	.	.	103	58	38	90	-144	1001	37.365
	14577	2761		.	.	.	129	104	31	95	-290	1082	39.189

f – Female . – Not applicable

Nominal Dose: Group 1 – 0 virus particles
Group 2 – 0.5×10^{11} virus particles

Appendix 6
Biodistribution Report
Ad26 (b) (4) 91-Day Intramuscular Single Dose
Biodistribution Study in New Zealand White Rabbits

(b) (4)

(b) (4)

REAL-TIME QUANTITATIVE POLYMERASE CHAIN REACTION ANALYSIS OF THE BIODISTRIBUTION OF Ad26 (b) (4) IN RABBIT

ABSTRACT: A qualified quantitative polymerase chain reaction (qPCR) assay was used to detect and quantify Ad26 (b) (4) in tissues and blood collected from (b) (4) (b) (4) ; a biodistribution study in rabbit. The assay detects a 162 base pair sequence, unique to the vector, using the ABI Prism 7700 Sequence Detection System. The number of copies of vector detected in up to one microgram of genomic DNA extracted from each tissue was quantified using serial dilutions of plasmid DNA containing the target sequence as standards. The lower limit of detection of the assay is 10 copies of Ad26 (b) (4) µg DNA; the lower limit of quantification is 50 copies of Ad26 (b) (4) µg DNA.

Prepared For: Beth Israel Deaconess Medical Center

(b) (4)

Operator:	(b) (4), (b) (6)	(b) (4), (b) (6)	Date: 06.27.07
Operator:			Date: 06.27.07
Operator:			Date: 06.27.07
Operator:			Date: 06.27.07
Operator:			Date: 06.27.07
Operator:			Date: 06.27.07
Principal Investigator:	(b) (4), (b) (6)		Date: 06.27.07
Quality Assurance:	(b) (4), (b) (6)		Date: 06.27.07

(b) (4)

Table of Contents

I. Study Information

(b) (4) **Statement of Work:** (b) (4)

Specimen Identification: Rabbit tissues and blood collected from (b) (4) Study (b) (4)

Objective: The objective of the study was to measure the number of copies of Ad26 (b) (4) per microgram of DNA purified from rabbit tissues and blood.

Sponsor: Beth Israel Deaconess Medical Center
Division of Viral Pathogenesis
41 Avenue Louis Pasteur
Boston, MA 02115

Sponsor Representative: (b) (4), (b) (6)
(b) (4), (b) (6)

Test Facility: (b) (4)

Study Director: (b) (4), (b) (6)
(b) (4), (b) (6)

Test Site: (b) (4)

Principal Investigator: (b) (4), (b) (6)
(b) (4), (b) (6)

Study Phase Schedule

Study Phase Initiation: 05/09/2007
Analysis Initiation: 05/10/2007
Analysis Completion: 06/04/2007
Study Phase Completion: The date of the Principal Investigator's signature in the *Principal Investigator's Approval* section of this study phase report.

Archives: Raw data, records, the statement of work, and a copy of the report will be maintained by (b) (4) Quality Assurance Department as described in (b) (4) Standard Operating Procedure (SOP) No. (b) (4) (b) (4)

(b) (4)

II. Assay Description and Methods

A. Assay Description

A TaqMan based assay was qualified to detect and quantify Ad26 (b) (4) DNA sequence in rabbit tissue. The assay design amplifies (b) (4) of the Ad26 (b) (4) DNA sequence. It was optimized to provide maximum sensitivity and specificity for detecting the target gene sequence in a background of rabbit tissue genomic DNA (gDNA). (b) (4)

B. Preparation of Standards

DNA standards were prepared by serially diluting Sponsor provided pAdapt26 (b) (4) plasmid DNA (b) (4) in a background of gDNA isolated from rabbit liver and prepared such that 1 µg of background gDNA was present per PCR. A dilution series was prepared to span the quantitative range of the assay with the following points: $1x10^6$ copies of vector DNA per microgram of animal model genomic DNA (copies/µg DNA), $1x10^5$ copies/µg DNA, $1x10^4$ copies/µg DNA, $1x10^3$ copies/µg DNA, $1x10^2$ copies/µg DNA and 50 copies/µg DNA. In addition to the standard curve, a point representing the assay's limit of detection of the assay is 10 copies of Ad26 (b) (4) /µg DNA.

C. Preparation of Specimens

DNA was extracted from tissue and blood specimens as described in (b) (4) (b) (4) *Operation and Maintenance of the BioRobot M48 Nucleic Acid Extraction System,* and/or (b) (4) *Isolation of Genomic DNA From Tissues or Biological Fluids*. A naive tissue, provided by (b) (4) was included with each batch of specimens to serve as an extraction contamination control (NEC-negative extraction control). The concentration of the DNA purified from each tissue was determined by absorbance at 260 nm (A260) according to (b) (4) (b) (4) *Determination of Nucleic Acid Concentration by Spectrophotometry* and the concentration subsequently adjusted to 100 ng/µL with water. Ten microliters (1 µg DNA) were used in each qPCR. For samples with DNA concentrations less than 100 ng/µL but greater than or equal to 50 ng/µL, the DNA was adjusted to 50 ng/µL, and

(b) (4)

20 µL (1 µg DNA) of the DNA preparation was run per reaction. Samples with DNA concentrations less than 50 ng/µL were run using 20 µL per qPCR. The mass or volume of DNA analyzed per PCR was recorded for each specimen and is reported in Appendix 1 of this report. Blood samples were run volumetrically with DNA from the equivalent of 10 microliters of blood analyzed in each reaction.

D. Real-Time Quantitative Polymerase Chain Reaction

qPCR amplification and fluorescence detection was performed using the ABI PRISM 7700 Sequence Detection System as described in (b) (4) *Operation of the ABI Sequence Detection System and Sequence Detector Software*, and (b) (4) *Quantitation of Target Sequences Using Universal Master Mix*. Three replicate qPCR reactions were performed on each specimen's DNA using the oligonucleotide primers and fluorescent probe described in the assay development report (b) (4) One of the three replicate reactions was spiked with 100 copies of vector to check for the presence of qPCR inhibitors. In addition to specimen DNA, each qPCR plate was run with one set of standards, a naïve rabbit genomic DNA negative control (0 copy) and the qPCR reagent control (NTC). Each extraction control (NEC) was included on at least one run with its corresponding specimens. These controls monitor the potential for non-specific amplification of animal model genomic DNA, contamination of the qPCR reagents, and contamination of specimen DNA during the extraction process, respectively. All controls were run in duplicate reactions.

E. Calculations and Data Analysis

For each qPCR run, the Sequence Detector Software v1.6.3 created a standard curve by plotting the mean C_T value (the cycle at which the reporter signal can be detected above baseline fluorescence) of each standard versus (LogN) starting copy number assigned to each standard. The software then performed a linear regression analysis to calculate the number of copies of the target sequence detected in each reaction for each specimen. The mean copy number of the duplicate reactions for each specimen was then calculated and the individual well and mean copy numbers were reported.

(b) (4)

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Data generated by the Sequence Detection Software was copied into a Microsoft Excel worksheet. Data for reactions containing less than one microgram of gDNA were mathematically adjusted to final reporting units of the number of copies per one microgram DNA. The mass or volume of DNA analyzed per reaction can be found in Appendix 1 of this report.

F. Acceptance Criteria

Acceptability of a qPCR assay was determined by the following criteria:

The correlation coefficient of the standard curve must be $\geq$0.980.

The Negative Extraction Control (NEC) must test below the limit of detection of the assay.

The qPCR reagent control (NTC) must test below the limit of detection of the assay by at least 10-fold.

Acceptability of the result for an individual specimen under analysis was determined by the following criteria:

For specimens with a quantifiable number of copies of the target sequence (within the range of quantification) the difference between C_T values of the duplicate reactions used for quantification must be less than or equal to 1 C_T.

The C_T of the spiked reaction must be less than the mean C_T of the limit of detection.

(b) (4)

III. Results

The number of copies of Ad26 (b) (4) per microgram of genomic DNA purified from each tissue is reported in Tables 1 and 2. The quantification of Ad26 (b) (4) in blood is expressed per 10 µL of blood. Specimens testing below the limit of detection of the assay are identified as "LLD" (less than the limit of detection). Specimens testing greater than 10 but less than 50 copies are detectable below the limit of quantification of the assay and are identified as "NQ" (not quantifiable). Inhibited reactions were re-analyzed using less DNA and results mathematically adjusted to copies per µg. Results of repeat analyses were multiplied by the appropriate dilution factor and reported. The mass of DNA analyzed in each reaction appears in Appendix 1.

(b) (4)

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Table 1- Biodistribution of Ad26 (b) (4) DNA at SD 11 and 61

Study Day	Treatment	Sex	Animal No.	Blood	Gonads	Liver	Thymus	Heart	Lung	Kidney	Spleen	Lymph Nodes		Bone Marrow	Brain	Injection Sites	
												Mesenteric	Iliac			Skin	Muscle
11	Placebo	Male	14530	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14531	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14532	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
		Female	14539	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14540	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14541	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
	Ad26 (b) (4) 0.5×10^{11} vp	Male	14548	LLD	LLD	LLD	LLD	LLD	LLD	LLD	50	LLD	960	LLD	LLD	LLD	LLD
			14549	LLD	LLD	LLD	LLD	LLD	LLD	LLD	92	LLD	119	LLD	LLD	LLD	5380
			14550	LLD	LLD	LLD	LLD	LLD	LLD	LLD	NQ	LLD	2439	LLD	LLD	LLD	61
			14551	LLD	LLD	LLD	LLD	LLD	LLD	LLD	95	LLD	2337	LLD	LLD	LLD	LLD
			14552	LLD	LLD	LLD	LLD	LLD	LLD	LLD	NQ	LLD	290	LLD	LLD	LLD	163
		Female	14563	LLD	LLD	LLD	LLD	LLD	LLD	LLD	NQ	LLD	8676	LLD	LLD	LLD	11981
			14564	LLD	LLD	LLD	LLD	LLD	LLD	LLD	116	LLD	4013	LLD	LLD	LLD	433
			14565	LLD	LLD	LLD	LLD	LLD	LLD	LLD	NQ	LLD	753	LLD	LLD	NQ	3313
			14566	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	456	LLD	LLD	LLD	2202
			14567	LLD	LLD	LLD	LLD	LLD	LLD	LLD	NQ	LLD	345	LLD	LLD	LLD	NQ
61	Placebo	Male	14533	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14534	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14535	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
		Female	14542	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14543	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14544	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
	Ad26 (b) (4) 0.5×10^{11} vp	Male	14553	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	115	LLD	LLD	LLD	LLD
			14554	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14555	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	NQ	LLD	LLD	LLD	LLD
			14556	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14557	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	84	LLD	LLD	LLD	LLD
		Female	14568	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14569	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14570	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	1400	LLD	LLD	LLD	NQ
			14571	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	239	LLD	LLD	LLD	NQ
			14572	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD

LLD = Lower than Limit of Detection (< 10 copies);
NQ = Not Quantifiable (> 10 copies and < 50 copies)

(b) (4)

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Table 2- Biodistribution of Ad26 (b) (4) DNA at SD 91

Study Day	Treatment	Sex	Animal No.	Blood	Gonads	Liver	Thymus	Heart	Lung	Kidney	Spleen	Lymph Nodes		Bone Marrow	Brain	Injection Sites	
												Mesenteric	Iliac			Skin	Muscle
91	Placebo	Male	14536	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14537	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14538	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
		Female	14545	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14546	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14547	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
	Ad26 (b) (4) 0.5×10^{11} vp	Male	14558	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14559	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14560	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	120
			14561	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	50	LLD	LLD	LLD	LLD
			14562	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	1807	LLD	LLD	LLD	LLD
		Female	14573	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	NQ
			14574	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14575	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14576	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD
			14577	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD	LLD

LLD = Lower than Limit of Detection (< 10 copies)
NQ = Not Quantifiable (> 10 copies and < 50 copies)

(b) (4)

IV. Conclusion

A TaqMan™ based qPCR assay was used to measure the biodistribution and persistence of Ad26 (b) (4) in a study conducted in rabbit (b) (4) Results of the qPCR analysis determined that the vaccine was primarily localized in the spleen, iliac lymph node, and the muscle at the site of injection. By study day 61, the vaccine was no longer detected in the spleen. By study day 91, detection of the vector in the iliac lymph nodes and muscle at the site of injection decreased to 2 out of 10 treated animals.

(b) (4)

V. Principal Investigator's Approval

This phase of (b) (4) was performed in compliance with Title 21 of the U.S. Code of Federal Regulations, Part 58, *Good Laboratory Practice for Nonclinical Laboratory Studies*, as applicable and according to (b) (4) (b) (4)

(b) (4), (b) (6)

Principal Investigator

06.27.07
Date

(b) (4)

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VI. Quality Assurance Statement

(b) (4) has been inspected and audited by the Quality Assurance Department of (b) (4) and as far as can be reasonably established, the methods described and the results incorporated in the report accurately reflect the raw data produced during the study. There were no deviations reported during the conduct of this study.

This study was subject to Quality Assurance inspection(s) and/or audit(s) as follows:

Inspection/Audit	Inspection/Audit Date	Date Reported to Management
Critical Phase Audit	02/22/07	02/22/07
Critical Phase Audit	04/10/07	04/10/07
Critical Phase Audit	05/08/07	05/08/07
Critical Phase Audit	05/30/07	06/01/07
Draft Report Audit	06/13/07	06/14/07
Final Report Audit	06/27/07	06/27/07

I certify that this study report provides a true and complete record of the data generated.

(b) (4), (b) (6)
Quality Assurance

06.27.07
Date

(b) (4)

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Appendix 1 – DNA Analyzed per Reaction

Study Day	Treatment	Sex	Animal No.	Blood	Gonads	Liver	Thymus	Heart	Lung	Kidney	Spleen	Lymph Nodes		Bone Marrow	Brain	Injection Sites	
												Mesenteric	Iliac			Skin	Muscle
11	Placebo	Male	14530	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.71	1.00	1.00
			14531	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14532	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.97	1.00	1.00
		Female	14539	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.98	1.00	1.00
			14540	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14541	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Ad26 (b) (4) 0.5×10^{11} vp	Male	14548	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14549	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14550	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14551	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14552	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
		Female	14563	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.77	1.00	1.00
			14564	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14565	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14566	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14567	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
61	Placebo	Male	14533	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.53	1.00	0.90
			14534	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.45	1.00	0.36	1.00	1.00
			14535	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.44	1.00	1.00
		Female	14542	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.37	1.00	1.00
			14543	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.39	1.00	1.00
			14544	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Ad26 (b) (4) 0.5×10^{11} vp	Male	14553	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.63	1.00	1.00
			14554	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14555	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.92	1.00	1.00
			14556	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14557	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.49	1.00	1.00
		Female	14568	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.98
			14569	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.65	1.00	1.00	1.00	0.92
			14570	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.28	1.00	1.00
			14571	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.98
			14572	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

Data expressed as micrograms (µg) for tissue and microliter (µL) for blood

(b) (4)

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Appendix 1 – Continued

Study Day	Treatment	Sex	Animal No.	Blood	Gonads	Liver	Thymus	Heart	Lung	Kidney	Spleen	Lymph Nodes		Bone Marrow	Brain	Injection Sites	
												Mesenteric	Iliac			Skin	Muscle
91	Placebo	Male	14536	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.61	1.00	1.00
			14537	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.11	1.00	1.00	1.00	1.00
			14538	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.45	1.00	1.00	1.00	1.00
		Female	14545	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.96	1.00	1.00	1.00	1.00
			14546	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.50	1.00	1.00
			14547	10	1.00	1.00	0.36	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.51
	Ad26 (b) (4) 0.5×10^{11} vp	Male	14558	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14559	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14560	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14561	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.32	1.00	1.00
			14562	10	1.00	1.00	1.00	1.00	0.92	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
		Female	14573	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14574	10	1.00	0.97	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14575	10	1.00	1.00	1.00	1.00	0.91	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
			14576	10	1.00	1.00	1.00	0.97	1.00	1.00	1.00	0.69	0.57	1.00	0.49	1.00	1.00
			14577	10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.98	1.00	1.00

Data expressed as micrograms (µg) for tissue and microliter (µL) for blood

(b) (4)

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Appendix 7
Protocol, Amendments, and Deviations
Ad26 (b) (4) 91-Day Intramuscular Single Dose
Biodistribution Study in New Zealand White Rabbits

(b) (4)

STUDY PROTOCOL

Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

(b) (4)

APPROVALS

(b) (4)

(b) (4), (b) (6) 1/8/07 Date
Senior Study Director

Beth Israel Deaconess:

(b) (4), (b) (6) 1/7/07 Date
Sponsor's Representative

(b) (4), (b) (6) 1-15-07 Date
(b) (4), (b) (6)
Vice President, Toxicology

(b) (4)

Beth Israel Deaconess (b) (4)

PROTOCOL

I. Study Title

Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits

II. Purpose

The purpose of this study is to determine the biodistribution of an adenovector-based (b) (4) vaccine in New Zealand White rabbits during a 91-day study period when administered by a single intramuscular injection.

III. III. Test Article Summary

The test article is purified, replication-incompetent, recombinant Adenovirus serotype 26 that expresses the clade A (b) (4) protein.

IV. Sponsor Information

A. Name and Address

Beth Israel Deaconess Medical Center
Division of Viral Pathogenesis
Research East Room 213
41 Avenue Louis Pasteur
Boston, MA 02115

B. Sponsor's Representative

(b) (4), (b) (6)

V. (b) (4)

A. Study Director

(b) (4), (b) (6)

Beth Israel Deaconess (b) (4)

B. Alternate Study Contact: (b) (4)

VI. Test Sites, Designated Archive Facilities and Contributing Scientists

A. Toxicology (b) (4)

B. Chemical Archive Facility

Crucell Holland BV
PO Box 2048
2301 CA Leiden
The Netherlands

C. Designated Archive Facility (b) (4)

D. Biodistribution Analysis (b) (4)

VII. Regulatory Information

A. Compliance

This study will be conducted according to the protocol and the company's Standard Operating Procedures (SOP). Portions of the study performed by the Sponsor or subcontractor(s) will be performed according to the protocol and their SOPs.

This study will be conducted in compliance with current U.S. FDA Good Laboratory Practice (GLP) Regulations for Non-clinical Laboratory Studies (21 CFR Part 58).

B. Quality Assurance

(b) (4) Quality Assurance Unit (QAU) will audit the study in accordance with the SOPs and GLPs.

Beth Israel Deaconess (b) (4)

Any portions of the study performed by the Sponsor or subcontractor(s) will be verified by their QAUs. The Quality Assurance Statement(s) will be provided to (b) (4) for inclusion in the final report.

C. Record Retention

All study data, including but not limited to, animal data, formulations data, necropsy data, professional reports, study protocol (including amendments), final report, and any communications concerning the conduct of the study will be retained in the (b) (4) Archive for a period of 5 years following issuance of the final report.

Due to a presumed limited stability, preserved tissues will be maintained for the 1-year period at (b) (4)

Study data generated by the Sponsor or subcontractors will be archived by the Sponsor or subcontractors.

Following the 5-year period (or before at Sponsor's request), the Sponsor will be contacted to determine the disposition of these materials. (b) (4) will maintain all electronic data. (b) (4) will maintain records regarding disposition of data and specimens.

VIII. Proposed Study Timetable

A. Study Initiation Date [a]	See Footnote
B. Experimental Start Date	Date of animal receipt
C. Day of Dosing	February 2, 2007
D. Necropsy	
SD 11:	February 12, 2007
SD 61:	April 3, 2007
SD 91:	May 3, 2007
E. Submission of Audited Draft Final Report	July 5, 2007
F. Study Completion Date [b]	See Footnote

[a] = The date Study Director signs protocol (Protocol must be signed before any study specific procedures are performed).
[b] = The date the report is finalized. The Study Director may finalize the report (by signature) 60 days after submission of the draft final report, if no Sponsor comments are received.

Beth Israel Deaconess (b) (4)

IX. Test and Control Articles

A. Identification and Supplier

1. **Test Article**

Ad26 (b) (4) (a purified, replication-incompetent, recombinant Adenovirus serotype 26 vector that expresses the clade A (b) (4) protein) will be supplied by the Sponsor via Crucell Holland BV. A Certificate of Analysis or equivalent documentation will be provided.

2. **Control Article/Diluent**

Placebo (Formulation Buffer) will be supplied by the Sponsor via Crucell Holland BV. A Certificate of Analysis or equivalent documentation will be provided.

B. Purity and Stability

1. **Test Article**

The purity and stability information for the neat test article will be provided by the Sponsor.

2. **Control Article/Diluent**

Stability can be indicated by a date of expiration in receipt paperwork or other associated documents.

C. Storage Conditions

1. **Test Article**

The adenovirus vaccine will be stored at -75±10°C.

2. **Control Article/Diluent**

The placebo will be stored at 2-8°C.

D. Reserve Samples and Test/Control Article Disposition

1. **Reserve Samples**

Reserve samples (1 vial each) of the neat test and control articles will be taken prior to initial use and will be stored under the same conditions as the neat materials, if reserve samples of the same lot materials have not been taken in other studies. Prior to report finalization, the reserve samples will be returned to Crucell Holland BV for archiving.

2. **Disposition**

Any remaining test and control articles will be returned to the Sponsor, used on subsequent studies, or disposed of at the direction of the Sponsor. Any empty test and control article containers will be disposed of after the final report is issued.

Beth Israel Deaconess (b) (4)

X. Dose Formulations, Sampling and Analysis

A. Formulation

1. **Frequency**

Formulation will not be required at (b) (4) because the control and test articles will be supplied in a ready-to-use form.

2. **Procedure**

Placebo – Remove from refrigerator approximately 30 minutes prior to dosing to let it warm up to room temperature.

Adenovirus vaccine - Thaw at room temperature (18-25°C, on table, not in flow cabinet), which will take approximately 30-45 minutes. After thawing, avoid temperature switches of the material as much as possible (do not transfer the material at 2-8°C or on ice). Start injection as soon as possible after thawing, and the injection needs to be completed within 4 hours after thawing.

3. **Disposition**

Excess formulations will be disposed in accordance with the company's SOPs, appropriate regulatory requirements, and/or information contained in the Material Safety Data Sheets.

B. Dose Formulation Analysis

1. **Formulation Sampling**

Since formulation will not be performed at (b) (4) formulation sampling will not be performed.

2. **Stability**

The date of expiration indicated on the Certificate of Analysis will serve for neat material stability under conditions of storage. Otherwise, data from a stability study or equivalent will be required for inclusion in the final report. Stability should be addressed at -75±10°C and room temperature since these will be the conditions of use for this study.

3. **Dose Analysis**

Dose formulation analysis will not be performed.

XI. Test System and Husbandry

A. Animals

1. **Strain/Source**

New Zealand White Rabbits

Beth Israel Deaconess (b) (4)

(b) (4)

2. **Age at Receipt**

   11 - 16 weeks

3. **Weight at Receipt**

   2-3 kg

4. **Number/Gender**

   48 total; 24 per sex with no more than 3 extras/sex ordered to ensure 48 suitable animals are assigned to study

5. **Identification**

   Individual ear tag and each cage will be labeled with a cage card

6. **Animal Welfare**

   (b) (4) Institutional Animal Care and Use Committee (IACUC) has reviewed this protocol for accordance with provisions of the USDA Animal Welfare Act, the PHS Policy on Humane Care and Use of Laboratory Animals and the U.S. Interagency Research Animal Committee Principals for the Utilization and Care of Research Animals prior to authorizing its execution.

   In the event of severe toxicity or other life threatening situations in which decisions are to be made regarding treatment or euthanasia of a study animal, the (b) (4) (b) (4) veterinarian and the Study Director will preserve the right for subsequent action.

B. Husbandry

1. **Housing**

   Animals will be individually housed in stainless steel and/or polycarbonate cages.

   Control animals will be housed in a separate room from that of test article-treated animals.

2. **Food**

   Animals will be fed Certified Teklad Global Rabbit Diet #2030, *ad libitum,* except when noted otherwise. Feeders will be changed at least once every two weeks.

   Feed is analyzed by the manufacturer for concentrations of specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates. General nutrient and contaminant lot release specifications are on file at (b) (4)

Beth Israel Deaconess (b) (4)

3. **Water**

Water is provided *ad libitum* via an automatic watering system and/or water bottles. The water is routinely analyzed for contaminants and specific microbes. The results of these analyses are on file at (b) (4)

4. **Contaminants**

Available information indicates that no substance is present in the diet or drinking water at a concentration likely to influence the outcome of this study.

5. **Environment**

Animals will be housed in a controlled environment (16-22°C and 30-70% relative humidity). Temperature and humidity will be monitored and recorded continuously in each animal room by an environmental monitoring system. In the event of a system failure, manual recording will be performed (once daily) as defined in the Standard Operating Procedures. A 12-hour light/12-hour dark cycle will be maintained except when interrupted by study-related events. These cycle interruptions will be documented in the study data. A minimum of ten air changes/hour will be maintained.

6. **Environmental Enrichment**

Cage enrichment and/or dietary supplements will be provided per the company's SOP.

C. Procedures for All Animals Prior to Randomization

Animals will be acclimated to the facility for at least 7 days prior to the first dose. During that time, animals will be evaluated as shown in **Table 1**. Based on these evaluations, animals considered unsuitable for the study will be excluded from randomization to study groups.

Table 1: Evaluations During Acclimation

Procedure	Frequency
Cageside Observations	≥ 2 daily
Clinical Observations	Prior to Study Day 1
Body Weight	Prior to Study Day 1

Note: Prior to Study Day 1, cageside observations may be recorded by exception.

D. Randomization

Animals will be assigned to study groups using computer generated random numbers. Males and females will be randomized separately. At the time of randomization, the mean body weight for each group will not be statistically different ($p<0.05$) from the control value. Permanent animal numbers will be assigned following randomization.

Beth Israel Deaconess (b) (4)

XII. Study Design

A. Justification for Species, Route of Administration and Dose Levels

This species will be used because of the US FDA recommendation for assessing the biodistribution of adenovirus-vectored vaccines. The intramuscular route was selected since it is the intended route of human exposure. The dose for this study was selected based on the largest amount of vaccine that can be delivered into the rabbit muscle with one injection.

B. Group Designation and Dosage Levels

Table 2: Group Designation and Dosage Levels

Group	Treatment	Dose Level	Dose Volume (mL)	Number of Animals	
				males	females
1	Placebo	0	0.5	9	9
2	Ad26 (b) (4)	0.5 x 10^{11} vp	0.5	15	15

C. Dosing Information

1. **Method of Administration**

   Animals will be dosed via intramuscular injection. Intramuscular injection will be a single 0.5-mL injection into right hind thigh muscle. Dose volume will not be adjusted for body weight. Injection will be administered using needle and syringe. Injection will be administered at a shaved/marked site.

2. **Frequency**

   Once on Study Day (SD) 1. The first day of dosing is designated as SD 1.

3. **Dose Volume**

   Single 0.5-mL injection.

Beth Israel Deaconess (b) (4)

D. Observation of Animals Following Randomization

Table 3: Observation of Animals Following Randomization

Procedure	Frequency of Testing
Cageside Observations [a]	≥ 2 Daily
Clinical Observations [b]	Prior to dose, weekly thereafter, and at termination
Body Weight	Prior to dose, weekly thereafter, and at termination

[a] = Cageside observations will include mortality, moribundity, general health and signs of toxicity.
[b] = Clinical observations will include skin and fur characteristics, eye and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, and somatomotor and behavior patterns.

E. Termination

1. **Unscheduled**

Gross necropsies will be conducted on all moribund animals and all animals not surviving to termination. Moribund animals will be euthanized by sodium pentobarbital or equivalent injection and exsanguinated prior to necropsy (gross necropsy, tissue preservation, histopathology, and bone marrow collection will be performed). Found dead animals will only have gross necropsy, tissue preservation and histopathology performed (no bone marrow collection performed).

2. **Scheduled**

All scheduled animals will be euthanized by sodium pentobarbital or equivalent injection and exsanguinated. Animals will be necropsied as close as possible to the time of sacrifice.

Table 4: Necropsy Schedule

Group	SD 11	SD 61	SD 91
1	3/sex	3/sex	3/sex
2	5/sex	5/sex	5/sex

F. Postmortem Procedures

1. **Gross Necropsy**

Animals will be subjected to a full gross necropsy, which includes examination of the external surface of the body, the injection sites, all orifices, and the cranial, thoracic, and abdominal cavities and their contents.

Beth Israel Deaconess (b) (4)

2. **Bone Marrow Collection**

Unscheduled Sacrifice: Two bone marrow smears will be prepared from the sternum of moribund sacrificed animals. Slides will be air-dried, fixed in methanol, and stored for possible future evaluation. If not evaluated, the slides will be discarded after report finalization.

Scheduled Biodistribution Animals: Bone marrow will be collected from the left femur. The samples will be snap frozen in liquid nitrogen and stored at -75±10°C.

3. **Tissue Collection – Scheduled Biodistribution Necropsy**

The following tissues will be collected in the order listed below with a fresh set of clean instruments for each organ of each animal. Gloves will be changed between each organ. Paired organs will be processed together. The tissues will be snap frozen in liquid nitrogen and stored at -75±10°C. The Group 1 (control) animals will be necropsied first, followed by Group 2 animals.

Blood (≥ 0.6 mL of blood will be collected into an EDTA tube and then transferred to a cryovial and snap frozen)
Ovaries/testis
Liver
Thymus
Heart
Lung
Kidney
Spleen
Mesenteric Lymph Nodes
Iliac Lymph Nodes
Skin and subcutis at injection site
Thigh muscle at injection site
Bone Marrow
Brain

All tissues will be shipped (on dry ice) to (b) (4) and will be processed for the presence of Ad26 (b) (4) in the tissues using a GLP validated method, qPCR (quantitative polymerase chain reaction). Tissues will not be pooled for analysis without prior discussion with the Sponsor. (b) (4) will be responsible for auditing the data generated and will provide a biodistribution report to be included in the final report.

4. **Tissue Collection – Unscheduled Necropsy**

The animal identification and all tissues (sex appropriate) identified to be collected in **Table 5** will be preserved in 10% neutral buffered formalin (NBF). Eye, optic nerve, testis and epididymis will be fixed in modified Davidson's fixative for 24-48 hours and then be transferred to 70% ethanol.

The tissues collected will be preserved for possible histopathologic evaluation. The preserved tissues will be kept at (b) (4) Tissues will be discarded when the

Beth Israel Deaconess (b) (4)

final report is issued following confirmation with the Sponsor and the Study Director.

Table 5: Tissue Preservation List

Tissue	Tissue Collected and Preserved
Adrenal gland	x
Aorta	x
Bone with marrow - femur	x
Bone with marrow - sternum	x
Brain	x
Cecum	x
Cervix	x
Colon	x
Duodenum	x
Epididymis	x
Esophagus	x
Eye	x
Gallbladder	x
Heart	x
Ileum	x
Jejunum	x
Kidney	x
Liver	x
Lung	x
Mammary gland (male and female)	x
Mandibular lymph node	x
Mandibular salivary gland	x
Mesenteric lymph node	x
Optic nerve	x
Ovary	x
Pancreas	x
Parathyroid gland	x
Pituitary	x
Prostate	x
Rectum	x
Sciatic nerve	x
Seminal vesicle	x
Skeletal muscle (biceps femoris)	x
Skin	x
Spinal cord (cervical, thoracic, lumbar)	x
Spleen	x
Stomach	x

Beth Israel Deaconess (b) (4)

Testis	x
Thymus	x
Thyroid gland	x
Tongue	x
Trachea	x
Urinary bladder	x
Uterus	x
Vagina	x
Gross Lesions	x
Injection site[1]	x

[1] Injection site will include underlying muscle.

XIII. Proposed Statistical Analyses

Descriptive statistics (mean, standard deviations, and N) will be presented for all applicable measurement data and shown in the summary tables. Data include but are not limited to:

Body Weight and Body Weight Change

Quantitative results will be analyzed using the Kolmogorov-Smirnov test for normality, the Levene Median test for equal variance and by one-way Analysis of the Variance (ANOVA). If either the normality or equal variance test fails, then the analysis will continue using the non-parametric Kruskal-Wallis ANOVA on rank-transformed data. For parametric data, if the ANOVA indicates statistical significance among experimental groups, then the Dunnett's t-test will be used to delineate which groups (if any) differ from the control. For non-parametric data, if the Kruskal-Wallis ANOVA indicates statistical significance among experimental groups then the Dunn's test will be used to delineate which groups (if any) differ from the control. The probability value of less than 0.05 (two-tailed) will be used as the critical level of significance for all tests.

Statistical analysis will be conducted using SigmaStat™ Statistical Software (b) (4)
(b) (4)

For any group where n=1, no statistical analysis will be performed.

XIV. Final Report

An unaudited and audited draft of the report will be sent to the Sponsor. At finalization, two paper copies (one bound, one unbound) and one electronic copy (PDF) of the final report, which includes the following information, but not limited to, will be submitted to the Sponsor.

Report Table of Contents:

COMPLIANCE STATEMENT

QUALITY ASSURANCE STATEMENT

SIGNATURE PAGE

SUMMARY

Beth Israel Deaconess (b) (4)

Beth Israel Deaconess (b) (4)

(b) (4)

PROTOCOL AMENDMENT

Study Number:	(b) (4)
Study Title:	Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits
Amendment Number:	1

1. **Subject: Section XII.E.2. Scheduled Termination**

   All scheduled animals will be euthanized by intravenous injection of sodium pentobarbital, or Euthasol, or equivalent and exsanguinated.

   Justification: Change to add alternative euthanasia method.

Approval:

(b) (4), (b) (6)
Senior Study Director — Date: 2/12/07

(b) (4), (b) (6)
Sponsor's Representative — Date: 2/9/07

Beth Israel Deaconess (b) (4)

(b) (4)

PROTOCOL AMENDMENT

Study Number:	(b) (4)
Study Title:	Ad26 (b) (4) : 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits
Amendment Number:	2

1. **Subject: Section IV.A. Study Director**

Effective on June 12, 2007, change Study Director to:

(b) (4), (b) (6)

Justification: Study Director is changed due to personnel change (b) (4)

Approval:

(b) (4), (b) (6)

(b) (4), (b) (6) 6-13-07 Date

Study Director

(b) (4), (b) (6)

6/13/07 Date

Sponsor's Representative

(b) (4), (b) (6)

6-13-07

Bridge GPS, Management

CONFIDENTIAL Page 1 of 1 June 12, 2007

(b) (4)

The following deviations from the protocol were noted:

No environmental monitoring data were collected for approximately 11 hours on February 2, 2007.

On several instances throughout the study, the relative humidity was below the protocol-specified lower limit of 30%.

The above-mentioned deviations did not impact this study, nor did they affect the quality or integrity of the study or the interpretation of the results in this report.

Janssen Vaccines & Prevention B.V. *

Pharmacokinetics Tabulated Summary

MODULE 2.6.5

VAC31518 JNJ-78436735

Prophylactic COVID-19 Vaccine

* Janssen Vaccines & Prevention B.V. is a Janssen pharmaceutical company of Johnson & Johnson and is hereafter referred to as the sponsor.

Issue Date: 4 November 2020
Document No.: (b) (4)

2.6.5.1 Pharmacokinetics: Overview

Test Article: Ad26.COV2.S

Type of Study	Test System	Route	Number of Injections	Test Article: Dose Level (Dose Volume)	GLP	Test Facility	Location in CTD/Study No.
Biodistribution Study with Ad26 vectored vaccine	NZW Rabbits	IM	Single Injection	Ad26 (b) (4) 5×10^{10} vp (0.5 mL)	Yes	(b) (4)	(b) (4)
Biodistribution Study with Ad26 vectored vaccine	NZW Rabbits	IM	Single Injection	Ad26 (b) (4) ± (b) (4) (b) (4) 1×10^{11} vp ± 150 µg (0.5 mL or 1 mL of mixture)	Yes	(b) (4)	(b) (4)

GLP = Good Laboratory Practice; IM = intramuscular; NZW = New Zealand White; SC = subcutaneous; $TCID_{50}$ = 50% tissue culture infective dose; vp = virus particles

2.6.5.5A Pharmacokinetics: Tissue/Organ Distribution

Test Article: Ad26 (b) (4)

Report Title:	Ad26 (b) (4) 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits
Study No.	(b) (4)
Species:	New Zealand White rabbits (HsdOkd)
No. of animals:	Total of 10 animals (5/sex) analyzed per timepoint per group (3/sex/timepoint in Group 1)
Test Article - Dose	Group 1 Placebo[a] 0 vp (0.5 mL) Group 2 Ad26 (b) (4) [b] $5x10^{10}$ vp in 0.5 mL
Route of Administration:	Intramuscular (IM) injection
Sampling timepoint:	Days 11, 61, 91
Tissues assessed by q-PCR:	Blood, gonads, liver, thymus, heart, lung, kidney, spleen, mesenteric lymph node, iliac lymph node, bone marrow, brain, skin at injection site, muscle at injection site
Assay Characteristics:	Limit of detection, LOD = 10 copies/µg DNA; Lower limit of quantitation, LLOQ = 50 copies/µg DNA

Tissue[c]	**Group 2 (Ad26 (b) (4) IM)**		
	Copies/µg DNA (min-max range of samples >LLOQ)	No. of animals >LLOQ	No. of animals >LOD and <LLOQ
Muscle at injection site			
Day 11	61 to 11,981	7/10	1/10
Day 61	-	0/10	2/10
Day 91	120	1/10	1/10
Skin at injection site			
Day 11	-	0/10	1/10
Day 61	-	0/10	0/10
Day 91	-	0/10	0/10
Iliac lymph nodes			
Day 11	119 to 8676	10/10	0/10
Day 61	84 to 1400	4/10	1/10
Day 91	50 to 1807	2/10	0/10
Spleen			
Day 11	50 to 116	4/10	5/10
Day 61	-	0/10	0/10
Day 91	-	0/10	0/10

[a] Ad26 (b) (4) placebo: (b) (4)

[b] Ad26 (b) (4) drug product: 1x10 vp/mL Ad26 (b) (4) formulated in (b) (4) (b) (4)

[c] Samples collected from Group 1 had Ad26 (b) (4) vector DNA results below the LOD of the assay for all tissues and fluids at all timepoints. For Group 2 animals, only tissues with vector DNA levels above LOD are listed. All other tissues collected had vector DNA results below the LOD of the assay at all time points.

- Levels for all animals were below LLOQ at this time point

IM = intramuscular(ly); LLOQ = lower limit of quantitation; LOD = limit of detection; q-PCR = quantitative polymerase chain reaction; vp = virus particles

2.6.5.5B Pharmacokinetics: Biodistribution: Ad26 (b) (4)

Test Article: Ad26 (b) (4)

Report Title:	A Single Dose Biodistribution Study of Ad26 (b) (4) by Intramuscular Injection in Rabbits with up to 180 Days Observation Period
Study No.	(b) (4)
Species:	New Zealand White Rabbit (Hra[NZW]SPF)
No. of animals:	Total of 10 animals (5/sex) analyzed per timepoint per group (3/sex/timepoint in Group 1)
Test Article - Dose	Group 1 Reference item[a] 0 vp (1 mL) Group 2 Ad26 (b) (4) [b] $1x10^{11}$ vp in 0.5 mL Group 3 Ad26 (b) (4) + (b) (4) [c] $1x10^{11}$ vp + 150 µg (b) (4) (1 mL of mixture)
Route of Administration:	Intramuscular (IM) injection
Sampling timepoint:	Days 11, 90, 120, and 180
Tissues assessed by q-PCR:	Blood, ovaries/testes, liver, spleen, kidney, iliac lymph node, heart, lung, brain, skin with subcutis over the injection, bicep femoris muscle at injection site, popliteal lymph node, bone marrow, thymus, mesenteric lymph node
Assay Characteristics:	Limit of detection, LOD = 7.1 copies/µg DNA Lower limit of quantitation, LLOQ = 28.6 copies/µg DNA

Tissue[d]	**Group 2 (Ad26 (b) (4) IM)**			**Group 3 (Ad26 (b) (4) + (b) (4) IM)**		
	Copies/µg DNA (min-max range of samples >LLOQ)	No. of animals >LLOQ	No. of animals >LOD and <LLOQ	Copies/µg DNA (min-max range of samples >LLOQ)	No. of animals >LLOQ	No. of animals >LOD and <LLOQ
Skin at injection site						
Day 11	39.1 to 6304.3	4/10	2/10	88.6 to 272.6	2/10	3/10
Day 90	280.1	1/10	0/10	42.7 to 175.1	2/10	0/10
Day 120	-	0/10	0/10	-	0/10	0/10
Day 180	NA	NA	NA	NA	NA	NA
Muscle at injection site						
Day 11	-	0/10	1/10	-	0/10	0/10
Day 90	-	0/10	0/10	-	0/10	0/10
Day 120	-	0/10	0/10	-	0/10	0/10
Day 180	NA	NA	NA	NA	NA	NA
Iliac lymph nodes						
Day 11	63.6 to 387.6	9/10	1/10	108.6 to 347.4	9/10	0/10
Day 90	48.1	1/10	3/10	25.9 to 35.3	2/10	3/10
Day 120	37.9 to 53.4	2/10	1/10	-	0/10	0/10
Day 180	37.6	1/10	2/10	-	0/10	2/10

2.6.5.5B Pharmacokinetics: Biodistribution: Ad26 (b) (4) (Continued)

Report Title: A Single Dose Biodistribution Study of Ad26 (b) (4) by Intramuscular Injection in Rabbits with up to 180 Days Observation Period
Study No. (b) (4)

Tissue[d]	**Group 2 (Ad26 (b) (4) IM)**			**Group 3 (Ad26 (b) (4) + (b) (4) IM)**		
	Copies/µg DNA (min-max range of samples >LLOQ)	No. of animals >LLOQ	No. of animals >LOD and <LLOQ	Copies/µg DNA (min-max range of samples >LLOQ)	No. of animals >LLOQ	No. of animals >LOD and <LLOQ
Popliteal lymph nodes						
Day 11	29.0	1/10	1/10	-	0/10	0/10
Day 90	-	0/10	0/10	-	0/10	0/10
Day 120	-	0/10	0/10	-	0/10	0/10
Day 180	NA	NA	NA	NA	NA	NA
Spleen						
Day 11	37.3 to 118.6	6/10	4/10	26.4 to 75.6	7/10	2/10
Day 90	-	0/10	0/10	-	0/10	0/10
Day 120	-	0/10	1/10	-	0/10	0/10
Day 180	-	0/10	0/10	-	0/10	0/10
Liver						
Day 11	-	0/10	0/10	-	0/10	1/10
Day 90	-	0/10	0/10	-	0/10	0/10
Day 120	NA	NA	NA	NA	NA	NA
Day 180	NA	NA	NA	NA	NA	NA

[a] Reference item: 0.9% Sodium Chloride for Injections, USP
[b] Ad26 (b) (4) $2x10^{11}$ vp/mL (in (b) (4))
[c] (b) (4) 0.3 mg/mL (in (b) (4))
[d] All tissues collected from euthanasia on Days 11, and 90 from all groups were analyzed for the presence of Ad26 vector DNA using q-PCR. From tissues collected from euthanasia on Days 120, only iliac lymph node, injection site skin, spleen, popliteal lymph node and injection site muscle were analyzed. From tissues collected from euthanasia on Days 180, only spleen and iliac lymph node were analyzed. Samples collected from Group 1 at Day 11 and Day 90 had Ad26 (b) (4) vector DNA results below the LOD of the assay for all tissues at all time points. For Group 2 and Group 3 animals, only tissues with vector DNA levels above LOD are listed. All other tissues collected had vector DNA results below the LOD of the assay at all time points.
- Levels for all animals were below LLOQ at this time point

IM = intramuscular(ly); LLOQ = lower limit of quantitation; LOD = limit of detection; q-PCR = quantitative polymerase chain reaction; NA = not analyzed; vp = virus particles

Janssen Vaccines & Prevention B.V.*

Pharmacokinetics Tabulated Summary

MODULE 2.6.5

VAC31518 JNJ-78436735

Prophylactic COVID-19 Vaccine

* Janssen Vaccines & Prevention B.V. is a Janssen pharmaceutical company of Johnson & Johnson and is hereafter referred to as the sponsor.

Issue Date: 18 June 2020
Document No.: (b) (4)

2.6.5.1 Pharmacokinetics: Overview: Ad26 (Platform) Studies

Type of Study (Target)	Test System (No. of animals)	Route	Vaccine Regimen, Interval, and Dose Level	GLP	Test Facility *(Study Period)*	Study No.
Biodistribution Study (b) (4)	NZW Rabbits (3-5/sex/group)	IM	Single injection: • Placebo buffer • Ad26 (b) (4) (5×10^{10} vp)	Yes	(b) (4) *(Jan – Sep 2007)*	(b) (4)
Biodistribution Study (b) (4)	NZW Rabbits (3-5/sex/group)	IM	Single injection: • Reference item (0.9% Sodium Chloride) • Ad26 (b) (4) (1×10^{11} vp) • Ad26 (b) (4) + (b) (4) (1×10^{11} vp + 150 µg)	Yes	(b) (4) *(Jun 2018 - May 2019)*	(b) (4)

Ad26: adenovirus type 26; GLP: Good Laboratory Practice; (b) (4) IM: intramuscular; NZW: New Zealand White; (b) (4) vp: virus particles

Janssen Vaccines & Prevention B.V. *

Pharmacokinetics Written Summary

MODULE 2.6.4

VAC31518 JNJ-78436735

Prophylactic COVID-19 Vaccine

* Janssen Vaccines & Prevention B.V. is a Janssen pharmaceutical company of Johnson & Johnson and is hereafter referred to as the sponsor.

Issue Date: 4 November 2020
Document No.: (b) (4)

TABLE OF CONTENTS

LIST OF IN-TEXT TABLES

LIST OF ABBREVIATIONS

Ad26	adenovirus type 26
CMV	cytomegalovirus
COVID-19	coronavirus disease 2019
DNA	deoxyribonucleic acid
E1	early region
EDTA	ethylenediaminetetraacetic acid
EMA	European Medicines Agency
FDA	Food and Drug Administration
GLP	Good Laboratory Practice
(b) (4)	
(b) (4)	
IM	intramuscular
NZW	New Zealand white
OECD	Organization for Economic Co-operation and Development
(b) (4)	
(b) (4)	
q-PCR	quantitative polymerase chain reaction
(b) (4)	
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
(b) (4)	
(b) (4)	
vp	virus particles
WHO	World Health Organization

Vectors and (Candidate) Vaccines

Ad26.COV2.S	Ad26 vector encoding a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Spike protein
Ad26 (b) (4)	Ad26 vector encoding (b) (4)
Ad26 (b) (4)	Ad26 vector encoding (b) (4)

1. BRIEF SUMMARY

Ad26.COV2.S (also known as VAC31518 or JNJ-78436735) is a monovalent, recombinant, replication-incompetent adenovirus type 26 (Ad26) vectored vaccine encoding a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Spike protein. It is being developed for prophylactic immunization against coronavirus disease 2019 (COVID-19), which has spread rapidly and globally since its emergence.

This Pharmacokinetics Written Summary provides an overview of the available pharmacokinetic data in support of the Ad26.COV2.S development. In accordance with the World Health Organization (WHO) Guidelines on Nonclinical Evaluation of Vaccines [6], pharmacokinetic studies are usually not needed for vaccines. However, in line with the European Medicines Agency (EMA) Guideline on quality, nonclinical and clinical aspects of live recombinant viral vectored vaccines [1] and the FDA Guidance on considerations for plasmid DNA vaccines for infectious disease indications [2], biodistribution studies have been conducted to assess the distribution, persistence, and clearance of the Ad26 vector (platform) following intramuscular (IM) injection.

The biodistribution profile of the Ad26 vector platform has been evaluated in the rabbit using an Ad26-based (b) (4) vaccine, i.e., Ad26 (b) (4) (Ad26 vector encoding the (b) (4) and an Ad26-based (b) (4) (b) (4) vaccine, i.e., Ad26 (b) (4) (Ad26 vector encoding (b) (4) (b) (4). An overview of the biodistribution studies is provided in Table 1. No pharmacokinetic or biodistribution studies have been conducted with Ad26.COV2.S specifically.

Table 1: Overview of Biodistribution Studies in Support of the Development of COVID-19 Vaccine Candidate Ad26.COV2.S

Study Type	GLP	Route	Species	Vaccines Administered	Number of Injections	Study No.
Biodistribution	Yes	IM	NZW rabbits	Ad26 (b) (4)	1-dose	(b) (4)
Biodistribution	Yes	IM	NZW rabbits	Ad26 (b) (4)	1-dose	(b) (4)

GLP = Good Laboratory Practice; IM = intramuscular; NZW = New Zealand white

The biodistribution studies for the Ad26 vector platform were conducted in compliance with U.S. FDA GLP Regulations (21 CFR Part 58) and/or the Organization for Economic Cooperation and Development (OECD) Principles of GLP in a country that is part of the OECD Mutual Acceptance of Data Process, and include the appropriate documentation. Information on e.g., study GLP status and test facility identity are provided in the Pharmacokinetics Overview Table in Mod2.6.5.1.

The biodistribution studies with Ad26 (b) (4) and Ad26 (b) (4) were conducted using the IM route, which is also the intended route for use of Ad26.COV2.S in humans.

The studies were done in rabbits as this is a widely accepted species to assess the nonclinical safety of vaccines. In nonclinical studies, Ad26-based vaccines (including Ad26.COV2.S, Ad26 (b) (4) and Ad26 (b) (4)) were shown to elicit immune responses in the animals, indicating the rabbit as a relevant nonclinical species for these vaccines. In addition, rabbits have sufficient muscle mass to receive a full human vaccine dose via the IM route with a single injection.

In the biodistribution studies with Ad26 (b) (4) (administered at a dose of 5×10^{10} virus particles [vp]) and Ad26 (b) (4) (administered at a dose of 1×10^{11} vp), animals were sacrificed on Days 11, 61, or 91 (Ad26 (b) (4)), and on Days 11, 90, 120 or 180 (Ad26 (b) (4)) following single IM injection. Tissues from these animals were harvested for analysis of Ad26 vector DNA using a quantitative polymerase chain reaction (q-PCR) assay. The Ad26 vector did not widely distribute following IM administration in the animals. Vector DNA was primarily detected at the site of injection, draining lymph nodes and (to a lesser extent) the spleen. Comparing the results from the respective necropsy timepoints, the number of animals with positive tissues and/or the vector copy number present in those positive tissues declined to levels close to, or below the detection limit of the q-PCR methods used, indicating clearance of the Ad26 vector from the animals/tissues. In addition, both Ad26-based vaccines tested in the biodistribution studies showed a similar pattern of (systemic) distribution and clearance when delivered via the IM route in the rabbit, despite carrying different transgene inserts.

The Ad26 vector backbone used for Ad26.COV2.S is identical to the vector backbone of the Ad26-based vaccines that were tested in the available biodistribution studies (i.e., Ad26 (b) (4) and Ad26 (b) (4)). The only difference between the vectors, apart from the encoded antigen transgene, is the insertion of a (b) (4) in the cytomegalovirus (CMV) promoter sequence of the transgene expression cassette of Ad26.COV2.S. This is not considered to impact the biodistribution profile of the Ad26 vector.

In conclusion, the Ad26 vector shows a limited distribution profile following IM injection. Clearance (reflected by a downward trend in number of positive tissues and vector copies over time, to levels close to, or below the detection limit of the q-PCR methods used) of the Ad26 vector was observed, indicating that the vector does not replicate and/or persist in the tissues following IM injection. These platform biodistribution data obtained from Ad26 (b) (4) and Ad26 (b) (4) are considered sufficient to inform on the biodistribution profile of Ad26.COV2.S, for which the same (replication-incompetent) Ad26 vector backbone is used. This position has been confirmed and agreed in a previous Scientific Advice by EMA (b) (4) and CBER (b) (4) (b) (4) It is further noted that the same platform biodistribution data were part of the MAA file for the Ebola vaccine component Ad26.ZEBOV (EU/1/20/1444/001).

2. METHODS OF ANALYSIS

In the biodistribution studies, specific PCR assays were used to detect and quantify Ad26-vector DNA in various tissues collected at specified time points following vector administration.

In GLP study No. (b) (4) (Ad26 (b) (4)), a TaqMan-based q-PCR assay was used to detect a target sequence of the Ad26 (b) (4) vector. The detection limit of this assay was 10 copies of Ad26 (b) (4) µg genomic DNA; the lower limit of quantification was 50 copies of Ad26 (b) (4) µg genomic DNA. A description of the assay is available in the report.

In GLP study No. (b) (4) (Ad26 (b) (4)), a TaqMan-based q-PCR assay was used for quantitation of a specific target sequence of the Ad26 (b) (4) vector. The detection limit of the assay was 7.1 copies/µg genomic DNA; the lower limit of quantification was 28.6 copies/µg genomic DNA. A method validation summary is available in the report.

3. ABSORPTION

Not applicable for vaccines.

4. DISTRIBUTION

To assess distribution, persistence, and clearance of the Ad26 viral vector (platform), IM biodistribution studies have been conducted in rabbits using an Ad26-based (b) (4) vaccine, i.e., Ad26 (b) (4) and an Ad26-based (b) (4) vaccine, i.e., Ad26 (b) (4). A comparison of the Ad26 (b) (4) and Ad26 (b) (4) biodistribution data is discussed in Section 9.

4.1. Ad26 (b) (4) (Study (b) (4))

Study Title (Report Date)	Ad26 (b) (4): 91-Day Intramuscular Single Dose Biodistribution Study in New Zealand White Rabbits (14 September 2007)
Conducting Laboratory, Location	(b) (4)
Sponsor	Beth Israel Deaconess Medical Center, Massachusetts, United States
GLP Compliance	Yes
Study Report	(b) (4)
Tabulated Summary	Mod2.6.5.5A

New Zealand White (NZW) rabbits were administered placebo or Ad26 (b) (4) at $5x10^{10}$ vp via a single IM injection into the right hind thigh muscle on Day 1 (Table 2). Parameters evaluated during the study included clinical and cage-side observations, body weights, and biodistribution. Necropsies were performed on 3 rabbits/sex in the placebo group and 5 rabbits/sex in the Ad26 (b) (4) group on Days 11, 61, and 91 to collect tissues for biodistribution analysis. These timepoints are in line with other biodistribution studies conducted with adenovirus type 5 (Ad5) and type 35 (Ad35) based vaccines [5] and were selected to cover sufficient time to assess clearance of the vector.

The following tissues were collected: blood, ovaries/testes, liver, thymus, heart, lung, kidney, spleen, mesenteric and iliac lymph nodes, bone marrow, brain, and skin, subcutis and muscle at the injection site. All tissues collected on Day 11, 61, and 91 were analyzed for the presence of the Ad26 (b) (4) DNA using a q-PCR method.

Table 2: Experimental Design of Biodistribution Study with Ad26 (b) (4) (Study (b) (4)

Group	Test Article	Dose Level	Dose Volume	Route	Scheduled Sacrifice Timepoint		
					Day 11	Day 61	Day 91
1	Placebo[a]	0	0.5 mL	IM	3/sex	3/sex	3/sex
2	Ad26 (b) (4)	5×10^{10} vp	0.5 mL	IM	5/sex	5/sex	5/sex

[a] (b) (4)
(b) (4)
(b) (4) mL formulated in (b) (4)
(b) (4)
(b) (4) IM = intramuscular; vp = virus particles

A single IM injection of Ad26 (b) (4) in male and female NZW rabbits was well tolerated with no effect on clinical/cage-side observations, or body weights.

For all Group 1 samples collected at Day 11, Day 61 or Day 91, Ad26 (b) (4) vector DNA was below the limit of detection of the assay (<10 copies/µg DNA).

Analysis of Group 2 samples on Day 11 indicated that Ad26 vector DNA was primarily localized in the injection site muscle, draining (iliac) lymph nodes and to a lesser extent the spleen. Ad26 (b) (4) vector DNA was below limit of detection in all other organs, except for one animal that showed a low signal in the injection site skin at a level below the lower limit of quantification (50 copies/µg DNA).

In the animals sacrificed on Day 61, the Ad26 vector DNA was no longer detected in the spleen, while vector DNA in the injection site muscle and iliac lymph nodes was detected at a reduced incidence and quantity compared to Day 11.

On Day 91, detection of the vector was limited to the injection site muscle and iliac lymph nodes in 2 of 10 treated animals and was below the limit of detection in all other examined tissues or animals.

4.2. Ad26 (b) (4) (Study (b) (4))

Study Title (Report Date)	Single Dose Biodistribution Study of Ad26 (b) (4) by Intramuscular Injection in Rabbits with up to 180 Days Observation Period (08 May 2019)
Conducting Laboratory, Location	(b) (4)
Sponsor	Janssen Infectious Diseases-Diagnostics, Belgium
GLP Compliance	Yes
Study Report	(b) (4)
Tabulated Summary	Mod2.6.5.5B

NZW rabbits were administered placebo or Ad26 (b) (4) at $1x10^{11}$ vp via a single IM injection into the right thigh. In one study arm, Ad26 (b) (4) was dosed in combination with 150 µg (b) (4) protein as a single injection (Table 3). The following parameters and end points were evaluated in this study: clinical signs, body weights, gross necropsy findings and biodistribution using q-PCR analysis. Tissues for q-PCR analysis were collected from 3 rabbits/sex in the placebo group and 5 rabbits/sex in the Ad26 (b) (4) groups on Days 11, 90, 120, and 180. To assess the clearance of the vector beyond 90 days (i.e., the last sampling

timepoint in the previous study with Ad26 (b) (4) , two additional later timepoints, Day 120 and 180, were included.

The following tissues were collected: blood, ovaries/testes, liver, thymus, heart, lung, kidney, spleen, mesenteric, iliac, and popliteal lymph nodes, bone marrow, brain, skin with subcutis at the injection site, and muscle at the injection site. All tissues collected from euthanasia on Days 11, and 90 from all groups were analyzed for the presence of Ad26 vector DNA using q-PCR. From the animals sacrificed on Day 120, only iliac lymph node, injection site skin, spleen, popliteal lymph node and injection site muscle were analyzed; from the animals sacrificed on Day 180, only spleen and iliac lymph node were analyzed. From Day 120 onwards, no Group 1 samples were analyzed given that they were negative on Day 11 and Day 90.

Table 3: Experimental Design of Biodistribution Study with Ad26 (b) (4) (Study (b) (4))

Group	Test Article	Dose Level	Dose Volume	Route	Scheduled Sacrifice Timepoint			
					Day 11	Day 90	Day 120	Day 180
1	Reference item[a]	0	1 mL	IM	3/sex	3/sex	3/sex	3/sex
2	Ad26 (b) (4) [b]	1×10^{11} vp	0.5 mL	IM	5/sex	5/sex	5/sex	5/sex
3	Ad26 (b) (4) [b] + (b) (4) [c]	1×10^{11} vp + 150 µg	1 mL (of mixture)	IM	5/sex	5/sex	5/sex	5/sex

[a] Reference item: 0.9% Sodium Chloride for Injections, USP
[b] Ad26 (b) (4) 2x10[11] vp/mL (in (b) (4))
[c] (b) (4) 0.3 mg/mL (in (b) (4) (b) (4))

IM = intramuscular; vp = virus particles

There were no Ad26 (b) (4) related changes noted in clinical observations, or body weights, and there were no treatment-related gross necropsy findings.

All samples collected from Group 1 at Day 11 and Day 90 had Ad26 (b) (4) vector DNA results below the limit of detection of the assay (<7.1 copies/µg DNA).

In samples collected from Group 2 and 3 on Day 11, Ad26 (b) (4) vector DNA was primarily detected in the skin at the injection site, iliac lymph nodes, and spleen. The skin at the injection site and the iliac lymph nodes presented the highest number of vector copies. The popliteal lymph node showed a low signal (around or below the lower limit of quantification of 28.6 copies/µg DNA) in 2 animals from Group 2. One animal from Group 3 showed a signal in the liver at a level below the lower limit of quantification.

In Group 2 and 3 animals sacrificed on Day 90, Ad26 (b) (4) vector DNA was detected only in the skin at the injection site and in the iliac lymph nodes, but at a reduced incidence, as well as a lower maximum quantity of vector DNA than on Day 11.

On Day 120, Ad26 (b) (4) vector DNA was only detected at a low vector copy number (close to, or below the lower limit of quantification) in a single spleen sample, and iliac lymph nodes in 3 of 10 treated animals from Group 2.

On Day 180, detection of the vector was limited to the iliac lymph nodes in 3 of 10 treated animals in Group 2 and 2 out of 10 animals in Group 3 at a level close to, or below the lower limit of quantification and was below the limit of detection in all other examined tissues or animals.

Animals from Group 2 and Group 3 showed a similar distribution pattern.

5. METABOLISM

Not applicable for vaccines.

6. EXCRETION

Not applicable for vaccines.

7. PHARMACOKINETIC DRUG INTERACTIONS

Not applicable for vaccines.

8. OTHER PHARMACOKINETIC STUDIES

Other pharmacokinetic studies were not performed.

9. DISCUSSION AND CONCLUSIONS

Pharmacokinetic or biodistribution studies have not been conducted with Ad26.COV2.S. To assess the distribution, persistence, and clearance of the Ad26 vector (platform), the biodistribution profile of the Ad26 vector has been evaluated using Ad26 (b) (4) and Ad26 (b) (4) following IM injection in the rabbit.

The Ad26 vector contains deletions in the early region (E1) of the Ad26 genome, rendering it replication-incompetent. Ad26-based vaccines require recombinant E1 complementing cell lines, like the PER.C6 (b) (4) cells, for virus replication. Outside of these specific cellular environments, Ad26-based vaccines cannot replicate or reproduce and are therefore expected to show a limited distribution and persistence following administration. This is confirmed by the biodistribution studies in rabbits in which the distribution, persistence and clearance of Ad26-based vaccines against (b) (4) (Ad26 (b) (4) study No. (b) (4) Section 4.1) and (b) (4) (Ad26 (b) (4) study No. (b) (4) Section 4.2) have been evaluated following IM administration. As a general pattern, both Ad26 vectors showed a similar and limited biodistribution profile, as they were primarily detected at the site of injection, regional (iliac) lymph nodes and (to a lesser extent) the spleen. No Ad26 vector DNA was detected in the gonads or in the brain.

Comparing the various necropsy timepoints following IM administration (Days 11, 61, and 91 for Ad26 (b) (4) Days 11, 90, 120 and 180 for Ad26 (b) (4) Table 4), a downward trend in number of positive tissues, and/or vector copies was observed, to levels close to, or below the respective limits of detection of the q-PCR assay used, indicating clearance of the Ad26 vector from the tissues. These data further indicate that the Ad26 vector does not replicate and/or persist in the tissues following IM injection.

Comparing the injection site tissues, in study (b) (4) vector DNA was mostly detected in the injection site muscle, while in study (b) (4) vector DNA was mostly detected in the injection site skin. Nevertheless, no clear differences in the systemic distribution and clearance profile of the Ad26 vector were observed between the two studies. Therefore, despite differences in the transgene insert, it can be concluded that both Ad26 vectors showed a similar pattern of (systemic) biodistribution and clearance when delivered via the IM route at full human doses in the rabbit.

The Ad26 vector backbone used for Ad26.COV2.S is identical to the vector backbone of the Ad26-based vaccines that were tested in the available biodistribution studies (i.e., Ad26 (b) (4) and Ad26 (b) (4). Ad26.COV2.S contains a (b) (4) in the CMV promoter sequence of the transgene expression cassette. This (b) (4) was not present in Ad26 (b) (4) and Ad26 (b) (4) Insertion of the (b) (4) is not considered to impact the biodistribution profile of the Ad26 vector. Adenoviruses are non-enveloped viruses whose cell entry, and therefore tropism, is dictated via interactions of structural capsid proteins (mainly the fiber and penton base) with specific cellular receptors [4]. The adenoviral capsid is a highly complex and organized structure [3] which does not easily allow for the introduction or exchange of other proteins. The transgene expression cassette, which is inserted into the site where the early E1 gene was previously located, is thus not considered to impact on the formation or the composition of the Ad26 vector capsid, and hence tropism of the vector. As a consequence, the biodistribution profile of the Ad26 vector is considered independent of the antigen transgene/expression cassette, which is supported by the comparable distribution profile observed for Ad26 (b) (4) and Ad26 (b) (4) Therefore, the biodistribution profile observed for Ad26 (b) (4) and Ad26 (b) (4) is considered sufficient to inform on the biodistribution profile of the Ad26.COV2.S construct when administered via the same route of administration (IM).

It is noted that for the Ad26 (b) (4) and Ad26 (b) (4) biodistribution studies, the Ad26 vector was formulated in different buffer formulations. The difference in formulation buffer between Ad26 (b) (4) (formulated in (b) (4)) and Ad26 (b) (4) (formulated in (b) (4)) did not impact the overall (systemic) distribution profile of the Ad26 vector. The Ad26.COV2.S vaccine is formulated in the same buffer as Ad26 (b) (4)

Overall, the biodistribution data obtained with Ad26 (b) (4) and Ad26 (b) (4) show a limited distribution profile and indicate clearance over time of the Ad26 vector following IM injection. The biodistribution results obtained with Ad26 (b) (4) and Ad26 (b) (4) are considered sufficient to inform on the biodistribution profile of Ad26.COV2.S, for which the same (replication-incompetent) Ad26 vector backbone is used. This position has been confirmed and agreed in a previous Scientific Advice by EMA (b) (4) and CBER (b) (4). It is further noted that the same

platform biodistribution data were part of the MAA file for the Ebola vaccine component Ad26.ZEBOV (EU/1/20/1444/001).

Table 4: Comparative Table of Biodistribution Data with Ad26-based Vaccines

Vector	Tissue[a]	Range[b] (No. of animals >LLOQ) [No. of animals >LOD and <LLOQ] [c]				
		Day 11	Day 61	Day 90/91	Day 120	Day 180
Ad26 (b) (4) (study (b) (4)	Inj Site Muscle	61-11,981 (7) [1]	<LLOQ [2]	120 (1) [1]	NA	NA
	Inj Site Skin	<LLOQ [1]	-	-	NA	NA
	Iliac Ln	119-8676 (10)	84-1400 (4) [1]	50-1807 (2)	NA	NA
	Spleen	50-116 (4) [5]	-	-	NA	NA
Ad26 (b) (4) (study (b) (4)	Inj Site Muscle	<LLOQ [1]	NA	-	-	-
	Inj Site Skin	39.1-6304.3 (4) [2]	NA	280.1 (1)	-	-
	Iliac Ln	63.6-387.6 (9) [1]	NA	48.1 (1) [3]	37.9-53.4 (2) [1]	37.6 (1) [2]
	Popliteal Ln[d]	29 (1) [1]	NA	-	-	-
	Spleen	37.3-118.6 (6) [4]	NA	-	<LLOQ [1]	-
Ad26 (b) (4) (b) (4) (study (b) (4)	Inj Site Skin	88.6-272.6 (2) [3]	NA	42.7-175.1 (2)	-	-
	Iliac Ln	108.6-347.4 (9)	NA	25.9-35.3 (2) [3]	-	<LLOQ [2]
	Spleen	26.4-75.6 (7) [2]	NA	-	-	-
	Liver	<LLOQ [1]	NA	-	-	-

(a) Only tissues with vector DNA levels above limit of detection (LOD) are listed. All other tissues collected had vector DNA results below the LOD of the assay at all time points
(b) Range in copies/µg genomic DNA
(c) No. of animals out of 10 animals per group
(d) Popliteal Ln was not sampled in Ad26 (b) (4) study [study (b) (4)
\- Levels for all animals were below LOD at this time point
NA Not available
LLOQ Lower limit of quantification (50 copies/µg DNA [study (b) (4) ; 28.6 copies/µg DNA [study (b) (4)])
LOD Limit of detection (10 copies/µg DNA [study (b) (4) ; 7.1 copies/µg DNA [study (b) (4))

10. TABLES AND FIGURES

Supplemental tables and figures are included at appropriate points throughout the summary within the text; additional information is provided within the Pharmacokinetic Tabulated Summaries, located in Mod2.6.5.

11. LIST OF LITERATURE CITATIONS

Literation citations are located in Mod4.3.

1. EMA Guideline on quality, nonclinical and clinical aspects of live recombinant viral vectored vaccines (CHMP/VWP/141697/2009).

2. FDA Guidance for Industry; Considerations for Plasmid DNA Vaccines for Infectious Disease Indications, 2007.

3. Liu, H., et al.. Atomic structure of human adenovirus by cryo-EM reveals interactions among protein networks. Science 2010; 329(5995): 1038-1043.

4. Sharma A, Li X, Bangari Ds, Mittal SK. Adenovirus receptors and their implications in gene delivery. Virus Res. 2009;143(2):184–194.

5. Sheets RL, Stein J, Bailer RT et al. Biodistribution and Toxicological Safety of Adenovirus Type 5 and Type 35 Vectored Vaccines Against Human Immunodeficiency Virus-1 (HIV-1), Ebola, or Marburg Are Similar Despite Differing Adenovirus Serotype Vector, Manufacturer's Construct, or Gene Inserts. J Immunotoxicol. 2008;5(3):315–335.

6. WHO Guidelines on Nonclinical Evaluation of Vaccines (WHO Technical Report Series No. 927, Annex 1, 2005).

Janssen Research & Development, B.V.*

Pharmacokinetics Written Summary

MODULE 2.6.4

VAC31518 JNJ-78436735

Prophylactic COVID-19 Vaccine

* Janssen Vaccines & Prevention B.V. is a Janssen pharmaceutical company of Johnson & Johnson and is hereafter referred to as the sponsor.

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LIST OF ABBREVIATIONS

Ad26	adenovirus type 26
Ad26 (b) (4)	Ad26 vector expressing (b) (4)
Ad26 (b) (4)	Ad26 vector encoding (b) (4)
COVID-19	coronavirus disease 2019
DNA	deoxyribonucleic acid
FDA	Food and Drug Administration
(b) (4)	
IM	intramuscular
LLOQ	lower limit of quantification
NZW	New Zealand white
OECD	Organization for Economic Co-operation and Development
(b) (4)	
qPCR	quantitative polymerase chain reaction
(b) (4)	
SARS	severe acute respiratory syndrome
SARS-CoV	severe acute respiratory syndrome coronavirus
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
(b) (4)	
vp	virus particles

1. BRIEF SUMMARY

Ad26COVS1 (also known as VAC31518 or JNJ-78436735) is a monovalent, recombinant, replication-incompetent adenovirus type 26 (Ad26) vectored vaccine encoding a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Spike protein. It is being developed for prophylactic immunization against coronavirus disease 2019 (COVID-19), which has spread rapidly and globally since its emergence.

This summary provides an overview of the available pharmacokinetic data in support of the Ad26COVS1 development. No specific pharmacokinetic studies have been performed with Ad26COVS1. However, to assess the distribution, persistence, and clearance of the Ad26 vector (platform), biodistribution studies were conducted in rabbits using two other Ad26-based vaccines encoding (b) (4) and (b) (4) antigens. The Ad26 vector did not widely distribute following intramuscular (IM) administration in the animals. Vector DNA was primarily detected at the site of injection, draining lymph nodes and (to a lesser extent) the spleen. Clearance of the Ad26 vector from the tissues was observed. These data indicate that the Ad26 vector does not replicate and/or persist in the tissues following IM injection. In addition, both Ad26-based vaccines tested in the biodistribution studies showed a similar pattern of distribution and clearance when delivered via the IM route in the rabbit. Therefore, the available biodistribution results are considered sufficient to inform on the biodistribution profile of Ad26COVS1, for which the same Ad26 vector backbone is used.

The biodistribution studies were conducted in accordance with the GLP standards (OECD), which conform with Food and Drug Administration (FDA) regulations. The dates of study conduct, and location of the raw data are noted in the individual reports; these reports have been submitted previously as part of other Investigational New Drug Applications. Information on study GLP status and test facility identity are provided in the Pharmacokinetics Overview Table in Mod2.6.5.1.

2. BIODISTRIBUTION

To assess distribution, persistence, and clearance of the Ad26 viral vector (platform), IM biodistribution studies have been conducted in rabbits using an Ad26-based (b) (4) ie, Ad26 (b) (4) (Ad26 vector encoding (b) (4) (b) (4)) and an Ad26-based (b) (4) ie, Ad26 (b) (4) (Ad26 vector encoding (b) (4)); see Sections 2.1 and 2.2, respectively.

2.1. Ad26 (b) (4)

New Zealand white (NZW) rabbits were administered placebo or Ad26 (b) (4) at 1×10^{11} vp (Group 2) via a single IM injection on Day 1. In an additional study arm, Ad26 (b) (4) was dosed in combination with 150 µg (b) (4) as a single IM injection (Group 3). Necropsies were performed on 3 rabbits/sex in the placebo group and 5 rabbits/sex in the Ad26 (b) (4) groups on Days 11, 90, 120, and 180 to collect tissues for biodistribution analysis. The following tissues were collected to assess the presence of Ad26 (b) (4) using a quantitative polymerase chain reaction (qPCR) method: blood, ovaries/testes, liver, thymus,

heart, lung, kidney, spleen, mesenteric, iliac, and popliteal lymph nodes, bone marrow, brain, skin with subcutis at the injection site, and muscle at the injection site (b) (4)

In samples collected from Group 2 and 3 on Day 11, Ad26 (b) (4) vector DNA was primarily detected in the skin at the injection site, iliac lymph nodes, and spleen. The skin at the injection site and the iliac lymph nodes presented the highest number of vector copies. The popliteal lymph node showed a low signal (around or below the lower limit of quantification (LLOQ) of 28.6 copies/µg DNA) in 2 animals from Group 2. One animal from Group 3 showed a signal in the liver at a level below the LLOQ.

In both Group 2 and 3 on Day 90, Ad26 (b) (4) vector DNA was detected only in the skin at the injection site and in the iliac lymph nodes, but at a reduced incidence, as well as a lower maximum quantity of vector DNA than on Day 11.

On Day 120, Ad26 (b) (4) vector DNA was only detected at a low vector copy number (close to, or below the LLOQ) in a single spleen sample and iliac lymph nodes in 3 of 10 treated animals from Group 2.

On Day 180, detection of the vector was limited to the iliac lymph nodes in 3 of 10 treated animals in Group 2 and 2 out of 10 animals in Group 3 at a level close to, or below the LLOQ and was below the limit of detection in all other examined tissues or animals.

Animals from Group 2 and Group 3 showed a similar distribution pattern, indicating that addition of a recombinant (b) (4) protein does not impact on the distribution pattern of the Ad26 vector.

2.2. Ad26 (b) (4)

NZW rabbits were administered placebo or Ad26 (b) (4) at 5 x 10^{10} vp via a single IM injection on Day 1. Necropsies were performed on 3 rabbits/sex in the placebo group and 5 rabbits/sex in the Ad26 (b) (4) group on Days 11, 61, and 91 to collect tissues for biodistribution analysis. The following tissues were analyzed for the presence of Ad26 (b) (4) using a qPCR method: blood, ovaries/testes, liver, thymus, heart, lung, kidney, spleen, mesenteric and iliac lymph nodes, bone marrow, brain, and skin, subcutis, and muscle at the injection site (b) (4)

Analysis on Day 11 indicated that the Ad26 (b) (4) vaccine was primarily localized in the injection site muscle, draining (iliac) lymph nodes and to a lesser extent the spleen. Ad26 (b) (4) vector DNA was below limit of detection in all other organs, except for one animal that showed a low signal in the injection site skin at a level below the lower limit of quantification (50 copies/µg DNA).

In the animals sacrificed on Day 61, the Ad26 vector DNA was no longer detected in the spleen while vector DNA in the injection site muscle and iliac lymph nodes was detected at a reduced incidence and quantity compared to Study Day 11.

On Day 91, detection of the vector was limited to the injection site muscle and iliac lymph nodes in 2 of 10 treated animals and was below the limit of detection in all other examined tissues or animals.

3. DISCUSSION AND CONCLUSIONS

As a general pattern, both Ad26 vectors (i.e. Ad26 (b) (4) and Ad26 (b) (4)) showed a similar and limited biodistribution profile following IM administration, as they were primarily detected at the site of injection, regional (iliac) lymph nodes and (to a lesser extent) the spleen.

Comparing the various necropsy timepoints following IM administration (ie, Days 11, 61, and 91 for Ad26 (b) (4) Days 11, 90, 120 and 180 for Ad26 (b) (4)), a downward trend in the number of positive tissues and/or vector copy number was observed, to levels close to, or below the respective limits of detection, indicating clearance of the Ad26 vector from the tissues. These data further indicate that the Ad26 vector does not replicate and/or persist in the tissues following IM injection.

Comparing the injection site tissues, Ad26 (b) (4) vector DNA was mostly detected in the injection site muscle, while Ad26 (b) (4) vector DNA was mostly detected in the injection site skin. While there is no clear explanation for this difference, it has no apparent impact on the (systemic) distribution and clearance profile of the Ad26 vector. Therefore, despite differences in the expressed transgene insert, it can be concluded that both Ad26 vectors showed a similar pattern of (systemic) biodistribution and clearance when delivered via the IM route at full human doses in the rabbit.

The Ad26 vector backbone used for Ad26COVS1 is identical to the vector backbone of the Ad26-based vaccines that were tested in the available biodistribution studies (ie, Ad26 (b) (4) and Ad26 (b) (4)). Ad26COVS1 contains a (b) (4) in the cytomegalovirus promoter sequence of the transgene expression cassette (for details, see (b) (4)). This (b) (4) was not present in Ad26 (b) (4) and Ad26 (b) (4) Insertion of the (b) (4) is not considered to impact the biodistribution profile of the Ad26 vector. Adenoviruses are non-enveloped viruses whose cell entry, and therefore tropism, is dictated via interactions of structural capsid proteins (mainly the fiber and penton base) with specific cellular receptors [1]. The transgene expression cassette itself, which is inserted into the site where the E1 gene was previously located, is not involved in the formation or the composition of the Ad26 vector capsid. Different antigen transgenes/expression cassettes are therefore not expected to alter cell tropism. As a consequence, the biodistribution profile of the Ad26 vector is considered independent of the antigen transgenes/expression cassette, which is supported by the comparable distribution profile observed for Ad26 (b) (4) and Ad26 (b) (4) Therefore, the biodistribution profile observed for Ad26 (b) (4) and

Ad26 (b) (4) is considered sufficient to inform on the biodistribution profile of the Ad26COVS1 construct when administered via the same route of administration (IM).

4. LIST OF LITERATURE CITATIONS

Literature references are located in Mod4.3.

1. Sharma A, Li X, Bangari Ds, Mittal SK. Adenovirus receptors and their implications in gene delivery. Virus Res. 2009;143(2):184–194.

(b) (4)

FINAL REPORT

Test Facility Study No. (b) (4)

Sponsor Reference No. (b) (4)

Sponsor EDMS No. (b) (4)

A Single Dose Biodistribution Study of Ad26 (b) (4) by Intramuscular Injection in Rabbits with up to 180 Days Observation Period

SPONSOR:
Janssen Infectious Diseases-Diagnostics BVBA
a member of the J&J group of companies
Turnhoutseweg 30
Beerse, B-2340
Belgium

TEST FACILITY:
(b) (4)

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QUALITY ASSURANCE STATEMENT

Study Number: (b) (4)

This Study has been audited by Quality Assurance in accordance with the applicable Good Laboratory Practice regulations. Reports were submitted in accordance with SOPs as follows:

QA INSPECTION DATES

		Dates Findings Submitted to:	
Date(s) of Audit	Phase(s) Audited	Study Director	Study Director Management
08-Jun-2018	Final Study Plan	08-Jun-2018	08-Jun-2018
12-Jun-2018	Study Plan Amendment 01	12-Jun-2018	12-Jun-2018
14-Jun-2018	Dose Preparation	14-Jun-2018	14-Jun-2018
04-Jul-2018	Body Weights	04-Jul-2018	04-Jul-2018
13-Jul-2018	Addition of Study Plan to Provantis	13-Jul-2018	13-Jul-2018
11-Oct-2018	Study Plan Amendment 02	11-Oct-2018	11-Oct-2018
11-Oct-2018	Study Plan Amendment 03	11-Oct-2018	11-Oct-2018
11-Oct-2018	Study Plan Amendment 04	11-Oct-2018	11-Oct-2018
07-Dec-2018	Study Plan Amendment 05	07-Dec-2018	07-Dec-2018
05-Feb-2019 - 07-Feb-2019	Data Review - Technical Operations	07-Feb-2019	07-Feb-2019
05-Feb-2019 - 06-Feb-2019	Report Preparation	07-Feb-2019	07-Feb-2019
06-Feb-2019	Data Review - Veterinary Services	07-Feb-2019	07-Feb-2019
06-Feb-2019	Data Review - Animal Care	07-Feb-2019	07-Feb-2019
06-Feb-2019	Data Review - Formulations	07-Feb-2019	07-Feb-2019
06-Feb-2019 - 07-Feb-2019	Report - Materials and Methods	07-Feb-2019	07-Feb-2019
27-Feb-2019 - 11-Mar-2019	Data Review - Bioanalysis & Immunology	11-Mar-2019	11-Mar-2019
27-Feb-2019 - 11-Mar-2019	Report Preparation	11-Mar-2019	11-Mar-2019
11-Mar-2019	Data Review - Shipping/Receiving	11-Mar-2019	11-Mar-2019
18-Mar-2019 - 19-Mar-2019	Phase Report - Deviation Log	19-Mar-2019	19-Mar-2019
19-Mar-2019	Data Review - Necropsy	20-Mar-2019	20-Mar-2019
19-Mar-2019	Phase Report - Pathology	20-Mar-2019	20-Mar-2019
19-Mar-2019	Report Preparation	20-Mar-2019	20-Mar-2019
19-Mar-2019	Study Plan Amendment 06	19-Mar-2019	19-Mar-2019
22-Mar-2019	Final Phase Report - Immunology	22-Mar-2019	22-Mar-2019
08-Apr-2019	Report Preparation	09-Apr-2019	09-Apr-2019
08-Apr-2019 - 09-Apr-2019	Final Phase Report - Immunology	09-Apr-2019	09-Apr-2019
15-Apr-2019	Study Plan Amendment 07	15-Apr-2019	15-Apr-2019
22-Apr-2019	Final Phase Report - Pathology	22-Apr-2019	22-Apr-2019

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

QUALITY ASSURANCE STATEMENT - Study Number: (b) (4)

QA INSPECTION DATES

Date(s) of Audit	Phase(s) Audited	Dates Findings Submitted to: Study Director	Study Director Management
23-Apr-2019 - 25-Apr-2019	Final Report	25-Apr-2019	25-Apr-2019
25-Apr-2019	Final CTD Table	25-Apr-2019	25-Apr-2019
01-May-2019	Study Plan Amendment 08	01-May-2019	01-May-2019

In addition to the above-mentioned audits, process-based and/or routine facility inspections were also conducted during the course of this study. Inspection findings, if any, specific to this study were reported by Quality Assurance to the Study Director and Management and listed as a Phase Audit on this Quality Assurance Statement.

The Final Report has been reviewed to assure that it accurately describes the materials and methods, and that the reported results accurately reflect the raw data.

DocuSigned by:

(b) (4), (b) (6)

Quality Assurance Auditor

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

COMPLIANCE STATEMENT

The study was performed in accordance with the OECD Principles of Good Laboratory Practice and as accepted by Regulatory Authorities throughout the European Union, United States of America (FDA), Japan (MHLW), and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

Exceptions from the above regulations are listed below.

- Characterization of the test items were performed by the Sponsor or Sponsor subcontractor at a laboratory that follows FDA Good Manufacturing Practice (GMP) regulations.
- Stability testing of the supplied test items was performed by the Sponsor or Sponsor subcontractor at a laboratory that follows FDA GMP regulations.
- Test Item (b) (4) Analysis for confirmation of positive identity was performed at the test site following FDA GMP regulations, however the study plan indicated the analysis would be conducted in accordance with the U.S. Department of Health and Human Services, Food and Drug Administration. As the analysis result confirmed the positive identity for (b) (4) this exception to Good Laboratory Practice (GLP) was not considered to have any impact on the study overall integrity or the study outcome.

This study was conducted in accordance with the procedures described herein. All deviations authorized/acknowledged by the Study Director are documented in the Study Records. The report represents an accurate and complete record of the results obtained.

There were no deviations from the above regulations that affected the overall integrity of the study or the interpretation of the study results and conclusions.

DocuSigned by:
(b) (4), (b) (6)

Study Director

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

1. RESPONSIBLE PERSONNEL

1.1. Test Facility

(b) (4), (b) (6)

1.2. Individual Scientist (IS) at Test Facility

(b) (4), (b) (6)

1.3. PI at Sponsor or Sponsor-designated Test Site

(b) (4), (b) (6)

2. SUMMARY

The objective of this study was to evalutate biodistribution and persistence of Ad26 (b) (4), a replication incompetent non-pathogenic Adenovirus Serotype 26 vector encoding the (b) (4) (b) (4) when given by single intramuscular injection (with or without co-administration with the (b) (4)) to NZW rabbits followed by an observation period of up to 180 days.

The study design was as follows:

Text Table 1
Experimental Design

Group No.	Test Material	Dose Level	Dose Volume (mL)	No. of Study Animals	
				Males	Females
1	Reference Item	0	1	12[a]	12[a]
2	Ad26 (b) (4)	1 x 10^{11} vp	0.5	20[b]	20[b]
3	Ad26 (b) (4) (b) (4)	1 x 10^{11} vp + 150µg	1 (of mixture)	20[b]	20[b]

[a] 3 animals/sex each euthanized on Days 11, 90, 120 and 180
[b] 5 animals/sex each euthanized on Days 11, 90, 120 and 180

The following parameters and end points were evaluated in this study: clinical signs, body weights, body weight changes, gross necropsy findings and tissue collection for qPCR analysis.

There were no Ad26 (b) (4) related changes noted in clinical observations, body weights or body weigth gains.

DNA isolation and qPCR analysis for the determination of Ad26 (b) (4) vector DNA was performed on a total of 920 rabbit tissue and fluid samples following a single intramuscular injection of Ad26 (b) (4) in the presence or absence of (b) (4) For all control (Group 1) samples collected at Day 11 or Day 90, Ad26 (b) (4) vector DNA results were below the LLOQ of the assay, as expected. Positive Ad26 (b) (4) vector DNA values were detected in the skin at the intramuscular injection site, the spleen, and in the iliac and popliteal lymph nodes at Day 11, with the highest vector copy number present in the skin. On Day 90, Ad26 (b) (4) vector DNA was no longer present in the popliteal lymph node and spleen, while the skin at the injection site and iliac lymph node were still positive, but showing a reduced incidence, as well as a lower maximum quantity of Ad26 (b) (4) vector DNA than those detected on Day 11. By Day 120, the vector was no longer present in the skin at the injection site, and only two animals from Group 2 were positive in the iliac lymph node. By Day 180, Ad26 (b) (4) vector DNA was no longer detected in any tissue, with the exception of 1 iliac lymph node, at a low vector copy number close to the LLOQ of the assay. Overall, this demonstrates a limited biodistribution profile as well as a clearance over time of the Ad26 (b) (4) vector following intramuscular injection. The presence of (b) (4) in the dosing mixture did not significantly impact on the biodistribution and the persistence of the Ad26 vector.

Following a single intramuscular injection of Ad26 (b) (4) and an observation period of up to 180 days, there were no treatment-related gross necropsy findings.

In conclusion, a single intramuscular injection into the lateral compartment of the right thigh in the rabbit at dose levels of 1 x 10^{11} vp Ad26 (b) (4) or 1 x 10^{11} vp Ad26 (b) (4) + 150µg (b) (4) (as a mixture) was clinically well tolerated. qPCR results for the determination of Ad26 (b) (4) Vector DNA in the control group were below the LLOQ of the assay, as expected. Positive Ad26 (b) (4) vector DNA values were detected in vaccine dosed groups in the skin at the intramuscular injection site, the spleen, and in the iliac and popliteal lymph nodes at Day 11, with the highest vector copy number present in the skin. By Day 180, Ad26 (b) (4) vector DNA was no longer detected in any tissue, with the exception of 1 iliac lymph node, at a low vector copy number close to the LLOQ of the assay. Overall, this demonstrates a limited biodistribution profile as well as a clearance over time of the Ad26 (b) (4) vector following intramuscular injection.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

3. TABULATED SUMMARY

3.1. Pharmacokinetics: Organ Distribution

Report Title: A Single Dose Biodistribution Study of Ad26 (b) (4) by Intramuscular Injection in Rabbits with up to 180 Days Observation Period

Species: Oryctolagus cuniculus / New Zealand White Rabbit (Hra[NZW]SPF)
Gender (M/F)/Number of animals: M52/F52
Feeding condition: 60 g on the day of arrival and 120 g/day thereafter
Vehicle/Formulation: 0.9% Sodium Chloride for Injections, USP
Method of Administration: Intramuscular injection
Dose (Viral Particles/Dose): 1 x 10^{11} vp Ad26 (b) (4) with or without 150µg (b) (4)
Sampling timepoint: Days 11, 90, 120, and 180

	Group 2 **Ad26** (b) (4) (copies/µg DNA) Range of Positive Samples	**N**	**Group 3** **Ad26** (b) (4) (copies/µg DNA) Range of Positive Samples	**N**
Tissues/organs				
Iliac Lymph Nodes				
Day 11	63.6 to 387.6	9	108.6 to 347.4	9
Day 90	48.1	1	25.9 to 35.3	2
Day 120	37.9 to 53.4	2	a	0
Day 180	37.6	1	a	0
Popliteal Lymph Nodes				
Day 11	29.0	1	a	0
Day 90	a	0	a	0
Day 120	a	0	a	0
Day 180	b	b	b	b
Skin				
Day 11	39.1 to 6304.3	4	88.6 to 272.6	2
Day 90	280.1	1	42.7 to 175.1	2
Day 120	a	0	a	0

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	Group 2 Ad26 (b) (4) (copies/µg DNA) Range of Positive Samples	N	Group 3 Ad26 (b) (4) (copies/µg DNA) Range of Positive Samples	N
Skin (Continued)				
Day 180	b	b	b	b
Spleen				
Day 11	37.3 to 118.6	6	26.4 to 75.6	7
Day 90	a	0	a	0
Day 120	a	0	a	0
Day 180	a	0	a	0

Additional information:

N = No. of animal with signal >LLOQ (theoretical value 20 copies per reaction or 28.6 copies/µg DNA) on a total of 10 animals (5M + 5F) analyzed per timepoint

a = Results <LLOQ

b = Not analyzed

4. INTRODUCTION

The objective of this study was to evalutate the biodistribution properties and persistence of a single dose of Ad26 (b) (4) a replication incompetent non-pathogenic Adenovirus Serotype 26 vector expressing the (b) (4) when given by intramuscular injection (with or without co-administration with the (b) (4)) to rabbits, followed by an observation period of up to 180 days.

The design of this study is based on WHO Guideline on nonclinical evaluation of vaccines, 2005; WHO Guideline on the non-clinical evaluation of vaccine adjuvants and adjuvanted vaccines Oct 2013; FDA Guidance Preclinical Assessment of Investigational Cellular and Gene Therapy Products; FDA 2006: Gene Therapy Clinical Trials – Observing Subjects for Delayed Adverse Events; and EMA guideline 2010: quality, non-clinical and clinical aspects of live recombinant viral vectored vaccines.

The Study Director signed the study plan on 29 May 2018, and dosing was initiated on 14 Jun 2018. The in-life phase of the study was completed on 11 Dec 2018. The experimental start date was 30 May 2018, and the experimental completion date was the signature date of the pathology report. The Deviations are presented in Section 9.

5. MATERIALS AND METHODS

5.1. Test and Reference Items

5.1.1. Test Items

Identification:	Ad26 (b) (4)
Batch (Lot) No.:	(b) (4)
Receipt Date:	07 Jun 2018
Expiration Date:	15 Nov 2018
Physical Description:	(b) (4)
Concentration:	2 x 10^{11} vp/mL
Storage Conditions:	Kept in a freezer set to maintain -80°C
Supplier:	Janssen Infectious Diseases-Diagnostics BVBA

Identification:	(b) (4)
Batch (Lot) No.:	(b) (4)
Receipt Date:	13 Jun 2018
Expiration Date:	17 Sep 2018
Concentration:	0.3 mg/mL
Physical Description:	(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Storage Conditions: Kept in a refrigerator set to maintain 5°C, protected from light

Supplier: Janssen Infectious Diseases-Diagnostics BVBA

5.1.2. Reference Item

Identification: 0.9% Sodium Chloride for Injections, USP

Batch (Lot) No.: (b) (4)

Expiration Date: Dec 2018

Physical Description: (b) (4)

Storage Conditions: Kept in a controlled temperature set to maintain 21°C

Supplier: (b) (4)

5.2. Test Items Characterization

The Sponsor provided to the Test Facility documentation of the identity, strength, purity, composition, and stability for the test items. A Certificate of Analysis was provided to the Test Facility and is presented in Appendix 1.

5.3. Test and Reference Items Inventory and Disposition

Records of the receipt, distribution, and storage of test and reference items were maintained. All unused test items were discarded before issurance of the Final Report.

5.4. Dose Formulation and Analysis

5.4.1. Preparation of Reference Item

The Reference Item, 0.9% Sodium Chloride for Injection, USP, was dispensed for administration to Group 1 control animals.

Any residual volumes were discarded.

5.4.2. Preparation of Test Item

5.4.2.1. (b) (4)

The protein vials (b) (4) were removed from the fridge on the day of dosing and allowed to warm to room temperature. The protein was mixed with Ad26 (b) (4) according to the preparation instruction and administered within 4 hours.

Two vials were returned to (b) (4), (b) (6) (b) (4) for confirmation for positive identity for (b) (4)

5.4.2.2. Ad26 (b) (4)

The vaccine (Ad26 (b) (4)) vial was removed from the freezer on the day of dosing and allowed to warm to room temperature. Thaw times, as determined by visual inspection, were documented. The vaccine was administered within 4 hours of thawing (group 2) or mixed and administered within 4 hours of thawing (Group 3).

Any thawed but unused vial was returned to a freezer set to maintain -80°C and kept until the end of the study.

5.4.2.3. Mixed Ad26 (b) (4)

The (b) (4) vials and the Ad26 (b) (4) vaccine vials were thawed Ad26 (b) (4) as previously described. A volume of 0.75 mL protein was added to a thawed vaccine vial. One (1) mL of the mixture was administered.

The mixture was administered within 4 hours of preparation completion.

Any residual volumes were discarded.

5.5. Sample Collection and Analysis

The test and reference items were used as received from the Sponsor; therefore, samples for dose formulation analysis were not collected by the Test Facility.

5.6. Stability Analysis

The Sponsor has provided data that demonstrate that the test items are stable in the vehicle when prepared and stored under the same conditions at concentrations bracketing those used in the present study. Stability data provided by the Sponsor have been retained in the study records.

5.7. Test System

5.7.1. Receipt

On 30 May 2018, fifty-three (53) New Zealand White Rabbit males and females were received from (b) (4) The animals were 5-6 months old with males weighing between 2.4 to 3.2 kg and females between 2.6 kg and 3.0 kg at initiation of dosing.

5.7.2. Justification for Test System and Number of Animals

The rabbit was chosen as the animal model for this study as it is an accepted nonrodent species for preclinical testing of vaccines by regulatory agencies.

The total number of animals to be used in this study was considered to be the minimum required to properly characterize the effects of the Test Item and has been designed such that it does not require an unnecessary number of animals to accomplish its objectives.

At this time, studies in laboratory animals provide the best available basis for extrapolation to humans and are required to support regulatory submissions. Acceptable models which do not use live animals currently do not exist.

5.7.3. Animal Identification

Each animal was identified using a subcutaneously implanted electronic identification chip.

5.7.4. Environmental Acclimation

A minimum acclimation period of two weeks was allowed between animal receipt and the start of treatment in order to accustom the animals to the laboratory environment.

5.7.5. Selection, Assignment, Replacement, and Disposition of Animals

Animals were assigned to groups by a stratified randomization scheme designed to achieve similar group mean body weights. Males and females were randomized separately. Animals at extremes of body weight range were not assigned to groups.

The disposition of all animals was documented in the study records.

5.7.6. Husbandry

5.7.6.1. Housing

On arrival, animals were individually housed in stainless steel perforated floor cages equipped with an automatic watering valve unless deemed inappropriate by the Study Director and/or Clinical Veterinarian. Each cage was clearly labeled with a color coded cage card indicating study, group, animal numbers and sex. Cages were arranged on the racks in group order. Where possible, control group animals were housed on a separate rack from the Test Item treated animals.These housing conditions were maintained unless deemed inappropriate by the Study Director and/or Clinical Veterinarian. The rooms in which the animals were kept were documented in the study records.

5.7.6.2. Environmental Conditions

Target temperatures of 17°C to 23°C with a relative target humidity of 30% to 70% were maintained. A 12-hour light/12-hour dark cycle was maintained.

5.7.6.3. Food

All animals were given a standard certified pelleted commercial laboratory diet (b) (4) (b) (4) Animals were fed 60g on the day of arrival and 120 g/day thereafter.

The feed was analyzed by the supplier for nutritional components and environmental contaminants. Results of the analysis are provided by the supplier and are on file at the Test Facility.

It was considered that there were no known contaminants in the feed that would have interfered with the objectives of the study.

5.7.6.4. Water

Municipal tap water after treatment by reverse osmosis and ultraviolet irradiation was freely available to each animal via an automatic watering system (except during designated procedures).

Periodic analysis of the water is performed, and results of these analyses are on file at the Test Facility.

It was considered that there were no known contaminants in the water that could have interfered with the outcome of the study.

5.7.6.5. Animal Enrichment

For psychological/environmental enrichment, animals were provided with toys, as well as food enrichment (fresh fruit/vegetables) and autoclaved hay, except during designated activities.

5.7.6.6. Brushing and Nail Trimming

Frequency: Brushing: at least weekly

Nail trimming: at least monthly

Procedure: Brushing: Rabbits were brushed gently to remove/prevent matting, clumping or tangling and to avoid ingestion of fur.

Nail trimming: the tips of the claws were cut with appropriate clippers.

5.7.6.7. Veterinary Care

Veterinary care was available throughout the course of the study, and animals were examined by the veterinary staff as warranted by clinical signs or other changes. All veterinary examinations and recommended therapeutic treatments were documented in the study records.

5.8. Experimental Design

Text Table 2
Experimental Design

Group No.	Test Material	Dose Level	Dose Volume (mL)	No. of Study Animals	
				Males	Females
1	Reference Item	0	1	12[a]	12[a]
2	Ad26 (b) (4)	1 x 10^{11} vp	0.5	20[b]	20[b]
3	Ad26 (b) (4) (b) (4)	1 x 10^{11} vp + 150µg	1 (of mixture)	20[b]	20[b]

[a] 3 animals/sex each euthanized on Days 11, 90, 120 and 180
[b] 5 animals/sex each euthanized on Days 11, 90, 120 and 180

5.8.1. Administration of Test and Reference Items

The test and reference items were administered to the appropriate animals via a single intramuscular injection (perpendicular to the thigh surface) into the lateral compartment of the right thigh (targeting the bicep femoris). The injection site was clipped free from fur the day prior to injection and marked with an indelible ink marker throughout the study. The volume for each dose was administered using a syringe and 25 gauge, 5/8 inch needle.

5.8.2. Justification of Route and Dose Levels

The intramuscular route of exposure was selected because this is the intended route of human exposure.

The dose selected for the Ad26 (b) (4) vaccine as well as the Ad26 (b) (4) (b) (4) mixture represented the maximum anticipated dose in the planned clinical studies, that is, full human doses were administered to the animals.

5.9. In-life Procedures, Observations, and Measurements

The in-life procedures, observations, and measurements listed below were performed for all study animals.

5.9.1. Mortality/Moribundity Checks

Throughout the study, animals were observed for general health/mortality and moribundity twice daily, once in the morning and once in the afternoon (Refer to Secion 9, for minor deviaitons). Animals were not removed from cage during observation, unless necessary for identification or confirmation of possible findings.

5.9.2. Clinical Observations

5.9.2.1. Cage Side Observations

Cage side observations were performed once daily, beginning on Day 3 to 9 and weekly thereafter. On the dosing day, these observations were performed 1 to 2 hours postdose and again at 24 hours postdose. Animals were not removed from cage during observation, unless necessary for identification or confirmation of possible findings.

5.9.2.2. Detailed Clinical Observations

The animals were removed from the cage, and a detailed clinical observation was performed weekly, beginning Day -8.

5.9.3. Body Weights

Animals were weighed weekly during the prestudy period, once prior to dosing, daily for 3 consecutive days postdose; and weekly commencing on Day 7. A weight was recorded on the day of necropsy.

5.10. Terminal Procedures

Terminal procedures are summarized in the following table:

Text Table 3
Terminal Procedures

Group No.	No. of Animals		Scheduled Euthanasia Day	Necropsy Procedures	
	M	F		Necropsy	Tissue Collection
1	3	3	11	X	*
2	5	5			
3	5	5			
1	3	3	90	X	*
2	5	5			
3	5	5			
1	3	3	120	X	*
2	5	5			
3	5	5			
1	3	3	180	X	*
2	5	5			
3	5	5			

X = Procedure to be conducted, - = Not applicable
*= Refer to Section 5.11.

5.10.1. Unscheduled Deaths

No animals died during the course of the study.

5.10.2. Scheduled Euthanasia

The control animals (Group 1) were euthanized first followed by treated animals (Group 2 and 3). All animals surviving until scheduled euthanasia had samples for qPCR analysis collected (as appropriate), and animals were euthanized by intravenous injection of sodium pentobarbital, followed by exsanguination by incision of the axillary or femoral arteries.

5.10.3. Necropsy

All animals were subjected to a complete necropsy examination, which included evaluation of the carcass and musculoskeletal system; all external surfaces and orifices; cranial cavity and external surfaces of the brain; and thoracic, abdominal, and pelvic cavities with their associated organs and tissues.

Necropsy procedures were performed by qualified personnel with appropriate training and experience in animal anatomy and gross pathology. A veterinary pathologist, or other suitably qualified person, was available.

5.10.4. Tissue Collection and Preservation

Representative samples of the tissues identified for qPCR analysis were collected using PCR clean removal procedures as per SOP. Remaining tissues were discarded without further examination.

5.11. Biodistribution Analysis by Quantitative Polymerase Chain Reaction (qPCR)

Quantitation of the Ad26 vector DNA was performed. The tissues/fluids listed below were assessed by qPCR. The analysis was conducted using a validated real-time qPCR assay (b) (4) (b) (4) The analytical procedures to be followed during the DNA isolation and qPCR analysis were detailed in (b) (4) (b) (4) (for the DNA isolation procedure), (b) (4) (for the PCR procedure) and (b) (4) (for tissue homogenization procedure). DNA quantity assessment procedure was documented in (b) (4) (b) (4) The results were included as an appendix to the report.

Tissues/fluids collection were performed according to (b) (4) clean removal and collected into PCR clean vials. A target amount of 0.5 - 1 g of each tissue was collected, when possible in duplicate (except skin with subcutis and biceps femorismuscle which were collected and weighed and bone marrow that was not weighed). Blood and tissue samples were snap frozen in liquid nitrogen, placed on dry ice, and then stored in a freezer set to maintain -80°C. Tissues were collected in the order below.

Samples were transferred to the appropriate laboratory at the Test Facility until analysis where DNA was isolated from:

- Blood
  - 2 samples each with a target volume of 1.0 mL, collected from the auricular artery into a K_2EDTA tube were transferred into PCR clean vials
- Ovaries/testes*
- Liver*
- Spleen (median region)*
- Kidney (hilar region)*
- Iliac lymph node*
- Heart (apex)*
- Lung (right caudal lobe)*
- Brain (4 quadrants: left and right near visual cortex, left and right forebrain)**
- Skin with subcutis over the injection*
- Bicep femoris muscle and full depth of underlying muscles to a maximum depth of 3 cm (at marked injection site)*
- Popliteal lymph node*
- Bone marrow (femur, flush with 1 mL of sterile saline, bilateral)*
- Thymus*
- Lymph node, mesenteric*

* The right side or sample aliquot 1 was processed. The remaining sample (left side or sample aliquot 2) was kept as a back-up.

** The right side of the forebrain was processed. The remaining 3 quadrants was kept as a back-up.

For all tissues except the muscle, up to 600 mg of tissue (or as appropriate) were first homogenized using the Geno/Grinder 2010 instrument. For the muscle, up to 8 g of tissue (or appropriate) separated in 2 aliquots (approximately 4 g each) were homogenized and pooled. Then the appropriate volume of tissue homogenate was treated with proteinase K enzyme. Up to 300 µL of whole blood and up to 400 µL of bone marrow were processed.

All tissues collected from euthanasia on Days 11, and 90 from all groups were analyzed for the presence of the Ad26 (b) (4) vector. Tissues from Day 120 were analyzed for iliac lymph node, injection site skin, spleen, popliteal lymph node and injection site muscle only and tissues from Day 180 were only analyzed for spleen and iliac lymph node. From Day 120 onwards, no Group 1 samples were analyzed given that they were negative for 2 consecutive time points (i.e. Day 11 and Day 90) for all tissues/fluids.

Remaining qPCR tissues and fluids will be retained for up to one year after issurance of the Draft Report.

6. CONSTRUCTED VARIABLES

Body Weight Gains: Calculated between at least each interval as well as between the beginning and end of each phase

All results presented in the tables of the report are calculated using non-rounded values as per the raw data rounding procedure and may not be exactly reproduced from the individual data presented.

For a description of the methods used in this study, refer to the last amended study plan, and deviations in Section 9.

7. STATISTICAL ANALYSIS

All statistical tests were conducted at the 5% significance level. All pairwise comparisons were conducted using two sided tests and were reported at the 0.1%, 1%, and 5% levels.

Numerical data collected on scheduled occasions for the listed variables were analyzed as indicated according to sex and occasion. Descriptive statistics number, mean and standard deviation were reported whenever possible. Values were also be expressed as a percentage of predose or control values when deemed appropriate. Inferential statistics was performed according to the matrix below when possible, but excluded semi-quantitative data, and any group with less than 3 observations.

Text Table 4
Statistical Matrix

Variables for Inferential Analysis	Statistical Method Parametric/ Non-Parametric
Body Weight	X
Body Weight Gains	X

The following pairwise comparisons were made:

Group 2 vs. Group 1

Group 3 vs. Group 1

7.1. Parametric/Non-Parametric

Levene's test was used to assess the homogeneity of group variances.

Datasets with at least 3 groups were compared using an overall one-way ANOVA *F*-test when Levene's test was not significant or the Kruskal-Wallis test when it was. When the overall *F*-test or Kruskal-Wallis test was found to be significant, then the above pairwise comparisons were conducted using Dunnett's or Dunn's test, respectively.

7.2. Statistical Method for qPCR Data Analysis

In order to assess the homogeneity of Days variances, the Group 2 qPCR numerical data corresponding to the five animals at each of Days 11, 90 and 120 (and day 180 if analysed) were submitted to Levene's tests. The Days were compared using an overall one-way ANOVA *F*-test when Levene's testwas not significant or the Kruskal-Wallis test when it was. When the overall *F*-test or Kruskal-Wallis test was found to be significant, then the three possible Days pairwise comparisons were conducted using Tukey test or Wilcoxon Rank Sum test respectively. Whenever the Wilcoxon Rank Sum test was used, adjustments for multiplicity of tests were made based on the square root of the number of pairwise comparisons.

A Summary Statistical Report was generated by SAS®, which was kept in the study records. The results of this analysis are indicated on summary data tables included in the study report.

7.3. Computerized Systems

Critical computerized systems used in the study are listed below or presented in the appropriate Phase Report. All computerized systems used in the conduct of this study have been validated; when a particular system has not satisfied all requirements, appropriate administrative and procedural controls were implemented to assure the quality and integrity of data.

Text Table 5
Critical Computerized Systems

System Name	Version No.	Description of Data Collected and/or Analyzed
Provantis	10	In-life (clinical observations, body weights); postmortem (necropsy)
Dispense	8 and/or 10	Test Material receipt, accountability and/or formulation activities.
In-house reporting software Nevis (using SAS)	Nevis 2 (SAS 9.2)	In-life (body weights)
Applied Biosystems QuantStudio™ 7 Flex Real-Time PCR System and QuantStudio™ 7 Flex software version	1.2	Data capture and analysis
Softmax Pro GXP	5.4.6	Data analysis
Deviation Information Library	2.1	Reporting and tracking of deviations

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

8. RETENTION OF RECORDS, SAMPLES, AND SPECIMENS

All study-specific raw data, documentation, study plan, samples, and specimens from this study were archived at the Test Facility by no later than the date of final report issue unless otherwise specified in the study plan. At least one year after issue of the draft report, the Sponsor will be contacted.

Electronic data generated by the Test Facility were archived as noted above, except the data collected using Provantis and reporting files stored on SDMS (including final reports), which were archived at the (b) (4)

All records, retained samples and specimens, and reports generated from phases or segments performed by Sponsor-designated subcontractors were returned to the Test Facility for archiving Archival location and duration are detailed in the applicable PI report(s) or details regarding the retention of the materials were provided to the Study Director for inclusion in the Final Report.

9. STUDY PLAN DEVIATIONS AND OTHER EVENTS

All deviations that occurred during the study have been authorized/acknowledged by the Study Director, assessed for impact, and documented in the study records. All study plan deviations that could have impacted the quality or integrity of the study are listed below.

None of the deviations were considered to have impacted the overall integrity of the study or the interpretation of the study results and conclusions.

In-life Observations, Measurements, and Evaluations

- A mortality/morbundity check was not performed on a few occasions. The animals were sufficiently monitored throughout the study during clinical observations therefore this deviations was considered not to adversely impact on the study outcome.
- The different DNA concentrations were used during the qPCR analysis of the popliteal lymph node for Animal No. 1003 Day 11 sample and Animal No. 3010 Day 90 sample due to an oversight. For Animal No. 1003 Day 11 sample, the final concentration analyzed was higher than the target concentration of 0.14 µg/µL. However, given that no PCR inhibition was observed during the analysis the use of a higher DNA concentration did not impact the analysis of this sample. For Animal No. 3010 Day 90 sample, a final DNA concentration of 0.08 µg/µL (1.6 µg of total DNA) instead of 0.14 µg/µl (2.8 µg of total DNA) was analyzed. However, the sample was successfully repeated using the appropriate concentration of DNA obtained in a new DNA isolation. Therefore, these deviations were considered to have no impact on the data and interpretation.

10. RESULTS

10.1. Mortality

(Appendix 2)

There were no unscheduled deaths over the course of the study.

10.2. Clinical Observations

(Table 1 and Appendix 3)

There were no Ad26 (b) (4) -related effects on clinical observations.

10.3. Body Weights and Body Weight Gains

(Figure 1, Figure 2,, Table 2, Table 3, Appendix 4, and Appendix 5)

There were no Ad26 (b) (4) -related effects on body weights or body weight gains.

10.4. qPCR Evaluation

(Appendix 6)

Positive samples were considered to be those samples which had detectable Ad26 (b) (4) vector DNA levels above the LLOQ. The results for positive samples are summarized in Text Table 6. All samples were analyzed within the validated parameters.

DNA isolation and qPCR analysis was performed on a total of 920 tissue and fluid samples collected at Day 11, Day 90, Day 120, and Day 180.

Samples collected from control animals (Group 1) at Day 11 and Day 90 had Ad26 (b) (4) vector DNA results below the LOD of the assay, as expected, for all tissues and fluids. For Group 2 and Group 3 animals, all matrices analyzed demonstrated Ad26 (b) (4) vector DNA results below the LLOQ (i.e. negative for Ad26 (b) (4) vector DNA) of the assay except for the skin with subcutis over the injection site, the spleen, and the iliac and popliteal lymph nodes. Low Ad26 (b) (4) Vector DNA (> LOD but ≤ LLOQ) were detected in some samples, including iliac and popliteal lymph nodes, liver, muscle, skin and spleen samples. The number of tissues with Ad26 (b) (4) Vector DNA copies between the LOD and the LLOQ decreased over time.

As per Text Table 6, only the skin at the injection site, the spleen (median region) as well as the iliac and popliteal lymph nodes were found to be positive for Ad26 (b) (4) vector DNA at Day 11. Although the skin at the injection site presented the highest number of vector copies (as observed for Group 2), the iliac lymph node was the tissue with the highest incidence of positive samples in both Group 2 and 3. The popliteal lymph node was only positive in one animal from Group 2. On Day 90, Ad26 (b) (4) vector DNA was no longer present in the popliteal lymph node and spleen, while the skin at the injection site and iliac lymph node were still positive, but showing a reduced incidence, as well as a lower maximum quantity of Ad26 (b) (4) vector DNA than those detected on Day 11. By Day 120, the vector was no longer present in the skin at the injection site, and only two animals from Group 2 were positive in the iliac lymph node. By

Day 180, one iliac lymph node sample was still positive but the number of copies detected was close to the LLOQ.

Given that no signal was detected at the injection site (muscle) on Day 11 and Day 90 following the initial analysis, a second analysis (leftover tissue analysis if available) was performed in order to ensure that Ad26 (b) (4) vector DNA was absent from the injection site muscle. Only the original results were reported in the absence of signal in the leftover tissue.

Throughout the study, the presence of (b) (4) in the dosing mixture did not affect the biodistribution and the persistence of the Ad26 vector, given that the overall distribution pattern (i.e. tissues showing a positive signal), the copy numbers detected, as well as the incidence of positive samples in Group 2 and 3 for a given timepoint were generally similar.

Collectively this data set demonstrates a limited distribution profile as well as clearance over time of Ad26 (b) (4) vector DNA following intramuscular injection.

Text Table 6
Range of Positive (>LLOQ, Theoretical Value 20 Copies Per Reaction or 28.6 copies/µg DNA) Samples for the Quantitative Determination of Ad (b) (4) vector DNA in New Zealand White Rabbits Tissue and Fluid Samples (Copies/µg DNA)

	D11				D90				D120				D180			
Tissues	**Gr 2**	**N**	**Gr 3**	**N**	**Gr 2**	**N**	**Gr 3**	**N**	**Gr 2**	**N**	**Gr 3**	**N**	**Gr 2**	**N**	**Gr 3**	**N**
Iliac LN	63.6 to 387.6	9	108.6 to 347.4	9	48.1	1	25.9 to 35.3	2	37.9 to 53.4	2	a	0	37.6	1	a	0
Popliteal LN	29.0	1	a	0	a	0	a	0	a	0	a	0	b	b	b	b
Skin	39.1 to 6304.3	4	88.6 to 272.6	2	280.1	1	42.7 to 175.1	2	a	0	a	0	b	b	b	b
Spleen	37.3 to 118.6	6	26.4 to 75.6	7	a	0	a	0	a	0	a	0	a	0	a	0

Gr = Group; N = Number of animals with signal >LLOQ on a total of 10 animals (5M + 5F) analyzed per timepoint; LN = Lymph Node
a = Results <LLOQ
b = Not analyzed

10.5. Gross Pathology – Terminal Euthanasia (Days 11, 90, 120 and 180)

(Appendix 7)

There were no Ad26 (b) (4) -related gross findings. Even though they were not always present in a concurrent control animal, the gross findings observed in treated animals were isolated (i.e., not more than 1 out of 5 animals per sex per group) and without any trend (i.e., no dose- or timepoint-relationship). Therefore, all gross findings observed were considered incidental, of the nature commonly observed in this strain and age of rabbits, and unrelated to administration of Ad26 (b) (4)

11. DISCUSSION

The biodistribution and persistance of a single dose of Ad26 (b) (4) a replication incompetent non-pathogenic Adenovirus Serotype 26 vector expressing the (b) (4) (b) (4) was evaluated when given by intramuscular injection at a dose level of 1 x 10 vp alone or combined with (b) (4) at 150µg, respectively in the lateral compartment of the right thigh with a maximum of 180-Day observation period. These doses were well tolerated as there were no clinical signs, body weight changes, or gross necropsy findings that were considered to be treament-related.

Positive (above the LLOQ) Ad26 (b) (4) vector DNA values were detected in the skin at the intramuscular injection site, the spleen, and in the iliac and popliteal lymph nodes at Day 11, with the highest vector copy number present in the skin. By Day 180, Ad26 (b) (4) vector DNA was no longer detected in any tissue, with the exception of 1 iliac lymph node, and at low vector copy numbers close to the LLOQ of the assay. Overall, this demonstrates a limited biodistribution profile as well as a clearance over time of Ad26 (b) (4) vector DNA following intramuscular injection. The presence of (b) (4) in the dosing mixture did not significantly impact on the biodistribution and the persistence of the Ad26 vector.

No Ad26 (b) (4) vector DNA could be detected in the injection site (muscle). Following review of the technician training records, dosing records and tissue sampling documentation, all procedures were appropriately followed and there was no indication that the dose could have been inadvertently given subcutaneous instead of intramuscular. This suggests that the vector was cleared rapidly (prior to the first sampling day, i.e. Day 11) from the injection site muscle tissue.

12. CONCLUSION

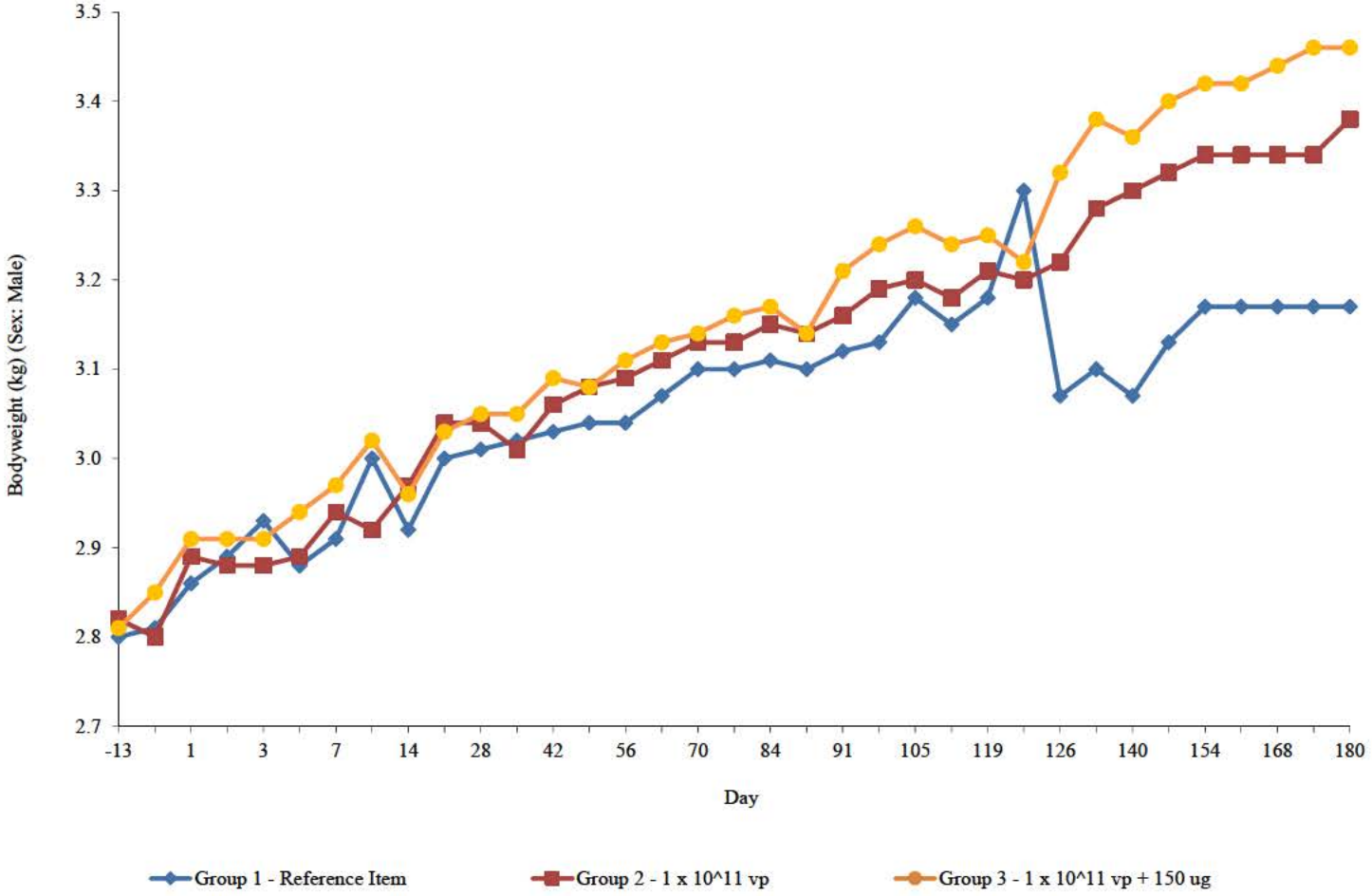
A single intramuscular injection into the lateral compartment of the right thigh in the rabbit at dose levels of 1 x 10^{11} vp Ad26 (b) (4) or 1 x 10^{11} vp Ad26 (b) (4) + 150µg (b) (4) (b) (4) (as a mixture) was clinically well tolerated. qPCR results for the determination of Ad26 (b) (4) Vector DNA in the control group were below the LLOQ of the assay, as expected. Positive Ad26 (b) (4) vector DNA values were detected in vaccine dosed groups in the skin at the intramuscular injection site, the spleen, and in the iliac and popliteal lymph nodes at Day 11, with the highest vector copy number present in the skin. By Day 180, Ad26 (b) (4) vector DNA was no longer detected in any tissue, with the exception of 1 iliac lymph node, at a low vector copy number close to the LLOQ of the assay. Overall, this demonstrates a limited biodistribution profile as well as a clearance over time of the Ad26 (b) (4) vector following intramuscular injection.

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Figure 1

Summary of Body Weights - Males

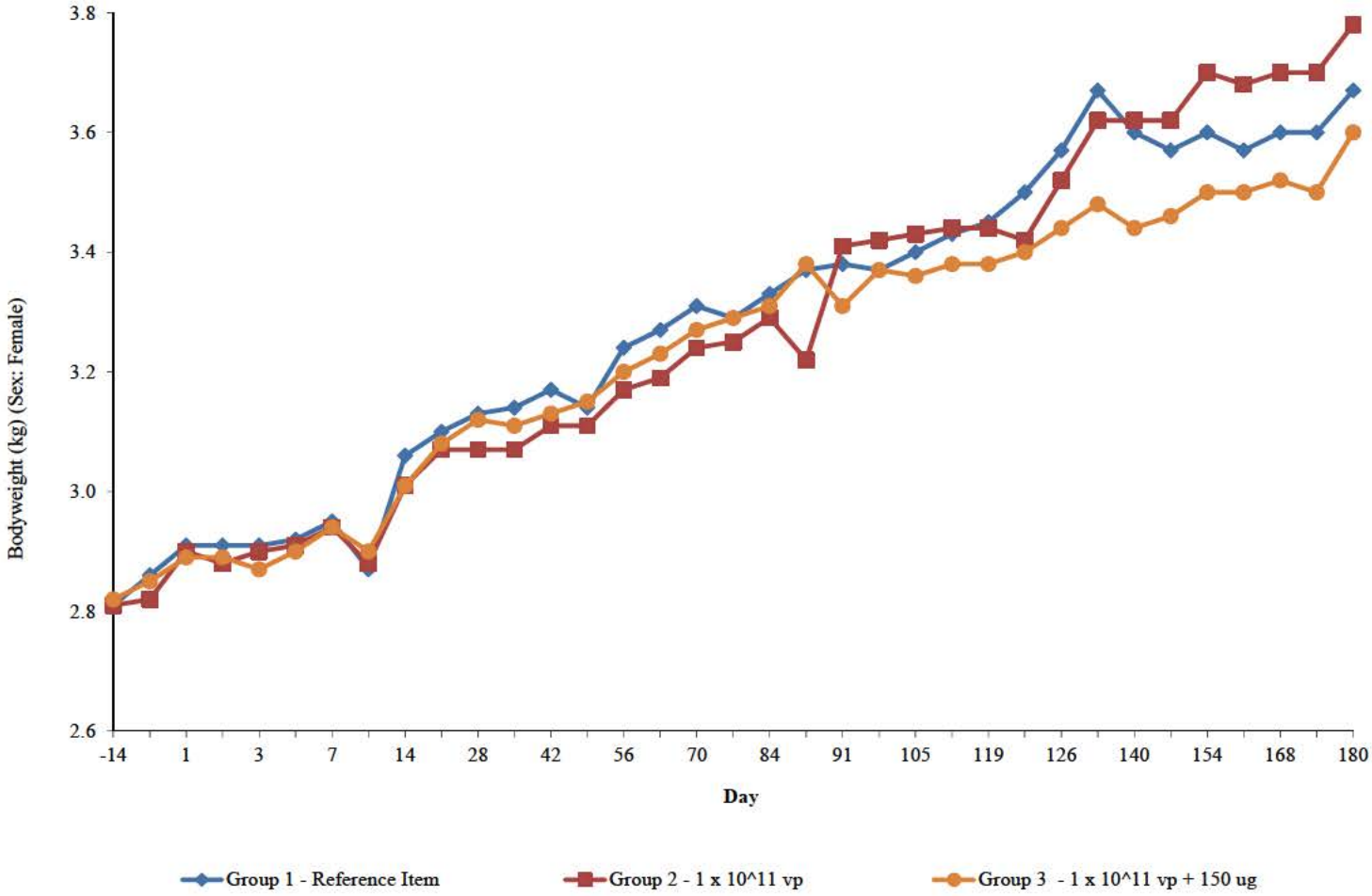


Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Figure 2

Summary of Body Weights - Females



Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 1

Summary of Clinical Observations Explanation Page

Note: Number of Observations equals the number of days the observation was seen.

Dosing Information

Dosing information is abbreviated on various data outputs; the following represents the dosing information for this study.

Group No.	Test Material	Dose Level
1	Reference Item	0
2	Ad26 (b) (4)	1×10^{11} vp
3	Ad26 (b) (4)	1×10^{11} vp + 150µg

Sponsor Reference No (b) (4) Test Facility Study No. (b) (4)

Table 1

Summary of Clinical Observations

(b) (4)

Observation Type: All Types From Day -16 (Start Date) to 180 (Start Date)	Male 0 Group 1	Male 1x10E11 vp Group 2	Male 1x10E11 vp+150 ug Group 3	Female 0 Group 1	Female 1x10E11 vp Group 2	Female 1x10E11 vp+150 ug Group 3
Activity Decreased						
Number of Animals Affected	0	0	0	1	0	0
Number of Times Recorded	0	0	0	2	0	0
First to Last seen	-	-	-	71 - 77	-	-
% of Affected Animals	0	0	0	8	0	0
Reduced Appetite						
Number of Animals Affected	0	0	0	1	1	1
Number of Times Recorded	0	0	0	5	4	4
First to Last seen	-	-	-	71 - 170	149 - 170	155 - 170
% of Affected Animals	0	0	0	8	5	5
Broken Toe Nail						
Number of Animals Affected	0	0	1	2	0	1
Number of Times Recorded	0	0	1	5	0	4
First to Last seen	-	-	120 - 120	96 - 154	-	-14 - 7
% of Affected Animals	0	0	5	17	0	5
Skin, Red						
Number of Animals Affected	1	0	0	3	0	1
Number of Times Recorded	1	0	0	4	0	2
First to Last seen	49 - 49	-	-	-1 - 175	-	84 - 161
% of Affected Animals	8	0	0	25	0	5
Skin, Dry						
Number of Animals Affected	0	1	0	1	0	1
Number of Times Recorded	0	1	0	2	0	1
First to Last seen	-	77 - 77	-	7 - 11	-	161 - 161
% of Affected Animals	0	5	0	8	0	5

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 1

Summary of Clinical Observations

(b) (4)

Observation Type: All Types From Day -16 (Start Date) to 180 (Start Date)	Male 0 Group 1	Male 1x10E11 vp Group 2	Male 1x10E11 vp+150 ug Group 3	Female 0 Group 1	Female 1x10E11 vp Group 2	Female 1x10E11 vp+150 ug Group 3
Skin, Lesion						
Number of Animals Affected	0	1	0	0	0	2
Number of Times Recorded	0	1	0	0	0	6
First to Last seen	-	112 - 112	-	-	-	56 - 77
% of Affected Animals	0	5	0	0	0	10
Skin, Scab						
Number of Animals Affected	2	0	2	0	0	5
Number of Times Recorded	6	0	5	0	0	11
First to Last seen	-15 - 56	-	-1 - 91	-	-	-1 - 119
% of Affected Animals	17	0	10	0	0	25
Fur, Loss						
Number of Animals Affected	0	0	0	0	2	4
Number of Times Recorded	0	0	0	0	2	4
First to Last seen	-	-	-	-	28 - 28	28 - 28
% of Affected Animals	0	0	0	0	10	20
Fur, Staining, Black						
Number of Animals Affected	1	1	0	1	0	0
Number of Times Recorded	1	1	0	3	0	0
First to Last seen	-8 - -8	-8 - -8	-	161 - 161	-	-
% of Affected Animals	8	5	0	8	0	0
Fur, Staining, Brown						
Number of Animals Affected	1	3	1	2	3	2
Number of Times Recorded	2	12	4	3	11	7
First to Last seen	91 - 98	-8 - 147	91 - 120	-8 - -1	-8 - 180	-8 - 168
% of Affected Animals	8	15	5	17	15	10

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 1

Summary of Clinical Observations

(b) (4)

Observation Type: All Types From Day -16 (Start Date) to 180 (Start Date)	Male 0 Group 1	 1x10E11 vp Group 2	 1x10E11 vp+150 ug Group 3	Female 0 Group 1	 1x10E11 vp Group 2	 1x10E11 vp+150 ug Group 3
Fur, Staining, Red						
Number of Animals Affected	0	0	0	1	0	0
Number of Times Recorded	0	0	0	1	0	0
First to Last seen	-	-	-	96 - 96	-	-
% of Affected Animals	0	0	0	8	0	0
Fur, Staining, Yellow						
Number of Animals Affected	4	10	9	6	8	10
Number of Times Recorded	36	148	80	60	143	200
First to Last seen	77 - 180	77 - 180	28 - 161	21 - 180	21 - 180	21 - 180
% of Affected Animals	33	50	45	50	40	50
Fur, Thin Cover						
Number of Animals Affected	0	0	3	0	2	4
Number of Times Recorded	0	0	18	0	9	31
First to Last seen	-	-	-8 - 120	-	-8 - 140	7 - 180
% of Affected Animals	0	0	15	0	10	20
Fur, Wet						
Number of Animals Affected	1	1	1	0	0	0
Number of Times Recorded	1	1	1	0	0	0
First to Last seen	77 - 77	84 - 84	14 - 14	-	-	-
% of Affected Animals	8	5	5	0	0	0
Penis, Protruding						
Number of Animals Affected	0	1	0	0	0	0
Number of Times Recorded	0	2	0	0	0	0
First to Last seen	-	-8 - -1	-	-	-	-
% of Affected Animals	0	5	0	0	0	0

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 1

Summary of Clinical Observations

(b) (4)

Observation Type: All Types From Day -16 (Start Date) to 180 (Start Date)	Male 0 Group 1	Male 1x10E11 vp Group 2	Male 1x10E11 vp+150 ug Group 3	Female 0 Group 1	Female 1x10E11 vp Group 2	Female 1x10E11 vp+150 ug Group 3
Feces, Absent						
Number of Animals Affected	0	3	3	0	0	0
Number of Times Recorded	0	3	4	0	0	0
First to Last seen	-	2 - 86	2 - 86	-	-	-
% of Affected Animals	0	15	15	0	0	0
Feces, Liquid						
Number of Animals Affected	0	0	0	0	1	0
Number of Times Recorded	0	0	0	0	1	0
First to Last seen	-	-	-	-	-5 - -5	-
% of Affected Animals	0	0	0	0	5	0
Feces, Output Decreased						
Number of Animals Affected	0	0	1	1	0	0
Number of Times Recorded	0	0	1	1	0	0
First to Last seen	-	-	107 - 107	73 - 73	-	-
% of Affected Animals	0	0	5	8	0	0
Feces, Size Reduced						
Number of Animals Affected	0	2	2	1	0	4
Number of Times Recorded	0	3	3	1	0	10
First to Last seen	-	6 - 100	100 - 107	73 - 73	-	1 - 142
% of Affected Animals	0	10	10	8	0	20
Feces, Soft						
Number of Animals Affected	0	1	0	0	1	0
Number of Times Recorded	0	3	0	0	1	0
First to Last seen	-	41 - 51	-	-	-5 - -5	-
% of Affected Animals	0	5	0	0	5	0

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 2

Summary of Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp
Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day -13	-8	1	2	3	4	7	11
1M	Mean	2.80	2.81	2.86	2.89	2.93	2.88	2.91	3.00
	SD	0.11	0.13	0.14	0.14	0.12	0.14	0.13	0.00
	N	12	12	12	12	12	12	12	3
2M	Mean	2.82	2.80	2.89	2.88	2.88	2.89	2.94	2.92
	SD	0.20	0.19	0.20	0.19	0.18	0.19	0.20	0.15
	N	20	20	20	20	20	20	20	5
	%Diff G1	0.54	-0.30	1.11	-0.40	-1.82	0.35	0.92	-2.67
3M	Mean	2.81	2.85	2.91	2.91	2.91	2.94	2.97	3.02
	SD	0.19	0.19	0.17	0.19	0.18	0.17	0.17	0.22
	N	20	20	20	20	20	20	20	5
	%Diff G1	0.36	1.31	1.81	0.63	-0.97	2.26	1.95	0.67

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 2

Summary of Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day 14	21	28	35	42	49	56	63
1M	Mean	2.92	3.00	3.01	3.02	3.03	3.04	3.04	3.07
	SD	0.16	0.17	0.15	0.16	0.21	0.20	0.21	0.21
	N	9	9	9	9	9	9	9	9
2M	Mean	2.97	3.04	3.04	3.01	3.06	3.08	3.09	3.11
	SD	0.23	0.20	0.20	0.20	0.18	0.21	0.18	0.20
	N	15	15	15	15	15	15	15	15
	%Diff G1	1.52	1.33	0.96	-0.29	0.88	1.17	1.39	1.52
3M	Mean	2.96	3.03	3.05	3.05	3.09	3.08	3.11	3.13
	SD	0.17	0.16	0.16	0.16	0.15	0.15	0.16	0.15
	N	15	15	15	15	15	15	15	15
	%Diff G1	1.29	0.89	1.18	1.03	1.76	1.17	2.26	1.96

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 2

Summary of Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day 70	77	84	90	91	98	105	112
1M	Mean	3.10	3.10	3.11	3.10	3.12	3.13	3.18	3.15
	SD	0.21	0.21	0.23	0.20	0.24	0.27	0.23	0.23
	N	9	9	9	3	6	6	6	6
2M	Mean	3.13	3.13	3.15	3.14	3.16	3.19	3.20	3.18
	SD	0.18	0.18	0.20	0.13	0.22	0.22	0.23	0.23
	N	15	15	15	5	10	10	10	10
	%Diff G1	1.08	0.86	1.36	1.29	1.39	1.81	0.52	0.95
3M	Mean	3.14	3.16	3.17	3.14	3.21	3.24	3.26	3.24
	SD	0.16	0.15	0.16	0.09	0.17	0.18	0.18	0.18
	N	15	15	15	5	10	10	10	10
	%Diff G1	1.29	1.94	2.00	1.29	2.99	3.40	2.41	2.86

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 2

Summary of Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day 119	120	126	133	140	147	154	161
1M	Mean	3.18	3.30	3.07	3.10	3.07	3.13	3.17	3.17
	SD	0.23	0.17	0.25	0.26	0.25	0.25	0.25	0.25
	N	6	3	3	3	3	3	3	3
2M	Mean	3.21	3.20	3.22	3.28	3.30	3.32	3.34	3.34
	SD	0.23	0.19	0.23	0.24	0.25	0.18	0.19	0.27
	N	10	5	5	5	5	5	5	5
	%Diff G1	0.84	-3.03	5.00	5.81	7.61	5.96	5.47	5.47
3M	Mean	3.25	3.22	3.32	3.38	3.36	3.40	3.42	3.42
	SD	0.17	0.13	0.23	0.22	0.22	0.19	0.23	0.23
	N	10	5	5	5	5	5	5	5
	%Diff G1	2.09	-2.42	8.26	9.03	9.57	8.51	8.00	8.00

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 2

Summary of Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp
Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day 168	Day 175	Day 180
1M	Mean	3.17	3.17	3.17
	SD	0.25	0.25	0.25
	N	3	3	3
2M	Mean	3.34	3.34	3.38
	SD	0.27	0.29	0.24
	N	5	5	5
	%Diff G1	5.47	5.47	6.74
3M	Mean	3.44	3.46	3.46
	SD	0.23	0.21	0.22
	N	5	5	5
	%Diff G1	8.63	9.26	9.26

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 2

Summary of Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp
Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day -14	-8	1	2	3	4	7	11
1F	Mean	2.81	2.86	2.91	2.91	2.91	2.92	2.95	2.87
	SD	0.08	0.09	0.10	0.07	0.08	0.07	0.07	0.06
	N	12	12	12	12	12	12	12	3
2F	Mean	2.81	2.82	2.90	2.88	2.90	2.91	2.94	2.88
	SD	0.12	0.13	0.13	0.12	0.14	0.10	0.13	0.04
	N	20	20	20	20	20	20	20	5
	%Diff G1	-0.12	-1.52	-0.46	-1.15	-0.29	-0.40	-0.51	0.47
3F	Mean	2.82	2.85	2.89	2.89	2.87	2.90	2.94	2.90
	SD	0.12	0.10	0.11	0.12	0.11	0.13	0.12	0.07
	N	20	20	20	20	20	20	20	5
	%Diff G1	0.24	-0.47	-0.80	-0.80	-1.32	-0.57	-0.34	1.16

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 2

Summary of Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day 14	21	28	35	42	49	56	63
1F	Mean	3.06	3.10	3.13	3.14	3.17	3.14	3.24	3.27
	SD	0.09	0.07	0.07	0.05	0.05	0.07	0.07	0.07
	N	9	9	9	9	9	9	9	9
2F	Mean	3.01	3.07	3.07	3.07	3.11	3.11	3.17	3.19
	SD	0.12	0.11	0.13	0.13	0.13	0.12	0.13	0.12
	N	15	15	15	15	15	15	15	15
	%Diff G1	-1.60	-1.08	-1.91	-2.26	-1.89	-0.99	-2.40	-2.24
3F	Mean	3.01	3.08	3.12	3.11	3.13	3.15	3.20	3.23
	SD	0.10	0.13	0.14	0.12	0.13	0.12	0.13	0.14
	N	15	15	15	15	15	15	15	15
	%Diff G1	-1.60	-0.65	-0.43	-1.20	-1.05	0.28	-1.37	-1.22

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 2

Summary of Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day 70	77	84	90	91	98	105	112
1F	Mean	3.31	3.29	3.33	3.37	3.38	3.37	3.40	3.43
	SD	0.06	0.08	0.09	0.15	0.08	0.08	0.06	0.08
	N	9	9	9	3	6	6	6	6
2F	Mean	3.24	3.25	3.29	3.22	3.41	3.42	3.43	3.44
	SD	0.12	0.14	0.12	0.08	0.10	0.10	0.12	0.12
	N	15	15	15	5	10	10	10	10
	%Diff G1	-2.15	-1.08	-1.40	-4.36	0.79	1.58	0.88	0.19
3F	Mean	3.27	3.29	3.31	3.38	3.31	3.37	3.36	3.38
	SD	0.14	0.13	0.14	0.16	0.14	0.18	0.17	0.15
	N	15	15	15	5	10	10	10	10
	%Diff G1	-1.14	0.14	-0.60	0.40	-2.17	0.10	-1.18	-1.55

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 2

Summary of Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day 119	120	126	133	140	147	154	161
1F	Mean	3.45	3.50	3.57	3.67	3.60	3.57	3.60	3.57
	SD	0.05	0.00	0.06	0.12	0.10	0.15	0.17	0.15
	N	6	3	3	3	3	3	3	3
2F	Mean	3.44	3.42	3.52	3.62	3.62	3.62	3.70	3.68
	SD	0.11	0.11	0.08	0.11	0.11	0.08	0.07	0.11
	N	10	5	5	5	5	5	5	5
	%Diff G1	-0.29	-2.29	-1.31	-1.27	0.56	1.50	2.78	3.18
3F	Mean	3.38	3.40	3.44	3.48	3.44	3.46	3.50	3.50
	SD	0.12	0.14	0.15	0.18	0.21	0.22	0.17	0.23
	N	10	5	5	5	5	5	5	5
	%Diff G1	-2.03	-2.86	-3.55	-5.09	-4.44	-2.99	-2.78	-1.87

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 2

Summary of Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp
Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day 168	175	180
1F	Mean	3.60	3.60	3.67
	SD	0.17	0.26	0.23
	N	3	3	3
2F	Mean	3.70	3.70	3.78
	SD	0.10	0.10	0.11
	N	5	5	5
	%Diff G1	2.78	2.78	3.09
3F	Mean	3.52	3.50	3.60
	SD	0.19	0.23	0.23
	N	5	5	5
	%Diff G1	-2.22	-2.78	-1.82

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 3

Summary of Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp
Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day							
		Change -13 - -8	Change -8 - 1	Change 1 - 2	Change 2 - 3	Change 3 - 4	Change 4 - 7	Change 7 - 11	Change 1 - 11
1M	Mean	0.01	0.05	0.03	0.04	-0.06	0.03	0.07	0.10
	SD	0.05	0.05	0.05	0.11	0.10	0.05	0.06	0.00
	N	12	12	12	12	12	12	3	3
2M	Mean	-0.02	0.09	-0.01d	0.00	0.01	0.05	0.04	0.10
	SD	0.06	0.06	0.03	0.03	0.04	0.06	0.05	0.00
	N	20	20	20	20	20	20	5	5
3M	Mean	0.04	0.07	0.00	-0.01	0.04b	0.03	0.04	0.06
	SD	0.10	0.06	0.05	0.06	0.07	0.04	0.05	0.05
	N	20	20	20	20	20	20	5	5

Significantly different from control group 1 value :a=p≤0.05,b=p≤0.01,c=p≤0.001 (Dunn)
d=p≤0.05,e=p≤0.01,f=p≤0.001 (Dunnett)

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 3

Summary of Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day							
		Change 7 - 14	Change 14 - 21	Change 21 - 28	Change 28 - 35	Change 35 - 42	Change 42 - 49	Change 49 - 56	Change 56 - 63
1M	Mean	0.02	0.08	0.01	0.01	0.01	0.01	0.00	0.02
	SD	0.04	0.04	0.03	0.06	0.09	0.03	0.05	0.07
	N	9	9	9	9	9	9	9	9
2M	Mean	0.01	0.07	0.00	-0.03	0.05	0.02	0.01	0.03
	SD	0.04	0.05	0.00	0.06	0.06	0.08	0.06	0.06
	N	15	15	15	15	15	15	15	15
3M	Mean	0.00	0.07	0.02	0.01	0.03	-0.01	0.03	0.01
	SD	0.04	0.07	0.06	0.05	0.07	0.06	0.05	0.05
	N	15	15	15	15	15	15	15	15

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 3

Summary of Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day							
		Change 63 - 70	Change 70 - 77	Change 77 - 84	Change 84 - 90	Change 1 - 90	Change 84 - 91	Change 91 - 98	Change 98 - 105
1M	Mean	0.03	0.00	0.01	-0.03	0.27	0.02	0.02	0.05
	SD	0.05	0.00	0.03	0.06	0.06	0.04	0.04	0.05
	N	9	9	9	3	3	6	6	6
2M	Mean	0.02	-0.01	0.03	0.04	0.26	-0.02	0.03	0.01
	SD	0.06	0.07	0.08	0.09	0.09	0.08	0.07	0.06
	N	15	15	15	5	5	10	10	10
3M	Mean	0.01	0.02	0.01	0.04	0.28	0.00	0.03	0.02
	SD	0.04	0.04	0.07	0.09	0.08	0.05	0.05	0.06
	N	15	15	15	5	5	10	10	10

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 3

Summary of Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day							
		Change 105 - 112	Change 112 - 119	Change 119 - 120	Change 1 - 120	Change 119 - 126	Change 126 - 133	Change 133 - 140	Change 140 - 147
1M	Mean	-0.03	0.03	-0.03	0.37	0.03	0.03	-0.03	0.07
	SD	0.05	0.05	0.06	0.06	0.06	0.06	0.06	0.06
	N	6	6	3	3	3	3	3	3
2M	Mean	-0.02	0.03	0.00	0.30	0.00	0.06	0.02	0.02
	SD	0.04	0.05	0.00	0.07	0.07	0.05	0.04	0.08
	N	10	10	5	5	5	5	5	5
3M	Mean	-0.02	0.01	0.00	0.32	0.04	0.06	-0.02	0.04
	SD	0.04	0.03	0.00	0.08	0.05	0.05	0.04	0.05
	N	10	10	5	5	5	5	5	5

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 3

Summary of Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day					
		Change 147 - 154	Change 154 - 161	Change 161 - 168	Change 168 - 175	Change 175 - 180	Change 1 - 180
1M	Mean	0.03	0.00	0.00	0.00	0.00	0.40
	SD	0.06	0.00	0.00	0.00	0.00	0.10
	N	3	3	3	3	3	3
2M	Mean	0.02	0.00	0.00	0.00	0.04	0.42
	SD	0.08	0.10	0.00	0.07	0.05	0.13
	N	5	5	5	5	5	5
3M	Mean	0.02	0.00	0.02	0.02	0.00	0.54
	SD	0.04	0.00	0.04	0.04	0.07	0.09
	N	5	5	5	5	5	5

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 3

Summary of Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp
Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day							
		Change -14 - -8	Change -8 - 1	Change 1 - 2	Change 2 - 3	Change 3 - 4	Change 4 - 7	Change 7 - 11	Change 1 - 11
1F	Mean	0.05	0.05	0.00	0.00	0.01	0.03	0.00	0.07
	SD	0.05	0.05	0.07	0.06	0.05	0.05	0.00	0.06
	N	12	12	12	12	12	12	3	3
2F	Mean	0.01	0.08	-0.02	0.03	0.01	0.03	0.02	0.04
	SD	0.07	0.06	0.04	0.06	0.10	0.09	0.04	0.05
	N	20	20	20	20	20	20	5	5
3F	Mean	0.03	0.04	0.00	-0.02	0.03	0.04	0.04	0.10
	SD	0.07	0.06	0.06	0.06	0.06	0.07	0.05	0.00
	N	20	20	20	20	20	20	5	5

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 3

Summary of Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day							
		Change 7 - 14	Change 14 - 21	Change 21 - 28	Change 28 - 35	Change 35 - 42	Change 42 - 49	Change 49 - 56	Change 56 - 63
1F	Mean	0.08	0.04	0.03	0.01	0.02	-0.02	0.10	0.02
	SD	0.07	0.05	0.05	0.06	0.04	0.08	0.09	0.07
	N	9	9	9	9	9	9	9	9
2F	Mean	0.05	0.06	0.01	0.00	0.03	0.01	0.05	0.03
	SD	0.05	0.06	0.06	0.04	0.06	0.07	0.07	0.07
	N	15	15	15	15	15	15	15	15
3F	Mean	0.04	0.07	0.04	-0.01	0.03	0.02	0.05	0.03
	SD	0.06	0.09	0.07	0.06	0.05	0.07	0.05	0.06
	N	15	15	15	15	15	15	15	15

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 3

Summary of Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day							
		Change 63 - 70	Change 70 - 77	Change 77 - 84	Change 84 - 90	Change 1 - 90	Change 84 - 91	Change 91 - 98	Change 98 - 105
1F	Mean	0.04	-0.02	0.04	0.03	0.40	0.05	-0.02	0.03
	SD	0.05	0.04	0.05	0.06	0.10	0.05	0.04	0.05
	N	9	9	9	3	3	6	6	6
2F	Mean	0.05	0.01	0.03	0.02	0.34	0.08	0.01	0.01
	SD	0.05	0.06	0.08	0.08	0.11	0.04	0.06	0.06
	N	15	15	15	5	5	10	10	10
3F	Mean	0.05	0.02	0.02	0.04	0.44	0.01	0.06a	-0.01
	SD	0.05	0.06	0.04	0.05	0.05	0.03	0.05	0.06
	N	15	15	15	5	5	10	10	10

Significantly different from control group 1 value :a=p≤0.05,b=p≤0.01,c=p≤0.001 (Dunnett)

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 3

Summary of Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day							
		Change 105 - 112	Change 112 - 119	Change 119 - 120	Change 1 - 120	Change 119 - 126	Change 126 - 133	Change 133 - 140	Change 140 - 147
1F	Mean	0.03	0.02	0.07	0.50	0.10	0.10	-0.07	-0.03
	SD	0.05	0.08	0.06	0.00	0.00	0.10	0.06	0.06
	N	6	6	3	3	3	3	3	3
2F	Mean	0.01	0.00	0.04	0.50	0.02	0.10	0.00	0.00
	SD	0.06	0.07	0.05	0.10	0.08	0.07	0.00	0.07
	N	10	10	5	5	5	5	5	5
3F	Mean	0.02	0.00	0.00	0.50	0.08	0.04	-0.04	0.02
	SD	0.06	0.05	0.00	0.07	0.04	0.05	0.05	0.04
	N	10	10	5	5	5	5	5	5

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Table 3

Summary of Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex		Day					
		Change 147 - 154	Change 154 - 161	Change 161 - 168	Change 168 - 175	Change 175 - 180	Change 1 - 180
1F	Mean	0.03	-0.03	0.03	0.00	0.07	0.80
	SD	0.06	0.06	0.06	0.10	0.06	0.26
	N	3	3	3	3	3	3
2F	Mean	0.08	-0.02	0.02	0.00	0.08	0.84
	SD	0.04	0.08	0.04	0.00	0.04	0.17
	N	5	5	5	5	5	5
3F	Mean	0.04	0.00	0.02	-0.02	0.10	0.70
	SD	0.05	0.07	0.04	0.08	0.07	0.19
	N	5	5	5	5	5	5

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

janssen
PHARMACEUTICAL COMPANIES of Johnson & Johnson

Certificate of Analysis

C18005 (b) (4)

Ad26 (b) (4) AP1, DP, 2e11 VP/ml, CTM

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

janssen
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Certificate of Analysis

C18005 (b) (4)

Ad26 (b) (4) AP1, DP, 2e11 VP/ml, CTM

(b) (4)

Data Decision info

Decision:	Approved
Responsible person:	(b) (6)
Date:	31-JAN-2018

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group Leiden Vaccines (JVL)	**Effective Date** 23-Apr-2018 09:14:03 EDT
Document Title Stablity shelf-life statement for Ad26 (b) (4) AP1, 2x10^11 VP/ml	

(b) (4)

Storage conditions
Store between -85°C and -55°C.

Storage instructions
Keep in original packaging until use

Transportation conditions
Ship at -20 ºC.
(see (b) (4) and specified allowance described in the Temperature Excursion Guideline (b) (4)
Proven temperature ranges

Printed On	08-Jun-2018 07:02:56 EDT	**Confidential**	PAGE : 1 of 5

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group Leiden Vaccines (JVL)	**Effective Date** 23-Apr-2018 09:14:03 EDT
Document Title Stablity shelf-life statement for Ad26 (b) (4) AP1, 2x10^11 VP/ml	

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group Leiden Vaccines (JVL)	**Effective Date** 23-Apr-2018 09:14:03 EDT
Document Title Stablity shelf-life statement for Ad26 (b) (4) AP1, 2x10^11 VP/ml	

(b) (4)

*****END OF DOCUMENT*****

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group Leiden Vaccines (JVL)	**Effective Date** 23-Apr-2018 09:14:03 EDT
Document Title Stablity shelf-life statement for Ad26 (b) (4) AP1, 2x10^11 VP/ml	

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group Leiden Vaccines (JVL)	**Effective Date** 23-Apr-2018 09:14 03 EDT
Document Title Stablity shelf-life statement for Ad26 (b) (4) AP1, 2x10^11 VP/ml	

(b) (4)

APPROVAL PAGE

Approver Name	Justification	Date
(b) (6)	Author Approval	23-Apr-2018 08:55 56 EDT
	Quality Integrator	23-Apr-2018 08 56:38 EDT
	Subject matter expert approval	23-Apr-2018 09:13 20 EDT
	Peer reviewer	23-Apr-2018 09:13 50 EDT

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

(b) (4)

(b) (4)

CERTIFICATE OF ANALYSIS

PRODUCT NAME: JNJ-64213175
(b) (4)

Printed On: 14-Jun-2018 03:18:21 EDT(-0400)	**Confidential**	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

(b) (4)

Test	Acceptance Criteria	Result
	(b) (4)	

END OF DOCUMENT

Printed On: 14-Jun-2018 03:18:21 EDT(-0400)	Confidential	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

(b) (4)

Document Revision History			
Version Number	**Section**	**Description of Change**	**Justification of Change**
1.0	All	JNJ-64213175 (b) (4) (b) (4) Drug Product (DP)	New Document

Printed On: 14-Jun-2018 03:18:21 EDT(-0400)	**Confidential**	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

(b) (4)

APPROVAL PAGE

Approver Name	Justification	Date
(b) (6)	Department Approval	17-Apr-2018 10 52 35 EDT
	Author Approval	17-Apr-2018 10:56:08 EDT

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group: PDMS Analytical Development	**Effective Date:** 25-Apr-2018 11:55:33 EDT
Document Title: Stability Statement for JNJ-64213175 (b) (4) Drug Product (DP)	

(b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group: PDMS Analytical Development	**Effective Date:** 25-Apr-2018 11:55:33 EDT
Document Title: Stability Statement for JNJ-64213175 (b) (4) Drug Product (DP)	

(b) (4)

5. REFERENCES

5.1 DS-SOP-20946 – "Management of Stability Statements for Large Molecule pharmaceutical products to be used during clinical trials".

5.2 DS-SPE-31204 Specification and justification of specification for (b) (4) DP

*****END OF DOCUMENT*****

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group: PDMS Analytical Development	**Effective Date:** 25-Apr-2018 11:55:33 EDT
Document Title: Stability Statement for JNJ-64213175 (b) (4) Drug Product (DP)	

Document Revision History			
Version Number	**Section**	**Description of Change**	**Justification of Change**
1.0	All	New document	New document

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group: PDMS Analytical Development	**Effective Date:** 25-Apr-2018 11:55:33 EDT
Document Title: Stability Statement for JNJ-64213175 (b) (4) Drug Product (DP)	

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group: PDMS Analytical Development	**Effective Date:** 25-Apr-2018 11:55:33 EDT
Document Title: Stability Statement for JNJ-64213175 (b) (4) Drug Product (DP)	

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group: PDMS Analytical Development	**Effective Date:** 25-Apr-2018 11:55:33 EDT
Document Title: Stability Statement for JNJ-64213175 (b) (4) Drug Product (DP)	

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group: PDMS Analytical Development	**Effective Date:** 25-Apr-2018 11:55:33 EDT
Document Title: Stability Statement for JNJ-64213175 (b) (4) Drug Product (DP)	

(b) (4)

Printed On	14-Jun-2018 03:19:12 EDT(-0400)	**Confidential**	PAGE : 7 of 10

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group: PDMS Analytical Development	**Effective Date:** 25-Apr-2018 11:55:33 EDT
Document Title: Stability Statement for JNJ-64213175 (b) (4) Drug Product (DP)	

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group: PDMS Analytical Development	**Effective Date:** 25-Apr-2018 11:55:33 EDT
Document Title: Stability Statement for JNJ-64213175 (b) (4) Drug Product (DP)	

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

Technical Document - Technical Document Stability Statement	
Owner Group: PDMS Analytical Development	**Effective Date:** 25-Apr-2018 11:55:33 EDT
Document Title: Stability Statement for JNJ-64213175 (b) (4) Drug Product (DP)	

(b) (4)

APPROVAL PAGE

Approver Name	Justification	Date
(b) (6)	AD-SI	25-Apr-2018 09 39 36 EDT
	Department Approval	25-Apr-2018 09:41:17 EDT
	Department Approval	25-Apr-2018 09:47:09 EDT
	DPD TI	25-Apr-2018 09:48:21 EDT
	Quality Approval	25-Apr-2018 11 54:48 EDT

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 1

(b) (4)	Quality Control Analysis Report (b) (4)	Page 1 of 1

References: (b) (4) Reporting Quality Control Test Results

Material Description: C148-104 (b) (4) Post-Shipment ID

Expiration Date: N/A

Results:

(b) (4)

Comments: NA

(b) (4), (b) (6)

(b) (4)

Appendix 2

Individual Mortality Explanation Page

Abbreviation	Description	Abbreviation	Description
AD or ACCD	Accidental death	PM SIR	Signs of ill health or reaction to treatment check in the afternoon
AM SIR	Signs of ill health or reaction to treatment check in the morning	REC	Recovery euthanasia
FD	Found dead	REL	Released
INTM	Interim	TE or TERM	Terminal euthanasia
NR	Not recorded	UE or UNSC	Unscheduled euthanasia

Note: This is a comprehensive list of abbreviations. All of the abbreviations listed may not be applicable to this report.

Note: Removal Time represents the time the removal was entered into the Provantis system and may not be representative of the time of death.

Dosing Information

Dosing information is abbreviated on various data outputs; the following represents the dosing information for this study.

Group No.	Test Material	Dose Level
1	Reference Item	0
2	Ad26 (b) (4)	1 x 10^{11} vp
3	Ad26 (b) (4)	1 x 10^{11} vp + 150µg

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 2

Individual Mortality

(b) (4)

Group	Dose Level	Sex	Animal	Cage	Removal Day	Removal Week	Removal Date	Removal Time	Time Slot	Removal Symptom	Pathology Reason
1	0	Male	1001	1001	11	2	24JUN2018	9:31	.	.	TERM
			1002	1002	11	2	24JUN2018	10:24	.	.	TERM
			1003	1003	11	2	24JUN2018	9:32	.	.	TERM
			1004	1004	90	13	11SEP2018	9:44	.	.	TERM
			1005	1005	90	13	11SEP2018	9:11	.	.	TERM
			1006	1006	90	13	11SEP2018	10:07	.	.	TERM
			1007	1007	120	18	11OCT2018	9:35	.	.	TERM
			1008	1008	120	18	11OCT2018	9:43	.	.	TERM
			1009	1009	120	18	11OCT2018	10:19	.	.	TERM
			1010	1010	180	26	10DEC2018	9:30	.	.	TERM
			1011	1011	180	26	10DEC2018	9:28	.	.	TERM
			1012	1012	180	26	10DEC2018	10:11	.	.	TERM
1	0	Female	1501	1501	11	2	25JUN2018	9:13	.	.	TERM
			1502	1502	11	2	25JUN2018	9:49	.	.	TERM
			1503	1503	11	2	25JUN2018	9:11	.	.	TERM
			1504	1504	90	13	12SEP2018	9:18	.	.	TERM
			1505	1505	90	13	12SEP2018	9:16	.	.	TERM
			1506	1506	90	13	12SEP2018	10:05	.	.	TERM
			1507	1507	120	18	12OCT2018	9:26	.	.	TERM
			1508	1508	120	18	12OCT2018	9:24	.	.	TERM
			1509	1509	120	18	12OCT2018	10:07	.	.	TERM
			1510	1510	180	26	11DEC2018	9:09	.	.	TERM
			1511	1511	180	26	11DEC2018	9:06	.	.	TERM
			1512	1512	180	26	11DEC2018	9:49	.	.	TERM
2	1x10E11 vp	Male	2001	2001	11	2	24JUN2018	11:12	.	.	TERM
			2002	2002	11	2	24JUN2018	12:02	.	.	TERM
			2003	2003	11	2	24JUN2018	10:30	.	.	TERM
			2004	2004	11	2	24JUN2018	11:11	.	.	TERM
			2005	2005	11	2	24JUN2018	11:55	.	.	TERM
			2006	2006	90	13	11SEP2018	10:05	.	.	TERM
			2007	2007	90	13	11SEP2018	10:46	.	.	TERM
			2008	2008	90	13	11SEP2018	10:36	.	.	TERM
			2009	2009	90	13	11SEP2018	11:19	.	.	TERM
			2010	2010	90	13	11SEP2018	11:18	.	.	TERM
			2011	2011	120	18	11OCT2018	10:21	.	.	TERM

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 2

Individual Mortality

(b) (4)

Group	Dose Level	Sex	Animal	Cage	Removal Day	Removal Week	Removal Date	Removal Time	Time Slot	Removal Symptom	Pathology Reason
2	1x10E11 vp	Male	2012	2012	120	18	11OCT2018	11:04	.	.	TERM
			2013	2013	120	18	11OCT2018	11:09	.	.	TERM
			2014	2014	120	18	11OCT2018	11:30	.	.	TERM
			2015	2015	120	18	11OCT2018	13:23	.	.	TERM
			2016	2016	180	26	10DEC2018	10:05	.	.	TERM
			2017	2017	180	26	10DEC2018	10:44	.	.	TERM
			2018	2018	180	26	10DEC2018	10:45	.	.	TERM
			2019	2019	180	26	10DEC2018	11:17	.	.	TERM
			2020	2020	180	26	10DEC2018	11:15	.	.	TERM
2	1x10E11 vp	Female	2501	2501	11	2	25JUN2018	10:22	.	.	TERM
			2502	2502	11	2	25JUN2018	10:56	.	.	TERM
			2503	2503	11	2	25JUN2018	9:52	.	.	TERM
			2504	2504	11	2	25JUN2018	10:24	.	.	TERM
			2505	2505	11	2	25JUN2018	10:58	.	.	TERM
			2506	2506	90	13	12SEP2018	9:57	.	.	TERM
			2507	2507	90	13	12SEP2018	10:55	.	.	TERM
			2508	2508	90	13	12SEP2018	11:07	.	.	TERM
			2509	2509	90	13	12SEP2018	11:33	.	.	TERM
			2510	2510	90	13	12SEP2018	11:30	.	.	TERM
			2511	2511	120	18	12OCT2018	10:05	.	.	TERM
			2512	2512	120	18	12OCT2018	10:42	.	.	TERM
			2513	2513	120	18	12OCT2018	10:42	.	.	TERM
			2514	2514	120	18	12OCT2018	11:16	.	.	TERM
			2515	2515	120	18	12OCT2018	11:15	.	.	TERM
			2516	2516	180	26	11DEC2018	9:50	.	.	TERM
			2517	2517	180	26	11DEC2018	10:26	.	.	TERM
			2518	2518	180	26	11DEC2018	10:26	.	.	TERM
			2519	2519	180	26	11DEC2018	11:01	.	.	TERM
			2520	2520	180	26	11DEC2018	10:59	.	.	TERM
3	1x10E11 vp+150	Male	3001	3001	11	2	24JUN2018	13:17	.	.	TERM
			3002	3002	11	2	24JUN2018	13:55	.	.	TERM
			3003	3003	11	2	24JUN2018	14:29	.	.	TERM
			3004	3004	11	2	24JUN2018	13:01	.	.	TERM
			3005	3005	11	2	24JUN2018	13:52	.	.	TERM
			3006	3006	90	13	11SEP2018	13:33	.	.	TERM

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 2

Individual Mortality

(b) (4)

Group	Dose Level	Sex	Animal	Cage	Removal Day	Removal Week	Removal Date	Removal Time	Time Slot	Removal Symptom	Pathology Reason
3	1x10E11 vp+150	Male	3007	3007	90	13	11SEP2018	13:27	.	.	TERM
			3008	3008	90	13	11SEP2018	14:12	.	.	TERM
			3009	3009	90	13	11SEP2018	14:11	.	.	TERM
			3010	3010	90	13	11SEP2018	14:48	.	.	TERM
			3011	3011	120	18	11OCT2018	13:16	.	.	TERM
			3012	3012	120	18	11OCT2018	13:59	.	.	TERM
			3013	3013	120	18	11OCT2018	13:56	.	.	TERM
			3014	3014	120	18	11OCT2018	14:41	.	.	TERM
			3015	3015	120	18	11OCT2018	14:37	.	.	TERM
			3016	3016	180	26	10DEC2018	13:27	.	.	TERM
			3017	3017	180	26	10DEC2018	13:25	.	.	TERM
			3018	3018	180	26	10DEC2018	14:02	.	.	TERM
			3019	3019	180	26	10DEC2018	13:57	.	.	TERM
			3020	3020	180	26	10DEC2018	14:36	.	.	TERM
3	1x10E11 vp+150	Female	3501	3501	11	2	25JUN2018	11:29	.	.	TERM
			3502	3502	11	2	25JUN2018	12:05	.	.	TERM
			3503	3503	11	2	25JUN2018	12:39	.	.	TERM
			3504	3504	11	2	25JUN2018	11:32	.	.	TERM
			3505	3505	11	2	25JUN2018	12:06	.	.	TERM
			3506	3506	90	13	12SEP2018	13:39	.	.	TERM
			3507	3507	90	13	12SEP2018	13:36	.	.	TERM
			3508	3508	90	13	12SEP2018	14:07	.	.	TERM
			3509	3509	90	13	12SEP2018	14:13	.	.	TERM
			3510	3510	90	13	12SEP2018	14:51	.	.	TERM
			3511	3511	120	18	12OCT2018	13:17	.	.	TERM
			3512	3512	120	18	12OCT2018	13:14	.	.	TERM
			3513	3513	120	18	12OCT2018	13:49	.	.	TERM
			3514	3514	120	18	12OCT2018	13:48	.	.	TERM
			3515	3515	120	18	12OCT2018	14:20	.	.	TERM
			3516	3516	180	26	11DEC2018	11:30	.	.	TERM
			3517	3517	180	26	11DEC2018	11:29	.	.	TERM
			3518	3518	180	26	11DEC2018	13:24	.	.	TERM
			3519	3519	180	26	11DEC2018	13:19	.	.	TERM
			3520	3520	180	26	11DEC2018	13:53	.	.	TERM

Appendix 3

Individual Clinical Observations Explanation Page

Abbreviation	Description	Abbreviation	Description
.	Not scheduled to be performed / Not seen / Dead	p #	Observation post dose
AM_S	Signs of ill health or reaction to treatment check in the morning	PM_S	Signs of ill health or reaction to treatment check in the afternoon
CAM	Cage side observation in the morning	pr #	Observation predose
Cp1	Cage side observation 1 to 2 hours post dose	SIRT	Signs of ill health or reaction to treatment
Cp2	Cage side observation 24 hours post dose	U #/Up #	Unscheduled examination post dose
Cpr	Cage side observation predose	UDu	Unscheduled examination during dosing
CSO	Cage side observation daily	Un #/Unsc #	Unscheduled examination
DE/D	Detailed examination	Upr	Unscheduled observation predose
DuRx	Observation during dosing	Vet	Anything observed by Vet Aid
Fev	Food evaluation	#	Number to avoid using the same timeslot/animal/day
OTHR	Other		

Note: This is a comprehensive list of abbreviations. All of the abbreviations listed may not be applicable to this report.

Note: Only animals with findings are presented in this appendix.

Dosing Information

Dosing information is abbreviated on various data outputs; the following represents the dosing information for this study.

Group No.	Test Material	Dose Level
1	Reference Item	0
2	Ad26 (b) (4)	1×10^{11} vp
3	Ad26 (b) (4)	1×10^{11} vp + 150µg

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-15 Vet	-8 DE	-1 DE	7 DE	28 DE	42 DE	49 DE
1007	Skin, Scab, Dorsal Thoracic	.	.	.	.	.	X	.
	Skin, Scab, Pinna, Left	X	.	X	X	.	.	.
	Fur, Wet, Lower Jaw	.	.	.	.	.	.	.
1008	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
1009	Skin, Red, Nasal Mucosa	.	.	.	.	.	.	X
	Fur, Staining, Black, Hindpaw, Left	.	X	.	.	.	.	.
	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
1011	Skin, Scab, Hindlimb, Right	.	.	.	.	X	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
1012	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		56 DE	77 DE	91 DE	98 DE	105 DE	112 DE	119 DE
1007	Skin, Scab, Dorsal Thoracic	.	.	.	.	.	.	.
	Skin, Scab, Pinna, Left	.	.	.	.	.	.	.
	Fur, Wet, Lower Jaw	.	X	.	.	.	.	.
1008	Fur, Staining, Yellow, Hindpaw, Left	.	X	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	X	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	X	.	.	.	.	.
1009	Skin, Red, Nasal Mucosa	.	.	.	.	.	.	.
	Fur, Staining, Black, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Brown, Tail	.	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	X	.	.	.	.
1011	Skin, Scab, Hindlimb, Right	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	X	X	.	.	.
1012	Fur, Staining, Yellow, Hindlimb, Left	.	.	X	X	X	X	X
	Fur, Staining, Yellow, Hindlimb, Right	.	.	X	X	X	X	X
	Fur, Staining, Yellow, Hindpaw, Left	.	X	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	X	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	X	X	X	X	X	X

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		126 DE	133 DE	140 DE	147 DE	154 DE	161 DE	168 DE
1007	Skin, Scab, Dorsal Thoracic	.	.	.	.	.	.	.
	Skin, Scab, Pinna, Left	.	.	.	.	.	.	.
	Fur, Wet, Lower Jaw	.	.	.	.	.	.	.
1008	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
1009	Skin, Red, Nasal Mucosa	.	.	.	.	.	.	.
	Fur, Staining, Black, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
1011	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
1012	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	X	X	X	X	X	X	X

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		175 DE	180 DE					
1007	Skin, Scab, Dorsal Thoracic	.	.					
	Skin, Scab, Pinna, Left	.	.					
	Fur, Wet, Lower Jaw	.	.					
1008	Fur, Staining, Yellow, Hindpaw, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
	Fur, Staining, Yellow, Tail	.	.					
1009	Skin, Red, Nasal Mucosa	.	.					
	Fur, Staining, Black, Hindpaw, Left	.	.					
	Fur, Staining, Brown, Tail	.	.					
	Fur, Staining, Yellow, Hindlimb, Left	.	.					
	Fur, Staining, Yellow, Hindlimb, Right	.	.					
1011	Skin, Scab, Hindlimb, Right	.	.					
	Fur, Staining, Yellow, Hindlimb, Left	.	.					
	Fur, Staining, Yellow, Hindlimb, Right	.	.					
1012	Fur, Staining, Yellow, Hindlimb, Left	.	.					
	Fur, Staining, Yellow, Hindlimb, Right	.	.					
	Fur, Staining, Yellow, Hindpaw, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
	Fur, Staining, Yellow, Tail	X	X					

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-8 DE	-1 DE	2 Cp2	6 CSO	41 AM_S	44 CSO	51 CSO
2002	Penis, Protruding	X	X	.	.	.	.	.
2003	Fur, Staining, Brown, Tail	X	X	.	.	.	.	.
2006	Skin, Dry, Pinna, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
2008	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
2010	Feces, Absent	.	.	.	.	.	.	.
2011	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
2012	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
2014	Fur, Staining, Brown, Muzzle	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	X	.	.	.
2015	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-8 DE	-1 DE	2 Cp2	6 CSO	41 AM_S	44 CSO	51 CSO
2015	Fur, Staining, Yellow, Lower Jaw	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Pinna, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Wet, Lower Jaw	.	.	.	.	.	.	.
	Feces, Absent	.	.	X	.	.	.	.
	Feces, Soft, Slight	.	.	.	.	.	X	X
	Feces, Soft, Severity Not Applicable	.	.	.	.	X	.	.
2016	Skin, Lesion, Hindlimb, Right, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Feces, Absent	.	.	X	.	.	.	.
2017	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2018	Fur, Staining, Black, Forepaw, Right	X	.	.	.	.	.	.
	Fur, Staining, Brown, Muzzle	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
2020	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-8 DE	-1 DE	2 Cp2	6 CSO	41 AM_S	44 CSO	51 CSO
2020	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		77 DE	84 DE	86 CSO	90 DE	91 DE	98 DE	100 CSO
2002	Penis, Protruding	.	.	.	.	.	.	.
2003	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
2006	Skin, Dry, Pinna, Left	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	X	.	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	X	.	X	.	.	.
	Fur, Staining, Yellow, Tail	X	X	.	X	.	.	.
2008	Fur, Staining, Yellow, Tail	X	.	.	.	.	.	.
2010	Feces, Absent	.	.	X	.	.	.	.
2011	Fur, Staining, Yellow, Cranium	X	X	.	.	X	X	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Tail	.	.	.	.	X	X	.
2012	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	X	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	X	.	.
2014	Fur, Staining, Brown, Muzzle	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Forelimb, Left	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Forelimb, Right	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	X	X	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	X
2015	Fur, Staining, Yellow, Cranium	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Forepaw, Left	X	X	.	.	X	X	.
	Fur, Staining, Yellow, Forepaw, Right	X	X	.	.	X	X	.
	Fur, Staining, Yellow, Hindpaw, Left	X	X	.	.	X	X	.
	Fur, Staining, Yellow, Hindpaw, Right	X	X	.	.	X	X	.

X=Present

Sponsor Reference No (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		77 DE	84 DE	86 CSO	90 DE	91 DE	98 DE	100 CSO
2015	Fur, Staining, Yellow, Lower Jaw	X	X	.	.	X	X	.
	Fur, Staining, Yellow, Pinna, Right	X	X	.	.	X	X	.
	Fur, Staining, Yellow, Tail	X	X	.	.	X	X	.
	Fur, Staining, Yellow, Ventral Cervical	.	.	.	.	X	X	.
	Fur, Wet, Lower Jaw	.	X	.	.	.	.	.
	Feces, Absent	.	.	.	.	.	.	.
	Feces, Soft, Slight	.	.	.	.	.	.	.
	Feces, Soft, Severity Not Applicable	.	.	.	.	.	.	.
2016	Skin, Lesion, Hindlimb, Right, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	X	X	.
	Feces, Absent	.	.	.	.	.	.	.
2017	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	X	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	X	.	.
2018	Fur, Staining, Black, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Brown, Muzzle	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	X	X	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	X
2020	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	X	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	X	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		77 DE	84 DE	86 CSO	90 DE	91 DE	98 DE	100 CSO
2020	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	X	X	.
	Fur, Staining, Yellow, Tail	X	X	.	.	X	X	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		105 DE	112 DE	119 DE	120 DE	126 DE	133 DE	140 DE
2002	Penis, Protruding	.	.	.	.	.	.	.
2003	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
2006	Skin, Dry, Pinna, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
2008	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
2010	Feces, Absent	.	.	.	.	.	.	.
2011	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	X	X	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	X	X	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
2012	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
2014	Fur, Staining, Brown, Muzzle	X	X	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
2015	Fur, Staining, Yellow, Cranium	X	X	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	X	X	X	X	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	X	X	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	X	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	X	X	X	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		105 DE	112 DE	119 DE	120 DE	126 DE	133 DE	140 DE
2015	Fur, Staining, Yellow, Lower Jaw	X	X	X	.	.	.	.
	Fur, Staining, Yellow, Pinna, Right	X	X	.	.	.	.	.
	Fur, Staining, Yellow, Tail	X	X	X	X	.	.	.
	Fur, Staining, Yellow, Ventral Cervical	X	X	X	X	.	.	.
	Fur, Wet, Lower Jaw	.	.	.	.	.	.	.
	Feces, Absent	.	.	.	.	.	.	.
	Feces, Soft, Slight	.	.	.	.	.	.	.
	Feces, Soft, Severity Not Applicable	.	.	.	.	.	.	.
2016	Skin, Lesion, Hindlimb, Right, Slight	.	X	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Feces, Absent	.	.	.	.	.	.	.
2017	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2018	Fur, Staining, Black, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Brown, Muzzle	.	X	X	.	X	X	X
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
2020	Fur, Staining, Yellow, Forepaw, Left	X	X	X	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	X	X	X	.	.	.	.

X=Present

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		105 DE	112 DE	119 DE	120 DE	126 DE	133 DE	140 DE
2020	Fur, Staining, Yellow, Hindpaw, Left	X	X	X	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	X	X	.	.	.	.
	Fur, Staining, Yellow, Tail	X	X	X	.	.	X	X

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		147 DE	154 DE	161 DE	168 DE	175 DE	180 DE	
2002	Penis, Protruding	.	.	.	.	.	.	
2003	Fur, Staining, Brown, Tail	.	.	.	.	.	.	
2006	Skin, Dry, Pinna, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	
2008	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	
2010	Feces, Absent	.	.	.	.	.	.	
2011	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	
2012	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	
2014	Fur, Staining, Brown, Muzzle	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forelimb, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forelimb, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	
2015	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	

Sponsor Reference No (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		147 DE	154 DE	161 DE	168 DE	175 DE	180 DE	
2015	Fur, Staining, Yellow, Lower Jaw	.	.	.	.	.	.	
	Fur, Staining, Yellow, Pinna, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	
	Fur, Staining, Yellow, Ventral Cervical	.	.	.	.	.	.	
	Fur, Wet, Lower Jaw	.	.	.	.	.	.	
	Feces, Absent	.	.	.	.	.	.	
	Feces, Soft, Slight	.	.	.	.	.	.	
	Feces, Soft, Severity Not Applicable	.	.	.	.	.	.	
2016	Skin, Lesion, Hindlimb, Right, Slight	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Feces, Absent	.	.	.	.	.	.	
2017	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
2018	Fur, Staining, Black, Forepaw, Right	.	.	.	.	.	.	
	Fur, Staining, Brown, Muzzle	X	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	
2020	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	

X=Present

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		147 DE	154 DE	161 DE	168 DE	175 DE	180 DE	
2020	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	X	X	X	X	X	X	

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-8 DE	-1 DE	2 Cp2	7 DE	14 DE	28 DE	35 DE
3002	Feces, Absent	.	.	X	.	.	.	.
3004	Feces, Absent	.	.	X	.	.	.	.
3005	Fur, Thin Cover, Dorsal Cervical	X	.	.	.	.	.	.
3006	Feces, Absent	.	.	X	.	.	.	.
3008	Fur, Wet, Lower Jaw	.	.	.	.	X	.	.
3009	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
3010	Skin, Scab, Upper Lip	.	.	.	.	X	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
3011	Broken Toe Nail, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Feces, Output Decreased, Severity Not Applicable	.	.	.	.	.	.	.
3012	Fur, Thin Cover, Abdominal	.	.	.	.	.	.	.
	Fur, Thin Cover, Urogenital	.	.	.	.	.	.	.
3013	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
3014	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3015	Fur, Staining, Brown, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Brown, Pinna, Right	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		-8 DE	-1 DE	2 Cp2	7 DE	14 DE	28 DE	35 DE
3015	Fur, Staining, Yellow, Cranium	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
3016	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Pinna, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
3018	Fur, Staining, Yellow, Lower Jaw	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Ventral Cervical	.	.	.	.	.	.	.
3019	Skin, Scab, Dorsal Cervical	.	X	.	X	X	.	.
	Skin, Scab, Pinna, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
	Fur, Thin Cover, Dorsal Cervical	.	X	.	X	X	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3020	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		42 DE	49 DE	56 DE	63 DE	70 DE	77 DE	84 DE
3002	Feces, Absent	.	.	.	.	.	.	.
3004	Feces, Absent	.	.	.	.	.	.	.
3005	Fur, Thin Cover, Dorsal Cervical	.	.	.	.	.	.	.
3006	Feces, Absent	.	.	.	.	.	.	.
3008	Fur, Wet, Lower Jaw	.	.	.	.	.	.	.
3009	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	X	X
3010	Skin, Scab, Upper Lip	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	X
3011	Broken Toe Nail, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Feces, Output Decreased, Severity Not Applicable	.	.	.	.	.	.	.
3012	Fur, Thin Cover, Abdominal	.	.	.	X	X	X	X
	Fur, Thin Cover, Urogenital	.	.	.	.	.	.	.
3013	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
3014	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	X	X
3015	Fur, Staining, Brown, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Brown, Pinna, Right	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		42 DE	49 DE	56 DE	63 DE	70 DE	77 DE	84 DE
3015	Fur, Staining, Yellow, Cranium	X	X	X	X	.	X	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	X	X
3016	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Pinna, Right	.	.	.	.	.	X	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	X	.
3018	Fur, Staining, Yellow, Lower Jaw	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Ventral Cervical	.	.	.	.	.	.	.
3019	Skin, Scab, Dorsal Cervical	.	.	.	.	.	.	.
	Skin, Scab, Pinna, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
	Fur, Thin Cover, Dorsal Cervical	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3020	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		86 CSO	90 DE	91 DE	98 DE	100 CSO	105 DE	107 CSO
3002	Feces, Absent	.	.	.	.	.	.	.
3004	Feces, Absent	.	.	.	.	.	.	.
3005	Fur, Thin Cover, Dorsal Cervical	.	.	.	.	.	.	.
3006	Feces, Absent	X	.	.	.	.	.	.
3008	Fur, Wet, Lower Jaw	.	.	.	.	.	.	.
3009	Fur, Staining, Yellow, Hindpaw, Left	.	X	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	X	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	X	.	.	.	.	.
3010	Skin, Scab, Upper Lip	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	X	.	.	.	.	.
3011	Broken Toe Nail, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	X	X	.	.	.
	Fur, Staining, Yellow, Tail	.	.	X	X	.	.	.
	Feces, Output Decreased, Severity Not Applicable	.	.	.	.	.	.	X
3012	Fur, Thin Cover, Abdominal	.	.	X	X	.	X	.
	Fur, Thin Cover, Urogenital	.	.	.	.	.	X	.
3013	Fur, Staining, Yellow, Hindpaw, Left	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	X	.	.	.	.
3014	Fur, Staining, Yellow, Hindpaw, Left	.	.	X	X	.	X	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	X	X	.	X	.
3015	Fur, Staining, Brown, Cranium	.	.	X	X	.	X	.
	Fur, Staining, Brown, Pinna, Right	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		86 CSO	90 DE	91 DE	98 DE	100 CSO	105 DE	107 CSO
3015	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	X	X	.	X	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	X	X	.	X	.
	Fur, Staining, Yellow, Tail	.	.	X	X	.	X	.
3016	Fur, Staining, Yellow, Hindpaw, Left	.	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	X	X	.	.	.
	Fur, Staining, Yellow, Pinna, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	X	X	.	.	.
3018	Fur, Staining, Yellow, Lower Jaw	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Ventral Cervical	.	.	X	.	.	.	.
3019	Skin, Scab, Dorsal Cervical	.	.	.	.	.	.	.
	Skin, Scab, Pinna, Left	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	X	X	.	.	.
	Fur, Staining, Yellow, Tail	.	.	X	X	.	X	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
	Fur, Thin Cover, Dorsal Cervical	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	X	.	.
3020	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	X	.	X

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		112 DE	119 DE	120 DE	147 DE	154 DE	161 DE	
3002	Feces, Absent	.	.	.	.	.	.	
3004	Feces, Absent	.	.	.	.	.	.	
3005	Fur, Thin Cover, Dorsal Cervical	.	.	.	.	.	.	
3006	Feces, Absent	.	.	.	.	.	.	
3008	Fur, Wet, Lower Jaw	.	.	.	.	.	.	
3009	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	
3010	Skin, Scab, Upper Lip	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	
3011	Broken Toe Nail, Hindpaw, Left	.	.	X	.	.	.	
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	
	Feces, Output Decreased, Severity Not Applicable	.	.	.	.	.	.	
3012	Fur, Thin Cover, Abdominal	X	X	X	.	.	.	
	Fur, Thin Cover, Urogenital	X	X	X	.	.	.	
3013	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	
3014	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
3015	Fur, Staining, Brown, Cranium	.	.	.	.	.	.	
	Fur, Staining, Brown, Pinna, Right	.	.	X	.	.	.	

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date						
		112 DE	119 DE	120 DE	147 DE	154 DE	161 DE	
3015	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	X	.	.	.	.	.	
3016	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Pinna, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	.	.	.	X	X	X	
3018	Fur, Staining, Yellow, Lower Jaw	.	.	.	.	.	.	
	Fur, Staining, Yellow, Ventral Cervical	.	.	.	.	.	.	
3019	Skin, Scab, Dorsal Cervical	.	.	.	.	.	.	
	Skin, Scab, Pinna, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	X	X	.	X	.	.	
	Fur, Staining, Yellow, Urogenital	.	.	.	X	.	.	
	Fur, Thin Cover, Dorsal Cervical	.	.	.	.	.	.	
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	
3020	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		-8 DE	-1 DE	7 DE	11 DE	21 DE	28 DE	35 DE
1502	Skin, Red, Hindlimb, Right	.	.	.	X	.	.	.
	Fur, Staining, Brown, Muzzle	X	X	.	.	.	.	.
1503	Skin, Red, Hindlimb, Right	.	X	.	X	.	.	.
	Skin, Dry, Hindlimb, Right	.	.	X	X	.	.	.
1504	Fur, Staining, Brown, Tail	X	.	.	.	.	.	.
1507	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	X	X
1508	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Muzzle	.	.	.	.	.	.	.
1509	Broken Toe Nail, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Red, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
1510	Activity Decreased	.	.	.	.	.	.	.
	Reduced Appetite	.	.	.	.	.	.	.
	Broken Toe Nail, Digit Forepaw, Right	.	.	.	.	.	.	.
	Broken Toe Nail, Digit Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Feces, Output Decreased, Severity Not Applicable	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
1511	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Pinna, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Pinna, Right	.	.	.	.	.	.	.
1512	Skin, Red, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Black, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Black, Hindlimb, Right	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		-8 DE	-1 DE	7 DE	11 DE	21 DE	28 DE	35 DE
1512	Fur, Staining, Black, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	X	X	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	X	X	X
	Fur, Staining, Yellow, Muzzle	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		42 DE	49 DE	56 DE	63 DE	70 DE	71 Unsc	72 CSO
1502	Skin, Red, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Brown, Muzzle	.	.	.	.	.	.	.
1503	Skin, Red, Hindlimb, Right	.	.	.	.	.	.	.
	Skin, Dry, Hindlimb, Right	.	.	.	.	.	.	.
1504	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
1507	Fur, Staining, Yellow, Forepaw, Left	X	X	X	X	X	.	.
	Fur, Staining, Yellow, Forepaw, Right	X	X	X	X	X	.	.
1508	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Muzzle	.	.	.	.	.	.	.
1509	Broken Toe Nail, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Red, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
1510	Activity Decreased	.	.	.	.	.	X	.
	Reduced Appetite	.	.	.	.	.	X	X
	Broken Toe Nail, Digit Forepaw, Right	.	.	.	.	.	.	.
	Broken Toe Nail, Digit Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Feces, Output Decreased, Severity Not Applicable	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
1511	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Pinna, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Pinna, Right	.	.	.	.	.	.	.
1512	Skin, Red, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Black, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Black, Hindlimb, Right	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		42 DE	49 DE	56 DE	63 DE	70 DE	71 Unsc	72 CSO
1512	Fur, Staining, Black, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	X	X	X	.	.	.
	Fur, Staining, Yellow, Muzzle	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		73 AM_S	77 DE	84 DE	96 Unsc	133 DE	140 DE	147 DE
1502	Skin, Red, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Brown, Muzzle	.	.	.	.	.	.	.
1503	Skin, Red, Hindlimb, Right	.	.	.	.	.	.	.
	Skin, Dry, Hindlimb, Right	.	.	.	.	.	.	.
1504	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
1507	Fur, Staining, Yellow, Forepaw, Left	.	X	X	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	X	X	.	.	.	.
1508	Fur, Staining, Yellow, Forepaw, Left	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Muzzle	.	.	X	.	.	.	.
1509	Broken Toe Nail, Hindpaw, Right	.	.	.	X	.	.	.
	Fur, Staining, Red, Hindpaw, Right	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Tail	.	.	X	.	.	.	.
1510	Activity Decreased	.	X	.	.	.	.	.
	Reduced Appetite	X	.	.	.	.	.	.
	Broken Toe Nail, Digit Forepaw, Right	.	.	.	.	.	.	.
	Broken Toe Nail, Digit Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	X	X	X
	Feces, Output Decreased, Severity Not Applicable	X	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	X	.	.	.	.	.	.
1511	Fur, Staining, Yellow, Cranium	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Pinna, Left	.	.	.	.	X	.	.
	Fur, Staining, Yellow, Pinna, Right	.	.	.	.	.	.	.
1512	Skin, Red, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Black, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Black, Hindlimb, Right	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		73 AM_S	77 DE	84 DE	96 Unsc	133 DE	140 DE	147 DE
1512	Fur, Staining, Black, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Muzzle	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	X	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		152 Unsc	154 DE	161 DE	163 CSO	168 DE	170 CSO	175 DE
1502	Skin, Red, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Brown, Muzzle	.	.	.	.	.	.	.
1503	Skin, Red, Hindlimb, Right	.	.	.	.	.	.	.
	Skin, Dry, Hindlimb, Right	.	.	.	.	.	.	.
1504	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
1507	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
1508	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Muzzle	.	.	.	.	.	.	.
1509	Broken Toe Nail, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Red, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
1510	Activity Decreased	.	.	.	.	.	.	.
	Reduced Appetite	.	.	.	X	.	X	.
	Broken Toe Nail, Digit Forepaw, Right	X	X	.	.	.	.	.
	Broken Toe Nail, Digit Hindpaw, Left	X	X	.	.	.	.	.
	Fur, Staining, Yellow, Tail	X	X	X	.	X	.	X
	Feces, Output Decreased, Severity Not Applicable	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
1511	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Pinna, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Pinna, Right	.	.	X	.	X	.	X
1512	Skin, Red, Hindlimb, Right	.	.	.	.	.	.	X
	Fur, Staining, Black, Hindlimb, Left	.	.	X	.	.	.	.
	Fur, Staining, Black, Hindlimb, Right	.	.	X	.	.	.	.

X=Present

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		152 Unsc	154 DE	161 DE	163 CSO	168 DE	170 CSO	175 DE
1512	Fur, Staining, Black, Tail	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Muzzle	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	X	.	X
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date 180 DE						
1502	Skin, Red, Hindlimb, Right	.						
	Fur, Staining, Brown, Muzzle	.						
1503	Skin, Red, Hindlimb, Right	.						
	Skin, Dry, Hindlimb, Right	.						
1504	Fur, Staining, Brown, Tail	.						
1507	Fur, Staining, Yellow, Forepaw, Left	.						
	Fur, Staining, Yellow, Forepaw, Right	.						
1508	Fur, Staining, Yellow, Forepaw, Left	.						
	Fur, Staining, Yellow, Forepaw, Right	.						
	Fur, Staining, Yellow, Muzzle	.						
1509	Broken Toe Nail, Hindpaw, Right	.						
	Fur, Staining, Red, Hindpaw, Right	.						
	Fur, Staining, Yellow, Tail	.						
1510	Activity Decreased	.						
	Reduced Appetite	.						
	Broken Toe Nail, Digit Forepaw, Right	.						
	Broken Toe Nail, Digit Hindpaw, Left	.						
	Fur, Staining, Yellow, Tail	X						
	Feces, Output Decreased, Severity Not Applicable	.						
	Feces, Size Reduced, Severity Not Applicable	.						
1511	Fur, Staining, Yellow, Cranium	.						
	Fur, Staining, Yellow, Pinna, Left	.						
	Fur, Staining, Yellow, Pinna, Right	X						
1512	Skin, Red, Hindlimb, Right	.						
	Fur, Staining, Black, Hindlimb, Left	.						
	Fur, Staining, Black, Hindlimb, Right	.						

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

0 Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		180 DE						
1512	Fur, Staining, Black, Tail	.						
	Fur, Staining, Yellow, Forepaw, Left	.						
	Fur, Staining, Yellow, Forepaw, Right	.						
	Fur, Staining, Yellow, Hindpaw, Left	.						
	Fur, Staining, Yellow, Hindpaw, Right	.						
	Fur, Staining, Yellow, Muzzle	.						
	Fur, Staining, Yellow, Tail	X						
	Fur, Staining, Yellow, Urogenital	.						

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		-8 DE	-5 Unsc	-1 DE	7 DE	14 DE	21 DE	28 DE
2506	Feces, Liquid, Slight	.	X	.	.	.	.	.
	Feces, Soft, Slight	.	X	.	.	.	.	.
2508	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
2511	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2512	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	X	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	X	.
2513	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2514	Fur, Loss, Slight	.	.	.	.	.	.	X
2515	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
2516	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Brown, Urogenital	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	X	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
2518	Fur, Loss, Slight	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		-8 DE	-5 Unsc	-1 DE	7 DE	14 DE	21 DE	28 DE
2519	Reduced Appetite	.	.	.	.	.	.	.
	Fur, Staining, Brown, Abdominal	X	.	.	.	.	.	.
	Fur, Staining, Brown, Tail	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
2520	Fur, Staining, Yellow, Cranium	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Muzzle	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Thin Cover, Dorsal Cervical	X	.	X	X	X	X	X

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		35 DE	42 DE	49 DE	56 DE	63 DE	70 DE	77 DE
2506	Feces, Liquid, Slight	.	.	.	.	.	.	.
	Feces, Soft, Slight	.	.	.	.	.	.	.
2508	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
2511	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2512	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2513	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2514	Fur, Loss, Slight	.	.	.	.	.	.	.
2515	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
2516	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Brown, Urogenital	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	X	X	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	X	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
2518	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		35 DE	42 DE	49 DE	56 DE	63 DE	70 DE	77 DE
2519	Reduced Appetite	.	.	.	.	.	.	.
	Fur, Staining, Brown, Abdominal	.	.	.	.	.	.	.
	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	X	X	X	X	X	X
	Fur, Staining, Yellow, Hindpaw, Right	X	X	X	X	X	X	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
2520	Fur, Staining, Yellow, Cranium	X	X	X	X	X	X	X
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Muzzle	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Thin Cover, Dorsal Cervical	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		84 DE	90 DE	91 DE	98 DE	105 DE	112 DE	119 DE
2506	Feces, Liquid, Slight	.	.	.	.	.	.	.
	Feces, Soft, Slight	.	.	.	.	.	.	.
2508	Fur, Staining, Brown, Tail	X	X	.	.	.	.	.
2511	Fur, Staining, Yellow, Forepaw, Left	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	.	X	X	.	.	.
2512	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2513	Fur, Staining, Yellow, Hindpaw, Left	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	.	.	.	.	.	.
2514	Fur, Loss, Slight	.	.	.	.	.	.	.
2515	Fur, Staining, Yellow, Cranium	X	.	.	.	.	.	.
2516	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Brown, Urogenital	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
2518	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		84 DE	90 DE	91 DE	98 DE	105 DE	112 DE	119 DE
2519	Reduced Appetite	.	.	.	.	.	.	.
	Fur, Staining, Brown, Abdominal	.	.	.	.	.	.	.
	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	X	.	X	X	X	X	X
	Fur, Staining, Yellow, Forepaw, Right	X	.	X	X	X	X	X
	Fur, Staining, Yellow, Hindpaw, Left	X	.	X	X	X	X	X
	Fur, Staining, Yellow, Hindpaw, Right	X	.	X	X	X	X	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
2520	Fur, Staining, Yellow, Cranium	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Muzzle	X	.	X	X	X	X	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Thin Cover, Dorsal Cervical	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		126 DE	133 DE	140 DE	147 DE	149 CSO	154 DE	156 CSO
2506	Feces, Liquid, Slight	.	.	.	.	.	.	.
	Feces, Soft, Slight	.	.	.	.	.	.	.
2508	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
2511	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2512	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2513	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
2514	Fur, Loss, Slight	.	.	.	.	.	.	.
2515	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
2516	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Brown, Urogenital	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	X	X	X	.	X	.
	Fur, Staining, Yellow, Urogenital	.	X	.	.	.	.	.
2518	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	X	X	X	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		126 DE	133 DE	140 DE	147 DE	149 CSO	154 DE	156 CSO
2519	Reduced Appetite	.	.	.	.	X	.	X
	Fur, Staining, Brown, Abdominal	.	.	.	.	.	.	.
	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	X	X	X	X	.	X	.
	Fur, Staining, Yellow, Forepaw, Right	X	X	X	X	.	X	.
	Fur, Staining, Yellow, Hindpaw, Left	X	X	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	X	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
2520	Fur, Staining, Yellow, Cranium	.	X	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Muzzle	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	X	.
	Fur, Thin Cover, Dorsal Cervical	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		161 DE	163 CSO	168 DE	170 CSO	175 DE	180 DE	
2506	Feces, Liquid, Slight	.	.	.	.	.	.	
	Feces, Soft, Slight	.	.	.	.	.	.	
2508	Fur, Staining, Brown, Tail	.	.	.	.	.	.	
2511	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
2512	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
2513	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
2514	Fur, Loss, Slight	.	.	.	.	.	.	
2515	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	
2516	Fur, Staining, Brown, Tail	.	.	.	.	X	X	
	Fur, Staining, Brown, Urogenital	.	.	.	.	X	X	
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	X	.	X	.	.	.	
	Fur, Staining, Yellow, Urogenital	X	.	.	.	.	.	
2518	Fur, Loss, Slight	.	.	.	.	.	.	
	Fur, Staining, Yellow, Cranium	.	.	X	.	.	.	
	Fur, Staining, Yellow, Tail	X	.	X	.	X	X	
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		161 DE	163 CSO	168 DE	170 CSO	175 DE	180 DE	
2519	Reduced Appetite	.	X	.	X	.	.	
	Fur, Staining, Brown, Abdominal	.	.	.	.	.	.	
	Fur, Staining, Brown, Tail	.	.	X	.	X	X	
	Fur, Staining, Yellow, Forepaw, Left	.	.	X	.	X	X	
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	X	X	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	X	.	X	.	X	X	
2520	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindlimb, Right	X	.	X	.	X	.	
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	
	Fur, Staining, Yellow, Muzzle	.	.	.	.	.	.	
	Fur, Staining, Yellow, Tail	X	.	X	.	X	X	
	Fur, Thin Cover, Dorsal Cervical	.	.	.	.	.	.	

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		-14 Unsc	-8 DE	-1 DE	1 Cp1	2 Cp2	3 CSO	4 CSO
3506	Skin, Scab, Hindlimb, Right	.	.	X	.	.	.	.
3507	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Interscapular	.	.	.	.	.	.	.
3508	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3509	Skin, Lesion, Ventral Cervical, Slight	.	.	.	.	.	.	.
	Skin, Scab, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Cervical	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	X	X	X	X
3513	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3514	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		-14 Unsc	-8 DE	-1 DE	1 Cp1	2 Cp2	3 CSO	4 CSO
3515	Broken Toe Nail, Hindpaw, Left	X	X	X	.	.	.	.
	Skin, Scab, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3516	Skin, Scab, Hindlimb, Right	.	.	X	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3517	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Thin Cover, Pinna, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3518	Skin, Red, Ventral Cervical	.	.	.	.	.	.	.
	Skin, Dry, Ventral Cervical	.	.	.	.	.	.	.
	Skin, Lesion, Ventral Cervical, Moderate	.	.	.	.	.	.	.
	Skin, Lesion, Ventral Cervical, Severe	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		-14 Unsc	-8 DE	-1 DE	1 Cp1	2 Cp2	3 CSO	4 CSO
3518	Skin, Scab, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Axillary, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Thoracic	.	.	.	.	.	.	.
3519	Reduced Appetite	.	.	.	.	.	.	.
	Fur, Staining, Brown, Anus	.	.	.	.	.	.	.
	Fur, Staining, Brown, Urogenital	.	X	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3520	Other (see comment)	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		-14 Unsc	-8 DE	-1 DE	1 Cp1	2 Cp2	3 CSO	4 CSO
3520	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		5 CSO	6 CSO	7 DE	7 CSO	14 DE	21 DE	28 DE
3506	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
3507	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Interscapular	.	.	X	.	X	.	.
3508	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3509	Skin, Lesion, Ventral Cervical, Slight	.	.	.	.	.	.	.
	Skin, Scab, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Cervical	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	X	X	.	X	.	.	.
3513	Fur, Loss, Slight	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3514	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		5 CSO	6 CSO	7 DE	7 CSO	14 DE	21 DE	28 DE
3515	Broken Toe Nail, Hindpaw, Left	.	.	X	.	.	.	.
	Skin, Scab, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	X	X
3516	Skin, Scab, Hindlimb, Right	.	.	X	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	X	X
3517	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Thin Cover, Pinna, Right	.	.	.	.	.	.	X
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3518	Skin, Red, Ventral Cervical	.	.	.	.	.	.	.
	Skin, Dry, Ventral Cervical	.	.	.	.	.	.	.
	Skin, Lesion, Ventral Cervical, Moderate	.	.	.	.	.	.	.
	Skin, Lesion, Ventral Cervical, Severe	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		5 CSO	6 CSO	7 DE	7 CSO	14 DE	21 DE	28 DE
3518	Skin, Scab, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	X
	Fur, Thin Cover, Axillary, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Thoracic	.	.	.	.	.	.	.
3519	Reduced Appetite	.	.	.	.	.	.	.
	Fur, Staining, Brown, Anus	.	.	.	.	.	.	X
	Fur, Staining, Brown, Urogenital	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3520	Other (see comment)	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		5 CSO	6 CSO	7 DE	7 CSO	14 DE	21 DE	28 DE
3520	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		35 DE	42 DE	49 DE	56 DE	56 Unsc	57 Unsc	63 DE
3506	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
3507	Fur, Staining, Yellow, Forepaw, Left	X	X	X	X	.	.	X
	Fur, Staining, Yellow, Forepaw, Right	X	X	X	X	.	.	X
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Interscapular	.	.	.	.	.	.	.
3508	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3509	Skin, Lesion, Ventral Cervical, Slight	.	.	.	.	.	X	.
	Skin, Scab, Ventral Cervical	.	.	.	.	.	.	X
	Fur, Thin Cover, Ventral Cervical	.	.	.	.	.	X	X
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3513	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3514	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		35 DE	42 DE	49 DE	56 DE	56 Unsc	57 Unsc	63 DE
3515	Broken Toe Nail, Hindpaw, Left	.	.	.	.	.	.	.
	Skin, Scab, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	X	X	X	.	.	X
	Fur, Staining, Yellow, Hindpaw, Right	X	X	X	X	.	.	X
3516	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	X	X	X	.	.	X
	Fur, Staining, Yellow, Hindpaw, Right	X	X	X	X	.	.	X
3517	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	X	X	.	.	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	X	X	.	.	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Thin Cover, Pinna, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3518	Skin, Red, Ventral Cervical	.	.	.	.	.	.	.
	Skin, Dry, Ventral Cervical	.	.	.	.	.	.	.
	Skin, Lesion, Ventral Cervical, Moderate	.	.	.	.	.	.	X
	Skin, Lesion, Ventral Cervical, Severe	.	.	.	X	X	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		35 DE	42 DE	49 DE	56 DE	56 Unsc	57 Unsc	63 DE
3518	Skin, Scab, Ventral Cervical	.	.	.	.	.	.	X
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	X	.	.	X
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	X	.	.	X
	Fur, Staining, Yellow, Hindpaw, Left	X	X	X	X	X	.	X
	Fur, Staining, Yellow, Hindpaw, Right	X	X	X	X	X	.	X
	Fur, Thin Cover, Axillary, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Cervical	.	.	.	X	X	.	X
	Fur, Thin Cover, Ventral Thoracic	.	.	.	.	.	.	.
3519	Reduced Appetite	.	.	.	.	.	.	.
	Fur, Staining, Brown, Anus	X	X	.	.	.	.	.
	Fur, Staining, Brown, Urogenital	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	X	X	.	.	X
	Fur, Staining, Yellow, Hindpaw, Left	.	.	X	X	.	.	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	X	X	.	.	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3520	Other (see comment)	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		35 DE	42 DE	49 DE	56 DE	56 Unsc	57 Unsc	63 DE
3520	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		70 DE	73 Unsc	77 DE	84 DE	105 DE	112 DE	119 DE
3506	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
3507	Fur, Staining, Yellow, Forepaw, Left	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	X	.	.	.
	Fur, Thin Cover, Interscapular	.	.	.	.	.	.	.
3508	Fur, Staining, Yellow, Forepaw, Left	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	X	.	.	.
3509	Skin, Lesion, Ventral Cervical, Slight	.	.	.	.	.	.	.
	Skin, Scab, Ventral Cervical	X	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Cervical	X	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3513	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	X	.	.	.
3514	Fur, Staining, Yellow, Forepaw, Left	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	X	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		70 DE	73 Unsc	77 DE	84 DE	105 DE	112 DE	119 DE
3515	Broken Toe Nail, Hindpaw, Left	.	.	.	.	.	.	.
	Skin, Scab, Hindlimb, Left	.	.	.	.	.	X	X
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	X	.	.	X
	Fur, Staining, Yellow, Hindpaw, Left	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	.	X	X	.	.	.
3516	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Cranium	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	.	.	.	.	.	.
3517	Fur, Staining, Brown, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	X	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	.	X	X	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	X	.	.	X
	Fur, Thin Cover, Pinna, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3518	Skin, Red, Ventral Cervical	.	.	.	X	.	.	.
	Skin, Dry, Ventral Cervical	.	.	.	.	.	.	.
	Skin, Lesion, Ventral Cervical, Moderate	.	X	X	.	.	.	.
	Skin, Lesion, Ventral Cervical, Severe	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		70 DE	73 Unsc	77 DE	84 DE	105 DE	112 DE	119 DE
3518	Skin, Scab, Ventral Cervical	X	X	X	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	X	.	.	.	.	.	.
	Fur, Thin Cover, Axillary, Left	.	.	.	.	X	X	X
	Fur, Thin Cover, Ventral Cervical	X	X	X	X	.	.	.
	Fur, Thin Cover, Ventral Thoracic	.	.	.	.	.	.	X
3519	Reduced Appetite	.	.	.	.	.	.	.
	Fur, Staining, Brown, Anus	.	.	.	.	.	.	.
	Fur, Staining, Brown, Urogenital	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	X	.	X	X
	Fur, Staining, Yellow, Forepaw, Right	X	.	.	X	.	X	X
	Fur, Staining, Yellow, Hindpaw, Left	X	.	.	X	.	X	X
	Fur, Staining, Yellow, Hindpaw, Right	X	.	.	X	.	X	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3520	Other (see comment)	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		70 DE	73 Unsc	77 DE	84 DE	105 DE	112 DE	119 DE
3520	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		120 DE	126 DE	133 DE	140 DE	142 CSO	147 DE	154 DE
3506	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
3507	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Interscapular	.	.	.	.	.	.	.
3508	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3509	Skin, Lesion, Ventral Cervical, Slight	.	.	.	.	.	.	.
	Skin, Scab, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Cervical	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3513	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3514	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		120 DE	126 DE	133 DE	140 DE	142 CSO	147 DE	154 DE
3515	Broken Toe Nail, Hindpaw, Left	.	.	.	.	.	.	.
	Skin, Scab, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	X	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3516	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Cranium	.	.	X	X	.	X	X
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3517	Fur, Staining, Brown, Tail	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	X	X	X	.	X	X
	Fur, Thin Cover, Pinna, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	X	.	.
3518	Skin, Red, Ventral Cervical	.	.	.	.	.	.	.
	Skin, Dry, Ventral Cervical	.	.	.	.	.	.	.
	Skin, Lesion, Ventral Cervical, Moderate	.	.	.	.	.	.	.
	Skin, Lesion, Ventral Cervical, Severe	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		120 DE	126 DE	133 DE	140 DE	142 CSO	147 DE	154 DE
3518	Skin, Scab, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Axillary, Left	.	X	X	X	.	X	X
	Fur, Thin Cover, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Thoracic	.	X	X	X	.	X	X
3519	Reduced Appetite	.	.	.	.	.	.	.
	Fur, Staining, Brown, Anus	.	.	.	.	.	.	.
	Fur, Staining, Brown, Urogenital	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	X	X	X	.	X	X
	Fur, Staining, Yellow, Forepaw, Right	.	X	X	X	.	X	X
	Fur, Staining, Yellow, Hindpaw, Left	.	X	X	X	.	X	X
	Fur, Staining, Yellow, Hindpaw, Right	.	X	X	X	.	X	X
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	X
	Fur, Staining, Yellow, Urogenital	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	X	.	.
3520	Other (see comment)	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	X	X	.	.	.	.

X=Present

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		120 DE	126 DE	133 DE	140 DE	142 CSO	147 DE	154 DE
3520	Fur, Staining, Yellow, Hindpaw, Right	.	X	X	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	X	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		155 AM_S	156 CSO	161 DE	163 CSO	168 DE	170 CSO	175 DE
3506	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
3507	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Interscapular	.	.	.	.	.	.	.
3508	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3509	Skin, Lesion, Ventral Cervical, Slight	.	.	.	.	.	.	.
	Skin, Scab, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Cervical	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3513	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3514	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	.	.	.	.	.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		155 AM_S	156 CSO	161 DE	163 CSO	168 DE	170 CSO	175 DE
3515	Broken Toe Nail, Hindpaw, Left	.	.	.	.	.	.	.
	Skin, Scab, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3516	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Cranium	.	.	X	.	X	.	X
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
3517	Fur, Staining, Brown, Tail	.	.	X	.	X	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindlimb, Left	.	.	.	.	X	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Tail	.	.	X	.	X	.	X
	Fur, Thin Cover, Pinna, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3518	Skin, Red, Ventral Cervical	.	.	X	.	.	.	.
	Skin, Dry, Ventral Cervical	.	.	X	.	.	.	.
	Skin, Lesion, Ventral Cervical, Moderate	.	.	.	.	.	.	.
	Skin, Lesion, Ventral Cervical, Severe	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		155 AM_S	156 CSO	161 DE	163 CSO	168 DE	170 CSO	175 DE
3518	Skin, Scab, Ventral Cervical	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Axillary, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Ventral Cervical	.	.	X	.	X	.	X
	Fur, Thin Cover, Ventral Thoracic	.	.	.	.	.	.	.
3519	Reduced Appetite	X	X	.	X	.	X	.
	Fur, Staining, Brown, Anus	.	.	.	.	.	.	.
	Fur, Staining, Brown, Urogenital	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Forelimb, Left	.	.	.	.	X	.	X
	Fur, Staining, Yellow, Forelimb, Right	.	.	.	.	X	.	X
	Fur, Staining, Yellow, Forepaw, Left	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Forepaw, Right	.	.	X	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	X	.	X	.	X
	Fur, Staining, Yellow, Hindpaw, Right	.	.	X	.	X	.	.
	Fur, Staining, Yellow, Tail	.	.	X	.	X	.	X
	Fur, Staining, Yellow, Urogenital	.	.	.	.	X	.	X
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.
3520	Other (see comment)	.	.	.	.	.	.	.
	Fur, Loss, Slight	.	.	.	.	.	.	.
	Fur, Staining, Yellow, Hindpaw, Left	.	.	.	.	.	.	.

X=Present

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		155 AM_S	156 CSO	161 DE	163 CSO	168 DE	170 CSO	175 DE
3520	Fur, Staining, Yellow, Hindpaw, Right	.	.	.	.	.	.	.
	Feces, Size Reduced, Severity Not Applicable	.	.	.	.	.	.	.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		176 PM_S	180 DE					
3506	Skin, Scab, Hindlimb, Right	.	.					
3507	Fur, Staining, Yellow, Forepaw, Left	.	.					
	Fur, Staining, Yellow, Forepaw, Right	.	.					
	Fur, Staining, Yellow, Hindpaw, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
	Fur, Thin Cover, Interscapular	.	.					
3508	Fur, Staining, Yellow, Forepaw, Left	.	.					
	Fur, Staining, Yellow, Forepaw, Right	.	.					
	Fur, Staining, Yellow, Hindpaw, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
3509	Skin, Lesion, Ventral Cervical, Slight	.	.					
	Skin, Scab, Ventral Cervical	.	.					
	Fur, Thin Cover, Ventral Cervical	.	.					
	Feces, Size Reduced, Severity Not Applicable	.	.					
3513	Fur, Loss, Slight	.	.					
	Fur, Staining, Yellow, Forepaw, Left	.	.					
	Fur, Staining, Yellow, Forepaw, Right	.	.					
	Fur, Staining, Yellow, Hindpaw, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
3514	Fur, Staining, Yellow, Forepaw, Left	.	.					
	Fur, Staining, Yellow, Forepaw, Right	.	.					
	Fur, Staining, Yellow, Hindpaw, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
	Fur, Staining, Yellow, Tail	.	.					

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		176 PM_S	180 DE					
3515	Broken Toe Nail, Hindpaw, Left	.	.					
	Skin, Scab, Hindlimb, Left	.	.					
	Fur, Staining, Yellow, Forepaw, Left	.	.					
	Fur, Staining, Yellow, Forepaw, Right	.	.					
	Fur, Staining, Yellow, Hindpaw, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
3516	Skin, Scab, Hindlimb, Right	.	.					
	Fur, Loss, Slight	.	.					
	Fur, Staining, Yellow, Cranium	.	X					
	Fur, Staining, Yellow, Hindpaw, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
3517	Fur, Staining, Brown, Tail	.	.					
	Fur, Staining, Yellow, Forepaw, Left	.	.					
	Fur, Staining, Yellow, Forepaw, Right	.	.					
	Fur, Staining, Yellow, Hindlimb, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
	Fur, Staining, Yellow, Tail	.	X					
	Fur, Thin Cover, Pinna, Right	.	.					
	Feces, Size Reduced, Severity Not Applicable	.	.					
3518	Skin, Red, Ventral Cervical	.	.					
	Skin, Dry, Ventral Cervical	.	.					
	Skin, Lesion, Ventral Cervical, Moderate	.	.					
	Skin, Lesion, Ventral Cervical, Severe	.	.					

X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		176 PM_S	180 DE					
3518	Skin, Scab, Ventral Cervical	.	.					
	Fur, Loss, Slight	.	.					
	Fur, Staining, Yellow, Forepaw, Left	.	.					
	Fur, Staining, Yellow, Forepaw, Right	.	.					
	Fur, Staining, Yellow, Hindpaw, Left	.	.					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
	Fur, Thin Cover, Axillary, Left	.	.					
	Fur, Thin Cover, Ventral Cervical	.	X					
	Fur, Thin Cover, Ventral Thoracic	.	.					
3519	Reduced Appetite	.	.					
	Fur, Staining, Brown, Anus	.	.					
	Fur, Staining, Brown, Urogenital	.	.					
	Fur, Staining, Yellow, Forelimb, Left	.	X					
	Fur, Staining, Yellow, Forelimb, Right	.	X					
	Fur, Staining, Yellow, Forepaw, Left	.	.					
	Fur, Staining, Yellow, Forepaw, Right	.	.					
	Fur, Staining, Yellow, Hindpaw, Left	.	X					
	Fur, Staining, Yellow, Hindpaw, Right	.	.					
	Fur, Staining, Yellow, Tail	.	X					
	Fur, Staining, Yellow, Urogenital	.	X					
	Feces, Size Reduced, Severity Not Applicable	.	.					
3520 !	Other (see comment)	X	.					
	Fur, Loss, Slight	.	.					
	Fur, Staining, Yellow, Hindpaw, Left	.	.					

!=Result comment recorded against 1 or more clinical observations. X=Present

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

1x10E11 vp+150 ug Group 3 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date						
		176 PM_S	180 DE					
3520 !	Fur, Staining, Yellow, Hindpaw, Right Feces, Size Reduced, Severity Not Applicable	. .	. .					

!=Result comment recorded against 1 or more clinical observations.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 3

Individual Clinical Observations

(b) (4)

Comment Information

Group	Sex	Animal	Day	Observation Type	Comment
3	Female	3520	176 (PM_S)	All Types	MODERATE FUR IN CAGE

Appendix 4

Individual Body Weights Explanation Page

Abbreviation	Description	Abbreviation	Description
--	Not scheduled to be performed / dead	TERR	Technical error
AVS	Suspected aberrant value	UPTD	Unable to perform due to technical difficulty
NT	Not taken	X	Excluded from mean
OA	Omitted activity		

Note: This is a comprehensive list of abbreviations. All of the abbreviations listed may not be applicable to this report.

Dosing Information

Dosing information is abbreviated on various data outputs; the following represents the dosing information for this study.

Group No.	Test Material	Dose Level
1	Reference Item	0
2	Ad26 (b) (4)	1×10^{11} vp
3	Ad26 (b) (4)	1×10^{11} vp + 150µg

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day -13	-8	1	2	3	4	7	11
1M	1001	2.8	2.8	2.9	2.9	2.9	2.9	2.9	3.0
	1002	2.8	2.8	2.9	2.9	2.9	2.9	2.9	3.0
	1003	2.9	2.9	2.9	3.0	2.9	2.9	3.0	3.0
	1004	2.8	2.8	2.9	2.9	2.9	2.9	2.9	--
	1005	3.0	3.0	3.0	3.1	3.1	3.0	3.1	--
	1006	2.7	2.6	2.6	2.7	2.7	2.7	2.7	--
	1007	2.8	2.8	2.9	2.9	2.9	2.9	2.9	--
	1008	2.7	2.8	2.8	2.9	2.9	2.8	2.9	--
	1009	2.9	3.0	3.1	3.1	3.1	3.1	3.1	--
	1010	2.7	2.7	2.8	2.8	3.1	2.8	2.8	--
	1011	2.6	2.6	2.6	2.6	2.8	2.6	2.7	--
	1012	2.9	2.9	2.9	2.9	3.0	3.0	3.0	--

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 14	21	28	35	42	49	56	63
1M	1001	--	--	--	--	--	--	--	--
	1002	--	--	--	--	--	--	--	--
	1003	--	--	--	--	--	--	--	--
	1004	2.9	3.0	3.0	3.0	3.0	3.0	3.0	3.0
	1005	3.1	3.2	3.2	3.2	3.3	3.3	3.2	3.3
	1006	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8
	1007	3.0	3.1	3.1	3.1	3.1	3.1	3.1	3.2
	1008	2.9	3.0	3.0	3.0	3.1	3.1	3.1	3.1
	1009	3.1	3.2	3.2	3.3	3.3	3.3	3.4	3.3
	1010	2.8	2.9	2.9	2.9	2.9	3.0	3.0	3.0
	1011	2.7	2.7	2.8	2.9	2.7	2.7	2.7	2.7
	1012	3.1	3.1	3.1	3.0	3.1	3.1	3.1	3.2

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 70	77	84	90	91	98	105	112
1M	1001	--	--	--	--	--	--	--	--
	1002	--	--	--	--	--	--	--	--
	1003	--	--	--	--	--	--	--	--
	1004	3.1	3.1	3.1	3.1	--	--	--	--
	1005	3.3	3.3	3.4	3.3	--	--	--	--
	1006	2.9	2.9	2.9	2.9	--	--	--	--
	1007	3.2	3.2	3.2	--	3.2	3.2	3.2	3.2
	1008	3.1	3.1	3.1	--	3.2	3.2	3.2	3.2
	1009	3.4	3.4	3.4	--	3.4	3.5	3.5	3.5
	1010	3.0	3.0	3.0	--	3.0	3.0	3.1	3.0
	1011	2.7	2.7	2.7	--	2.7	2.7	2.8	2.8
	1012	3.2	3.2	3.2	--	3.2	3.2	3.3	3.2

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 119	120	126	133	140	147	154	161
1M	1001	--	--	--	--	--	--	--	--
	1002	--	--	--	--	--	--	--	--
	1003	--	--	--	--	--	--	--	--
	1004	--	--	--	--	--	--	--	--
	1005	--	--	--	--	--	--	--	--
	1006	--	--	--	--	--	--	--	--
	1007	3.3	3.2	--	--	--	--	--	--
	1008	3.2	3.2	--	--	--	--	--	--
	1009	3.5	3.5	--	--	--	--	--	--
	1010	3.1	--	3.1	3.2	3.1	3.1	3.2	3.2
	1011	2.8	--	2.8	2.8	2.8	2.9	2.9	2.9
	1012	3.2	--	3.3	3.3	3.3	3.4	3.4	3.4

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 168	175	180
1M	1001	--	--	--
	1002	--	--	--
	1003	--	--	--
	1004	--	--	--
	1005	--	--	--
	1006	--	--	--
	1007	--	--	--
	1008	--	--	--
	1009	--	--	--
	1010	3.2	3.2	3.2
	1011	2.9	2.9	2.9
	1012	3.4	3.4	3.4

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day -13	-8	1	2	3	4	7	11
2M	2001	2.8	2.8	2.8	2.8	2.8	2.8	2.9	2.9
	2002	2.9	2.9	3.0	3.0	3.0	3.0	3.1	3.1
	2003	2.8	2.7	2.8	2.8	2.8	2.8	2.8	2.9
	2004	2.6	2.6	2.6	2.6	2.6	2.6	2.7	2.7
	2005	2.8	2.8	2.9	2.9	2.9	2.9	2.9	3.0
	2006	3.0	3.0	3.1	3.1	3.1	3.1	3.1	--
	2007	2.9	2.9	3.0	3.0	3.0	3.0	3.1	--
	2008	2.7	2.7	2.8	2.8	2.8	2.8	2.8	--
	2009	2.5	2.5	2.7	2.7	2.7	2.7	2.7	--
	2010	2.9	2.7	2.8	2.8	2.8	2.8	2.9	--
	2011	2.7	2.7	2.8	2.8	2.9	2.8	2.8	--
	2012	3.1	3.1	3.1	3.1	3.1	3.2	3.2	--
	2013	2.5	2.5	2.6	2.6	2.6	2.6	2.7	--
	2014	2.7	2.7	2.8	2.8	2.8	2.8	2.8	--
	2015	3.0	3.0	3.2	3.1	3.1	3.1	3.2	--
	2016	2.8	2.9	3.0	2.9	2.9	3.0	3.0	--
	2017	2.6	2.6	2.6	2.6	2.6	2.6	2.7	--
	2018	2.7	2.7	2.8	2.8	2.8	2.8	2.8	--
	2019	3.1	3.1	3.2	3.2	3.1	3.1	3.3	--
	2020	3.2	3.1	3.2	3.2	3.2	3.2	3.2	--

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 14	21	28	35	42	49	56	63
2M	2001	--	--	--	--	--	--	--	--
	2002	--	--	--	--	--	--	--	--
	2003	--	--	--	--	--	--	--	--
	2004	--	--	--	--	--	--	--	--
	2005	--	--	--	--	--	--	--	--
	2006	3.2	3.2	3.2	3.2	3.3	3.3	3.3	3.3
	2007	3.1	3.2	3.2	3.1	3.2	3.3	3.2	3.2
	2008	2.8	2.9	2.9	2.8	2.9	3.0	3.0	3.0
	2009	2.7	2.8	2.8	2.8	2.9	3.0	3.0	2.9
	2010	2.9	3.0	3.0	2.9	3.0	2.9	2.9	3.0
	2011	2.8	2.9	2.9	2.9	3.0	3.0	3.0	3.0
	2012	3.2	3.3	3.3	3.2	3.2	3.3	3.3	3.3
	2013	2.7	2.8	2.8	2.8	2.8	2.8	2.8	2.8
	2014	2.8	2.9	2.9	2.9	2.9	2.9	3.0	3.0
	2015	3.2	3.2	3.2	3.2	3.2	3.3	3.3	3.3
	2016	3.0	3.1	3.1	3.0	3.1	3.0	3.1	3.2
	2017	2.7	2.8	2.8	2.8	2.9	2.8	2.9	3.0
	2018	2.8	2.9	2.9	2.9	2.9	2.9	2.9	2.9
	2019	3.3	3.3	3.3	3.3	3.3	3.4	3.3	3.4
	2020	3.3	3.3	3.3	3.4	3.3	3.3	3.3	3.4

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 70	77	84	90	91	98	105	112
2M	2001	--	--	--	--	--	--	--	--
	2002	--	--	--	--	--	--	--	--
	2003	--	--	--	--	--	--	--	--
	2004	--	--	--	--	--	--	--	--
	2005	--	--	--	--	--	--	--	--
	2006	3.3	3.3	3.3	3.3	--	--	--	--
	2007	3.3	3.2	3.2	3.2	--	--	--	--
	2008	3.0	3.2	3.0	3.2	--	--	--	--
	2009	3.0	2.9	3.0	3.0	--	--	--	--
	2010	3.0	3.0	3.0	3.0	--	--	--	--
	2011	3.0	3.0	3.0	--	3.1	3.2	3.1	3.1
	2012	3.4	3.3	3.4	--	3.4	3.4	3.4	3.4
	2013	2.9	2.9	2.9	--	2.9	2.9	2.9	2.9
	2014	3.0	3.0	3.0	--	3.0	3.0	3.1	3.0
	2015	3.3	3.3	3.3	--	3.3	3.3	3.4	3.4
	2016	3.2	3.2	3.3	--	3.1	3.3	3.3	3.2
	2017	3.0	3.0	3.0	--	3.0	3.0	3.0	3.0
	2018	2.9	2.9	3.0	--	2.9	2.9	2.9	2.9
	2019	3.4	3.4	3.5	--	3.5	3.5	3.5	3.5
	2020	3.3	3.3	3.4	--	3.4	3.4	3.4	3.4

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 119	120	126	133	140	147	154	161
2M	2001	--	--	--	--	--	--	--	--
	2002	--	--	--	--	--	--	--	--
	2003	--	--	--	--	--	--	--	--
	2004	--	--	--	--	--	--	--	--
	2005	--	--	--	--	--	--	--	--
	2006	--	--	--	--	--	--	--	--
	2007	--	--	--	--	--	--	--	--
	2008	--	--	--	--	--	--	--	--
	2009	--	--	--	--	--	--	--	--
	2010	--	--	--	--	--	--	--	--
	2011	3.1	3.1	--	--	--	--	--	--
	2012	3.4	3.4	--	--	--	--	--	--
	2013	3.0	3.0	--	--	--	--	--	--
	2014	3.1	3.1	--	--	--	--	--	--
	2015	3.4	3.4	--	--	--	--	--	--
	2016	3.2	--	3.2	3.3	3.3	3.3	3.4	3.3
	2017	3.0	--	3.0	3.1	3.1	3.2	3.2	3.2
	2018	2.9	--	3.0	3.0	3.0	3.1	3.1	3.0
	2019	3.6	--	3.5	3.6	3.6	3.5	3.6	3.7
	2020	3.4	--	3.4	3.4	3.5	3.5	3.4	3.5

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 168	175	180
2M	2001	--	--	--
	2002	--	--	--
	2003	--	--	--
	2004	--	--	--
	2005	--	--	--
	2006	--	--	--
	2007	--	--	--
	2008	--	--	--
	2009	--	--	--
	2010	--	--	--
	2011	--	--	--
	2012	--	--	--
	2013	--	--	--
	2014	--	--	--
	2015	--	--	--
	2016	3.3	3.4	3.4
	2017	3.2	3.1	3.2
	2018	3.0	3.0	3.1
	2019	3.7	3.7	3.7
	2020	3.5	3.5	3.5

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day -13	-8	1	2	3	4	7	11
3M	3001	2.6	2.6	2.7	2.7	2.6	2.7	2.7	2.7
	3002	2.6	3.0	3.0	3.0	3.0	3.0	3.0	3.1
	3003	3.2	3.2	3.2	3.2	3.2	3.3	3.3	3.3
	3004	2.9	2.9	3.0	3.0	3.0	3.0	3.0	3.0
	3005	2.9	2.8	2.9	2.9	2.9	2.9	2.9	3.0
	3006	2.6	2.7	2.8	2.8	2.8	2.8	2.8	--
	3007	2.7	2.8	2.8	2.8	2.8	2.8	2.9	--
	3008	3.0	3.0	3.0	3.0	3.0	3.1	3.1	--
	3009	2.7	2.8	2.8	2.8	2.8	2.9	2.9	--
	3010	2.8	2.8	2.9	2.9	2.9	2.9	2.9	--
	3011	3.0	3.0	3.1	3.1	3.1	3.1	3.2	--
	3012	2.7	2.7	2.7	2.7	2.7	2.7	2.8	--
	3013	2.8	2.7	2.8	2.8	2.7	2.9	2.9	--
	3014	2.7	2.7	2.8	2.8	2.9	2.8	2.9	--
	3015	3.0	3.0	3.1	3.1	3.1	3.1	3.1	--
	3016	2.4	2.4	2.6	2.5	2.6	2.7	2.7	--
	3017	2.8	2.9	2.9	3.0	2.9	3.0	3.0	--
	3018	2.8	2.8	2.9	2.8	2.9	2.9	2.9	--
	3019	3.1	3.2	3.2	3.3	3.2	3.2	3.3	--
	3020	2.9	2.9	3.0	3.0	3.0	3.0	3.0	--

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 14	21	28	35	42	49	56	63
3M	3001	--	--	--	--	--	--	--	--
	3002	--	--	--	--	--	--	--	--
	3003	--	--	--	--	--	--	--	--
	3004	--	--	--	--	--	--	--	--
	3005	--	--	--	--	--	--	--	--
	3006	2.8	2.9	2.9	2.9	2.9	2.9	3.0	3.0
	3007	2.9	2.9	3.0	3.0	3.0	3.0	3.0	3.1
	3008	3.1	3.1	3.1	3.1	3.2	3.2	3.2	3.2
	3009	2.8	3.0	2.9	3.0	3.0	3.0	3.0	3.1
	3010	2.9	3.1	3.1	3.0	3.2	3.0	3.1	3.1
	3011	3.2	3.2	3.3	3.3	3.3	3.3	3.4	3.3
	3012	2.8	2.9	2.9	2.9	3.0	3.0	3.0	3.0
	3013	2.9	2.9	2.9	2.9	3.0	3.0	3.0	3.0
	3014	2.9	2.9	3.0	3.0	3.0	3.0	3.0	3.0
	3015	3.1	3.2	3.2	3.2	3.2	3.2	3.2	3.2
	3016	2.7	2.8	2.8	2.8	2.9	2.9	2.9	2.9
	3017	3.0	3.0	3.1	3.1	3.1	3.2	3.2	3.2
	3018	2.9	3.0	3.0	3.1	3.0	3.0	3.1	3.1
	3019	3.3	3.4	3.4	3.4	3.4	3.4	3.5	3.5
	3020	3.1	3.1	3.1	3.1	3.1	3.1	3.1	3.2

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 70	77	84	90	91	98	105	112
3M	3001	--	--	--	--	--	--	--	--
	3002	--	--	--	--	--	--	--	--
	3003	--	--	--	--	--	--	--	--
	3004	--	--	--	--	--	--	--	--
	3005	--	--	--	--	--	--	--	--
	3006	3.0	3.0	3.0	3.0	--	--	--	--
	3007	3.1	3.1	3.1	3.2	--	--	--	--
	3008	3.2	3.2	3.1	3.2	--	--	--	--
	3009	3.1	3.1	3.2	3.1	--	--	--	--
	3010	3.2	3.2	3.1	3.2	--	--	--	--
	3011	3.4	3.4	3.4	--	3.4	3.4	3.5	3.4
	3012	3.0	3.0	3.1	--	3.1	3.2	3.1	3.1
	3013	3.0	3.0	3.1	--	3.1	3.1	3.1	3.1
	3014	3.0	3.0	3.0	--	3.0	3.0	3.1	3.1
	3015	3.2	3.3	3.2	--	3.3	3.3	3.3	3.3
	3016	2.9	3.0	3.0	--	3.0	3.0	3.1	3.0
	3017	3.2	3.2	3.3	--	3.3	3.3	3.3	3.3
	3018	3.1	3.2	3.2	--	3.2	3.2	3.2	3.2
	3019	3.5	3.5	3.6	--	3.5	3.6	3.6	3.6
	3020	3.2	3.2	3.2	--	3.2	3.3	3.3	3.3

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 119	120	126	133	140	147	154	161
3M	3001	--	--	--	--	--	--	--	--
	3002	--	--	--	--	--	--	--	--
	3003	--	--	--	--	--	--	--	--
	3004	--	--	--	--	--	--	--	--
	3005	--	--	--	--	--	--	--	--
	3006	--	--	--	--	--	--	--	--
	3007	--	--	--	--	--	--	--	--
	3008	--	--	--	--	--	--	--	--
	3009	--	--	--	--	--	--	--	--
	3010	--	--	--	--	--	--	--	--
	3011	3.4	3.4	--	--	--	--	--	--
	3012	3.1	3.1	--	--	--	--	--	--
	3013	3.2	3.2	--	--	--	--	--	--
	3014	3.1	3.1	--	--	--	--	--	--
	3015	3.3	3.3	--	--	--	--	--	--
	3016	3.0	--	3.1	3.1	3.1	3.2	3.2	3.2
	3017	3.3	--	3.3	3.4	3.4	3.4	3.4	3.4
	3018	3.2	--	3.2	3.3	3.3	3.3	3.3	3.3
	3019	3.6	--	3.7	3.7	3.7	3.7	3.8	3.8
	3020	3.3	--	3.3	3.4	3.3	3.4	3.4	3.4

(b) (4)

Sponsor Reference No (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 168	175	180
3M	3001	--	--	--
	3002	--	--	--
	3003	--	--	--
	3004	--	--	--
	3005	--	--	--
	3006	--	--	--
	3007	--	--	--
	3008	--	--	--
	3009	--	--	--
	3010	--	--	--
	3011	--	--	--
	3012	--	--	--
	3013	--	--	--
	3014	--	--	--
	3015	--	--	--
	3016	3.2	3.3	3.2
	3017	3.5	3.5	3.5
	3018	3.3	3.3	3.4
	3019	3.8	3.8	3.8
	3020	3.4	3.4	3.4

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day -14	-8	1	2	3	4	7	11
1F	1501	2.7	2.7	2.7	2.8	2.8	2.8	2.8	2.8
	1502	2.8	2.9	2.9	2.9	2.9	2.9	2.9	2.9
	1503	2.7	2.8	2.8	2.8	2.8	2.8	2.9	2.9
	1504	2.9	3.0	3.0	2.9	3.0	2.9	3.0	--
	1505	2.9	2.9	3.0	2.9	2.9	3.0	3.0	--
	1506	2.8	2.8	2.9	3.0	2.9	2.9	2.9	--
	1507	2.9	2.9	3.0	3.0	3.0	3.0	3.0	--
	1508	2.9	3.0	3.0	3.0	3.0	3.0	3.0	--
	1509	2.8	2.9	3.0	2.9	3.0	3.0	3.0	--
	1510	2.8	2.8	2.9	2.9	2.9	2.9	3.0	--
	1511	2.7	2.8	2.8	2.9	2.8	2.9	2.9	--
	1512	2.8	2.8	2.9	2.9	2.9	2.9	3.0	--

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 14	21	28	35	42	49	56	63
1F	1501	--	--	--	--	--	--	--	--
	1502	--	--	--	--	--	--	--	--
	1503	--	--	--	--	--	--	--	--
	1504	3.0	3.1	3.1	3.2	3.2	3.0	3.3	3.4
	1505	3.1	3.1	3.1	3.1	3.1	3.1	3.2	3.3
	1506	3.0	3.0	3.1	3.1	3.1	3.1	3.1	3.2
	1507	3.2	3.2	3.2	3.2	3.2	3.2	3.3	3.2
	1508	3.1	3.2	3.2	3.2	3.2	3.2	3.3	3.3
	1509	3.1	3.1	3.1	3.1	3.2	3.2	3.2	3.2
	1510	3.0	3.1	3.2	3.2	3.2	3.2	3.3	3.3
	1511	2.9	3.0	3.0	3.1	3.2	3.1	3.2	3.2
	1512	3.1	3.1	3.2	3.1	3.1	3.2	3.3	3.3

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 70	77	84	90	91	98	105	112
1F	1501	--	--	--	--	--	--	--	--
	1502	--	--	--	--	--	--	--	--
	1503	--	--	--	--	--	--	--	--
	1504	3.4	3.4	3.5	3.5	--	--	--	--
	1505	3.3	3.3	3.3	3.4	--	--	--	--
	1506	3.3	3.2	3.2	3.2	--	--	--	--
	1507	3.2	3.2	3.3	--	3.3	3.3	3.4	3.4
	1508	3.3	3.3	3.4	--	3.4	3.4	3.4	3.4
	1509	3.3	3.3	3.3	--	3.4	3.4	3.4	3.4
	1510	3.3	3.2	3.3	--	3.3	3.3	3.3	3.4
	1511	3.3	3.3	3.3	--	3.4	3.3	3.4	3.4
	1512	3.4	3.4	3.4	--	3.5	3.5	3.5	3.6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 119	120	126	133	140	147	154	161
1F	1501	--	--	--	--	--	--	--	--
	1502	--	--	--	--	--	--	--	--
	1503	--	--	--	--	--	--	--	--
	1504	--	--	--	--	--	--	--	--
	1505	--	--	--	--	--	--	--	--
	1506	--	--	--	--	--	--	--	--
	1507	3.4	3.5	--	--	--	--	--	--
	1508	3.5	3.5	--	--	--	--	--	--
	1509	3.4	3.5	--	--	--	--	--	--
	1510	3.5	--	3.6	3.6	3.5	3.4	3.4	3.4
	1511	3.4	--	3.5	3.6	3.6	3.6	3.7	3.6
	1512	3.5	--	3.6	3.8	3.7	3.7	3.7	3.7

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 168	175	180
1F	1501	--	--	--
	1502	--	--	--
	1503	--	--	--
	1504	--	--	--
	1505	--	--	--
	1506	--	--	--
	1507	--	--	--
	1508	--	--	--
	1509	--	--	--
	1510	3.4	3.3	3.4
	1511	3.7	3.7	3.8
	1512	3.7	3.8	3.8

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day -14	-8	1	2	3	4	7	11
2F	2501	2.7	2.7	2.8	2.8	2.8	2.7	2.8	2.8
	2502	2.8	2.8	2.9	2.8	2.9	2.8	2.9	2.9
	2503	2.7	2.8	2.9	2.9	2.9	2.9	2.9	2.9
	2504	2.8	2.8	2.8	2.8	2.8	2.9	2.9	2.9
	2505	2.7	2.7	2.8	2.8	2.8	2.8	2.8	2.9
	2506	2.8	2.9	3.0	2.9	2.9	3.0	3.0	--
	2507	2.9	2.8	2.9	2.9	2.9	2.9	2.9	--
	2508	2.9	2.9	2.9	2.9	2.9	2.9	2.9	--
	2509	2.6	2.5	2.6	2.6	2.6	2.9	2.6	--
	2510	2.9	2.8	3.0	3.0	3.0	3.0	3.0	--
	2511	2.6	2.7	2.7	2.7	2.7	2.8	2.8	--
	2512	2.9	2.9	2.9	2.9	2.9	2.9	3.0	--
	2513	3.0	3.0	3.1	3.1	3.1	3.1	3.2	--
	2514	3.0	3.0	3.1	3.0	3.0	3.0	3.1	--
	2515	2.7	2.7	2.8	2.8	2.8	2.8	2.9	--
	2516	2.8	3.0	3.0	3.0	3.0	3.0	3.1	--
	2517	2.9	2.9	2.9	2.9	3.0	3.0	3.0	--
	2518	2.9	2.9	3.0	3.0	3.2	3.0	3.1	--
	2519	2.8	2.8	3.0	2.9	3.0	2.9	2.9	--
	2520	2.7	2.7	2.8	2.8	2.8	2.8	2.9	--

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 14	21	28	35	42	49	56	63
2F	2501	--	--	--	--	--	--	--	--
	2502	--	--	--	--	--	--	--	--
	2503	--	--	--	--	--	--	--	--
	2504	--	--	--	--	--	--	--	--
	2505	--	--	--	--	--	--	--	--
	2506	3.0	3.1	3.1	3.1	3.1	3.1	3.2	3.2
	2507	3.0	3.1	3.0	3.0	3.1	3.1	3.0	3.2
	2508	3.0	3.0	3.0	3.0	3.0	3.0	3.1	3.1
	2509	2.7	2.9	2.8	2.8	2.9	2.9	2.9	3.0
	2510	3.0	3.0	3.0	3.0	3.0	3.0	3.1	3.1
	2511	2.9	2.9	2.9	2.9	3.0	2.9	3.0	3.0
	2512	3.0	3.1	3.1	3.1	3.2	3.2	3.2	3.2
	2513	3.2	3.3	3.3	3.3	3.3	3.3	3.3	3.4
	2514	3.1	3.2	3.2	3.1	3.1	3.2	3.2	3.2
	2515	2.9	3.0	3.0	3.0	2.9	3.1	3.1	3.1
	2516	3.1	3.2	3.2	3.2	3.3	3.2	3.3	3.3
	2517	3.1	3.1	3.2	3.2	3.2	3.2	3.4	3.3
	2518	3.1	3.1	3.2	3.2	3.2	3.2	3.3	3.3
	2519	3.0	3.0	3.0	3.1	3.1	3.1	3.2	3.2
	2520	3.0	3.0	3.1	3.1	3.2	3.2	3.2	3.3

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 70	77	84	90	91	98	105	112
2F	2501	--	--	--	--	--	--	--	--
	2502	--	--	--	--	--	--	--	--
	2503	--	--	--	--	--	--	--	--
	2504	--	--	--	--	--	--	--	--
	2505	--	--	--	--	--	--	--	--
	2506	3.2	3.3	3.2	3.3	--	--	--	--
	2507	3.2	3.1	3.3	3.3	--	--	--	--
	2508	3.1	3.2	3.2	3.2	--	--	--	--
	2509	3.0	3.0	3.2	3.1	--	--	--	--
	2510	3.1	3.1	3.1	3.2	--	--	--	--
	2511	3.1	3.1	3.1	--	3.2	3.2	3.2	3.2
	2512	3.3	3.3	3.3	--	3.4	3.4	3.4	3.4
	2513	3.4	3.4	3.4	--	3.5	3.5	3.6	3.6
	2514	3.3	3.3	3.3	--	3.4	3.5	3.5	3.4
	2515	3.2	3.2	3.2	--	3.3	3.3	3.3	3.4
	2516	3.4	3.5	3.5	--	3.5	3.4	3.5	3.5
	2517	3.4	3.3	3.4	--	3.4	3.4	3.4	3.4
	2518	3.3	3.4	3.4	--	3.5	3.5	3.5	3.6
	2519	3.3	3.3	3.3	--	3.4	3.5	3.4	3.4
	2520	3.3	3.3	3.4	--	3.5	3.5	3.5	3.5

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 119	120	126	133	140	147	154	161
2F	2501	--	--	--	--	--	--	--	--
	2502	--	--	--	--	--	--	--	--
	2503	--	--	--	--	--	--	--	--
	2504	--	--	--	--	--	--	--	--
	2505	--	--	--	--	--	--	--	--
	2506	--	--	--	--	--	--	--	--
	2507	--	--	--	--	--	--	--	--
	2508	--	--	--	--	--	--	--	--
	2509	--	--	--	--	--	--	--	--
	2510	--	--	--	--	--	--	--	--
	2511	3.3	3.3	--	--	--	--	--	--
	2512	3.4	3.5	--	--	--	--	--	--
	2513	3.5	3.5	--	--	--	--	--	--
	2514	3.4	3.5	--	--	--	--	--	--
	2515	3.3	3.3	--	--	--	--	--	--
	2516	3.6	--	3.5	3.7	3.7	3.6	3.7	3.6
	2517	3.4	--	3.4	3.5	3.5	3.5	3.6	3.6
	2518	3.6	--	3.6	3.7	3.7	3.7	3.8	3.8
	2519	3.4	--	3.5	3.5	3.5	3.6	3.7	3.6
	2520	3.5	--	3.6	3.7	3.7	3.7	3.7	3.8

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 168	175	180
2F	2501	--	--	--
	2502	--	--	--
	2503	--	--	--
	2504	--	--	--
	2505	--	--	--
	2506	--	--	--
	2507	--	--	--
	2508	--	--	--
	2509	--	--	--
	2510	--	--	--
	2511	--	--	--
	2512	--	--	--
	2513	--	--	--
	2514	--	--	--
	2515	--	--	--
	2516	3.7	3.7	3.7
	2517	3.6	3.6	3.7
	2518	3.8	3.8	3.9
	2519	3.6	3.6	3.7
	2520	3.8	3.8	3.9

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day -14	-8	1	2	3	4	7	11
3F	3501	2.6	2.7	2.7	2.6	2.7	2.7	2.7	2.8
	3502	2.7	2.8	2.8	2.9	2.8	2.8	2.9	2.9
	3503	2.7	2.8	2.8	2.8	2.8	2.8	2.9	2.9
	3504	2.9	2.8	2.9	2.9	2.9	2.9	2.9	3.0
	3505	2.7	2.8	2.8	2.9	2.8	2.9	2.9	2.9
	3506	2.8	2.8	2.8	2.9	2.8	2.8	2.9	--
	3507	2.9	2.9	3.0	3.0	2.9	2.8	3.0	--
	3508	3.0	3.0	3.1	3.1	3.1	3.1	3.1	--
	3509	2.8	2.8	2.9	2.9	2.9	3.0	3.0	--
	3510	2.8	2.8	2.9	2.8	2.9	2.9	2.9	--
	3511	2.9	2.9	2.9	3.0	3.0	3.1	3.0	--
	3512	2.6	2.7	2.7	2.7	2.7	2.7	2.7	--
	3513	2.7	2.7	2.8	2.8	2.8	2.8	2.9	--
	3514	3.0	3.0	3.1	3.0	3.0	3.1	3.1	--
	3515	2.9	3.0	3.0	3.0	3.0	3.0	3.1	--
	3516	2.9	3.0	2.9	2.9	2.9	2.9	3.0	--
	3517	2.8	2.9	2.9	2.9	2.8	2.9	2.9	--
	3518	3.0	2.9	3.0	3.0	3.0	3.1	3.1	--
	3519	2.8	2.8	2.8	2.7	2.7	2.8	2.8	--
	3520	2.8	2.8	2.9	2.9	2.9	2.9	3.0	--

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 14	21	28	35	42	49	56	63
3F	3501	--	--	--	--	--	--	--	--
	3502	--	--	--	--	--	--	--	--
	3503	--	--	--	--	--	--	--	--
	3504	--	--	--	--	--	--	--	--
	3505	--	--	--	--	--	--	--	--
	3506	3.0	3.1	3.0	3.0	3.0	3.1	3.1	3.2
	3507	3.0	3.1	3.2	3.1	3.1	3.2	3.3	3.3
	3508	3.0	3.3	3.3	3.3	3.3	3.4	3.4	3.5
	3509	3.1	3.1	3.1	3.1	3.2	3.2	3.2	3.2
	3510	3.0	3.1	3.1	3.1	3.1	3.2	3.2	3.1
	3511	3.0	3.1	3.1	3.1	3.1	3.1	3.1	3.2
	3512	2.8	2.8	2.9	2.9	2.9	2.9	3.0	3.0
	3513	2.9	3.0	3.0	3.1	3.1	3.1	3.1	3.2
	3514	3.1	3.2	3.3	3.3	3.3	3.3	3.4	3.4
	3515	3.1	3.2	3.2	3.2	3.2	3.2	3.3	3.3
	3516	3.1	3.1	3.3	3.1	3.2	3.2	3.3	3.3
	3517	3.0	2.9	3.0	3.0	3.1	3.0	3.1	3.1
	3518	3.1	3.2	3.2	3.2	3.2	3.2	3.2	3.3
	3519	2.8	2.9	2.9	2.9	2.9	3.0	3.0	3.0
	3520	3.1	3.1	3.2	3.2	3.3	3.2	3.3	3.3

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 70	77	84	90	91	98	105	112
3F	3501	--	--	--	--	--	--	--	--
	3502	--	--	--	--	--	--	--	--
	3503	--	--	--	--	--	--	--	--
	3504	--	--	--	--	--	--	--	--
	3505	--	--	--	--	--	--	--	--
	3506	3.2	3.2	3.2	3.2	--	--	--	--
	3507	3.4	3.4	3.4	3.5	--	--	--	--
	3508	3.5	3.5	3.6	3.6	--	--	--	--
	3509	3.2	3.3	3.3	3.3	--	--	--	--
	3510	3.2	3.2	3.2	3.3	--	--	--	--
	3511	3.3	3.3	3.3	--	3.3	3.4	3.4	3.4
	3512	3.0	3.0	3.1	--	3.1	3.1	3.1	3.1
	3513	3.2	3.3	3.3	--	3.3	3.4	3.4	3.4
	3514	3.5	3.4	3.4	--	3.5	3.6	3.6	3.6
	3515	3.3	3.3	3.4	--	3.4	3.4	3.5	3.4
	3516	3.3	3.4	3.4	--	3.4	3.5	3.4	3.4
	3517	3.2	3.2	3.2	--	3.2	3.2	3.2	3.3
	3518	3.4	3.4	3.4	--	3.4	3.5	3.5	3.5
	3519	3.1	3.1	3.1	--	3.1	3.1	3.1	3.2
	3520	3.3	3.4	3.4	--	3.4	3.5	3.4	3.5

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 119	120	126	133	140	147	154	161
3F	3501	--	--	--	--	--	--	--	--
	3502	--	--	--	--	--	--	--	--
	3503	--	--	--	--	--	--	--	--
	3504	--	--	--	--	--	--	--	--
	3505	--	--	--	--	--	--	--	--
	3506	--	--	--	--	--	--	--	--
	3507	--	--	--	--	--	--	--	--
	3508	--	--	--	--	--	--	--	--
	3509	--	--	--	--	--	--	--	--
	3510	--	--	--	--	--	--	--	--
	3511	3.4	3.4	--	--	--	--	--	--
	3512	3.2	3.2	--	--	--	--	--	--
	3513	3.4	3.4	--	--	--	--	--	--
	3514	3.6	3.6	--	--	--	--	--	--
	3515	3.4	3.4	--	--	--	--	--	--
	3516	3.4	--	3.5	3.6	3.5	3.6	3.6	3.6
	3517	3.3	--	3.4	3.4	3.4	3.4	3.5	3.5
	3518	3.5	--	3.6	3.6	3.6	3.6	3.6	3.7
	3519	3.2	--	3.2	3.2	3.1	3.1	3.2	3.1
	3520	3.4	--	3.5	3.6	3.6	3.6	3.6	3.6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 4

Individual Body Weights (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day 168	175	180
3F	3501	--	--	--
	3502	--	--	--
	3503	--	--	--
	3504	--	--	--
	3505	--	--	--
	3506	--	--	--
	3507	--	--	--
	3508	--	--	--
	3509	--	--	--
	3510	--	--	--
	3511	--	--	--
	3512	--	--	--
	3513	--	--	--
	3514	--	--	--
	3515	--	--	--
	3516	3.6	3.7	3.7
	3517	3.5	3.5	3.6
	3518	3.7	3.6	3.7
	3519	3.2	3.1	3.2
	3520	3.6	3.6	3.8

(b) (4)

Appendix 5

Individual Body Weight Gains Explanation Page

Abbreviation	Description	Abbreviation	Description
--	Not scheduled to be performed / dead	TERR	Technical error
AVS	Suspected aberrant value	UPTD	Unable to perform due to technical difficulty
NC	Not calculable	X	Excluded from mean
OA	Omitted activity		

Note: This is a comprehensive list of abbreviations. All of the abbreviations listed may not be applicable to this report.

Dosing Information

Dosing information is abbreviated on various data outputs; the following represents the dosing information for this study.

Group No.	Test Material	Dose Level
1	Reference Item	0
2	Ad26 (b) (4)	1×10^{11} vp
3	Ad26 (b) (4)	1×10^{11} vp + 150µg

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp
Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day							
		Change -13 - -8	Change -8 - 1	Change 1 - 2	Change 2 - 3	Change 3 - 4	Change 4 - 7	Change 7 - 11	Change 7 - 14
1M	1001	0.0	0.1	0.0	0.0	0.0	0.0	0.1	--
	1002	0.0	0.1	0.0	0.0	0.0	0.0	0.1	--
	1003	0.0	0.0	0.1	-0.1	0.0	0.1	0.0	--
	1004	0.0	0.1	0.0	0.0	0.0	0.0	--	0.0
	1005	0.0	0.0	0.1	0.0	-0.1	0.1	--	0.0
	1006	-0.1	0.0	0.1	0.0	0.0	0.0	--	0.0
	1007	0.0	0.1	0.0	0.0	0.0	0.0	--	0.1
	1008	0.1	0.0	0.1	0.0	-0.1	0.1	--	0.0
	1009	0.1	0.1	0.0	0.0	0.0	0.0	--	0.0
	1010	0.0	0.1	0.0	0.3	-0.3	0.0	--	0.0
	1011	0.0	0.0	0.0	0.2	-0.2	0.1	--	0.0
	1012	0.0	0.0	0.0	0.1	0.0	0.0	--	0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 14 - 21	Change 21 - 28	Change 28 - 35	Change 35 - 42	Change 42 - 49	Change 49 - 56	Change 56 - 63	Change 63 - 70
1M	1001	--	--	--	--	--	--	--	--
	1002	--	--	--	--	--	--	--	--
	1003	--	--	--	--	--	--	--	--
	1004	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.1
	1005	0.1	0.0	0.0	0.1	0.0	-0.1	0.1	0.0
	1006	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.1
	1007	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0
	1008	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0
	1009	0.1	0.0	0.1	0.0	0.0	0.1	-0.1	0.1
	1010	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0
	1011	0.0	0.1	0.1	-0.2	0.0	0.0	0.0	0.0
	1012	0.0	0.0	-0.1	0.1	0.0	0.0	0.1	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 70 - 77	Change 77 - 84	Change 84 - 90	Change 84 - 91	Change 91 - 98	Change 98 - 105	Change 105 - 112	Change 112 - 119
1M	1001	--	--	--	--	--	--	--	--
	1002	--	--	--	--	--	--	--	--
	1003	--	--	--	--	--	--	--	--
	1004	0.0	0.0	0.0	--	--	--	--	--
	1005	0.0	0.1	-0.1	--	--	--	--	--
	1006	0.0	0.0	0.0	--	--	--	--	--
	1007	0.0	0.0	--	0.0	0.0	0.0	0.0	0.1
	1008	0.0	0.0	--	0.1	0.0	0.0	0.0	0.0
	1009	0.0	0.0	--	0.0	0.1	0.0	0.0	0.0
	1010	0.0	0.0	--	0.0	0.0	0.1	-0.1	0.1
	1011	0.0	0.0	--	0.0	0.0	0.1	0.0	0.0
	1012	0.0	0.0	--	0.0	0.0	0.1	-0.1	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day							
		Change 119 - 120	Change 119 - 126	Change 126 - 133	Change 133 - 140	Change 140 - 147	Change 147 - 154	Change 154 - 161	Change 161 - 168
1M	1001	--	--	--	--	--	--	--	--
	1002	--	--	--	--	--	--	--	--
	1003	--	--	--	--	--	--	--	--
	1004	--	--	--	--	--	--	--	--
	1005	--	--	--	--	--	--	--	--
	1006	--	--	--	--	--	--	--	--
	1007	-0.1	--	--	--	--	--	--	--
	1008	0.0	--	--	--	--	--	--	--
	1009	0.0	--	--	--	--	--	--	--
	1010	--	0.0	0.1	-0.1	0.0	0.1	0.0	0.0
	1011	--	0.0	0.0	0.0	0.1	0.0	0.0	0.0
	1012	--	0.1	0.0	0.0	0.1	0.0	0.0	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 168 - 175	Day Change 175 - 180
1M	1001	--	--
	1002	--	--
	1003	--	--
	1004	--	--
	1005	--	--
	1006	--	--
	1007	--	--
	1008	--	--
	1009	--	--
	1010	0.0	0.0
	1011	0.0	0.0
	1012	0.0	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day							
		Change -13 - -8	Change -8 - 1	Change 1 - 2	Change 2 - 3	Change 3 - 4	Change 4 - 7	Change 7 - 11	Change 7 - 14
2M	2001	0.0	0.0	0.0	0.0	0.0	0.1	0.0	--
	2002	0.0	0.1	0.0	0.0	0.0	0.1	0.0	--
	2003	-0.1	0.1	0.0	0.0	0.0	0.0	0.1	--
	2004	0.0	0.0	0.0	0.0	0.0	0.1	0.0	--
	2005	0.0	0.1	0.0	0.0	0.0	0.0	0.1	--
	2006	0.0	0.1	0.0	0.0	0.0	0.0	--	0.1
	2007	0.0	0.1	0.0	0.0	0.0	0.1	--	0.0
	2008	0.0	0.1	0.0	0.0	0.0	0.0	--	0.0
	2009	0.0	0.2	0.0	0.0	0.0	0.0	--	0.0
	2010	-0.2	0.1	0.0	0.0	0.0	0.1	--	0.0
	2011	0.0	0.1	0.0	0.1	-0.1	0.0	--	0.0
	2012	0.0	0.0	0.0	0.0	0.1	0.0	--	0.0
	2013	0.0	0.1	0.0	0.0	0.0	0.1	--	0.0
	2014	0.0	0.1	0.0	0.0	0.0	0.0	--	0.0
	2015	0.0	0.2	-0.1	0.0	0.0	0.1	--	0.0
	2016	0.1	0.1	-0.1	0.0	0.1	0.0	--	0.0
	2017	0.0	0.0	0.0	0.0	0.0	0.1	--	0.0
	2018	0.0	0.1	0.0	0.0	0.0	0.0	--	0.0
	2019	0.0	0.1	0.0	-0.1	0.0	0.2	--	0.0
	2020	-0.1	0.1	0.0	0.0	0.0	0.0	--	0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 14 - 21	Change 21 - 28	Change 28 - 35	Change 35 - 42	Change 42 - 49	Change 49 - 56	Change 56 - 63	Change 63 - 70
2M	2001	--	--	--	--	--	--	--	--
	2002	--	--	--	--	--	--	--	--
	2003	--	--	--	--	--	--	--	--
	2004	--	--	--	--	--	--	--	--
	2005	--	--	--	--	--	--	--	--
	2006	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
	2007	0.1	0.0	-0.1	0.1	0.1	-0.1	0.0	0.1
	2008	0.1	0.0	-0.1	0.1	0.1	0.0	0.0	0.0
	2009	0.1	0.0	0.0	0.1	0.1	0.0	-0.1	0.1
	2010	0.1	0.0	-0.1	0.1	-0.1	0.0	0.1	0.0
	2011	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0
	2012	0.1	0.0	-0.1	0.0	0.1	0.0	0.0	0.1
	2013	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.1
	2014	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0
	2015	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0
	2016	0.1	0.0	-0.1	0.1	-0.1	0.1	0.1	0.0
	2017	0.1	0.0	0.0	0.1	-0.1	0.1	0.1	0.0
	2018	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	2019	0.0	0.0	0.0	0.0	0.1	-0.1	0.1	0.0
	2020	0.0	0.0	0.1	-0.1	0.0	0.0	0.1	-0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 70 - 77	Change 77 - 84	Change 84 - 90	Change 84 - 91	Change 91 - 98	Change 98 - 105	Change 105 - 112	Change 112 - 119
2M	2001	--	--	--	--	--	--	--	--
	2002	--	--	--	--	--	--	--	--
	2003	--	--	--	--	--	--	--	--
	2004	--	--	--	--	--	--	--	--
	2005	--	--	--	--	--	--	--	--
	2006	0.0	0.0	0.0	--	--	--	--	--
	2007	-0.1	0.0	0.0	--	--	--	--	--
	2008	0.2	-0.2	0.2	--	--	--	--	--
	2009	-0.1	0.1	0.0	--	--	--	--	--
	2010	0.0	0.0	0.0	--	--	--	--	--
	2011	0.0	0.0	--	0.1	0.1	-0.1	0.0	0.0
	2012	-0.1	0.1	--	0.0	0.0	0.0	0.0	0.0
	2013	0.0	0.0	--	0.0	0.0	0.0	0.0	0.1
	2014	0.0	0.0	--	0.0	0.0	0.1	-0.1	0.1
	2015	0.0	0.0	--	0.0	0.0	0.1	0.0	0.0
	2016	0.0	0.1	--	-0.2	0.2	0.0	-0.1	0.0
	2017	0.0	0.0	--	0.0	0.0	0.0	0.0	0.0
	2018	0.0	0.1	--	-0.1	0.0	0.0	0.0	0.0
	2019	0.0	0.1	--	0.0	0.0	0.0	0.0	0.1
	2020	0.0	0.1	--	0.0	0.0	0.0	0.0	0.0

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day							
		Change 119 - 120	Change 119 - 126	Change 126 - 133	Change 133 - 140	Change 140 - 147	Change 147 - 154	Change 154 - 161	Change 161 - 168
2M	2001	--	--	--	--	--	--	--	--
	2002	--	--	--	--	--	--	--	--
	2003	--	--	--	--	--	--	--	--
	2004	--	--	--	--	--	--	--	--
	2005	--	--	--	--	--	--	--	--
	2006	--	--	--	--	--	--	--	--
	2007	--	--	--	--	--	--	--	--
	2008	--	--	--	--	--	--	--	--
	2009	--	--	--	--	--	--	--	--
	2010	--	--	--	--	--	--	--	--
	2011	0.0	--	--	--	--	--	--	--
	2012	0.0	--	--	--	--	--	--	--
	2013	0.0	--	--	--	--	--	--	--
	2014	0.0	--	--	--	--	--	--	--
	2015	0.0	--	--	--	--	--	--	--
	2016	--	0.0	0.1	0.0	0.0	0.1	-0.1	0.0
	2017	--	0.0	0.1	0.0	0.1	0.0	0.0	0.0
	2018	--	0.1	0.0	0.0	0.1	0.0	-0.1	0.0
	2019	--	-0.1	0.1	0.0	-0.1	0.1	0.1	0.0
	2020	--	0.0	0.0	0.1	0.0	-0.1	0.1	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad2 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 168 - 175	Day Change 175 - 180
2M	2001	--	--
	2002	--	--
	2003	--	--
	2004	--	--
	2005	--	--
	2006	--	--
	2007	--	--
	2008	--	--
	2009	--	--
	2010	--	--
	2011	--	--
	2012	--	--
	2013	--	--
	2014	--	--
	2015	--	--
	2016	0.1	0.0
	2017	-0.1	0.1
	2018	0.0	0.1
	2019	0.0	0.0
	2020	0.0	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change -13 - -8	Change -8 - 1	Change 1 - 2	Change 2 - 3	Change 3 - 4	Change 4 - 7	Change 7 - 11	Change 7 - 14
3M	3001	0.0	0.1	0.0	-0.1	0.1	0.0	0.0	--
	3002	0.4	0.0	0.0	0.0	0.0	0.0	0.1	--
	3003	0.0	0.0	0.0	0.0	0.1	0.0	0.0	--
	3004	0.0	0.1	0.0	0.0	0.0	0.0	0.0	--
	3005	-0.1	0.1	0.0	0.0	0.0	0.0	0.1	--
	3006	0.1	0.1	0.0	0.0	0.0	0.0	--	0.0
	3007	0.1	0.0	0.0	0.0	0.0	0.1	--	0.0
	3008	0.0	0.0	0.0	0.0	0.1	0.0	--	0.0
	3009	0.1	0.0	0.0	0.0	0.1	0.0	--	-0.1
	3010	0.0	0.1	0.0	0.0	0.0	0.0	--	0.0
	3011	0.0	0.1	0.0	0.0	0.0	0.1	--	0.0
	3012	0.0	0.0	0.0	0.0	0.0	0.1	--	0.0
	3013	-0.1	0.1	0.0	-0.1	0.2	0.0	--	0.0
	3014	0.0	0.1	0.0	0.1	-0.1	0.1	--	0.0
	3015	0.0	0.1	0.0	0.0	0.0	0.0	--	0.0
	3016	0.0	0.2	-0.1	0.1	0.1	0.0	--	0.0
	3017	0.1	0.0	0.1	-0.1	0.1	0.0	--	0.0
	3018	0.0	0.1	-0.1	0.1	0.0	0.0	--	0.0
	3019	0.1	0.0	0.1	-0.1	0.0	0.1	--	0.0
	3020	0.0	0.1	0.0	0.0	0.0	0.0	--	0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 14 - 21	Change 21 - 28	Change 28 - 35	Change 35 - 42	Change 42 - 49	Change 49 - 56	Change 56 - 63	Change 63 - 70
3M	3001	--	--	--	--	--	--	--	--
	3002	--	--	--	--	--	--	--	--
	3003	--	--	--	--	--	--	--	--
	3004	--	--	--	--	--	--	--	--
	3005	--	--	--	--	--	--	--	--
	3006	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0
	3007	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.0
	3008	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
	3009	0.2	-0.1	0.1	0.0	0.0	0.0	0.1	0.0
	3010	0.2	0.0	-0.1	0.2	-0.2	0.1	0.0	0.1
	3011	0.0	0.1	0.0	0.0	0.0	0.1	-0.1	0.1
	3012	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0
	3013	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
	3014	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0
	3015	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	3016	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0
	3017	0.0	0.1	0.0	0.0	0.1	0.0	0.0	0.0
	3018	0.1	0.0	0.1	-0.1	0.0	0.1	0.0	0.0
	3019	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0
	3020	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 70 - 77	Change 77 - 84	Change 84 - 90	Change 84 - 91	Change 91 - 98	Change 98 - 105	Change 105 - 112	Change 112 - 119
3M	3001	--	--	--	--	--	--	--	--
	3002	--	--	--	--	--	--	--	--
	3003	--	--	--	--	--	--	--	--
	3004	--	--	--	--	--	--	--	--
	3005	--	--	--	--	--	--	--	--
	3006	0.0	0.0	0.0	--	--	--	--	--
	3007	0.0	0.0	0.1	--	--	--	--	--
	3008	0.0	-0.1	0.1	--	--	--	--	--
	3009	0.0	0.1	-0.1	--	--	--	--	--
	3010	0.0	-0.1	0.1	--	--	--	--	--
	3011	0.0	0.0	--	0.0	0.0	0.1	-0.1	0.0
	3012	0.0	0.1	--	0.0	0.1	-0.1	0.0	0.0
	3013	0.0	0.1	--	0.0	0.0	0.0	0.0	0.1
	3014	0.0	0.0	--	0.0	0.0	0.1	0.0	0.0
	3015	0.1	-0.1	--	0.1	0.0	0.0	0.0	0.0
	3016	0.1	0.0	--	0.0	0.0	0.1	-0.1	0.0
	3017	0.0	0.1	--	0.0	0.0	0.0	0.0	0.0
	3018	0.1	0.0	--	0.0	0.0	0.0	0.0	0.0
	3019	0.0	0.1	--	-0.1	0.1	0.0	0.0	0.0
	3020	0.0	0.0	--	0.0	0.1	0.0	0.0	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day							
		Change 119 - 120	Change 119 - 126	Change 126 - 133	Change 133 - 140	Change 140 - 147	Change 147 - 154	Change 154 - 161	Change 161 - 168
3M	3001	--	--	--	--	--	--	--	--
	3002	--	--	--	--	--	--	--	--
	3003	--	--	--	--	--	--	--	--
	3004	--	--	--	--	--	--	--	--
	3005	--	--	--	--	--	--	--	--
	3006	--	--	--	--	--	--	--	--
	3007	--	--	--	--	--	--	--	--
	3008	--	--	--	--	--	--	--	--
	3009	--	--	--	--	--	--	--	--
	3010	--	--	--	--	--	--	--	--
	3011	0.0	--	--	--	--	--	--	--
	3012	0.0	--	--	--	--	--	--	--
	3013	0.0	--	--	--	--	--	--	--
	3014	0.0	--	--	--	--	--	--	--
	3015	0.0	--	--	--	--	--	--	--
	3016	--	0.1	0.0	0.0	0.1	0.0	0.0	0.0
	3017	--	0.0	0.1	0.0	0.0	0.0	0.0	0.1
	3018	--	0.0	0.1	0.0	0.0	0.0	0.0	0.0
	3019	--	0.1	0.0	0.0	0.0	0.1	0.0	0.0
	3020	--	0.0	0.1	-0.1	0.1	0.0	0.0	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 168 - 175	Day Change 175 - 180
3M	3001	--	--
	3002	--	--
	3003	--	--
	3004	--	--
	3005	--	--
	3006	--	--
	3007	--	--
	3008	--	--
	3009	--	--
	3010	--	--
	3011	--	--
	3012	--	--
	3013	--	--
	3014	--	--
	3015	--	--
	3016	0.1	-0.1
	3017	0.0	0.0
	3018	0.0	0.1
	3019	0.0	0.0
	3020	0.0	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day							
		Change -14 - -8	Change -8 - 1	Change 1 - 2	Change 2 - 3	Change 3 - 4	Change 4 - 7	Change 7 - 11	Change 7 - 14
1F	1501	0.0	0.0	0.1	0.0	0.0	0.0	0.0	--
	1502	0.1	0.0	0.0	0.0	0.0	0.0	0.0	--
	1503	0.1	0.0	0.0	0.0	0.0	0.1	0.0	--
	1504	0.1	0.0	-0.1	0.1	-0.1	0.1	--	0.0
	1505	0.0	0.1	-0.1	0.0	0.1	0.0	--	0.1
	1506	0.0	0.1	0.1	-0.1	0.0	0.0	--	0.1
	1507	0.0	0.1	0.0	0.0	0.0	0.0	--	0.2
	1508	0.1	0.0	0.0	0.0	0.0	0.0	--	0.1
	1509	0.1	0.1	-0.1	0.1	0.0	0.0	--	0.1
	1510	0.0	0.1	0.0	0.0	0.0	0.1	--	0.0
	1511	0.1	0.0	0.1	-0.1	0.1	0.0	--	0.0
	1512	0.0	0.1	0.0	0.0	0.0	0.1	--	0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 14 - 21	Change 21 - 28	Change 28 - 35	Change 35 - 42	Change 42 - 49	Change 49 - 56	Change 56 - 63	Change 63 - 70
1F	1501	--	--	--	--	--	--	--	--
	1502	--	--	--	--	--	--	--	--
	1503	--	--	--	--	--	--	--	--
	1504	0.1	0.0	0.1	0.0	-0.2	0.3	0.1	0.0
	1505	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.0
	1506	0.0	0.1	0.0	0.0	0.0	0.0	0.1	0.1
	1507	0.0	0.0	0.0	0.0	0.0	0.1	-0.1	0.0
	1508	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0
	1509	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.1
	1510	0.1	0.1	0.0	0.0	0.0	0.1	0.0	0.0
	1511	0.1	0.0	0.1	0.1	-0.1	0.1	0.0	0.1
	1512	0.0	0.1	-0.1	0.0	0.1	0.1	0.0	0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 70 - 77	Change 77 - 84	Change 84 - 90	Change 84 - 91	Change 91 - 98	Change 98 - 105	Change 105 - 112	Change 112 - 119
1F	1501	--	--	--	--	--	--	--	--
	1502	--	--	--	--	--	--	--	--
	1503	--	--	--	--	--	--	--	--
	1504	0.0	0.1	0.0	--	--	--	--	--
	1505	0.0	0.0	0.1	--	--	--	--	--
	1506	-0.1	0.0	0.0	--	--	--	--	--
	1507	0.0	0.1	--	0.0	0.0	0.1	0.0	0.0
	1508	0.0	0.1	--	0.0	0.0	0.0	0.0	0.1
	1509	0.0	0.0	--	0.1	0.0	0.0	0.0	0.0
	1510	-0.1	0.1	--	0.0	0.0	0.0	0.1	0.1
	1511	0.0	0.0	--	0.1	-0.1	0.1	0.0	0.0
	1512	0.0	0.0	--	0.1	0.0	0.0	0.1	-0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 119 - 120	Change 119 - 126	Change 126 - 133	Change 133 - 140	Change 140 - 147	Change 147 - 154	Change 154 - 161	Change 161 - 168
1F	1501	--	--	--	--	--	--	--	--
	1502	--	--	--	--	--	--	--	--
	1503	--	--	--	--	--	--	--	--
	1504	--	--	--	--	--	--	--	--
	1505	--	--	--	--	--	--	--	--
	1506	--	--	--	--	--	--	--	--
	1507	0.1	--	--	--	--	--	--	--
	1508	0.0	--	--	--	--	--	--	--
	1509	0.1	--	--	--	--	--	--	--
	1510	--	0.1	0.0	-0.1	-0.1	0.0	0.0	0.0
	1511	--	0.1	0.1	0.0	0.0	0.1	-0.1	0.1
	1512	--	0.1	0.2	-0.1	0.0	0.0	0.0	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 168 - 175	Day Change 175 - 180
1F	1501	--	--
	1502	--	--
	1503	--	--
	1504	--	--
	1505	--	--
	1506	--	--
	1507	--	--
	1508	--	--
	1509	--	--
	1510	-0.1	0.1
	1511	0.0	0.1
	1512	0.1	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day							
		Change -14 - -8	Change -8 - 1	Change 1 - 2	Change 2 - 3	Change 3 - 4	Change 4 - 7	Change 7 - 11	Change 7 - 14
2F	2501	0.0	0.1	0.0	0.0	-0.1	0.1	0.0	--
	2502	0.0	0.1	-0.1	0.1	-0.1	0.1	0.0	--
	2503	0.1	0.1	0.0	0.0	0.0	0.0	0.0	--
	2504	0.0	0.0	0.0	0.0	0.1	0.0	0.0	--
	2505	0.0	0.1	0.0	0.0	0.0	0.0	0.1	--
	2506	0.1	0.1	-0.1	0.0	0.1	0.0	--	0.0
	2507	-0.1	0.1	0.0	0.0	0.0	0.0	--	0.1
	2508	0.0	0.0	0.0	0.0	0.0	0.0	--	0.1
	2509	-0.1	0.1	0.0	0.0	0.3	-0.3	--	0.1
	2510	-0.1	0.2	0.0	0.0	0.0	0.0	--	0.0
	2511	0.1	0.0	0.0	0.0	0.1	0.0	--	0.1
	2512	0.0	0.0	0.0	0.0	0.0	0.1	--	0.0
	2513	0.0	0.1	0.0	0.0	0.0	0.1	--	0.0
	2514	0.0	0.1	-0.1	0.0	0.0	0.1	--	0.0
	2515	0.0	0.1	0.0	0.0	0.0	0.1	--	0.0
	2516	0.2	0.0	0.0	0.0	0.0	0.1	--	0.0
	2517	0.0	0.0	0.0	0.1	0.0	0.0	--	0.1
	2518	0.0	0.1	0.0	0.2	-0.2	0.1	--	0.0
	2519	0.0	0.2	-0.1	0.1	-0.1	0.0	--	0.1
	2520	0.0	0.1	0.0	0.0	0.0	0.1	--	0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 14 - 21	Change 21 - 28	Change 28 - 35	Change 35 - 42	Change 42 - 49	Change 49 - 56	Change 56 - 63	Change 63 - 70
2F	2501	--	--	--	--	--	--	--	--
	2502	--	--	--	--	--	--	--	--
	2503	--	--	--	--	--	--	--	--
	2504	--	--	--	--	--	--	--	--
	2505	--	--	--	--	--	--	--	--
	2506	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0
	2507	0.1	-0.1	0.0	0.1	0.0	-0.1	0.2	0.0
	2508	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
	2509	0.2	-0.1	0.0	0.1	0.0	0.0	0.1	0.0
	2510	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
	2511	0.0	0.0	0.0	0.1	-0.1	0.1	0.0	0.1
	2512	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.1
	2513	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0
	2514	0.1	0.0	-0.1	0.0	0.1	0.0	0.0	0.1
	2515	0.1	0.0	0.0	-0.1	0.2	0.0	0.0	0.1
	2516	0.1	0.0	0.0	0.1	-0.1	0.1	0.0	0.1
	2517	0.0	0.1	0.0	0.0	0.0	0.2	-0.1	0.1
	2518	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0
	2519	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.1
	2520	0.0	0.1	0.0	0.1	0.0	0.0	0.1	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 70 - 77	Change 77 - 84	Change 84 - 90	Change 84 - 91	Change 91 - 98	Change 98 - 105	Change 105 - 112	Change 112 - 119
2F	2501	--	--	--	--	--	--	--	--
	2502	--	--	--	--	--	--	--	--
	2503	--	--	--	--	--	--	--	--
	2504	--	--	--	--	--	--	--	--
	2505	--	--	--	--	--	--	--	--
	2506	0.1	-0.1	0.1	--	--	--	--	--
	2507	-0.1	0.2	0.0	--	--	--	--	--
	2508	0.1	0.0	0.0	--	--	--	--	--
	2509	0.0	0.2	-0.1	--	--	--	--	--
	2510	0.0	0.0	0.1	--	--	--	--	--
	2511	0.0	0.0	--	0.1	0.0	0.0	0.0	0.1
	2512	0.0	0.0	--	0.1	0.0	0.0	0.0	0.0
	2513	0.0	0.0	--	0.1	0.0	0.1	0.0	-0.1
	2514	0.0	0.0	--	0.1	0.1	0.0	-0.1	0.0
	2515	0.0	0.0	--	0.1	0.0	0.0	0.1	-0.1
	2516	0.1	0.0	--	0.0	-0.1	0.1	0.0	0.1
	2517	-0.1	0.1	--	0.0	0.0	0.0	0.0	0.0
	2518	0.1	0.0	--	0.1	0.0	0.0	0.1	0.0
	2519	0.0	0.0	--	0.1	0.1	-0.1	0.0	0.0
	2520	0.0	0.1	--	0.1	0.0	0.0	0.0	0.0

(b) (4)

Sponsor Reference No (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day							
		Change 119 - 120	Change 119 - 126	Change 126 - 133	Change 133 - 140	Change 140 - 147	Change 147 - 154	Change 154 - 161	Change 161 - 168
2F	2501	--	--	--	--	--	--	--	--
	2502	--	--	--	--	--	--	--	--
	2503	--	--	--	--	--	--	--	--
	2504	--	--	--	--	--	--	--	--
	2505	--	--	--	--	--	--	--	--
	2506	--	--	--	--	--	--	--	--
	2507	--	--	--	--	--	--	--	--
	2508	--	--	--	--	--	--	--	--
	2509	--	--	--	--	--	--	--	--
	2510	--	--	--	--	--	--	--	--
	2511	0.0	--	--	--	--	--	--	--
	2512	0.1	--	--	--	--	--	--	--
	2513	0.0	--	--	--	--	--	--	--
	2514	0.1	--	--	--	--	--	--	--
	2515	0.0	--	--	--	--	--	--	--
	2516	--	-0.1	0.2	0.0	-0.1	0.1	-0.1	0.1
	2517	--	0.0	0.1	0.0	0.0	0.1	0.0	0.0
	2518	--	0.0	0.1	0.0	0.0	0.1	0.0	0.0
	2519	--	0.1	0.0	0.0	0.1	0.1	-0.1	0.0
	2520	--	0.1	0.1	0.0	0.0	0.0	0.1	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 168 - 175	Day Change 175 - 180
2F	2501	--	--
	2502	--	--
	2503	--	--
	2504	--	--
	2505	--	--
	2506	--	--
	2507	--	--
	2508	--	--
	2509	--	--
	2510	--	--
	2511	--	--
	2512	--	--
	2513	--	--
	2514	--	--
	2515	--	--
	2516	0.0	0.0
	2517	0.0	0.1
	2518	0.0	0.1
	2519	0.0	0.1
	2520	0.0	0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change -14 - -8	Change -8 - 1	Change 1 - 2	Change 2 - 3	Change 3 - 4	Change 4 - 7	Change 7 - 11	Change 7 - 14
3F	3501	0.1	0.0	-0.1	0.1	0.0	0.0	0.1	--
	3502	0.1	0.0	0.1	-0.1	0.0	0.1	0.0	--
	3503	0.1	0.0	0.0	0.0	0.0	0.1	0.0	--
	3504	-0.1	0.1	0.0	0.0	0.0	0.0	0.1	--
	3505	0.1	0.0	0.1	-0.1	0.1	0.0	0.0	--
	3506	0.0	0.0	0.1	-0.1	0.0	0.1	--	0.1
	3507	0.0	0.1	0.0	-0.1	-0.1	0.2	--	0.0
	3508	0.0	0.1	0.0	0.0	0.0	0.0	--	-0.1
	3509	0.0	0.1	0.0	0.0	0.1	0.0	--	0.1
	3510	0.0	0.1	-0.1	0.1	0.0	0.0	--	0.1
	3511	0.0	0.0	0.1	0.0	0.1	-0.1	--	0.0
	3512	0.1	0.0	0.0	0.0	0.0	0.0	--	0.1
	3513	0.0	0.1	0.0	0.0	0.0	0.1	--	0.0
	3514	0.0	0.1	-0.1	0.0	0.1	0.0	--	0.0
	3515	0.1	0.0	0.0	0.0	0.0	0.1	--	0.0
	3516	0.1	-0.1	0.0	0.0	0.0	0.1	--	0.1
	3517	0.1	0.0	0.0	-0.1	0.1	0.0	--	0.1
	3518	-0.1	0.1	0.0	0.0	0.1	0.0	--	0.0
	3519	0.0	0.0	-0.1	0.0	0.1	0.0	--	0.0
	3520	0.0	0.1	0.0	0.0	0.0	0.1	--	0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 14 - 21	Change 21 - 28	Change 28 - 35	Change 35 - 42	Change 42 - 49	Change 49 - 56	Change 56 - 63	Change 63 - 70
3F	3501	--	--	--	--	--	--	--	--
	3502	--	--	--	--	--	--	--	--
	3503	--	--	--	--	--	--	--	--
	3504	--	--	--	--	--	--	--	--
	3505	--	--	--	--	--	--	--	--
	3506	0.1	-0.1	0.0	0.0	0.1	0.0	0.1	0.0
	3507	0.1	0.1	-0.1	0.0	0.1	0.1	0.0	0.1
	3508	0.3	0.0	0.0	0.0	0.1	0.0	0.1	0.0
	3509	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
	3510	0.1	0.0	0.0	0.0	0.1	0.0	-0.1	0.1
	3511	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.1
	3512	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0
	3513	0.1	0.0	0.1	0.0	0.0	0.0	0.1	0.0
	3514	0.1	0.1	0.0	0.0	0.0	0.1	0.0	0.1
	3515	0.1	0.0	0.0	0.0	0.0	0.1	0.0	0.0
	3516	0.0	0.2	-0.2	0.1	0.0	0.1	0.0	0.0
	3517	-0.1	0.1	0.0	0.1	-0.1	0.1	0.0	0.1
	3518	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.1
	3519	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.1
	3520	0.0	0.1	0.0	0.1	-0.1	0.1	0.0	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 70 - 77	Change 77 - 84	Change 84 - 90	Change 84 - 91	Change 91 - 98	Change 98 - 105	Change 105 - 112	Change 112 - 119
3F	3501	--	--	--	--	--	--	--	--
	3502	--	--	--	--	--	--	--	--
	3503	--	--	--	--	--	--	--	--
	3504	--	--	--	--	--	--	--	--
	3505	--	--	--	--	--	--	--	--
	3506	0.0	0.0	0.0	--	--	--	--	--
	3507	0.0	0.0	0.1	--	--	--	--	--
	3508	0.0	0.1	0.0	--	--	--	--	--
	3509	0.1	0.0	0.0	--	--	--	--	--
	3510	0.0	0.0	0.1	--	--	--	--	--
	3511	0.0	0.0	--	0.0	0.1	0.0	0.0	0.0
	3512	0.0	0.1	--	0.0	0.0	0.0	0.0	0.1
	3513	0.1	0.0	--	0.0	0.1	0.0	0.0	0.0
	3514	-0.1	0.0	--	0.1	0.1	0.0	0.0	0.0
	3515	0.0	0.1	--	0.0	0.0	0.1	-0.1	0.0
	3516	0.1	0.0	--	0.0	0.1	-0.1	0.0	0.0
	3517	0.0	0.0	--	0.0	0.0	0.0	0.1	0.0
	3518	0.0	0.0	--	0.0	0.1	0.0	0.0	0.0
	3519	0.0	0.0	--	0.0	0.0	0.0	0.1	0.0
	3520	0.1	0.0	--	0.0	0.1	-0.1	0.1	-0.1

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day							
		Change 119 - 120	Change 119 - 126	Change 126 - 133	Change 133 - 140	Change 140 - 147	Change 147 - 154	Change 154 - 161	Change 161 - 168
3F	3501	--	--	--	--	--	--	--	--
	3502	--	--	--	--	--	--	--	--
	3503	--	--	--	--	--	--	--	--
	3504	--	--	--	--	--	--	--	--
	3505	--	--	--	--	--	--	--	--
	3506	--	--	--	--	--	--	--	--
	3507	--	--	--	--	--	--	--	--
	3508	--	--	--	--	--	--	--	--
	3509	--	--	--	--	--	--	--	--
	3510	--	--	--	--	--	--	--	--
	3511	0.0	--	--	--	--	--	--	--
	3512	0.0	--	--	--	--	--	--	--
	3513	0.0	--	--	--	--	--	--	--
	3514	0.0	--	--	--	--	--	--	--
	3515	0.0	--	--	--	--	--	--	--
	3516	--	0.1	0.1	-0.1	0.1	0.0	0.0	0.0
	3517	--	0.1	0.0	0.0	0.0	0.1	0.0	0.0
	3518	--	0.1	0.0	0.0	0.0	0.0	0.1	0.0
	3519	--	0.0	0.0	-0.1	0.0	0.1	-0.1	0.1
	3520	--	0.1	0.1	0.0	0.0	0.0	0.0	0.0

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 5

Individual Body Weight Gains (kg)

Group 1 - Reference Item Group 2 - Ad26 (b) (4) 1 x 10^11 vp

Group 3 - Ad26 (b) (4) 1 x 10^11 vp + 150 µg

Group / Sex	Animal No.	Day Change 168 - 175	Day Change 175 - 180
3F	3501	--	--
	3502	--	--
	3503	--	--
	3504	--	--
	3505	--	--
	3506	--	--
	3507	--	--
	3508	--	--
	3509	--	--
	3510	--	--
	3511	--	--
	3512	--	--
	3513	--	--
	3514	--	--
	3515	--	--
	3516	0.1	0.0
	3517	0.0	0.1
	3518	-0.1	0.1
	3519	-0.1	0.1
	3520	0.0	0.2

(b) (4)

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

FINAL REPORT

Study Phase: Molecular Biology

Test Facility Study No. (b) (4)

Sponsor Reference No. (b) (4)

TEST FACILITY:
(b) (4)

Appendix 6

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Appendix 6

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Appendix 6

1. INTRODUCTION

This report describes the biodistribution evaluation of Ad26 (b) (4) vector DNA in New Zealand White Rabbit tissue and fluid samples collected from the study entitled: "A Single Dose Biodistribution Study of Ad26 (b) (4) vector DNA by Intramuscular Injection in Rabbits with up to 180 Days Observation Period". Quality standards applicable to this report are discussed in the main study report.

The objective of this portion of the study, performed at (b) (4) was to determine the biodistribution of Ad26 (b) (4) vector DNA in Male and Female New Zealand White Rabbit tissue and fluid samples using a Real-Time Quantitative Polymerase Chain Reaction (qPCR). The study was sponsored by Janssen Infectious Diseases & Diagnostics BVBA, Beerse, Belgium. (b) (4), (b) (6) served as the Study Director.

For the work detailed in this report, the Molecular Biology phase Experimental start date was 31 Aug 2018 and the Molecular Biology phase Experimental completion date was 30 Jan 2019.

2. EXPERIMENTAL DESIGN

Experimental procedures applicable to the Molecular Biology phase analysis are summarized in Text Table 1.

Text Table 1
Experimental Design

Group No.	Test Material	Dose Level	Dose Volume (mL)	Necropsy Day	No. of Main Study Animals per Necropsy Day	
					Males	Females
1	Reference Item	0	1	11,90,120,180	3	3
2	Ad26 (b) (4) vector DNA	1 x 10^{11} vp	0.5		5	5
3	Ad26 (b) (4) (b) (4)	1 x 10^{11} vp + 150µg	1 (of mixture)		5	5

The experimental design applicable to the biodistribution portion was used for tissue and fluid samples collected at the Test Facility as listed in Text Table 2.

Appendix 6

Text Table 2
Samples Collected for Analysis

Tissues and Fluids List:	
Blood	Lung (right caudal lobe)
Bone marrow (femur, flush with 1 mL of sterile saline, bilateral)	Bicep femoris muscle and full depth of underlying muscles to a maximum depth of 3 cm (at marked injection site)
Brain (Right Forebrain)	Ovaries
Heart (apex)	Testes
Iliac lymph node	Skin with subcutis over the injection
Popliteal lymph node	Spleen (median region)
Kidney (hilar region)	Thymus
Liver	Lymph node, mesenteric

Tissues collected from euthanasia on Day 11 and Day 90 were analyzed for all treatment groups. Tissues from Day 120 were analyzed for iliac lymph node, skin with subcutis over the injection, spleen, popliteal lymph node, and muscle (injection site); tissues from Day 180 were analyzed for spleen and iliac lymph node given that these tissues were found to be positive for the presence of Ad26 (b) (4) vector DNA at the previous timepoints. No Group 1 samples were analyzed at the 2 latest timepoints (Day 120, Day 180) given that they found to be negative for 2 consecutive time points for all tissues/fluids.

3. MATERIALS AND METHODS

3.1. Primer No.1

Identity: Ad26 (b) (4) DP-FP ((b) (4))

Supplier: (b) (4)

Concentration: (b) (4)

Lot No. : (b) (4)

Sequence: (b) (4)

Length: 17 bases

Storage Conditions: Kept in a freezer set to maintain -20°C

Expiry Date: 05 Jun 2023 (for Lot number (b) (4)) and 28 Jun 2023 (for Lot numbers (b) (4))

Lot number corresponded to the Reference number indicated on the specification sheet.

Appendix 6

3.2. Primer No.2

Identity:	Ad26 (b) (4) DP-RP ((b) (4))
Supplier:	(b) (4)
Concentration:	(b) (4)
Lot No. :	(b) (4)
Sequence:	(b) (4)
Length:	22 bases
Storage Conditions:	Kept in a freezer set to maintain -20°C
Expiry Date:	05 Jun 2023 (for Lot number (b) (4)) and 28 Jun 2023 (for Lot numbers (b) (4)) Lot number corresponded to the Reference number indicated on the specification sheet.

3.3. Probe

Identity:	Ad26 (b) (4) DP -Probe TaqMan probe (b) (4)
Supplier:	(b) (4)
Concentration:	(b) (4)
Catalog No.:	(b) (4)
Tube number:	(b) (4)
Sequence:	(b) (4)
Length:	18 bases
Storage Conditions:	Kept in a freezer set to maintain -20°C, protected from light when possible
Expiry Date:	22 Jun 2019 (for Lot numbers (b) (4) , 01 Oct 2019 (for Lot number (b) (4)) and 24 Oct 2019 (for Lot numbers (b) (4)

3.4. Reference Standard

Identity:	Ad26 (b) (4)
Description:	Ad26 (b) (4) DP RM (b) (4)
Supplier:	Sponsor
Concentration:	1.9×10^{11} VP/mL (1.9×10^{8} copies/µL)
Batch No.:	(b) (4)
Storage Conditions:	Kept in a freezer set to maintain -80°C
Expiry Date:	28 Feb 2019

Appendix 6

A Certificate of Analysis (CofA) for the Reference Standard is provided in Appendix 5.

3.5. Blank Matrix

Identity:	Rabbit Genomic DNA
Description:	Pool of New Zealand White Rabbit genomic DNA
Supplier:	(b) (4)
Tissue Type:	Mesenteric Lymph Nodes, Thymus
Quantity:	1 mL/aliquot
Concentration:	1154.6 µg/mL in Elution Buffer
Batch No.:	(b) (4)
Storage Conditions:	Kept in a freezer set to maintain -20°C
Expiry Date:	The stability was monitored and deemed acceptable based on the assay's performance.

3.6. Calibration Standards

Serial dilutions of Ad26 (b) (4) vector DNA reference standard Vector DNA were prepared in blank matrix (0.14 µg/µL rabbit genomic DNA) for the calibration curve, covering the theoretical concentration range of 20 copies per reaction or 28.6 copies/µg DNA (Lower Limit of Quantitation, LLOQ) to 1 X 10^6 copies per reaction or 1428571.4 copies/µg DNA (Upper Limit of Quantitation, ULOQ) of Ad26 (b) (4) vector DNA. Calibration standards were generated in bulk and stored until use in the qPCR assay. A zero standard, also called No Template Control (or NTC), containing no Ad26 (b) (4) vector DNA, was loaded on each plate. The No Template Control consisted of the blank matrix diluted, in nuclease-free water, to the appropriate genomic DNA concentration (e.g. 0.14 µg/µL target sample DNA concentration). Refer to the latest version of the qPCR analytical procedure, (b) (4) for details (Appendix 4).

3.7. Quality Control Samples

Quality control (QC) samples of Ad26 (b) (4) vector DNA reference standard Vector DNA were prepared in blank matrix (0.14 µg/µL) at theoretical concentrations of 60, 5000 and 250000 copies per reaction, and were assayed in replicates of three, in duplicate. Quality controls were generated in bulk and stored until use in qPCR assay. Refer to the latest version of the qPCR analytical procedure, (b) (4) for details (Appendix 4).

Appendix 6

3.8. Study Samples

Total DNA for qPCR biodistribution analysis was isolated from Tissue and fluid study samples using the Maxwell ® 16 LEV Blood DNA Kit from Promega as per the analytical procedures (b) (4) The latest version of the APs are attached as Appendix 1 and Appendix 2, respectively.

Up to 300 µL of whole blood and up to 400 µL of bone marrow were processed. For all tissues except the muscle, up to 600 mg of tissue was first homogenized using the Geno/Grinder 2010 instrument. For the muscle, given that up to 15 g of tissue were collected, approximately 8 g of tissue separated in 2 aliquots (approximately 4 g each) was first homogenized and pooled. Then the appropriate volume of tissue homogenate was treated with the proteinase K enzyme. Given that no signal was detected at the injection site (muscle) on Day 11 and Day 90 following the initial analysis, a second analysis (leftover tissue if available) was performed in order to ensure that Ad26 (b) (4) vector DNA was absent from the total amount of collected tissue from the the muscle (injection site).

It should be noted that during the course of the sample analysis study, efforts were made to improve the DNA isolation results given that they were not in line with those obtained during the validation. Improvements in the DNA isolation procedure for the iliac lymph node, the liver, the brain (forebrain) and the thymus samples were performed by increasing the tissue homogenate volume loaded into the Maxwell cartridges in order to yield a higher DNA concentration. This update had no impact on the assays performed given that the total volume loaded in the Maxwell cartridges remained unchanged and that the final concentration of DNA isolated was the critical factor to perform the subsequent qPCR assay.

Additionally, the DNA isolation was repeated for some samples following the initial isolation due to a DNA concentration or a 260/280 ratio below the target specified in AP. For those samples, if a qPCR result was available, it was not considered as being appropriate. The qPCR assay was therefore repeated using a DNA sample meeting the specifications for concentration and ratio. Details concerning the repeated sample analysis are presented in Table 9.

DNA quantity was determined by spectrophotometry as per (b) (4) for the study samples (refer to Appendix 3) or standard Operating Procedure (SOP) (b) (4) for the Pool of New Zealand White Rabbit genomic DNA used as the blank matrix for the calibration curve. Once isolated, total DNA was stored in a freezer set to maintain -20°C until qPCR analysis as (b) (4) (refer to Appendix 4).

Study samples were prepared to a target DNA concentration of 0.14 µg/µL (0.7 µg DNA per well) in nuclease-free water for all matrices, when possible. In order to minimally process the total target concentration of 2 µg DNA unspiked and 1 µg DNA spiked with the reference standard, the unspiked study samples were analyzed in quadruplicate (4 PCR wells) and the spiked study samples were analyzed in duplicate (2 PCR wells) where possible. Study samples with DNA concentration results ≤ 0.14 µg/µL were processed neat in the appropriate number of PCR wells to achieve a total quantity of at least 2 µg of DNA analyzed, where possible, and flagged as such in the results table. Study samples with a 260/280 ratio < 1.7 were analyzed but

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flagged as such in the results table. The mastermix in blank matrix spiked with Ad26 (b) (4) vector DNA reference standard Vector DNA (spiked NTC) was analyzed in triplicate (3 PCR wells) and the results were used as the nominal concentration of the spiked study samples.

3.9. Analytical Method

The real-time quantitative PCR assay is a TaqMan 5'-nuclease assay consisting of two oligonucleotide primers (forward and reverse) for target gene amplification and signal detection with a VIC dye-labeled TaqMan MGB (minor groove binder) probe. During the PCR assay, cleavage of the probe by the DNA polymerase separates the reporter dye (at the 5'- end of the probe) and the quencher (at the 3'- end of the probe). The increase of the resulting signal after each cycle is directly proportional to the amount of target sequence amplified. The oligonucleotide primer set is specific for amplifying Ad26 (b) (4) vector DNA reference standard (b) (4).

The calibration standards and quality control samples were mixed with a PCR cocktail ("Master Mix") containing the target-specific oligonucleotide primers and fluorogenic probe. The study samples were mixed with both PCR cocktail ("Master Mix") and Spiked Control PCR cocktail ("SpC Master Mix") in order to assess PCR efficiency. The SpC Master Mix was prepared with a quantity of Ad26 (b) (4) vector DNA reference standard Vector DNA corresponding to the QC3 level (60 copies/reaction). The results of the SpC NTC wells were used as the nominal concentration of the spiked study samples.

PCR reactions were assembled in 384-well plates and run on the Applied Biosystems QuantStudioTM 7 Flex Real-Time PCR System. The data was further imported in Softmax Pro for processing and analysis.

Negative control reactions (containing no reference standard, only blank matrix), also called "No Template Controls" and Spiked control Master Mix No Template Control (SpC NTC), were generated in bulk and stored until use in qPCR assay.

3.10. Method Validation

The analytical method validation conducted at (b) (4) under Study No. (b) (4) was subjected to the following experimental checks to ensure it was suitable for its intended use: range of response, intra- and inter-assay precision and accuracy, specificity and selectivity, limit of detection, linearity of dilution. Short-term, long-term, and freeze-thaw matrix stability assessments have been completed for all matrices. Refer to the Method Validation Summary (Appendix 6) for the validation details.

3.11. Calculation of Ad26 (b) (4) Vector DNA Copies, PCR Efficiency (PCRE) and Coefficient of Variation (CV)

The study sample Ad26 (b) (4) vector DNA concentration in copies per µg of host genomic DNA was calculated using the formula below:

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$$\text{Copies/}\mu\text{g} = \frac{\text{Mean back-calculated copies per reaction}}{\text{Total } \mu\text{g of DNA tested per reaction}}$$

In order to verify that potential inhibitors carried over from the DNA isolation were not affecting the qPCR assay, all study samples were analyzed in two separate reactions. In the first reaction, the samples were added to a PCR cocktail (Master Mix) that contained only the components of the PCR Master Mix. The results from this analysis were used to calculate and report the number of copies/µg per reaction of Ad26 (b) (4) vector DNA detected in the study samples. In the second reaction, study samples were added to a Spiked PCR cocktail (Spiked Control Master Mix or SpC Master Mix) containing the components of the PCR Master Mix and a known quantity of Ad26 (b) (4) vector DNA reference standard (spiked). The amount of Ad26 (b) (4) vector DNA spiked (nominal value) in the SpC Master Mix was determined for each run using SpC NTC wells without Study Sample DNA.

Samples with PCRE (PCR efficiency) ≥ 50% were considered acceptable. For each study sample the PCRE was calculated using the expression:

$$\text{PCRE} = \frac{\text{SpC Sample Mean BCC (Copies per Reaction)}}{\text{SpC Theoretical}} \times 100$$

Where:

$$\text{SpC Theoretical} = \text{SpC NTC Mean BCC (Copies per Reaction)} + \text{UnSpC Sample Mean BCC (Copies per Reaction)}$$

Note: Mean BCC= Mean back-calculated concentration

Precision expressed as coefficient of variation (CV) was calculated using the formula below:

$$\%\ \text{CV} = \frac{\text{(Standard Deviation)}}{\text{Mean}} \times 100$$

3.12. Computerized Systems

Critical computerized systems used in this study phase are listed below (see Text Table 3).

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Text Table 3
Computerized Systems

System Name	Version No.	Description of Data Collected and/or Analyzed
Applied Biosystems QuantStudio™ 7 Flex Real-Time PCR System and QuantStudio™ 7 Flex software version	1.2	Data capture and analysis
Softmax Pro GXP	5.4.6	Data analysis
Watson LIMS	7.4.2	Sample management
Excel	2016	Data tabulation
Word	2016	Reporting of data in the report
Mesa Laboratories AmegaView CMS	version 3.0 Build 1208.8	Continuous Monitoring System. Monitoring of standalone fridges, freezers, incubators, and selected laboratories to measure temperature, relative humidity, and CO_2, as appropriate
Johnson Controls Metasys	MVE 7.0 (M5)	Building Automation System. Control of HVAC and other building systems, as well as temperature/humidity control and trending in selected laboratories and animal rooms
Deviation Information Library	2.1.29	Reporting and tracking of deviations

4. DEVIATIONS

The following deviations from the Analytical procedures occurred during the sample analysis:

- The wrong DNA concentration was used during the qPCR analysis of the popliteal lymph node for sample Day 11 1003 and Day 90 3010 due to an oversight. For the sample 1003, the final concentration analyzed was higher than the target concentration of 0.14 µg/µL. However, given that no PCR inhibition was observed during the analysis the use of a higher DNA concentration did not impact the analysis of this sample. For sample 3010, a final DNA concentration of 0.08 µg/µL (1.6 µg of total DNA) instead of 0.14 µg/µl (2.8 µg of total DNA) was analyzed. However, the sample 3010 was successfully repeated using the appropriate concentration of DNA obtained in a new DNA isolation. Therefore, this deviation was considered to have no impact on the data.
- Additional minor deviations from the Analytical Procedures and/or Standard Operating Procedures occurred during the study and were documented in the raw data. The deviations were minor in nature and had no impact upon the integrity of the study nor the conclusions drawn for its intended purpose. No deviation to the study plan occurred during this study.

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5. RESULTS AND DISCUSSIONS

5.1. PCR Standard Curve and QC Samples

All standards and QC samples met acceptance criteria from all reported assays. The assay failure rate is 0.0%.

The PCR calibration standards and QC sample results are summarized in Table 2, Table 3, Table 4, Table 5, and Table 6. A summary of each assay run during the course of the study is also presented in Table 1.

5.2. DNA Isolation

Several blood samples, some bone marrow and iliac lymph node samples, and an incidental ovary sample presented a 260/280 absorbance ratio below 1.7, indicating that some impurities were present in the DNA isolate. Regardless of the presence of impurities, Ad26 (b) (4) vector DNA could be detected in all samples, as shown by the positive signal observed in all spiked samples (results kept in the raw data), indicating that the impurities had no impact on the quality of the PCR reaction. However, the presence of impurities may have contributed to an overestimation of the quantity of DNA present in these samples, meaning that a lower actual quantity of DNA may have been analyzed for some of these samples. Moreover, some blood, bone marrow, iliac lymph node, and incidental skin samples were below the target DNA concentration of 0.14 µg/uL upon analysis, meaning that the sensitivity of the copy numbers detected for these samples may have been affected. Generally, it was possible to analyze a total amount of 2 µg of DNA. Nevertheless, even when this was not feasible, as the Ad26 (b) (4) vector DNA copies measured are normalized to the amount of DNA analyzed, the lower quantity of DNA recovered at the isolation step had a limited impact on the actual copy number reported.

5.3. Detection of Ad26 (b) (4) vector DNA in No Template Controls, Spiked No Template Controls and Spiked Control Samples

Ad26 (b) (4) vector DNA levels were below the validated Limit of Detection (LOD) established at 5 copies per reaction (7.1 copies/µg DNA) in all NTC samples indicating that no contamination was detected in the qPCR assay setup.

The SpC NTC %CV of the replicates was ≤ 30% for all assays. A variability in the SpC NTC nominal concentration values was noticed across the assays. This was considered to have no impact since the nominal value, which is reflecting the actual amount of the reference standard spiked in the master mix, was used to test the efficiency of the PCR assay in a background of each study sample DNA.

All samples met PCR efficiency acceptance criteria in all reported results.

5.4. Detection of Ad26 (b) (4) Vector DNA in Study Samples

The results from the qPCR analysis for each matrix are summarized in Table 7. Positive samples were considered to be those samples which had detectable Ad26 (b) (4) vector DNA levels

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above the LLOQ. The results for positive samples are summarized in Text Table 4. The samples that were below the LLOQ but above the LOD (limit of detection) were indicated as < LLOQ and the samples that were below the LOD were indicated as such in the results table. All samples were analyzed within the validated parameters.

DNA isolation and qPCR analysis was performed on a total of 920 tissue and fluid samples collected at Day 11, Day 90, Day 120, and Day 180.

Samples collected from control animals (Group 1) at Day 11 and Day 90 had Ad26 (b) (4) vector DNA results below the LOD of the assay, as expected, for all tissues and fluids. For Group 2 and Group 3 animals, all matrices analyzed demonstrated Ad26 (b) (4) vector DNA results below the LLOQ (i.e. negative for Ad26 (b) (4) vector DNA) of the assay except for the skin with subcutis over the injection site, the spleen, and the iliac and popliteal lymph nodes. Low Ad26 (b) (4) Vector DNA (> LOD but ≤ LLOQ) were detected in some samples, including iliac and popliteal lymph nodes, liver, muscle, skin and spleen samples. The number of tissues with Ad26 (b) (4) Vector DNA copies between the LOD and the LLOQ decreased over time. The number of samples with results > LOD but ≤ LLOQ are summarized in Text Table 5.

As per Text Table 4, only the skin at the injection site, the spleen (median region) as well as the iliac and popliteal lymph nodes were found to be positive for Ad26 (b) (4) vector DNA at Day 11. Although the skin at the injection site presented the highest number of vector copies (as observed for Group 2), the iliac lymph node was the tissue with the highest incidence of positive samples in both Group 2 and 3. The popliteal lymph node was only positive in one animal from Group 2. On Day 90, Ad26 (b) (4) vector DNA was no longer detected in the popliteal lymph node. On day 120 Ad26 (b) (4) vector DNA was detected at low level only (> LOD but ≤ LLOQ) in the spleen while the skin at the injection site and iliac lymph node were still positive, but showing a reduced incidence, as well as a lower maximum quantity of Ad26 (b) (4) vector DNA than those detected on Day 11. By Day 120, the skin at the injection site was no longer presented vector copies of Ad26 (b) (4) vector DNA, and only two animals from Group 2 were positive in the iliac lymph node. By Day 180, one iliac lymph node sample was still positive but the number of copies detected was close to the LLOQ.

Given that no signal was detected at the injection site (muscle) on Day 11 and Day 90 following the initial analysis, a second analysis (leftover tissue analysis if available) was performed in order to ensure that Ad26 (b) (4) vector DNA was absent from the injection site muscle. Only the original results were reported in the absence of signal in the leftover tissue.

Throughout the study, the presence of (b) (4) in the dosing mixture did not affect the biodistribution and the persistence of the Ad26 vector, given that the overall distribution pattern (i.e. tissues showing a positive signal), the copy numbers detected, as well as the incidence of positive samples in Group 2 and 3 for a given timepoint were generally similar.

Collectively this data set demonstrates a limited distribution profile as well as clearance over time of Ad26 (b) (4) vector DNA following intramuscular injection.

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Text Table 4
Range of Positive (>LLOQ, Theoretical Value 20 Copies Per Reaction or 28.6 Vopies/µg DNA) Samples for the Quantitative Determination of Ad.26 (b) (4) Vector DNA in New Zealand White Rabbits Tissue and Fluid Samples (Copies/µg DNA)

	D11				D90				D120				D180			
Tissues	**Gr 2**	**N**	**Gr 3**	**N**	**Gr 2**	**N**	**Gr 3**	**N**	**Gr 2**	**N**	**Gr 3**	**N**	**Gr 2**	**N**	**Gr 3**	**N**
Iliac LN	63.6 to 387.6	9	108.6 to 347.4	9	48.1	1	25.9 to 35.3	2	37.9 to 53.4	2	a	0	37.6	1	a	0
Popliteal LN	29.0	1	a	0	a	0	a	0	a	0	a	0	b	b	b	b
Skin	39.1 to 6304.3	4	88.6 to 272.6	2	280.1	1	42.7 to 175.1	2	a	0	a	0	b	b	b	b
Spleen	37.3 to 118.6	6	26.4 to 75.6	7	a	0	a	0	a	0	a	0	a	0	a	0

Gr = Group; N = Number of animals with signal >LLOQ on a total of 10 animals (5M + 5F) analyzed per timepoint;
LN = Lymph Node
a = Results <LLOQ/LOD
b = Not analyzed

Text Table 5
Summary of the Number of Samples with Results > LOD (5 Copies per Reaction or 7.1 Copies/µg DNA) but ≤ LLOQ (20 Copies per Reaction or 28.6 Copies/µg DNA) for the Quantitative Determination of Ad.26 (b) (4) Vector DNA in New Zealand White Rabbits Tissue and Fluid Samples (Copies/µg DNA)

	D11		D90		D120		D180	
Tissues	**Group 2***	**Group 3***	**Group 2***	**Group 3***	**Group 2***	**Group 3***	**Group 2***	**Group 3***
Iliac LN	1	0	3	3	1	0	2	2
Liver	0	1	0	0	a	a	a	a
Muscle	1	0	0	0	0	0	a	a
Popliteal LN	1	0	0	0	0	0	a	a
Skin	2	3	0	0	0	0	a	a
Spleen	4	2	0	0	1	0	0	0

LN = Lymph Node
* Total of 10 animals (5M + 5F) analyzed per timepoint
a = Not analyzed

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6. CONCLUSION

DNA isolation and qPCR analysis for the determination of Ad26 (b) (4) vector DNA was performed on a total of 920 rabbit tissue and fluid samples following a single intramuscular injection of Ad26 (b) (4) vector DNA in the presence or absence of (b) (4) For all control (Group 1) samples collected at Day 11 or Day 90, Ad26 (b) (4) vector DNA results were below the LLOQ of the assay, as expected. Positive Ad26 (b) (4) vector DNA values were detected in the skin at the intramuscular injection site, the spleen, and in the iliac and popliteal lymph nodes at Day 11, with the highest vector copy number present in the skin. By Day 180, Ad26 (b) (4) vector DNA was no longer detected in any tissue, with the exception of 1 iliac lymph node, and at low vector copy numbers close to the LLOQ of the assay. Overall, this demonstrates a limited biodistribution profile as well as a clearance over time of Ad26 (b) (4) vector DNA following intramuscular injection. The presence of (b) (4) in the dosing mixture did not significantly impact on the biodistribution and the persistence of the Ad26 vector.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

7. REPORT APPROVAL

DocuSigned by:
(b) (4), (b) (6)

Individual Scientist, Immunology

Appendix 6

Table 1
Assay Run Summary for the Quantitative Determination of Ad26 (b) (4) DNA in Rabbit Tissues and Fluids

Appendix 6

Assay Run Summary for the Quantitative Determination of Ad26 (b) (4) DNA in Rabbit Tissues and Fluids

Assay ID	Assay Date	Accepted/Rejected	Comments
Pro-01	31-Aug-2018	N/Ap	DNA
Pro-02	31-Aug-2018	N/Ap	DNA
Pro-03	04-Sep-2018	N/Ap	DNA
Pro-04	06-Sep-2018	N/Ap	DNA
Pro-05	05-Sep-2018	N/Ap	DNA
Pro-06	05-Sep-2018	N/Ap	DNA
Pro-07	06-Sep-2018	Accepted	Bulk Spiking 1 + qPCR Spike check 1
Pro-08	07-Sep-2018	N/Ap	DNA
Pro-09	07-Sep-2018	Accepted	QPCR
Pro-10	07-Sep-2018	Accepted	QPCR
Pro-11	10-Sep-2018	N/Ap	DNA
Pro-12	10-Sep-2018	N/Ap	DNA
Pro-13	10-Sep-2018	Accepted	QPCR
Pro-14	11-Sep-2018	N/Ap	DNA
Pro-15	12-Sep-2018	N/Ap	DNA
Pro-16AB	13-Sep-2018	N/Ap	DNA
Pro-16CD	14-Sep-2018	N/Ap	DNA
Pro-17	14-Sep-2018	N/Ap	DNA
Pro-18	17-Sep-2018	N/Ap	DNA
Pro-19	14-Sep-2018	Accepted	QPCR
Pro-20	14-Sep-2018	Accepted	QPCR
Pro-21	18-Sep-2018	Accepted	QPCR
Pro-22	18-Sep-2018	Accepted	QPCR
Pro-23	18-Sep-2018	N/Ap	DNA
Pro-24	19-Sep-2018	N/Ap	DNA
Pro-25	19-Sep-2018	Accepted	QPCR
Pro-26	19-Sep-2018	Accepted	QPCR

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Assay Run Summary for the Quantitative Determination of Ad26 (b) (4) DNA in Rabbit Tissues and Fluids

Assay ID	Assay Date	Accepted/Rejected	Comments
Pro-27	20-Sep-2018	N/Ap	DNA
Pro-28	20-Sep-2018	Accepted	QPCR
Pro-29	20-Sep-2018	Accepted	QPCR
Pro-30	21-Sep-2018	Accepted	QPCR
Pro-31	21-Sep-2018	Accepted	QPCR
Pro-32	24-Sep-2018	N/Ap	DNA
Pro-33	24-Sep-2018	N/Ap	DNA
Pro-34	25-Sep-2018	N/Ap	DNA
Pro-35	26-Sep-2018	N/Ap	DNA
Pro-36	26-Sep-2018	N/Ap	DNA
Pro-37	27-Sep-2018	N/Ap	DNA
Pro-38	27-Sep-2018	N/Ap	DNA
Pro-39	28-Sep-2018	Accepted	QPCR
Pro-40	28-Sep-2018	Accepted	QPCR
Pro-41	28-Sep-2018	N/Ap	DNA
Pro-42	28-Sep-2018	N/Ap	DNA
Pro-43	01-Oct-2018	N/Ap	DNA
Pro-44	01-Oct-2018	N/Ap	DNA
Pro-45	02-Oct-2018	N/Ap	DNA
Pro-46	02-Oct-2018	N/Ap	DNA
Pro-47	03-Oct-2018	N/Ap	DNA
Pro-48	03-Oct-2018	N/Ap	DNA
Pro-49	03-Oct-2018	Accepted	Bulk Spiking 2 + qPCR Spike check 2
Pro-50	04-Oct-2018	N/Ap	DNA
Pro-51	04-Oct-2018	N/Ap	DNA
Pro-52	04-Oct-2018	N/Ap	DNA
Pro-53	05-Oct-2018	N/Ap	DNA

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Assay Run Summary for the Quantitative Determination of Ad26 (b) (4) DNA in Rabbit Tissues and Fluids

Assay ID	Assay Date	Accepted/Rejected	Comments
Pro-54	05-Oct-2018	N/Ap	DNA
Pro-55	24-Oct-2018	N/Ap	Bulk Spiking 3
Pro-55A	26-Oct-2018	Accepted	Spike Check 3
Pro-56	09-Oct-2018	Accepted	QPCR
Pro-57	09-Oct-2018	Accepted	QPCR
Pro-58	10-Oct-2018	N/Ap	DNA
Pro-59	11-Oct-2018	N/Ap	DNA
Pro-60	10-Oct-2018	Accepted	QPCR
Pro-61	10-Oct-2018	Accepted	QPCR
Pro-62	12-Oct-2018	N/Ap	DNA
Pro-63	15-Oct-2018	N/Ap	DNA
Pro-64	15-Oct-2018	Accepted	QPCR
Pro-65	15-Oct-2018	Accepted	QPCR
Pro-66	16-Oct-2018	Accepted	QPCR
Pro-67	16-Oct-2018	Accepted	QPCR
Pro-68	16-Oct-2018	N/Ap	DNA
Pro-69	17-Oct-2018	Accepted	QPCR
Pro-70	17-Oct-2018	Accepted	QPCR
Pro-71	17-Oct-2018	N/Ap	DNA
Pro-72	18-Oct-2018	Accepted	QPCR
Pro-73	18-Oct-2018	Accepted	QPCR
Pro-74	19-Oct-2018	N/Ap	DNA
Pro-75	31-Oct-2018	N/Ap	DNA
Pro-76	23-Oct-2018	Accepted	QPCR
Pro-77	23-Oct-2018	Accepted	QPCR
Pro-78	25-Oct-2018	N/Ap	DNA
Pro-79	29-Oct-2018	N/Ap	DNA

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Assay Run Summary for the Quantitative Determination of Ad26 (b) (4) DNA in Rabbit Tissues and Fluids

Assay ID	Assay Date	Accepted/Rejected	Comments
Pro-80	29-Oct-2018	N/Ap	DNA
Pro-81	30-Oct-2018	N/Ap	DNA
Pro-82	30-Oct-2018	N/Ap	DNA
Pro-83	31-Oct-2018	N/Ap	DNA
Pro-84	01-Nov-2018	Accepted	QPCR
Pro-85	01-Nov-2018	Accepted	QPCR
Pro-86	01-Nov-2018	N/Ap	DNA
Pro-87	05-Nov-2018	N/Ap	DNA
Pro-88	05-Nov-2018	N/Ap	DNA
Pro-89	06-Nov-2018	Accepted	QPCR
Pro-90	06-Nov-2018	Accepted	QPCR
Pro-91	06-Nov-2018	N/Ap	DNA
Pro-92	07-Nov-2018	Accepted	QPCR
Pro-93	07-Nov-2018	Accepted	QPCR
Pro-94	17-Nov-2018	Accepted	QPCR
Pro-95	22-Nov-2018	Accepted	DNA + QPCR
Pro-96	11-Dec-2018	N/Ap	DNA
Pro-97	12-Dec-2018	N/Ap	DNA
Pro-98	13-Dec-2018	Accepted	QPCR
Pro-99	13-Dec-2018	Accepted	QPCR
Pro-100	30-Jan-2019	Accepted	QPCR

Assay Failure Rate: 0.0%
N/Ap: Not applicable

Appendix 6

Table 2
Calibration Curve Parameters for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White rabbits Tissues and Fluids

Appendix 6

Calibration Curve Parameters for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Intercept	Slope	Coefficient of Correlation (R2)
Pro-07	39.5	-3.40	0.999
Pro-09	39.4	-3.38	0.999
Pro-10	39.4	-3.40	0.999
Pro-13	39.6	-3.43	0.999
Pro-19	39.4	-3.40	1.000
Pro-20	39.4	-3.39	0.998
Pro-21	39.6	-3.39	0.999
Pro-22	39.8	-3.42	0.999
Pro-25	39.4	-3.41	0.999
Pro-26	39.6	-3.45	0.999
Pro-28	39.4	-3.39	0.999
Pro-29	39.5	-3.42	0.999
Pro-30	39.6	-3.44	0.999
Pro-31	39.6	-3.43	0.999
Pro-39	39.3	-3.37	0.999
Pro-40	39.7	-3.46	0.998
Pro-49	39.5	-3.38	0.999
Pro-55A	39.5	-3.41	0.999
Pro-56	39.7	-3.47	0.998
Pro-57	39.6	-3.45	0.999
Pro-60	39.4	-3.42	0.999
Pro-61	39.5	-3.42	0.999
Pro-64	39.3	-3.39	1.000
Pro-65	39.5	-3.42	0.999

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Calibration Curve Parameters for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Intercept	Slope	Coefficient of Correlation (R2)
Pro-66	39.3	-3.39	0.999
Pro-67	39.3	-3.38	0.999
Pro-69	39.5	-3.41	0.999
Pro-70	39.6	-3.44	0.999
Pro-72	39.5	-3.42	0.999
Pro-73	39.6	-3.45	0.999
Pro-76	39.7	-3.45	0.998
Pro-77	39.5	-3.39	0.999
Pro-84	39.5	-3.41	0.999
Pro-85	39.4	-3.39	0.998
Pro-89	39.5	-3.40	0.999
Pro-90	39.8	-3.47	0.999
Pro-92	39.4	-3.39	0.999
Pro-93	39.7	-3.46	0.999
Pro-94	39.4	-3.40	0.999
Pro-95	39.7	-3.45	0.999
Pro-98	39.4	-3.44	0.999
Pro-99	39.6	-3.46	0.998
Pro-100	39.7	-3.48	0.999

Appendix 6

Table 3
Mean Back-Calculated Concentration of Calibration Standards for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Appendix 6

Mean Back-Calculated Concentration of Calibration Standards for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction)								
	STD 1 1000000.0 copies/rxn	STD 2 100000.0 copies/rxn	STD 3 10000.0 copies/rxn	STD 4 1000.0 copies/rxn	STD 5 250.0 copies/rxn	STD 6 125.0 copies/rxn	STD 7 35.0 copies/rxn	STD 8 20.0 copies/rxn	STD 9 10.0 copies/rxn
Pro-07	985160.3	102265.0	9981.7	1019.6	270.3	119.7	32.1	19.1	11.4
Pro-09	1030328.5	102620.0	10177.4	956.4	242.2	116.0	38.0	17.7	11.8
Pro-10	960173.9	102608.9	10061.0	1033.4	249.6	126.5	39.6	20.2	8.8
Pro-13	990900.8	97528.5	10014.6	1056.4	268.9	127.3	30.6	22.0	9.4 b
Pro-19	1002547.3	101628.1	10190.7	968.0	246.3	123.1	33.8	21.5	10.0
Pro-20	1010669.4	101504.7	10078.9	955.3	250.4	121.7	33.3	25.8	9.1
Pro-21	1013210.0	100617.7	9772.0	971.2	243.5	127.5	38.6	21.8	9.1
Pro-22	992667.9	99808.7	10246.8	993.7	264.1	116.4	42.8 a	17.0	10.8
Pro-25	985951.7	101031.8	10104.9	982.8	254.6	127.3	34.6	20.2	10.1
Pro-26	947917.1	100733.3	9991.4	1030.8	278.2	125.5	41.3	17.6	8.7 a
Pro-28	1001088.0	101908.5	9976.7	1004.1	236.1	121.8	34.4	24.9	8.5 a
Pro-29	998378.6	98349.7	10080.0	994.9	259.5	132.4	32.3	21.3 a	9.9
Pro-30	992823.9	100014.0	10261.4	970.5	248.1	138.2	34.6	18.4	10.8
Pro-31	975603.6	100160.6	9981.3	1038.6	276.0	122.2	35.9	15.0 a	11.0
Pro-39	1031580.9	103050.6	9808.5	959.5	238.1	118.5	35.8	19.9	11.2
Pro-40	921341.6	97980.6	9927.9	1075.2	270.9	153.9	36.5	21.2	7.3
Pro-49	1043389.3	102702.8	9942.4	950.7	237.6	112.8	35.5	21.2	12.0 a
Pro-55A	971585.7	103445.5	10259.0	945.0	261.7	131.4	36.6	18.3 a	9.9
Pro-56	915897.4	99808.5	10021.5	1048.7	269.4	155.3	34.0	24.3 a	7.3
Pro-57	971307.4	99432.5	9839.9	1038.2	266.6	137.4	36.3	17.6	9.9
Pro-60	1005100.5	99805.3	10097.0	998.5	252.4	121.6	34.9	25.2 b	9.5 a
Pro-61	1002606.6	101414.1	9774.4	992.6	253.2	136.2	33.8	19.1	10.4 a

Appendix 6

Mean Back-Calculated Concentration of Calibration Standards for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction)								
	STD 1 1000000.0 copies/rxn	STD 2 100000.0 copies/rxn	STD 3 10000.0 copies/rxn	STD 4 1000.0 copies/rxn	STD 5 250.0 copies/rxn	STD 6 125.0 copies/rxn	STD 7 35.0 copies/rxn	STD 8 20.0 copies/rxn	STD 9 10.0 copies/rxn
Pro-64	1014652.1	101122.3	9965.6	960.3	245.4	127.3	33.8	20.8	10.4
Pro-65	996543.1	103307.7	9908.9	976.2	255.6	130.0	31.6	18.0	12.2
Pro-66	1035212.7	101016.3	9565.6	934.6	262.5	127.8	32.9	22.3	9.8
Pro-67	1063183.0	99490.0	10280.8	922.4	228.6	116.5	35.3	22.4	10.9
Pro-69	991650.3	100195.6	10103.5	967.5	258.8	127.1	36.1	21.1	9.6
Pro-70	975384.5	102110.0	9817.4	989.5	262.3	135.5	33.5	21.5	9.4
Pro-72	1004045.6	100387.7	10097.6	1000.2	251.5	121.1	35.7	17.9 a	11.2
Pro-73	984399.8	99499.7	10029.5	992.3	268.9	127.2	37.2	17.2 b	9.3 a
Pro-76	968768.7	98526.3	9941.1	993.4	281.8	130.8	40.5	20.6	8.1
Pro-77	1030106.0	101807.8	9789.0	977.6	234.6	126.2	37.3	18.7	10.9
Pro-84	1030581.9	100132.3	9489.8	964.8	239.5	132.8	38.9	21.3	8.4 a
Pro-85	1068308.7	98870.8	9549.8	977.9	242.0	133.6	33.6	16.3	13.0
Pro-89	1030667.9	100011.4	9812.0	968.6	249.7	128.4	33.9	19.5	11.6 a
Pro-90	965451.1	97976.1	9981.2	1033.4	290.0	126.1	33.8	21.4	8.9
Pro-92	1013304.3	100753.0	9743.5	945.0	256.1	131.8	33.6	25.9 a	9.1
Pro-93	958796.9	99711.1	10006.5	1028.3	261.9	141.2	38.5	16.8	9.5 a
Pro-94	1053978.7	98622.6	9716.8	991.2	244.5	124.0	36.6	17.2	12.0
Pro-95	975809.7	99331.3	10067.7	1022.6	257.7	132.0	38.7	18.2 a	9.2
Pro-98	970773.6	100801.6	10091.8	1034.2	267.4	128.7	34.6	19.8	9.5
Pro-99	965605.0	101227.1	10056.4	1031.6	272.3	134.2	32.9	18.5	11.6 b

Appendix 6

Mean Back-Calculated Concentration of Calibration Standards for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction)								
	STD 1 1000000.0 copies/rxn	STD 2 100000.0 copies/rxn	STD 3 10000.0 copies/rxn	STD 4 1000.0 copies/rxn	STD 5 250.0 copies/rxn	STD 6 125.0 copies/rxn	STD 7 35.0 copies/rxn	STD 8 20.0 copies/rxn	STD 9 10.0 copies/rxn
Pro-100	961915.0	105568.3	10505.9	933.7	256.6	129.5	29.8	22.9	- c
Mean	995566.7	100671.8	9979.3	991.4	256.4	128.5	35.4	20.2	10.0
N	43	43	43	43	43	43	43	43	42
SD	33999.0	1684.3	204.4	36.7	13.8	8.6	2.8	2.6	1.3
CV(%)	3.4	1.7	2.0	3.7	5.4	6.7	7.9	12.9	13.0
% Nominal	99.6	100.7	99.8	99.1	102.6	102.8	101.1	101.0	100.0

Descriptions:
STD: Standard
Rxn: Reaction
STD 8: LLOQ
STD 9: Accessory
Comments:
a = 1 out of 3 replicates values masked
b = 2 out of 3 replicates values masked
c = 3 out of 3 replicates values masked

Appendix 6

Table 4
Mean Ct value of Calibration Standards for the Quantitative Determination of Ad26 (b) (4) (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Appendix 6

Mean Ct value of Calibration Standards for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction)								
	STD 1	STD 2	STD 3	STD 4	STD 5	STD 6	STD 7	STD 8	STD 9
	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct
Pro-07	19.13	22.48	25.92	29.29	31.28	32.48	34.41	35.18	35.97
Pro-09	19.08	22.49	25.87	29.34	31.36	32.45	34.08	35.21	35.81
Pro-10	19.10	22.40	25.84	29.19	31.29	32.30	34.01	35.01	36.24
Pro-13	19.01	22.47	25.86	29.21	31.25	32.38	34.51	35.02	36.25 b
Pro-19	19.05	22.43	25.83	29.30	31.32	32.34	34.25	34.92	36.04
Pro-20	19.02	22.41	25.83	29.28	31.26	32.33	34.23	34.63	36.17
Pro-21	19.30	22.70	26.13	29.53	31.55	32.51	34.27	35.13	36.41
Pro-22	19.32	22.73	26.12	29.57	31.54	32.75	34.25 a	35.61	36.32
Pro-25	19.00	22.38	25.78	29.23	31.23	32.26	34.19	35.00	36.04
Pro-26	18.97	22.33	25.79	29.19	31.15	32.35	34.02	35.32	36.33 a
Pro-28	19.03	22.40	25.82	29.20	31.33	32.31	34.18	34.66	36.26 a
Pro-29	18.98	22.42	25.81	29.25	31.25	32.25	34.34	34.99 a	36.10
Pro-30	19.00	22.43	25.83	29.35	31.39	32.26	34.35	35.29	36.09
Pro-31	19.01	22.40	25.84	29.21	31.19	32.41	34.23	35.54 a	35.99
Pro-39	19.02	22.39	25.83	29.23	31.27	32.29	34.04	34.91	35.76
Pro-40	19.00	22.37	25.82	29.16	31.24	32.09	34.25	35.09	36.70
Pro-49	19.15	22.55	25.97	29.42	31.45	32.57	34.24	35.02	35.84 a
Pro-55A	19.16	22.47	25.89	29.42	31.32	32.34	34.23	35.25 a	36.17
Pro-56	19.06	22.40	25.86	29.26	31.30	32.14	34.44	34.93 a	36.77
Pro-57	18.96	22.37	25.83	29.20	31.23	32.22	34.23	35.33	36.17
Pro-60	18.89	22.32	25.73	29.17	31.20	32.29	34.17	34.63 b	36.08 a
Pro-61	18.94	22.34	25.82	29.21	31.25	32.16	34.24	35.08	35.98 a
Pro-64	18.98	22.38	25.79	29.24	31.25	32.21	34.17	34.88	35.92

Appendix 6

Mean Ct value of Calibration Standards for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction)								
	STD 1	STD 2	STD 3	STD 4	STD 5	STD 6	STD 7	STD 8	STD 9
	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct
Pro-65	18.94	22.31	25.79	29.23	31.23	32.23	34.34	35.19	35.76
Pro-66	18.95	22.37	25.84	29.26	31.13	32.19	34.18	34.76	35.97
Pro-67	18.90	22.38	25.71	29.25	31.30	32.29	34.06	34.72	35.80
Pro-69	19.04	22.43	25.83	29.30	31.25	32.30	34.18	34.98	36.17
Pro-70	18.99	22.36	25.85	29.29	31.27	32.25	34.34	35.04	36.25
Pro-72	18.99	22.41	25.82	29.26	31.31	32.39	34.25	35.24 a	35.96
Pro-73	18.95	22.38	25.82	29.27	31.23	32.36	34.19	35.34 b	36.28 a
Pro-76	19.09	22.51	25.94	29.38	31.27	32.42	34.19	35.22	36.61
Pro-77	19.08	22.50	25.94	29.34	31.45	32.36	34.16	35.18	35.96
Pro-84	18.98	22.43	25.92	29.31	31.37	32.25	34.07	34.95	36.35 a
Pro-85	18.98	22.49	25.94	29.29	31.36	32.24	34.27	35.33	35.67
Pro-89	19.04	22.48	25.91	29.32	31.32	32.32	34.31	35.09	35.86 a
Pro-90	19.10	22.54	25.98	29.39	31.30	32.57	34.56	35.24	36.57
Pro-92	19.00	22.40	25.84	29.28	31.20	32.19	34.23	34.59 a	36.15
Pro-93	18.95	22.36	25.81	29.23	31.29	32.22	34.19	35.42	36.28 a
Pro-94	18.95	22.45	25.87	29.25	31.31	32.31	34.11	35.26	35.77
Pro-95	19.05	22.47	25.92	29.33	31.39	32.40	34.24	35.36 a	36.41
Pro-98	18.87	22.25	25.69	29.10	31.10	32.20	34.15	34.99	36.09
Pro-99	18.94	22.33	25.80	29.21	31.21	32.30	34.42	35.26	35.95 b

Appendix 6

Mean Ct value of Calibration Standards for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction)								
	STD 1	STD 2	STD 3	STD 4	STD 5	STD 6	STD 7	STD 8	STD 9
	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct
Pro-100	18.83	22.17	25.67	29.32	31.29	32.33	34.53	34.93	- c
Mean	19.02	22.42	25.85	29.28	31.29	32.32	34.24	35.09	36.13
N	43	43	43	43	43	43	43	43	42
SD	0.10	0.10	0.09	0.09	0.09	0.13	0.13	0.24	0.26
CV(%)	0.5	0.4	0.3	0.3	0.3	0.4	0.4	0.7	0.7

Descriptions:
STD: Standard
STD 8: LLOQ
STD 9: Accessory
Ct: Cycle Threshold
Comments:
a = 1 out of 3 replicates values masked
b = 2 out of 3 replicates values masked
c = 3 out of 3 replicates values masked

Appendix 6

Table 5
Mean Back-Calculated Concentration of Run Quality Control Samples for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Appendix 6

Mean Back-Calculated Concentration of Run Quality Control Samples for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction, mean results of replicate wells)					
	QC 1		QC 2		QC-3	
	QC 1-1	QC 1-2	QC 2-1	QC 2-2	QC 3-1	QC 3-2
	250000.0 copies/rxn	250000.0 copies/rxn	5000.0 copies/rxn	5000.0 copies/rxn	60.0 copies/rxn	60.0 copies/rxn
Pro-07	230388.5	242714.6	4764.2	5061.2	65.6	69.1
Pro-09	265722.4	250381.5	4980.5	4868.1	63.3	53.9
Pro-10	282145.4	265525.7	5407.6	5127.3	58.6	64.6
Pro-13	257969.5	246714.4	5182.1	5105.7	61.1	73.0
Pro-19	256486.3	254057.9	5047.9	5107.3	63.0	68.9
Pro-20	261903.7	258519.0	5085.1	5029.8	66.7	65.7
Pro-21	261029.7	260060.9	4762.8	5283.5	61.1	67.5
Pro-22	253863.9	258140.5	5190.9	5228.0	67.4	68.6
Pro-25	252280.6	257596.2	4988.0	5183.0	65.2	63.7
Pro-26	246944.4	252387.7	5121.5	5225.2	59.5	55.4
Pro-28	256533.1	256059.3	5117.9	5048.6	68.9	64.7
Pro-29	256346.0	249488.0	5363.0	5183.1	66.1	66.4
Pro-30	241728.1	240520.3	4947.1	5116.0	67.8	66.7
Pro-31	252851.1	247638.1	5210.3	5127.4	66.4	69.8
Pro-39	264738.4	262370.0	5038.6	4960.5	66.4	59.7
Pro-40	239284.2	236646.2	4982.4	5225.0	69.3	70.0
Pro-49	271363.4	265532.8	5287.0	5131.9	68.7	64.3
Pro-55A	264609.1	272311.5	5091.9	5161.0	69.7	69.7
Pro-56	239211.9	240816.7	5176.6	5339.9	63.7	63.5
Pro-57	241447.8	245606.2	5180.6	5039.0	60.7	72.5
Pro-60	257559.0	263071.5	5387.9	5192.7	72.3	68.2

Appendix 6

Mean Back-Calculated Concentration of Run Quality Control Samples for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction, mean results of replicate wells)					
	QC 1		QC 2		QC-3	
	QC 1-1	QC 1-2	QC 2-1	QC 2-2	QC 3-1	QC 3-2
	250000.0 copies/rxn	250000.0 copies/rxn	5000.0 copies/rxn	5000.0 copies/rxn	60.0 copies/rxn	60.0 copies/rxn
Pro-61	262757.7	247363.5	5553.9	5328.3	63.7	56.7
Pro-64	255293.0	257068.7	5109.6	5143.9	53.7	66.7
Pro-65	259322.1	252062.7	5145.7	5126.7	65.2	66.9
Pro-66	256379.9	257924.2	4810.1	5036.8	60.0	58.7
Pro-67	265693.4	257769.5	4993.8	4948.8	61.2	55.1
Pro-69	262285.3	259546.2	5159.2	5119.7	57.6	69.2
Pro-70	261478.6	251587.9	5570.8	5213.2	65.6	63.6
Pro-72	257369.6	256024.9	5465.2	5235.8	72.5	67.6
Pro-73	260736.0	242436.0	5260.3	5071.1	64.6	60.6
Pro-76	238043.9	234248.5	5186.9	5197.9	66.5	66.9
Pro-77	249010.5	245935.7	5192.5	5041.3	71.8	66.2
Pro-84	266938.3	257969.1	5370.4	5187.5	63.0	57.6
Pro-85	263280.3	267545.1	5149.4	5060.5	79.9 a	63.8
Pro-89	255433.4	241537.7	5183.0	4951.4	63.3	59.0
Pro-90	237045.5	238844.1	5199.8	5293.1	73.2	65.8
Pro-92	255896.4	248327.3	5003.8	4862.0	61.4	63.1
Pro-93	255168.8	238645.9	5240.8	5081.6	64.6	59.6
Pro-94	261502.6	247005.2	4817.7	4434.6	60.0	62.5
Pro-95	261827.0	243725.6	5386.2	5033.2	79.2 a	71.0
Pro-98	277866.5	267420.3	5620.4	5607.2	70.1	69.3
Pro-99	259720.4	252170.2	5496.0	5337.6	74.5	69.7

Appendix 6

Mean Back-Calculated Concentration of Run Quality Control Samples for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction, mean results of replicate wells)					
	QC 1		QC 2		QC-3	
	QC 1-1	QC 1-2	QC 2-1	QC 2-2	QC 3-1	QC 3-2
	250000.0 copies/rxn	250000.0 copies/rxn	5000.0 copies/rxn	5000.0 copies/rxn	60.0 copies/rxn	60.0 copies/rxn
Pro-100	216534.9	195689.6	4606.8	4408.0	65.0	67.6
Mean	255674.2	250860.6	5159.0	5103.8	65.8	65.0
N	43	43	43	43	43	43
SD	12182.3	12641.4	225.1	203.9	5.4	4.8
CV(%)	4.8	5.0	4.4	4.0	8.2	7.4
% Nominal	102.3	100.3	103.2	102.1	109.7	108.3

Descriptions:
QC: Quality Control
Rxn: Reaction
Comments:
a = % Nominal out of acceptance criteria

Appendix 6

Table 6
Mean Ct Value of Quality Control for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Appendix 6

Mean Ct value of Quality Control for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction)					
	QC 1-1	QC 1-2	QC 2-1	QC 2-2	QC 3-1	QC 3-2
	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct
Pro-07	21.30	21.20	27.03	26.94	33.37	33.28
Pro-09	21.07	21.16	26.91	26.95	33.35	33.57
Pro-10	20.93	21.00	26.75	26.83	33.43	33.30
Pro-13	21.02	21.08	26.84	26.86	33.47	33.20
Pro-19	21.07	21.10	26.86	26.84	33.34	33.20
Pro-20	21.02	21.03	26.82	26.83	33.20	33.23
Pro-21	21.30	21.30	27.19	27.03	33.59	33.45
Pro-22	21.34	21.32	27.12	27.11	33.58	33.55
Pro-25	21.02	20.99	26.83	26.77	33.25	33.29
Pro-26	20.98	20.95	26.79	26.76	33.46	33.57
Pro-28	21.03	21.04	26.80	26.82	33.15	33.24
Pro-29	21.00	21.04	26.75	26.80	33.29	33.29
Pro-30	21.11	21.12	26.91	26.86	33.32	33.35
Pro-31	21.02	21.05	26.81	26.83	33.34	33.24
Pro-39	21.01	21.02	26.80	26.83	33.14	33.29
Pro-40	21.03	21.05	26.86	26.78	33.29	33.27
Pro-49	21.13	21.16	26.90	26.94	33.27	33.39
Pro-55A	21.08	21.04	26.92	26.91	33.28	33.28
Pro-56	21.08	21.07	26.85	26.81	33.47	33.49
Pro-57	21.04	21.02	26.79	26.83	33.45	33.18
Pro-60	20.91	20.89	26.66	26.71	33.06	33.17
Pro-61	20.93	21.04	26.66	26.74	33.29	33.46
Pro-64	21.01	21.00	26.77	26.77	33.48	33.17

Appendix 6

Mean Ct value of Quality Control for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction)					
	QC 1-1	QC 1-2	QC 2-1	QC 2-2	QC 3-1	QC 3-2
	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct
Pro-65	20.94	20.99	26.76	26.77	33.26	33.22
Pro-66	21.00	20.99	26.85	26.78	33.34	33.33
Pro-67	20.93	20.98	26.77	26.78	33.23	33.39
Pro-69	21.01	21.02	26.82	26.83	33.48	33.20
Pro-70	20.96	21.01	26.70	26.81	33.34	33.41
Pro-72	21.01	21.02	26.74	26.80	33.16	33.26
Pro-73	20.94	21.05	26.78	26.83	33.37	33.47
Pro-76	21.20	21.21	26.91	26.91	33.43	33.42
Pro-77	21.17	21.19	26.87	26.92	33.21	33.31
Pro-84	20.98	21.03	26.77	26.82	33.36	33.49
Pro-85	21.05	21.02	26.85	26.87	33.00 a	33.32
Pro-89	21.10	21.18	26.85	26.91	33.34	33.46
Pro-90	21.21	21.20	26.96	26.93	33.38	33.54
Pro-92	21.03	21.07	26.82	26.87	33.33	33.28
Pro-93	20.95	21.04	26.78	26.83	33.39	33.55
Pro-94	21.01	21.09	26.90	27.04	33.39	33.35
Pro-95	21.04	21.13	26.84	26.94	33.17 a	33.32
Pro-98	20.73	20.80	26.56	26.57	33.12	33.15
Pro-99	20.92	20.96	26.70	26.74	33.15	33.25

Appendix 6

Mean Ct value of Quality Control for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Assay ID	Ad26 (b) (4) Vector DNA Concentration (copies/reaction)					
	QC 1-1	QC 1-2	QC 2-1	QC 2-2	QC 3-1	QC 3-2
	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct	Mean Ct
Pro-100	21.08	21.24	26.91	26.97	33.36	33.33
Mean	21.04	21.07	26.83	26.85	33.32	33.34
N	43	43	43	43	43	43
SD	0.11	0.10	0.11	0.10	0.13	0.12
CV(%)	0.5	0.5	0.4	0.4	0.4	0.4

Descriptions:
QC: Quality Control
Ct: Cycle Threshold
Comments:
a = % Nominal concentration out of acceptance criteria

Appendix 6

Table 7
QPCR results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1001	Blood	D11	0.1222	1.6	Pro-13	10-Sep-2018	0.12	<LOD	4	2.400	b
1	1001	Bone Marrow	D11	0.0239	1.2	Pro-94	17-Nov-2018	0.02	<LOD	10	1.000	a,b
1	1001	Forebrain RT	D11	0.2859	2.2	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Heart	D11	0.5839	2.1	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Iliac LN	D11	2.2546	2.2	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Kidney	D11	1.2089	2.0	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Liver	D11	0.1955	1.9	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Lung RT	D11	1.9092	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Mesenteric LN	D11	8.8813	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Muscle	D11	0.3006	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Popliteal LN	D11	6.9956	2.2	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Skin	D11	0.2761	2.0	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Spleen	D11	2.1643	2.0	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Testis	D11	0.5564	2.1	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1001	Thymus	D11	0.1586	2.0	Pro-30	21-Sep-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1002	Blood	D11	0.1050	1.5	Pro-94	17-Nov-2018	0.11	<LOD	5	2.750	b
1	1002	Bone Marrow	D11	0.0258	1.5	Pro-94	17-Nov-2018	0.03	<LOD	10	1.500	a,b
1	1002	Forebrain RT	D11	0.1556	2.1	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Heart	D11	0.3309	2.1	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Iliac LN	D11	1.5299	2.2	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Kidney	D11	1.0116	1.9	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Liver	D11	0.2266	2.0	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Lung RT	D11	0.7502	1.9	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Mesenteric LN	D11	13.3475	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Muscle	D11	0.3089	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Popliteal LN	D11	3.8013	2.2	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Skin	D11	0.4275	2.1	Pro-30	21-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Spleen	D11	0.9468	2.0	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Testis	D11	2.9127	2.1	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1002	Thymus	D11	3.2729	1.9	Pro-30	21-Sep-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1003	Blood	D11	0.1246	1.5	Pro-94	17-Nov-2018	0.12	<LOD	5	3.000	b
1	1003	Bone Marrow	D11	0.8266	1.7	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Forebrain RT	D11	0.2496	2.1	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Heart	D11	0.4032	2.2	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Iliac LN	D11	0.1314	1.9	Pro-10	07-Sep-2018	0.13	<LOD	4	2.600	b
1	1003	Kidney	D11	0.8180	2.1	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Liver	D11	0.2521	2.1	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Lung RT	D11	0.7212	1.9	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Mesenteric LN	D11	8.7309	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Muscle	D11	0.3032	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Popliteal LN	D11	2.1557	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Skin	D11	0.2632	2.0	Pro-30	21-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Spleen	D11	0.4572	2.1	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Testis	D11	1.5956	2.1	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1003	Thymus	D11	0.7029	1.7	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1501	Blood	D11	0.1112	1.5	Pro-94	17-Nov-2018	0.11	<LOD	5	2.750	b
1	1501	Bone Marrow	D11	0.0326	1.4	Pro-94	17-Nov-2018	0.03	<LOD	10	1.500	a,b
1	1501	Forebrain RT	D11	0.3037	2.2	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Heart	D11	0.2326	1.9	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Iliac LN	D11	0.7959	2.1	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Kidney	D11	1.8762	2.3	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Liver	D11	0.2087	1.9	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Lung RT	D11	0.5877	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Mesenteric LN	D11	12.6195	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Muscle	D11	0.3047	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Ovaries	D11	3.4775	1.8	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Popliteal LN	D11	6.4636	2.2	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Skin	D11	0.2813	2.0	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Spleen	D11	0.4347	2.1	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1501	Thymus	D11	2.2682	1.9	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1502	Blood	D11	0.0985	1.4	Pro-94	17-Nov-2018	0.10	<LOD	5	2.500	b
1	1502	Bone Marrow	D11	0.0180	1.3	Pro-94	17-Nov-2018	0.02	<LOD	10	1.000	a,b
1	1502	Forebrain RT	D11	0.3149	2.2	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Heart	D11	0.2373	2.1	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Iliac LN	D11	1.1630	2.1	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Kidney	D11	2.0091	2.1	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Liver	D11	0.2592	1.8	Pro-30	21-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Lung RT	D11	1.1943	2.0	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Mesenteric LN	D11	10.6893	2.0	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Muscle	D11	0.3799	2.0	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Ovaries	D11	4.1535	1.6	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	b
1	1502	Popliteal LN	D11	6.4448	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Skin	D11	0.2987	2.0	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Spleen	D11	0.6765	2.1	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1502	Thymus	D11	0.4182	1.9	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1503	Blood	D11	0.1164	1.5	Pro-94	17-Nov-2018	0.12	<LOD	5	3.000	b
1	1503	Bone Marrow	D11	0.3671	1.8	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Forebrain RT	D11	0.3801	2.2	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Heart	D11	0.4134	2.2	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Iliac LN	D11	0.3318	2.0	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Kidney	D11	1.9541	2.0	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Liver	D11	0.1762	1.8	Pro-10	07-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Lung RT	D11	1.2389	1.9	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Mesenteric LN	D11	8.0644	2.1	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Muscle	D11	0.3614	2.0	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Ovaries	D11	2.6689	1.9	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Popliteal LN	D11	5.0813	2.2	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Skin	D11	0.4613	2.0	Pro-09	07-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Spleen	D11	1.0122	2.2	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	
1	1503	Thymus	D11	2.2541	1.7	Pro-13	10-Sep-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2001	Blood	D11	0.1143	1.6	Pro-19	14-Sep-2018	0.11	<LOD	4	2.200	b
2	2001	Bone Marrow	D11	0.1884	1.8	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Forebrain RT	D11	0.1996	2.0	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Heart	D11	0.3088	2.1	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Iliac LN	D11	0.7823	2.1	Pro-20	14-Sep-2018	0.14	<LLOQ	4	2.800	
2	2001	Kidney	D11	2.5529	1.9	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Liver	D11	0.3749	1.9	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Lung RT	D11	1.6478	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Mesenteric LN	D11	0.6956	2.1	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Muscle	D11	0.2423	2.0	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Popliteal LN	D11	5.2721	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Skin	D11	0.2358	1.9	Pro-19	14-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Spleen	D11	1.1156	2.2	Pro-19	14-Sep-2018	0.14	<LLOQ	4	2.800	
2	2001	Testis	D11	3.4596	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2001	Thymus	D11	0.1817	2.0	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2002	Blood	D11	0.1204	1.6	Pro-19	14-Sep-2018	0.12	<LOD	4	2.400	b
2	2002	Bone Marrow	D11	0.6779	2.0	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	
2	2002	Forebrain RT	D11	0.4432	1.9	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2002	Heart	D11	0.4208	1.9	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2002	Iliac LN	D11	1.2744	2.1	Pro-20	14-Sep-2018	0.14	63.6	4	2.800	
2	2002	Kidney	D11	1.0458	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2002	Liver	D11	0.8202	2.1	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2002	Lung RT	D11	0.3894	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2002	Mesenteric LN	D11	1.8251	2.1	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2002	Muscle	D11	0.1648	2.1	Pro-28	20-Sep-2018	0.14	<LLOQ	4	2.800	
2	2002	Popliteal LN	D11	3.1378	2.2	Pro-22	18-Sep-2018	0.14	<LLOQ	4	2.800	
2	2002	Skin	D11	0.1840	2.0	Pro-19	14-Sep-2018	0.14	<LOD	4	2.800	
2	2002	Spleen	D11	0.9060	2.2	Pro-19	14-Sep-2018	0.14	37.3	4	2.800	
2	2002	Testis	D11	3.2747	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2002	Thymus	D11	0.3779	1.7	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2003	Blood	D11	0.1324	1.4	Pro-84	01-Nov-2018	0.13	<LOD	4	2.600	b
2	2003	Bone Marrow	D11	0.3506	2.0	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Forebrain RT	D11	0.2230	1.9	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Heart	D11	0.4448	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Iliac LN	D11	4.0629	2.1	Pro-20	14-Sep-2018	0.14	197.6	4	2.800	
2	2003	Kidney	D11	2.0536	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Liver	D11	1.0710	2.1	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Lung RT	D11	0.5787	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Mesenteric LN	D11	1.1852	1.9	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Muscle	D11	0.1437	2.1	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Popliteal LN	D11	5.6214	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Skin	D11	0.7566	2.1	Pro-19	14-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Spleen	D11	1.2104	2.2	Pro-19	14-Sep-2018	0.14	80.7	4	2.800	
2	2003	Testis	D11	3.7336	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2003	Thymus	D11	3.1978	1.9	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2004	Blood	D11	0.2084	1.5	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	b
2	2004	Bone Marrow	D11	0.6480	2.1	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	
2	2004	Forebrain RT	D11	0.2270	1.9	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2004	Heart	D11	0.3298	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2004	Iliac LN	D11	0.5232	2.0	Pro-20	14-Sep-2018	0.14	140.6	4	2.800	
2	2004	Kidney	D11	1.6886	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2004	Liver	D11	1.2645	2.1	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2004	Lung RT	D11	0.5689	1.9	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2004	Mesenteric LN	D11	6.6756	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2004	Muscle	D11	0.1838	2.1	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
2	2004	Popliteal LN	D11	6.3891	2.2	Pro-22	18-Sep-2018	0.14	29.0	4	2.800	
2	2004	Skin	D11	0.2475	1.9	Pro-19	14-Sep-2018	0.14	295.1	4	2.800	
2	2004	Spleen	D11	1.1885	2.2	Pro-19	14-Sep-2018	0.14	85.6	4	2.800	
2	2004	Testis	D11	3.3443	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2004	Thymus	D11	2.5817	1.8	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2005	Blood	D11	0.1459	1.6	Pro-19	14-Sep-2018	0.14	<LOD	4	2.800	b
2	2005	Bone Marrow	D11	0.5219	1.9	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	
2	2005	Forebrain RT	D11	0.3532	1.9	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2005	Heart	D11	0.4971	1.9	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2005	Iliac LN	D11	4.5868	2.1	Pro-20	14-Sep-2018	0.14	256.1	4	2.800	
2	2005	Kidney	D11	1.7459	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2005	Liver	D11	0.4453	1.9	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2005	Lung RT	D11	0.4750	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2005	Mesenteric LN	D11	1.0692	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2005	Muscle	D11	0.2398	2.1	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
2	2005	Popliteal LN	D11	6.5007	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2005	Skin	D11	0.4950	2.1	Pro-19	14-Sep-2018	0.14	39.1	4	2.800	
2	2005	Spleen	D11	1.1089	2.2	Pro-19	14-Sep-2018	0.14	<LLOQ	4	2.800	
2	2005	Testis	D11	2.2491	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2005	Thymus	D11	1.2673	1.8	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2501	Blood	D11	0.1181	1.5	Pro-19	14-Sep-2018	0.12	<LOD	4	2.400	b
2	2501	Bone Marrow	D11	0.0246	1.5	Pro-84	01-Nov-2018	0.02	<LOD	9	0.900	a,b
2	2501	Forebrain RT	D11	0.2610	1.8	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2501	Heart	D11	0.8289	2.2	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2501	Iliac LN	D11	0.8639	2.1	Pro-20	14-Sep-2018	0.14	90.4	4	2.800	
2	2501	Kidney	D11	1.0535	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2501	Liver	D11	0.3212	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2501	Lung RT	D11	1.0325	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2501	Mesenteric LN	D11	6.0428	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2501	Muscle	D11	0.2181	1.8	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
2	2501	Ovaries	D11	1.0602	2.1	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2501	Popliteal LN	D11	2.6236	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2501	Skin	D11	0.7904	2.0	Pro-19	14-Sep-2018	0.14	<LLOQ	4	2.800	
2	2501	Spleen	D11	0.8469	2.1	Pro-19	14-Sep-2018	0.14	<LLOQ	4	2.800	
2	2501	Thymus	D11	0.2275	2.0	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2502	Blood	D11	0.1517	1.4	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	b
2	2502	Bone Marrow	D11	0.0850	1.8	Pro-84	01-Nov-2018	0.09	<LOD	5	2.250	b
2	2502	Forebrain RT	D11	0.1514	2.0	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2502	Heart	D11	0.3438	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2502	Iliac LN	D11	2.3239	2.1	Pro-20	14-Sep-2018	0.14	144.0	4	2.800	
2	2502	Kidney	D11	1.2952	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2502	Liver	D11	0.3613	1.9	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2502	Lung RT	D11	0.5225	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2502	Mesenteric LN	D11	1.5520	1.8	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2502	Muscle	D11	0.5120	2.1	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	
2	2502	Ovaries	D11	1.5493	1.9	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2502	Popliteal LN	D11	5.3399	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2502	Skin	D11	0.7377	2.1	Pro-19	14-Sep-2018	0.14	<LOD	4	2.800	
2	2502	Spleen	D11	1.0094	2.2	Pro-19	14-Sep-2018	0.14	79.3	4	2.800	
2	2502	Thymus	D11	1.0282	1.8	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2503	Blood	D11	0.1595	1.5	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	b
2	2503	Bone Marrow	D11	3.5558	1.6	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	b
2	2503	Forebrain RT	D11	0.3003	2.0	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2503	Heart	D11	0.6910	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2503	Iliac LN	D11	2.9382	2.1	Pro-20	14-Sep-2018	0.14	184.6	4	2.800	
2	2503	Kidney	D11	1.3341	2.1	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2503	Liver	D11	0.1491	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2503	Lung RT	D11	0.8463	1.9	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2503	Mesenteric LN	D11	7.8453	1.8	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2503	Muscle	D11	0.4060	2.1	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	
2	2503	Ovaries	D11	3.8627	1.9	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2503	Popliteal LN	D11	3.1729	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2503	Skin	D11	0.4558	2.1	Pro-19	14-Sep-2018	0.14	1207.0	4	2.800	
2	2503	Spleen	D11	0.9944	2.2	Pro-19	14-Sep-2018	0.14	118.6	4	2.800	
2	2503	Thymus	D11	1.3338	1.9	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2504	Blood	D11	0.1058	1.6	Pro-19	14-Sep-2018	0.11	<LOD	4	2.200	b
2	2504	Bone Marrow	D11	0.3835	2.0	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	
2	2504	Forebrain RT	D11	0.7078	2.1	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2504	Heart	D11	0.1789	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2504	Iliac LN	D11	6.2430	2.1	Pro-20	14-Sep-2018	0.14	387.6	4	2.800	
2	2504	Kidney	D11	1.6211	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2504	Liver	D11	0.4643	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2504	Lung RT	D11	1.6419	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2504	Mesenteric LN	D11	3.3062	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2504	Muscle	D11	0.5165	2.0	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	
2	2504	Ovaries	D11	1.5696	2.1	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2504	Popliteal LN	D11	6.5699	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2504	Skin	D11	0.5110	2.1	Pro-19	14-Sep-2018	0.14	6304.3	4	2.800	
2	2504	Spleen	D11	1.1276	2.2	Pro-19	14-Sep-2018	0.14	47.0	4	2.800	
2	2504	Thymus	D11	0.1608	2.0	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2505	Blood	D11	0.1246	1.5	Pro-19	14-Sep-2018	0.12	<LOD	4	2.400	b
2	2505	Bone Marrow	D11	1.1957	1.9	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	
2	2505	Forebrain RT	D11	0.1937	2.1	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2505	Heart	D11	0.2932	1.7	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2505	Iliac LN	D11	4.6309	2.1	Pro-20	14-Sep-2018	0.14	153.1	4	2.800	
2	2505	Kidney	D11	1.7245	2.0	Pro-20	14-Sep-2018	0.14	<LOD	4	2.800	
2	2505	Liver	D11	0.1579	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2505	Lung RT	D11	1.0592	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2505	Mesenteric LN	D11	3.3818	2.0	Pro-21	18-Sep-2018	0.14	<LOD	4	2.800	
2	2505	Muscle	D11	0.2460	2.1	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
2	2505	Ovaries	D11	1.3929	2.1	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2505	Popliteal LN	D11	5.8893	2.2	Pro-22	18-Sep-2018	0.14	<LOD	4	2.800	
2	2505	Skin	D11	0.4314	2.1	Pro-19	14-Sep-2018	0.14	<LLOQ	4	2.800	
2	2505	Spleen	D11	0.8928	2.1	Pro-19	14-Sep-2018	0.14	<LLOQ	4	2.800	
2	2505	Thymus	D11	0.3963	1.7	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3001	Blood	D11	0.1128	1.6	Pro-29	20-Sep-2018	0.11	<LOD	4	2.200	b
3	3001	Bone Marrow	D11	0.0697	1.9	Pro-29	20-Sep-2018	0.07	<LOD	6	2.100	b
3	3001	Forebrain RT	D11	0.1948	2.0	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3001	Heart	D11	0.4573	1.9	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
3	3001	Iliac LN	D11	5.2047	2.0	Pro-31	21-Sep-2018	0.14	111.6	4	2.800	
3	3001	Kidney	D11	3.7021	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3001	Liver	D11	0.4872	2.3	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	
3	3001	Lung RT	D11	1.3728	2.1	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3001	Mesenteric LN	D11	1.0184	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3001	Muscle	D11	0.2738	2.1	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3001	Popliteal LN	D11	0.5566	1.9	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3001	Skin	D11	0.1472	2.4	Pro-56	09-Oct-2018	0.14	<LLOQ	4	2.800	
3	3001	Spleen	D11	1.5847	2.1	Pro-26	19-Sep-2018	0.14	27.4	4	2.800	
3	3001	Testis	D11	2.5319	2.1	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3001	Thymus	D11	0.1673	1.8	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3002	Blood	D11	0.1167	1.7	Pro-29	20-Sep-2018	0.12	<LOD	4	2.400	b
3	3002	Bone Marrow	D11	0.0851	1.7	Pro-29	20-Sep-2018	0.09	<LOD	5	2.250	b
3	3002	Forebrain RT	D11	0.9349	2.3	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	
3	3002	Heart	D11	0.6331	2.2	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
3	3002	Iliac LN	D11	5.6156	2.0	Pro-31	21-Sep-2018	0.14	159.3	4	2.800	
3	3002	Kidney	D11	1.5945	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3002	Liver	D11	0.2347	2.2	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	
3	3002	Lung RT	D11	2.2953	2.1	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3002	Mesenteric LN	D11	1.4900	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3002	Muscle	D11	0.2537	2.2	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3002	Popliteal LN	D11	3.0775	1.8	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3002	Skin	D11	0.1758	2.0	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3002	Spleen	D11	0.9682	2.1	Pro-26	19-Sep-2018	0.14	<LLOQ	4	2.800	
3	3002	Testis	D11	1.0807	2.1	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3002	Thymus	D11	1.8929	1.9	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3003	Blood	D11	0.1262	1.7	Pro-29	20-Sep-2018	0.13	<LOD	4	2.600	b
3	3003	Bone Marrow	D11	0.2061	1.8	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	
3	3003	Forebrain RT	D11	0.1896	2.0	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3003	Heart	D11	0.2840	2.1	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3003	Iliac LN	D11	1.5673	2.1	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3003	Kidney	D11	1.4064	2.1	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3003	Liver	D11	0.2868	1.9	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	
3	3003	Lung RT	D11	1.6230	1.9	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3003	Mesenteric LN	D11	1.5907	1.9	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3003	Muscle	D11	0.2910	2.2	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3003	Popliteal LN	D11	0.3365	2.0	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3003	Skin	D11	1.0056	2.1	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3003	Spleen	D11	0.7908	2.1	Pro-26	19-Sep-2018	0.14	36.0	4	2.800	
3	3003	Testis	D11	2.9850	2.1	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3003	Thymus	D11	1.0664	1.7	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3004	Blood	D11	0.1080	1.7	Pro-29	20-Sep-2018	0.11	<LOD	4	2.200	b
3	3004	Bone Marrow	D11	0.1046	2.0	Pro-29	20-Sep-2018	0.10	<LOD	5	2.500	b
3	3004	Forebrain RT	D11	0.1451	2.2	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
3	3004	Heart	D11	0.4227	2.1	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3004	Iliac LN	D11	4.6110	2.0	Pro-31	21-Sep-2018	0.14	168.3	4	2.800	
3	3004	Kidney	D11	1.2263	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3004	Liver	D11	0.3968	2.1	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	
3	3004	Lung RT	D11	1.5628	2.1	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3004	Mesenteric LN	D11	1.1225	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3004	Muscle	D11	0.3116	2.1	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3004	Popliteal LN	D11	1.1207	1.9	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3004	Skin	D11	0.2517	2.0	Pro-28	20-Sep-2018	0.14	<LLOQ	4	2.800	
3	3004	Spleen	D11	1.7241	2.1	Pro-26	19-Sep-2018	0.14	75.6	4	2.800	
3	3004	Testis	D11	3.4796	2.1	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3004	Thymus	D11	0.5729	2.0	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3005	Blood	D11	0.1418	1.6	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	b
3	3005	Bone Marrow	D11	0.1478	1.7	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	
3	3005	Forebrain RT	D11	0.2218	2.0	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3005	Heart	D11	0.3885	2.1	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3005	Iliac LN	D11	4.3219	2.0	Pro-31	21-Sep-2018	0.14	182.4	4	2.800	
3	3005	Kidney	D11	1.0244	1.9	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3005	Liver	D11	0.2056	1.8	Pro-56	09-Oct-2018	0.14	<LLOQ	4	2.800	
3	3005	Lung RT	D11	2.2085	2.1	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3005	Mesenteric LN	D11	1.0571	2.1	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3005	Muscle	D11	0.2788	2.0	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3005	Popliteal LN	D11	1.3110	2.0	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3005	Skin	D11	0.2506	2.0	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3005	Spleen	D11	1.5532	2.1	Pro-26	19-Sep-2018	0.14	66.9	4	2.800	
3	3005	Testis	D11	2.8127	2.1	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3005	Thymus	D11	0.1775	1.9	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3501	Blood	D11	0.0511	1.3	Pro-84	01-Nov-2018	0.05	<LOD	8	2.000	b
3	3501	Bone Marrow	D11	0.0647	1.7	Pro-84	01-Nov-2018	0.06	<LOD	8	2.400	b
3	3501	Forebrain RT	D11	0.1553	2.1	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3501	Heart	D11	0.4636	2.0	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3501	Iliac LN	D11	7.0389	2.1	Pro-31	21-Sep-2018	0.14	248.0	4	2.800	
3	3501	Kidney	D11	2.3981	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3501	Liver	D11	0.4396	2.3	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	
3	3501	Lung RT	D11	1.6141	2.1	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3501	Mesenteric LN	D11	2.3822	1.9	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3501	Muscle	D11	0.3903	2.1	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3501	Ovaries	D11	2.9903	1.8	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3501	Popliteal LN	D11	2.4049	1.9	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3501	Skin	D11	0.2245	2.0	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3501	Spleen	D11	1.8605	2.0	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3501	Thymus	D11	0.6498	1.9	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3502	Blood	D11	0.1045	1.7	Pro-29	20-Sep-2018	0.10	<LOD	4	2.000	b
3	3502	Bone Marrow	D11	0.0898	1.8	Pro-29	20-Sep-2018	0.09	<LOD	5	2.250	b
3	3502	Forebrain RT	D11	0.1456	2.0	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3502	Heart	D11	1.5351	2.2	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3502	Iliac LN	D11	3.5934	2.0	Pro-31	21-Sep-2018	0.14	347.4	4	2.800	
3	3502	Kidney	D11	2.0553	2.1	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3502	Liver	D11	0.2304	1.8	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	
3	3502	Lung RT	D11	2.6886	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3502	Mesenteric LN	D11	1.1529	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3502	Muscle	D11	0.3683	2.2	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3502	Ovaries	D11	2.3898	2.1	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3502	Popliteal LN	D11	0.9358	2.0	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3502	Skin	D11	0.2961	2.0	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3502	Spleen	D11	1.4087	2.1	Pro-26	19-Sep-2018	0.14	<LLOQ	4	2.800	
3	3502	Thymus	D11	0.2168	1.9	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3503	Blood	D11	0.1532	1.4	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	b
3	3503	Bone Marrow	D11	0.1135	1.3	Pro-29	20-Sep-2018	0.11	<LOD	4	2.200	b
3	3503	Forebrain RT	D11	0.1615	2.2	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
3	3503	Heart	D11	1.0716	1.7	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3503	Iliac LN	D11	4.1837	2.0	Pro-31	21-Sep-2018	0.14	108.6	4	2.800	
3	3503	Kidney	D11	1.6999	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3503	Liver	D11	0.2102	1.8	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	
3	3503	Lung RT	D11	2.5552	2.1	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3503	Mesenteric LN	D11	1.5954	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3503	Muscle	D11	0.4456	2.0	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3503	Ovaries	D11	0.8721	1.9	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3503	Popliteal LN	D11	2.5068	1.9	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3503	Skin	D11	2.1040	2.2	Pro-28	20-Sep-2018	0.14	272.6	4	2.800	
3	3503	Spleen	D11	1.4821	2.1	Pro-26	19-Sep-2018	0.14	47.7	4	2.800	
3	3503	Thymus	D11	2.9293	1.8	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3504	Blood	D11	0.1115	1.5	Pro-29	20-Sep-2018	0.11	<LOD	4	2.200	b
3	3504	Bone Marrow	D11	1.5186	1.4	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	b
3	3504	Forebrain RT	D11	0.3552	1.9	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3504	Heart	D11	0.6284	2.1	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3504	Iliac LN	D11	5.7924	2.1	Pro-31	21-Sep-2018	0.14	208.1	4	2.800	
3	3504	Kidney	D11	1.2273	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3504	Liver	D11	0.3050	2.2	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	
3	3504	Lung RT	D11	1.2238	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3504	Mesenteric LN	D11	0.6205	1.9	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3504	Muscle	D11	0.4316	2.1	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3504	Ovaries	D11	2.1876	2.1	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3504	Popliteal LN	D11	1.4042	2.0	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3504	Skin	D11	3.2728	2.1	Pro-28	20-Sep-2018	0.14	88.6	4	2.800	
3	3504	Spleen	D11	1.4705	2.2	Pro-26	19-Sep-2018	0.14	70.9	4	2.800	
3	3504	Thymus	D11	0.8450	2.0	Pro-77	23-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3505	Blood	D11	0.1021	1.6	Pro-29	20-Sep-2018	0.10	<LOD	4	2.000	b
3	3505	Bone Marrow	D11	0.1884	1.5	Pro-29	20-Sep-2018	0.14	<LOD	4	2.800	b
3	3505	Forebrain RT	D11	0.1841	2.0	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3505	Heart	D11	1.1160	2.1	Pro-31	21-Sep-2018	0.14	<LOD	4	2.800	
3	3505	Iliac LN	D11	8.0655	2.1	Pro-31	21-Sep-2018	0.14	264.0	4	2.800	
3	3505	Kidney	D11	1.6346	2.0	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3505	Liver	D11	0.1420	1.8	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	
3	3505	Lung RT	D11	1.3793	2.1	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3505	Mesenteric LN	D11	1.8539	1.9	Pro-25	19-Sep-2018	0.14	<LOD	4	2.800	
3	3505	Muscle	D11	0.3939	2.1	Pro-28	20-Sep-2018	0.14	<LOD	4	2.800	
3	3505	Ovaries	D11	2.4843	2.0	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3505	Popliteal LN	D11	0.4391	2.0	Pro-26	19-Sep-2018	0.14	<LOD	4	2.800	
3	3505	Skin	D11	0.9183	2.0	Pro-28	20-Sep-2018	0.14	<LLOQ	4	2.800	
3	3505	Spleen	D11	1.6574	2.1	Pro-26	19-Sep-2018	0.14	26.4	4	2.800	
3	3505	Thymus	D11	0.2238	1.9	Pro-56	09-Oct-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1004	Blood	D90	0.0766	1.7	Pro-92	07-Nov-2018	0.08	<LOD	5	2.000	b
1	1004	Bone Marrow	D90	0.5676	1.9	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1004	Forebrain RT	D90	0.3999	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1004	Heart	D90	0.4779	2.2	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1004	Iliac LN	D90	1.7798	2.0	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1004	Kidney	D90	1.7115	2.2	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1004	Liver	D90	0.2943	2.0	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1004	Lung RT	D90	0.8683	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1004	Mesenteric LN	D90	4.3897	2.1	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1004	Muscle	D90	0.8159	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1004	Popliteal LN	D90	4.6784	2.0	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1004	Skin	D90	0.2034	2.0	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1004	Spleen	D90	1.3289	2.2	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1004	Testis	D90	1.0840	2.2	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1004	Thymus	D90	1.8963	1.9	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1005	Blood	D90	0.0908	1.8	Pro-92	07-Nov-2018	0.09	<LOD	5	2.250	b
1	1005	Bone Marrow	D90	0.7675	1.8	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1005	Forebrain RT	D90	0.3692	2.3	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1005	Heart	D90	0.5294	2.2	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1005	Iliac LN	D90	0.0325	1.6	Pro-39	28-Sep-2018	0.03	<LOD	8	1.200	a,b
1	1005	Kidney	D90	2.3807	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1005	Liver	D90	0.2079	2.0	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1005	Lung RT	D90	0.8634	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1005	Mesenteric LN	D90	9.0392	2.1	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1005	Muscle	D90	0.6179	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1005	Popliteal LN	D90	7.5552	2.1	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1005	Skin	D90	0.1664	2.0	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1005	Spleen	D90	1.5492	2.1	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1005	Testis	D90	1.8961	2.2	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1005	Thymus	D90	0.9514	2.0	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1006	Blood	D90	0.0878	1.8	Pro-92	07-Nov-2018	0.09	<LOD	5	2.250	b
1	1006	Bone Marrow	D90	0.4060	1.9	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1006	Forebrain RT	D90	0.5880	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1006	Heart	D90	0.5026	2.2	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1006	Iliac LN	D90	0.4681	1.8	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1006	Kidney	D90	1.8559	2.2	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1006	Liver	D90	0.3273	1.9	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1006	Lung RT	D90	0.9621	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1006	Mesenteric LN	D90	5.0373	2.0	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1006	Muscle	D90	0.6009	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1006	Popliteal LN	D90	4.0058	2.1	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1006	Skin	D90	0.1404	2.0	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1006	Spleen	D90	1.4627	2.1	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1006	Testis	D90	1.1727	2.2	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1006	Thymus	D90	0.9233	2.1	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1504	Blood	D90	0.0757	1.7	Pro-92	07-Nov-2018	0.08	<LOD	5	2.000	b
1	1504	Bone Marrow	D90	0.6055	2.0	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1504	Forebrain RT	D90	0.5202	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1504	Heart	D90	0.3797	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1504	Iliac LN	D90	0.7015	1.9	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1504	Kidney	D90	1.7277	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1504	Liver	D90	0.1869	2.1	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1504	Lung RT	D90	0.8754	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1504	Mesenteric LN	D90	4.3052	2.1	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1504	Muscle	D90	0.5918	2.1	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1504	Ovaries	D90	1.3374	2.1	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1504	Popliteal LN	D90	5.2830	2.1	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1504	Skin	D90	0.4011	2.1	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1504	Spleen	D90	1.4541	2.1	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1504	Thymus	D90	1.3180	2.0	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1505	Blood	D90	0.0822	1.8	Pro-92	07-Nov-2018	0.08	<LOD	5	2.000	b
1	1505	Bone Marrow	D90	0.7675	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1505	Forebrain RT	D90	0.2956	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1505	Heart	D90	0.4179	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1505	Iliac LN	D90	0.1404	1.4	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	b
1	1505	Kidney	D90	2.1509	2.2	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1505	Liver	D90	0.4925	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1505	Lung RT	D90	1.0212	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1505	Mesenteric LN	D90	2.0740	2.2	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1505	Muscle	D90	0.6149	2.0	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1505	Ovaries	D90	2.3836	2.0	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1505	Popliteal LN	D90	5.5144	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1505	Skin	D90	0.4700	2.0	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1505	Spleen	D90	1.3860	2.1	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1505	Thymus	D90	1.6381	2.0	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
1	1506	Blood	D90	0.0803	1.7	Pro-92	07-Nov-2018	0.08	<LOD	5	2.000	b
1	1506	Bone Marrow	D90	1.3622	2.0	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1506	Forebrain RT	D90	0.1855	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1506	Heart	D90	0.5953	2.2	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1506	Iliac LN	D90	0.1067	1.5	Pro-39	28-Sep-2018	0.11	<LOD	4	2.200	b
1	1506	Kidney	D90	1.8462	2.2	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1506	Liver	D90	0.3643	2.1	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1506	Lung RT	D90	1.0756	2.1	Pro-39	28-Sep-2018	0.14	<LOD	4	2.800	
1	1506	Mesenteric LN	D90	3.3694	2.2	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1506	Muscle	D90	0.5918	2.2	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1506	Ovaries	D90	1.4662	2.2	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1506	Popliteal LN	D90	6.8648	2.0	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	
1	1506	Skin	D90	0.1693	2.0	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1506	Spleen	D90	1.4678	2.2	Pro-40	28-Sep-2018	0.14	<LOD	4	2.800	
1	1506	Thymus	D90	1.6991	2.0	Pro-76	23-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2006	Blood	D90	0.1995	1.5	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2006	Bone Marrow	D90	2.1838	1.9	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Forebrain RT	D90	0.1545	2.1	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Heart	D90	0.3289	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Iliac LN	D90	1.3133	2.1	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Kidney	D90	0.7764	2.0	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Liver	D90	0.3006	1.9	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Lung RT	D90	1.9511	2.0	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Mesenteric LN	D90	0.9562	1.8	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Muscle	D90	0.3004	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Popliteal LN	D90	3.6549	2.0	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Skin	D90	0.1087	1.9	Pro-84	01-Nov-2018	0.11	<LOD	5	2.750	b
2	2006	Spleen	D90	1.3774	2.1	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Testis	D90	3.0944	2.0	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2006	Thymus	D90	1.2929	2.2	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2007	Blood	D90	0.1417	1.5	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2007	Bone Marrow	D90	0.3034	1.6	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2007	Forebrain RT	D90	0.1524	2.1	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Heart	D90	0.5400	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Iliac LN	D90	0.8434	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Kidney	D90	1.0302	2.1	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Liver	D90	0.4272	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Lung RT	D90	1.1716	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Mesenteric LN	D90	0.9802	1.9	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Muscle	D90	0.2521	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Popliteal LN	D90	9.4879	2.0	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Skin	D90	0.1502	1.9	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Spleen	D90	0.2178	2.1	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Testis	D90	0.7899	2.0	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2007	Thymus	D90	1.4315	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2008	Blood	D90	0.3020	1.4	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2008	Bone Marrow	D90	1.1108	1.7	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Forebrain RT	D90	0.1417	2.2	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Heart	D90	0.2501	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Iliac LN	D90	0.4721	2.0	Pro-60	10-Oct-2018	0.14	<LLOQ	4	2.800	
2	2008	Kidney	D90	1.5078	2.0	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Liver	D90	0.2765	2.0	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Lung RT	D90	1.8548	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Mesenteric LN	D90	0.8653	2.0	Pro-84	01-Nov-2018	0.14	<LOD	4	2.800	
2	2008	Muscle	D90	0.2858	2.1	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Popliteal LN	D90	3.1170	1.9	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Skin	D90	0.1577	2.0	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Spleen	D90	1.4233	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Testis	D90	2.7330	2.2	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2008	Thymus	D90	0.9367	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2009	Blood	D90	0.2020	1.5	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2009	Bone Marrow	D90	0.2343	1.6	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2009	Forebrain RT	D90	0.9021	2.2	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Heart	D90	0.1846	2.1	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Iliac LN	D90	1.7103	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Kidney	D90	0.8229	2.1	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Liver	D90	0.1567	2.0	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Lung RT	D90	1.8188	2.0	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Mesenteric LN	D90	7.9910	1.8	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Muscle	D90	0.2888	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Popliteal LN	D90	6.4102	2.1	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Skin	D90	0.3679	2.0	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Spleen	D90	1.4517	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Testis	D90	2.2248	2.1	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2009	Thymus	D90	0.9424	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2010	Blood	D90	0.0772	1.4	Pro-67	16-Oct-2018	0.08	<LOD	5	2.000	b
2	2010	Bone Marrow	D90	1.8770	1.9	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Forebrain RT	D90	0.7728	2.3	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Heart	D90	0.2900	1.8	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Iliac LN	D90	0.3705	1.6	Pro-60	10-Oct-2018	0.14	<LLOQ	4	2.800	b
2	2010	Kidney	D90	0.8633	2.1	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Liver	D90	0.4966	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Lung RT	D90	2.9735	2.0	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Mesenteric LN	D90	2.6437	1.9	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Muscle	D90	0.2547	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Popliteal LN	D90	7.8687	2.1	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Skin	D90	0.1739	2.0	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Spleen	D90	0.9418	2.1	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Testis	D90	3.0019	2.1	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2010	Thymus	D90	1.5697	2.2	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2506	Blood	D90	0.3704	1.3	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2506	Bone Marrow	D90	1.5653	2.0	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Forebrain RT	D90	0.8352	2.2	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Heart	D90	0.5785	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Iliac LN	D90	2.4897	2.1	Pro-60	10-Oct-2018	0.14	48.1	4	2.800	
2	2506	Kidney	D90	1.5036	2.0	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Liver	D90	0.2086	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Lung RT	D90	1.9775	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Mesenteric LN	D90	0.7596	2.0	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Muscle	D90	0.3833	2.1	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Ovaries	D90	2.4406	2.1	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Popliteal LN	D90	8.8390	2.1	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Skin	D90	0.5207	2.0	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Spleen	D90	1.7640	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
2	2506	Thymus	D90	1.8296	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2507	Blood	D90	0.2230	1.4	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2507	Bone Marrow	D90	0.2789	1.8	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Forebrain RT	D90	0.7812	2.2	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Heart	D90	0.2763	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Iliac LN	D90	0.2281	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Kidney	D90	1.0165	2.0	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Liver	D90	0.3106	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Lung RT	D90	1.4321	2.0	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Mesenteric LN	D90	0.9900	1.9	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Muscle	D90	0.2583	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Ovaries	D90	1.4506	2.1	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Popliteal LN	D90	2.5640	1.9	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Skin	D90	0.4921	2.0	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Spleen	D90	1.9012	2.1	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
2	2507	Thymus	D90	1.2589	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2508	Blood	D90	0.3720	1.3	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2508	Bone Marrow	D90	0.8617	2.0	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Forebrain RT	D90	0.1448	2.1	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Heart	D90	0.2010	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Iliac LN	D90	2.5784	2.1	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Kidney	D90	2.4613	2.0	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Liver	D90	0.2404	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Lung RT	D90	2.5945	1.9	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Mesenteric LN	D90	0.9197	1.8	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Muscle	D90	0.1733	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Ovaries	D90	2.8615	2.0	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Popliteal LN	D90	3.9957	2.0	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Skin	D90	0.2846	2.0	Pro-73	18-Oct-2018	0.14	280.1	4	2.800	
2	2508	Spleen	D90	1.6512	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
2	2508	Thymus	D90	2.4181	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2509	Blood	D90	0.1791	1.6	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2509	Bone Marrow	D90	3.3530	1.8	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Forebrain RT	D90	0.2596	2.0	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Heart	D90	0.5843	2.1	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Iliac LN	D90	0.1493	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Kidney	D90	0.8905	2.1	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Liver	D90	0.5558	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Lung RT	D90	2.4534	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Mesenteric LN	D90	0.4052	1.9	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Muscle	D90	0.2519	2.1	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Ovaries	D90	4.0219	1.9	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Popliteal LN	D90	6.4934	2.0	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Skin	D90	0.2399	2.0	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Spleen	D90	1.7673	2.1	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
2	2509	Thymus	D90	2.0305	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2510	Blood	D90	0.2771	1.4	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
2	2510	Bone Marrow	D90	0.9105	1.9	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Forebrain RT	D90	0.2356	2.0	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Heart	D90	0.5469	1.9	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Iliac LN	D90	1.8315	2.0	Pro-60	10-Oct-2018	0.14	<LLOQ	4	2.800	
2	2510	Kidney	D90	1.6452	2.1	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Liver	D90	0.3072	2.0	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Lung RT	D90	1.9369	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Mesenteric LN	D90	0.3901	2.0	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Muscle	D90	0.2822	1.9	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Ovaries	D90	0.9101	2.1	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Popliteal LN	D90	4.8484	2.2	Pro-57	09-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Skin	D90	0.4867	2.0	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Spleen	D90	1.6886	2.1	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
2	2510	Thymus	D90	1.5384	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3006	Blood	D90	0.2300	1.5	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3006	Bone Marrow	D90	0.7350	1.5	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3006	Forebrain RT	D90	0.7499	2.2	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Heart	D90	0.7872	2.1	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Iliac LN	D90	1.2084	2.1	Pro-72	18-Oct-2018	0.14	<LLOQ	4	2.800	
3	3006	Kidney	D90	1.8151	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Liver	D90	0.7312	2.3	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Lung RT	D90	0.9122	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Mesenteric LN	D90	11.4633	2.1	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Muscle	D90	0.1560	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Popliteal LN	D90	5.4144	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Skin	D90	0.2265	2.1	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Spleen	D90	1.5440	2.2	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Testis	D90	3.0747	2.2	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
3	3006	Thymus	D90	0.7695	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3007	Blood	D90	0.1760	1.4	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3007	Bone Marrow	D90	1.2576	1.9	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	
3	3007	Forebrain RT	D90	0.9377	2.3	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3007	Heart	D90	0.5113	1.8	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
3	3007	Iliac LN	D90	3.1485	2.1	Pro-72	18-Oct-2018	0.14	25.9	4	2.800	
3	3007	Kidney	D90	2.4074	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3007	Liver	D90	0.1396	1.9	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	b
3	3007	Lung RT	D90	0.9931	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
3	3007	Mesenteric LN	D90	12.2427	2.1	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3007	Muscle	D90	0.1889	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3007	Popliteal LN	D90	1.4212	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3007	Skin	D90	0.2232	2.1	Pro-69	17-Oct-2018	0.14	175.1	4	2.800	
3	3007	Spleen	D90	1.6025	2.2	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3007	Testis	D90	3.1360	2.2	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
3	3007	Thymus	D90	0.6449	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3008	Blood	D90	0.2418	1.5	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3008	Bone Marrow	D90	0.6764	1.5	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3008	Forebrain RT	D90	0.8751	2.2	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Heart	D90	0.2216	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Iliac LN	D90	1.8475	2.0	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Kidney	D90	2.2883	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Liver	D90	0.7247	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Lung RT	D90	0.9607	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Mesenteric LN	D90	2.6123	2.1	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Muscle	D90	0.2534	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Popliteal LN	D90	1.7084	1.7	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Skin	D90	0.3345	2.1	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Spleen	D90	1.4174	2.2	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Testis	D90	2.7524	2.2	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
3	3008	Thymus	D90	1.1491	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3009	Blood	D90	0.1378	1.4	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3009	Bone Marrow	D90	0.3290	2.0	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Forebrain RT	D90	1.0444	2.3	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Heart	D90	0.4861	2.1	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Iliac LN	D90	1.4210	2.1	Pro-72	18-Oct-2018	0.14	<LLOQ	4	2.800	
3	3009	Kidney	D90	2.3085	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Liver	D90	0.2710	2.0	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Lung RT	D90	0.7562	2.2	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Mesenteric LN	D90	1.9352	2.1	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Muscle	D90	0.2146	2.2	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Popliteal LN	D90	3.2449	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Skin	D90	0.2969	2.1	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Spleen	D90	1.8627	2.2	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Testis	D90	3.8434	2.2	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
3	3009	Thymus	D90	2.1920	2.0	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3010	Blood	D90	0.1797	1.4	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3010	Bone Marrow	D90	0.8169	1.4	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3010	Forebrain RT	D90	0.9218	2.3	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3010	Heart	D90	0.6575	2.1	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
3	3010	Iliac LN	D90	3.4041	2.1	Pro-72	18-Oct-2018	0.14	35.3	4	2.800	
3	3010	Kidney	D90	1.9735	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3010	Liver	D90	0.4105	2.0	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3010	Lung RT	D90	1.0407	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
3	3010	Mesenteric LN	D90	9.1090	2.1	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3010	Muscle	D90	0.2202	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3010	Popliteal LN	D90	2.9564	2.0	Pro-95	22-Nov-2018	0.14	<LOD	4	2.800	
3	3010	Skin	D90	0.2891	2.1	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3010	Spleen	D90	1.2349	2.2	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3010	Testis	D90	2.4401	2.2	Pro-73	18-Oct-2018	0.14	<LOD	4	2.800	
3	3010	Thymus	D90	0.4460	1.9	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3506	Blood	D90	0.1336	1.4	Pro-67	16-Oct-2018	0.13	<LOD	4	2.600	b
3	3506	Bone Marrow	D90	1.1430	1.6	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3506	Forebrain RT	D90	0.9519	2.3	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Heart	D90	0.6387	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Iliac LN	D90	0.4393	2.0	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Kidney	D90	1.9304	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Liver	D90	0.2919	2.0	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Lung RT	D90	1.0284	2.2	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Mesenteric LN	D90	11.5766	2.1	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Muscle	D90	0.3681	1.7	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Ovaries	D90	2.9000	2.0	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Popliteal LN	D90	5.2284	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Skin	D90	0.6331	1.9	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Spleen	D90	1.4307	2.2	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3506	Thymus	D90	0.2642	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3507	Blood	D90	0.1358	1.4	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3507	Bone Marrow	D90	0.7047	1.7	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Forebrain RT	D90	0.8974	2.3	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Heart	D90	0.9320	2.0	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Iliac LN	D90	3.8446	2.0	Pro-72	18-Oct-2018	0.14	<LLOQ	4	2.800	
3	3507	Kidney	D90	2.4650	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Liver	D90	0.2863	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Lung RT	D90	1.1828	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Mesenteric LN	D90	5.9462	2.2	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Muscle	D90	0.3392	2.0	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Ovaries	D90	2.2976	2.0	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Popliteal LN	D90	3.3125	1.8	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Skin	D90	0.6430	1.9	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Spleen	D90	0.9593	1.9	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3507	Thymus	D90	1.6257	2.0	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3508	Blood	D90	0.1343	1.5	Pro-67	16-Oct-2018	0.13	<LOD	4	2.600	b
3	3508	Bone Marrow	D90	0.4755	1.6	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3508	Forebrain RT	D90	0.8835	2.3	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Heart	D90	0.5191	2.1	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Iliac LN	D90	0.0262	1.5	Pro-84	01-Nov-2018	0.03	<LOD	10	1.500	a,b
3	3508	Kidney	D90	1.7670	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Liver	D90	0.1707	1.9	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Lung RT	D90	0.9756	2.2	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Mesenteric LN	D90	9.8466	2.2	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Muscle	D90	0.2855	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Ovaries	D90	3.4374	2.0	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Popliteal LN	D90	0.7249	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Skin	D90	0.6232	1.9	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Spleen	D90	1.3795	2.2	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3508	Thymus	D90	1.1118	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3509	Blood	D90	0.2464	1.5	Pro-67	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3509	Bone Marrow	D90	0.3195	1.6	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3509	Forebrain RT	D90	0.9938	2.3	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Heart	D90	0.3857	1.8	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Iliac LN	D90	0.7101	1.9	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Kidney	D90	2.4790	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Liver	D90	0.6269	2.1	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Lung RT	D90	1.0336	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Mesenteric LN	D90	6.9775	2.0	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Muscle	D90	0.3922	1.9	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Ovaries	D90	1.9638	2.0	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Popliteal LN	D90	2.4214	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Skin	D90	0.4627	2.0	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Spleen	D90	1.3652	2.1	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3509	Thymus	D90	0.6992	2.1	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3510	Blood	D90	0.1201	1.5	Pro-67	16-Oct-2018	0.12	<LOD	4	2.400	b
3	3510	Bone Marrow	D90	1.1527	1.5	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	b
3	3510	Forebrain RT	D90	0.6520	2.2	Pro-69	17-Oct-2018	0.14	<LOD	4	2.800	
3	3510	Heart	D90	0.6449	2.1	Pro-60	10-Oct-2018	0.14	<LOD	4	2.800	
3	3510	Iliac LN	D90	0.0621	1.7	Pro-84	01-Nov-2018	0.06	<LOD	7	2.100	b
3	3510	Kidney	D90	1.8234	2.2	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3510	Liver	D90	1.4034	2.2	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3510	Lung RT	D90	0.9153	2.1	Pro-61	10-Oct-2018	0.14	<LOD	4	2.800	
3	3510	Mesenteric LN	D90	5.0798	2.2	Pro-72	18-Oct-2018	0.14	<LOD	4	2.800	
3	3510	Muscle	D90	0.3353	2.0	Pro-70	17-Oct-2018	0.14	<LOD	4	2.800	
3	3510	Ovaries	D90	3.2907	1.9	Pro-65	15-Oct-2018	0.14	<LOD	4	2.800	
3	3510	Popliteal LN	D90	2.9603	2.0	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3510	Skin	D90	0.4373	1.9	Pro-69	17-Oct-2018	0.14	42.7	4	2.800	
3	3510	Spleen	D90	1.3046	2.2	Pro-64	15-Oct-2018	0.14	<LOD	4	2.800	
3	3510	Thymus	D90	0.6097	2.0	Pro-66	16-Oct-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2011	Iliac LN	D120	0.4507	1.6	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	b
2	2011	Muscle	D120	0.4884	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
2	2011	Popliteal LN	D120	3.9334	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
2	2011	Skin	D120	0.2179	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2011	Spleen	D120	1.2970	2.2	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2012	Iliac LN	D120	3.9096	1.5	Pro-85	01-Nov-2018	0.14	37.9	4	2.800	b
2	2012	Muscle	D120	0.5009	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
2	2012	Popliteal LN	D120	3.8100	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
2	2012	Skin	D120	0.2819	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2012	Spleen	D120	1.6003	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2013	Iliac LN	D120	0.5545	1.9	Pro-85	01-Nov-2018	0.14	<LLOQ	4	2.800	
2	2013	Muscle	D120	0.4742	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
2	2013	Popliteal LN	D120	3.6456	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
2	2013	Skin	D120	0.3450	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2013	Spleen	D120	1.4117	2.2	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2014	Iliac LN	D120	1.5147	1.3	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	b
2	2014	Muscle	D120	0.4620	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
2	2014	Popliteal LN	D120	3.4066	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
2	2014	Skin	D120	0.3520	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2014	Spleen	D120	1.4127	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2015	Iliac LN	D120	5.2047	1.4	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	b
2	2015	Muscle	D120	0.4342	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
2	2015	Popliteal LN	D120	3.0963	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
2	2015	Skin	D120	0.1575	2.0	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2015	Spleen	D120	1.0773	2.0	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2511	Iliac LN	D120	2.7129	1.6	Pro-85	01-Nov-2018	0.14	53.4	4	2.800	b
2	2511	Muscle	D120	0.4548	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
2	2511	Popliteal LN	D120	1.8365	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
2	2511	Skin	D120	0.6102	1.9	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2511	Spleen	D120	1.4142	2.1	Pro-90	06-Nov-2018	0.14	<LLOQ	4	2.800	
2	2512	Iliac LN	D120	1.7682	1.3	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	b
2	2512	Muscle	D120	0.3981	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
2	2512	Popliteal LN	D120	3.6289	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
2	2512	Skin	D120	0.5352	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2512	Spleen	D120	1.8548	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2513	Iliac LN	D120	1.2553	1.2	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	b
2	2513	Muscle	D120	0.4941	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
2	2513	Popliteal LN	D120	0.8229	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
2	2513	Skin	D120	0.4276	2.2	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2513	Spleen	D120	1.3706	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2514	Iliac LN	D120	1.9258	1.4	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	b
2	2514	Muscle	D120	0.4604	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
2	2514	Popliteal LN	D120	1.7670	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
2	2514	Skin	D120	0.5713	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2514	Spleen	D120	1.3614	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2515	Iliac LN	D120	1.3997	1.2	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	b
2	2515	Muscle	D120	0.5028	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
2	2515	Popliteal LN	D120	5.2922	2.0	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
2	2515	Skin	D120	0.5687	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
2	2515	Spleen	D120	1.2865	2.0	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
3	3011	Iliac LN	D120	1.0539	1.3	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	b
3	3011	Muscle	D120	0.3557	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
3	3011	Popliteal LN	D120	10.7983	2.0	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
3	3011	Skin	D120	0.3957	2.0	Pro-93	07-Nov-2018	0.14	<LOD	4	2.800	
3	3011	Spleen	D120	1.2247	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
3	3012	Iliac LN	D120	0.4122	1.3	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	b
3	3012	Muscle	D120	0.4003	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
3	3012	Popliteal LN	D120	2.2214	2.0	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
3	3012	Skin	D120	0.2999	2.0	Pro-93	07-Nov-2018	0.14	<LOD	4	2.800	
3	3012	Spleen	D120	1.0947	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3013	Iliac LN	D120	2.4092	1.2	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	b
3	3013	Muscle	D120	0.3939	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
3	3013	Popliteal LN	D120	6.6547	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
3	3013	Skin	D120	0.4181	2.0	Pro-93	07-Nov-2018	0.14	<LOD	4	2.800	
3	3013	Spleen	D120	1.2493	2.0	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
3	3014	Iliac LN	D120	0.0496	1.4	Pro-89	06-Nov-2018	0.05	<LOD	8	2.000	a,b
3	3014	Muscle	D120	0.3555	2.0	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
3	3014	Popliteal LN	D120	5.2476	2.0	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
3	3014	Skin	D120	0.3084	2.0	Pro-93	07-Nov-2018	0.14	<LOD	4	2.800	
3	3014	Spleen	D120	1.0654	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
3	3015	Iliac LN	D120	0.8448	1.2	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	b
3	3015	Muscle	D120	0.2826	2.2	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
3	3015	Popliteal LN	D120	5.1442	2.0	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
3	3015	Skin	D120	0.4427	2.0	Pro-93	07-Nov-2018	0.14	<LOD	4	2.800	
3	3015	Spleen	D120	1.3810	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
3	3511	Iliac LN	D120	0.5516	1.5	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	b
3	3511	Muscle	D120	0.4052	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
3	3511	Popliteal LN	D120	5.7110	1.9	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
3	3511	Skin	D120	0.1584	1.9	Pro-93	07-Nov-2018	0.14	<LOD	4	2.800	
3	3511	Spleen	D120	1.3000	2.0	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	

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QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3512	Iliac LN	D120	0.3603	1.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	b
3	3512	Muscle	D120	0.3332	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
3	3512	Popliteal LN	D120	6.4899	2.0	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
3	3512	Skin	D120	0.2629	2.0	Pro-93	07-Nov-2018	0.14	<LOD	4	2.800	
3	3512	Spleen	D120	1.3435	2.1	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
3	3513	Iliac LN	D120	0.8189	1.2	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	b
3	3513	Muscle	D120	0.3740	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
3	3513	Popliteal LN	D120	0.9760	2.0	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
3	3513	Skin	D120	0.1841	2.0	Pro-93	07-Nov-2018	0.14	<LOD	4	2.800	
3	3513	Spleen	D120	1.3049	2.0	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
3	3514	Iliac LN	D120	5.6155	1.4	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	b
3	3514	Muscle	D120	0.3251	2.2	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
3	3514	Popliteal LN	D120	1.3457	2.1	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
3	3514	Skin	D120	0.2437	1.9	Pro-93	07-Nov-2018	0.14	<LOD	4	2.800	
3	3514	Spleen	D120	1.2836	1.8	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	
3	3515	Iliac LN	D120	0.8169	1.3	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	b
3	3515	Muscle	D120	0.3956	2.1	Pro-85	01-Nov-2018	0.14	<LOD	4	2.800	
3	3515	Popliteal LN	D120	6.2345	1.9	Pro-89	06-Nov-2018	0.14	<LOD	4	2.800	
3	3515	Skin	D120	0.5641	2.0	Pro-93	07-Nov-2018	0.14	<LOD	4	2.800	
3	3515	Spleen	D120	1.1410	2.0	Pro-90	06-Nov-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2016	Iliac LN	D180	0.8995	2.0	Pro-100	30-Jan-2019	0.14	37.6	4	2.800	
2	2016	Spleen	D180	1.3218	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
2	2017	Iliac LN	D180	1.9611	2.0	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
2	2017	Spleen	D180	0.9777	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
2	2018	Iliac LN	D180	0.0532	1.6	Pro-98	13-Dec-2018	0.05	<LOD	10	2.500	b
2	2018	Spleen	D180	1.0460	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
2	2019	Iliac LN	D180	1.8306	2.0	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
2	2019	Spleen	D180	1.0489	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
2	2020	Iliac LN	D180	0.9732	1.9	Pro-98	13-Dec-2018	0.14	<LLOQ	4	2.800	
2	2020	Spleen	D180	1.0685	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
2	2516	Iliac LN	D180	1.1672	1.9	Pro-98	13-Dec-2018	0.14	<LLOQ	4	2.800	
2	2516	Spleen	D180	1.1709	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
2	2517	Iliac LN	D180	0.2469	1.8	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
2	2517	Spleen	D180	1.0700	1.9	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
2	2518	Iliac LN	D180	0.8971	1.9	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
2	2518	Spleen	D180	1.0170	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
2	2519	Iliac LN	D180	3.0260	1.8	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
2	2519	Spleen	D180	1.0383	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
2	2520	Iliac LN	D180	1.1307	1.9	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
2	2520	Spleen	D180	0.9449	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
3	3016	Iliac LN	D180	1.0885	1.9	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
3	3016	Spleen	D180	0.9981	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
3	3017	Iliac LN	D180	0.8972	1.9	Pro-98	13-Dec-2018	0.14	<LLOQ	4	2.800	
3	3017	Spleen	D180	1.1459	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
3	3018	Iliac LN	D180	1.3829	2.0	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
3	3018	Spleen	D180	0.9633	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
3	3019	Iliac LN	D180	0.4261	1.9	Pro-98	13-Dec-2018	0.14	<LLOQ	4	2.800	
3	3019	Spleen	D180	1.0069	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
3	3020	Iliac LN	D180	0.8487	2.0	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
3	3020	Spleen	D180	0.9941	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
3	3516	Iliac LN	D180	0.9202	1.9	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
3	3516	Spleen	D180	0.8866	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	

Appendix 6

QPCR Results for the Quantitative Determination of Ad.26 (b) (4) vector DNA in Day 11, Day 90, Day 120 and Day 180 New Zealand White Rabbits Tissue and Fluid Samples

Group	Animal ID	Matrix	Time point	DNA Con. (µg/µL)	Ratio	PCR Assay ID	PCR Assay Date	PCR DNA Con. (µg/µL)	Reported Value (copies/µg)	Total Wells	Total DNA (µg)	FLAG
3	3517	Iliac LN	D180	1.2625	1.9	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
3	3517	Spleen	D180	0.9831	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
3	3518	Iliac LN	D180	0.0168	1.1	Pro-98	13-Dec-2018	0.02	<LOD	10	1.000	a,b
3	3518	Spleen	D180	0.9747	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
3	3519	Iliac LN	D180	1.2140	1.9	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
3	3519	Spleen	D180	1.2224	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	
3	3520	Iliac LN	D180	3.4774	1.8	Pro-98	13-Dec-2018	0.14	<LOD	4	2.800	
3	3520	Spleen	D180	0.9260	2.0	Pro-99	13-Dec-2018	0.14	<LOD	4	2.800	

a: Less than 2 µg of DNA were analyzed in the qPCR Assay. Study sample loaded into the 384-well plate was capped at the maximum replicates due to the sample limitation

b: DNA concentration or ratio below the corresponding target of 0.1400 µg/µL or 1.7, respectively

The LLOQ and the LOD of the method were established in the associated validation study to be 20 copies/reaction (28.6 copies/µg DNA) and 5 copies/reaction (7.1 copies/µg DNA) respectively.

<LLOQ: Result below the LLOQ (lower limit of quantification) but above the LOD (limit of detection)

<LOD: Result below the LOD (limit of detection)

Appendix 6

Table 8
Summary of qPCR Results for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

Appendix 6

Summary of qPCR Results for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

DNA (copies/µg)
Males
Group 2 - Ad26 (b) (4) 1 x 10^{11} vp

Tissue	Summary Information	Day 11	Day 90
Testes	Mean	14.30	14.30
	SD	0.00	0.00
	N	5	5
Blood	Mean	14.30	14.30
	SD	0.00	0.00
	N	5	5
Bone Marrow	Mean	14.30	14.30
	SD	0.00	0.00
	N	5	5
Forebrain Right	Mean	14.30	14.30
	SD	0.00	0.00
	N	5	5

Day 90 significantly different from Day 11 value: A - $P \leq 0.05$ B - $P \leq 0.01$ C - $P \leq 0.001$ (Tukey)
a - $P' \leq 0.05$ b - $P' \leq 0.01$ c - $P' \leq 0.001$(Wilcoxon)
Day 90, Day 120 and Day 180 significantly different from Day 11 value: D - $P \leq 0.05$ E - $P \leq 0.01$ F - $P \leq 0.001$ (Tukey)
d - $P' \leq 0.05$ e - $P' \leq 0.01$ f - $P' \leq 0.001$(adjusted Wilcoxon)
Day 120 and Day 180 significantly different from Day 90 value: G - $P \leq 0.05$ H - $P \leq 0.01$ I - $P \leq 0.001$ (Tukey)
g - $P' \leq 0.05$ h - $P' \leq 0.01$ i - $P' \leq 0.001$(adjusted Wilcoxon)
Day 180 significantly different from Day 120 value: J - $P \leq 0.05$ K - $P \leq 0.01$ M - $P \leq 0.001$ (Tukey)
j - $P' \leq 0.05$ k - $P' \leq 0.01$ m - $P' \leq 0.001$(adjusted Wilcoxon)
where P' = adjusted p-value (multiplicity based on the square root of the number of pairwise comparisons)
The LLOQ and the LOD of the method were established in the associated validation study to be 20 copies/reaction (28.6 copies/µg DNA) and 5 copies/reaction (7.1 copies/µg DNA) respectively. For the purpose of the statistical analysis and the calculations of the descriptive statistics (arithmetic, standard deviation), the results that are < LLOQ were processed as the LLOQ / 2 (20. / 2 = 10 copies/rxn or 28.6/2 = 14.3 copies/µg DNA).

Appendix 6

Summary of qPCR Results for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

DNA (copies/µg)
Males
Group 2 - Ad26 (b) (4) 1 x 10^{11} vp

Tissue	Summary Information	Day 11	Day 90	Day 120	Day 180
Heart	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		
Iliac Lymph Node	Mean	134.44	14.30	19.02	18.96
	SD	97.83	0.00	10.55	10.42
	N	5	5	5	5
Kidney	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		
Liver	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		

Day 90 significantly different from Day 11 value: A - P ≤ 0.05 B - P ≤ 0.01 C - P ≤ 0.001 (Tukey)
a - P' ≤ 0.05 b - P' ≤ 0.01 c - P' ≤ 0.001(Wilcoxon)
Day 90, Day 120 and Day 180 significantly different from Day 11 value: D - P ≤ 0.05 E - P ≤ 0.01 F - P ≤ 0.001 (Tukey)
d - P' ≤ 0.05 e - P' ≤ 0.01 f - P' ≤ 0.001(adjusted Wilcoxon)
Day 120 and Day 180 significantly different from Day 90 value: G - P ≤ 0.05 H - P ≤ 0.01 I - P ≤ 0.001 (Tukey)
g - P' ≤ 0.05 h - P' ≤ 0.01 i - P' ≤ 0.001(adjusted Wilcoxon)
Day 180 significantly different from Day 120 value: J - P ≤ 0.05 K - P ≤ 0.01 M - P ≤ 0.001 (Tukey)
j - P' ≤ 0.05 k - P' ≤ 0.01 m - P' ≤ 0.001(adjusted Wilcoxon)
where P' = adjusted p-value (multiplicity based on the square root of the number of pairwise comparisons)
The LLOQ and the LOD of the method were established in the associated validation study to be 20 copies/reaction (28.6 copies/µg DNA) and 5 copies/reaction (7.1 copies/µg DNA) respectively. For the purpose of the statistical analysis and the calculations of the descriptive statistics (arithmetic, standard deviation), the results that are < LLOQ were processed as the LLOQ / 2 (20. / 2 = 10 copies/rxn or 28.6/2 = 14.3 copies/µg DNA).

Appendix 6

Summary of qPCR Results for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

DNA (copies/µg)
Males
Group 2 - Ad26 (b) (4) 1 x 10^{11} vp

Tissue	Summary Information	Day 11	Day 90	Day 120	Day 180
Lung Right Caudal Lobe	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		
Mesenteric Lymph Node	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		
Muscle	Mean	14.30	14.30	14.30	
	SD	0.00	0.00	0.00	
	N	5	5	5	
Popliteal Lymph Node	Mean	17.24	14.30	14.30	
	SD	6.57	0.00	0.00	
	N	5	5	5	

Day 90 significantly different from Day 11 value: A - P ≤ 0.05 B - P ≤ 0.01 C - P ≤ 0.001 (Tukey)
a - P' ≤ 0.05 b - P' ≤ 0.01 c - P' ≤ 0.001(Wilcoxon)
Day 90, Day 120 and Day 180 significantly different from Day 11 value: D - P ≤ 0.05 E - P ≤ 0.01 F - P ≤ 0.001 (Tukey)
d - P' ≤ 0.05 e - P' ≤ 0.01 f - P' ≤ 0.001(adjusted Wilcoxon)
Day 120 and Day 180 significantly different from Day 90 value: G - P ≤ 0.05 H - P ≤ 0.01 I - P ≤ 0.001 (Tukey)
g - P' ≤ 0.05 h - P' ≤ 0.01 i - P' ≤ 0.001(adjusted Wilcoxon)
Day 180 significantly different from Day 120 value: J - P ≤ 0.05 K - P ≤ 0.01 M - P ≤ 0.001 (Tukey)
j - P' ≤ 0.05 k - P' ≤ 0.01 m - P' ≤ 0.001(adjusted Wilcoxon)
where P' = adjusted p-value (multiplicity based on the square root of the number of pairwise comparisons)
The LLOQ and the LOD of the method were established in the associated validation study to be 20 copies/reaction (28.6 copies/µg DNA) and 5 copies/reaction (7.1 copies/µg DNA) respectively. For the purpose of the statistical analysis and the calculations of the descriptive statistics (arithmetic, standard deviation), the results that are < LLOQ were processed as the LLOQ / 2 (20. / 2 = 10 copies/rxn or 28.6/2 = 14.3 copies/µg DNA).

Appendix 6

Summary of qPCR Results for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

DNA (copies/µg)
Males
Group 2 - Ad26 (b) (4) 1 x 10^{11} vp

Tissue	Summary Information	Day 11	Day 90	Day 120	Day 180
Skin	Mean	75.42	14.30	14.30	
	SD	123.27	0.00	0.00	
	N	5	5	5	
Spleen	Mean	46.44	14.30	14.30	14.30
	SD	34.85	0.00	0.00	0.00
	N	5	5	5	5
Thymus	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		

Day 90 significantly different from Day 11 value: A - P ≤ 0.05 B - P ≤ 0.01 C - P ≤ 0.001 (Tukey)
a - P' ≤ 0.05 b - P' ≤ 0.01 c - P' ≤ 0.001(Wilcoxon)
Day 90, Day 120 and Day 180 significantly different from Day 11 value: D - P ≤ 0.05 E - P ≤ 0.01 F - P ≤ 0.001 (Tukey)
d - P' ≤ 0.05 e - P' ≤ 0.01 f - P' ≤ 0.001(adjusted Wilcoxon)
Day 120 and Day 180 significantly different from Day 90 value: G - P ≤ 0.05 H - P ≤ 0.01 I - P ≤ 0.001 (Tukey)
g - P' ≤ 0.05 h - P' ≤ 0.01 i - P' ≤ 0.001(adjusted Wilcoxon)
Day 180 significantly different from Day 120 value: J - P ≤ 0.05 K - P ≤ 0.01 M - P ≤ 0.001 (Tukey)
j - P' ≤ 0.05 k - P' ≤ 0.01 m - P' ≤ 0.001(adjusted Wilcoxon)
where P' = adjusted p-value (multiplicity based on the square root of the number of pairwise comparisons)
The LLOQ and the LOD of the method were established in the associated validation study to be 20 copies/reaction (28.6 copies/µg DNA) and 5 copies/reaction (7.1 copies/µg DNA) respectively. For the purpose of the statistical analysis and the calculations of the descriptive statistics (arithmetic, standard deviation), the results that are < LLOQ were processed as the LLOQ / 2 (20. / 2 = 10 copies/rxn or 28.6/2 = 14.3 copies/µg DNA).

Appendix 6

Summary of qPCR Results for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

DNA (copies/µg)
Females
Group 2 - Ad26 (b) (4) 1 x 10^{11} vp

Tissue	Summary Information	Day 11	Day 90
Ovaries	Mean	14.30	14.30
	SD	0.00	0.00
	N	5	5
Blood	Mean	14.30	14.30
	SD	0.00	0.00
	N	5	5
Bone Marrow	Mean	14.30	14.30
	SD	0.00	0.00
	N	5	5
Forebrain Right	Mean	14.30	14.30
	SD	0.00	0.00
	N	5	5

Day 90 significantly different from Day 11 value: A - P ≤ 0.05 B - P ≤ 0.01 C - P ≤ 0.001 (Tukey)
a - P' ≤ 0.05 b - P' ≤ 0.01 c - P' ≤ 0.001(Wilcoxon)
Day 90, Day 120 and Day 180 significantly different from Day 11 value: D - P ≤ 0.05 E - P ≤ 0.01 F - P ≤ 0.001 (Tukey)
d - P' ≤ 0.05 e - P' ≤ 0.01 f - P' ≤ 0.001(adjusted Wilcoxon)
Day 120 and Day 180 significantly different from Day 90 value: G - P ≤ 0.05 H - P ≤ 0.01 I - P ≤ 0.001 (Tukey)
g - P' ≤ 0.05 h - P' ≤ 0.01 i - P' ≤ 0.001(adjusted Wilcoxon)
Day 180 significantly different from Day 120 value: J - P ≤ 0.05 K - P ≤ 0.01 M - P ≤ 0.001 (Tukey)
j - P' ≤ 0.05 k - P' ≤ 0.01 m - P' ≤ 0.001(adjusted Wilcoxon)
where P' = adjusted p-value (multiplicity based on the square root of the number of pairwise comparisons)
The LLOQ and the LOD of the method were established in the associated validation study to be 20 copies/reaction (28.6 copies/µg DNA) and 5 copies/reaction (7.1 copies/µg DNA) respectively. For the purpose of the statistical analysis and the calculations of the descriptive statistics (arithmetic, standard deviation), the results that are < LLOQ were processed as the LLOQ / 2 (20. / 2 = 10 copies/rxn or 28.6/2 = 14.3 copies/µg DNA).

Appendix 6

Summary of qPCR Results for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

DNA (copies/µg)
Females
Group 2 - Ad26 (b) (4) 1 x 10^{11} vp

Tissue	Summary Information	Day 11	Day 90	Day 120	Day 180
Heart	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		
Iliac Lymph Node	Mean	191.94	21.06 d	22.12 d	14.30 d
	SD	114.51	15.12	17.49	0.00
	N	5	5	5	5
Kidney	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		
Liver	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		

Day 90 significantly different from Day 11 value: A - P ≤ 0.05 B - P ≤ 0.01 C - P ≤ 0.001 (Tukey)
a - P' ≤ 0.05 b - P' ≤ 0.01 c - P' ≤ 0.001(Wilcoxon)
Day 90, Day 120 and Day 180 significantly different from Day 11 value: D - P ≤ 0.05 E - P ≤ 0.01 F - P ≤ 0.001 (Tukey)
d - P' ≤ 0.05 e - P' ≤ 0.01 f - P' ≤ 0.001(adjusted Wilcoxon)
Day 120 and Day 180 significantly different from Day 90 value: G - P ≤ 0.05 H - P ≤ 0.01 I - P ≤ 0.001 (Tukey)
g - P' ≤ 0.05 h - P' ≤ 0.01 i - P' ≤ 0.001(adjusted Wilcoxon)
Day 180 significantly different from Day 120 value: J - P ≤ 0.05 K - P ≤ 0.01 M - P ≤ 0.001 (Tukey)
j - P' ≤ 0.05 k - P' ≤ 0.01 m - P' ≤ 0.001(adjusted Wilcoxon)
where P' = adjusted p-value (multiplicity based on the square root of the number of pairwise comparisons)
The LLOQ and the LOD of the method were established in the associated validation study to be 20 copies/reaction (28.6 copies/µg DNA) and 5 copies/reaction (7.1 copies/µg DNA) respectively. For the purpose of the statistical analysis and the calculations of the descriptive statistics (arithmetic, standard deviation), the results that are < LLOQ were processed as the LLOQ / 2 (20. / 2 = 10 copies/rxn or 28.6/2 = 14.3 copies/µg DNA).

Appendix 6

Summary of qPCR Results for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

DNA (copies/µg)
Females
Group 2 - Ad26 (b) (4) 1 x 10^{11} vp

Tissue	Summary Information	Day 11	Day 90	Day 120	Day 180
Lung Right Caudal Lobe	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		
Mesenteric Lymph Node	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		
Muscle	Mean	14.30	14.30	14.30	
	SD	0.00	0.00	0.00	
	N	5	5	5	
Popliteal Lymph Node	Mean	14.30	14.30	14.30	
	SD	0.00	0.00	0.00	
	N	5	5	5	

Day 90 significantly different from Day 11 value: A - $P \leq 0.05$ B - $P \leq 0.01$ C - $P \leq 0.001$ (Tukey)
a - $P' \leq 0.05$ b - $P' \leq 0.01$ c - $P' \leq 0.001$(Wilcoxon)
Day 90, Day 120 and Day 180 significantly different from Day 11 value: D - $P \leq 0.05$ E - $P \leq 0.01$ F - $P \leq 0.001$ (Tukey)
d - $P' \leq 0.05$ e - $P' \leq 0.01$ f - $P' \leq 0.001$(adjusted Wilcoxon)
Day 120 and Day 180 significantly different from Day 90 value: G - $P \leq 0.05$ H - $P \leq 0.01$ I - $P \leq 0.001$ (Tukey)
g - $P' \leq 0.05$ h - $P' \leq 0.01$ i - $P' \leq 0.001$(adjusted Wilcoxon)
Day 180 significantly different from Day 120 value: J - $P \leq 0.05$ K - $P \leq 0.01$ M - $P \leq 0.001$ (Tukey)
j - $P' \leq 0.05$ k - $P' \leq 0.01$ m - $P' \leq 0.001$(adjusted Wilcoxon)
where P' = adjusted p-value (multiplicity based on the square root of the number of pairwise comparisons)
The LLOQ and the LOD of the method were established in the associated validation study to be 20 copies/reaction (28.6 copies/µg DNA) and 5 copies/reaction (7.1 copies/µg DNA) respectively. For the purpose of the statistical analysis and the calculations of the descriptive statistics (arithmetic, standard deviation), the results that are < LLOQ were processed as the LLOQ / 2 (20. / 2 = 10 copies/rxn or 28.6/2 = 14.3 copies/µg DNA).

Appendix 6

Summary of qPCR Results for the Quantitative Determination of Ad26 (b) (4) Vector DNA in New Zealand White Rabbits Tissues and Fluids

DNA (copies/µg)
Females
Group 2 - Ad26 (b) (4) 1 x 10^{11} vp

Tissue	Summary Information	Day 11	Day 90	Day 120	Day 180
Skin	Mean	1510.84	67.46	14.30	
	SD	2728.94	118.87	0.00	
	N	5	5	5	
Spleen	Mean	54.70	14.30	14.30	14.30
	SD	44.75	0.00	0.00	0.00
	N	5	5	5	5
Thymus	Mean	14.30	14.30		
	SD	0.00	0.00		
	N	5	5		

Day 90 significantly different from Day 11 value: A - P ≤ 0.05 B - P ≤ 0.01 C - P ≤ 0.001 (Tukey)
a - P' ≤ 0.05 b - P' ≤ 0.01 c - P' ≤ 0.001(Wilcoxon)
Day 90, Day 120 and Day 180 significantly different from Day 11 value: D - P ≤ 0.05 E - P ≤ 0.01 F - P ≤ 0.001 (Tukey)
d - P' ≤ 0.05 e - P' ≤ 0.01 f - P' ≤ 0.001(adjusted Wilcoxon)
Day 120 and Day 180 significantly different from Day 90 value: G - P ≤ 0.05 H - P ≤ 0.01 I - P ≤ 0.001 (Tukey)
g - P' ≤ 0.05 h - P' ≤ 0.01 i - P' ≤ 0.001(adjusted Wilcoxon)
Day 180 significantly different from Day 120 value: J - P ≤ 0.05 K - P ≤ 0.01 M - P ≤ 0.001 (Tukey)
j - P' ≤ 0.05 k - P' ≤ 0.01 m - P' ≤ 0.001(adjusted Wilcoxon)
where P' = adjusted p-value (multiplicity based on the square root of the number of pairwise comparisons)
The LLOQ and the LOD of the method were established in the associated validation study to be 20 copies/reaction (28.6 copies/µg DNA) and 5 copies/reaction (7.1 copies/µg DNA) respectively. For the purpose of the statistical analysis and the calculations of the descriptive statistics (arithmetic, standard deviation), the results that are < LLOQ were processed as the LLOQ / 2 (20. / 2 = 10 copies/rxn or 28.6/2 = 14.3 copies/µg DNA).

Appendix 6

Table 9
Repeated Samples for the Quantitative Determination of Ad.26 (b) (4) Vector DNA in New Zealand White Rabbits Tissue and Fluid Samples

Appendix 6

Repeated Samples for the Quantitative Determination of Ad.26 (b) (4) vector DNA in New Zealand White Rabbits Tissue and Fluid Samples

Subject	Tissue Type	Study day	Initial Assay		Repeat #1		Repeat #2		Repeat #3		Reported Results	
			Assay ID	Assay type	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason
1003	Iliac LN	D11	Pro-04	DNA Isolation	Pro-24	g	-	-	-	-	Pro-04	a
1003	Popliteal LN	D11	Pro-02	Spectrophotometry	Pro-02 Repeat	Repeated by error	-	-	-	-	Pro-02 Repeat	b
3010	Popliteal LN	D90	Pro-64	QPCR	Pro-95	Wrong concentration used in Pro-64	-	-	-	-	Pro-95	c
2001	Muscle	D11	Pro-28	QPCR	Pro-56	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	d
2002	Muscle	D11	Pro-28	QPCR	Pro-77	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
2003	Muscle	D11	Pro-28	QPCR	Pro-77	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
2004	Muscle	D11	Pro-28	QPCR	Pro-77	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
2005	Muscle	D11	Pro-28	QPCR	Pro-56	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
2501	Muscle	D11	Pro-28	QPCR	Pro-56	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
2502	Muscle	D11	Pro-77	QPCR	Pro-77	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-77	
2504	Muscle	D11	Pro-77	QPCR	Pro-77	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-77	
2505	Muscle	D11	Pro-28	QPCR	Pro-57	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

Repeated Samples for the Quantitative Determination of Ad.26 (b) (4) vector DNA in New Zealand White Rabbits Tissue and Fluid Samples

Subject	Tissue Type	Study day	Initial Assay		Repeat #1		Repeat #2		Repeat #3		Reported Results	
			Assay ID	Assay type	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason
3001	Muscle	D11	Pro-28	QPCR	Pro-57	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	d
3002	Muscle	D11	Pro-28	QPCR	Pro-57	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
3003	Muscle	D11	Pro-28	QPCR	Pro-57	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
3004	Muscle	D11	Pro-28	QPCR	Pro-57	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
3005	Muscle	D11	Pro-28	QPCR	Pro-57	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
3501	Muscle	D11	Pro-28	QPCR	Pro-57	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
3502	Muscle	D11	Pro-28	QPCR	Pro-57	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
3504	Muscle	D11	Pro-28	QPCR	Pro-57	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-28	
2010	Muscle	D90	Pro-65	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-65	
2506	Muscle	D90	Pro-65	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-65	
2507	Muscle	D90	Pro-65	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-65	
2508	Muscle	D90	Pro-65	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-65	

Appendix 6

Repeated Samples for the Quantitative Determination of Ad.26 (b) (4) vector DNA in New Zealand White Rabbits Tissue and Fluid Samples

Subject	Tissue Type	Study day	Initial Assay		Repeat #1		Repeat #2		Repeat #3		Reported Results	
			Assay ID	Assay type	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason
2509	Muscle	D90	Pro-65	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-65	d
2510	Muscle	D90	Pro-65	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-65	
3007	Muscle	D90	Pro-70	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-70	
3009	Muscle	D90	Pro-70	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-70	
3506	Muscle	D90	Pro-70	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-70	
3507	Muscle	D90	Pro-70	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-70	
3508	Muscle	D90	Pro-70	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-70	
3509	Muscle	D90	Pro-70	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-70	
3510	Muscle	D90	Pro-70	QPCR	Pro-92	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-70	
2011	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
2012	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
2013	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	

Appendix 6

Repeated Samples for the Quantitative Determination of Ad.26 (b) (4) vector DNA in New Zealand White Rabbits Tissue and Fluid Samples

Subject	Tissue Type	Study day	Initial Assay		Repeat #1		Repeat #2		Repeat #3		Reported Results	
			Assay ID	Assay type	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason
2014	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	d
2015	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
2511	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
2512	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
2513	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
2514	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
2515	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
3011	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
3012	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
3013	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
3014	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
3015	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

Repeated Samples for the Quantitative Determination of Ad.26 (b) (4) vector DNA in New Zealand White Rabbits Tissue and Fluid Samples

Subject	Tissue Type	Study day	Initial Assay		Repeat #1		Repeat #2		Repeat #3		Reported Results	
			Assay ID	Assay type	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason
3511	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
3512	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
3513	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	d
3514	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
3515	Muscle	D120	Pro-85	QPCR	Pro-93	Leftover tissue analyzed for confirmation	-	-	-	-	Pro-85	
1001	Bone Marrow	D11	Pro-13	QPCR	Pro-77	Less than 2 µg of DNA analyzed	Pro-94	Less than 2 µg of DNA analyzed	-	-	Pro-94	e
1002	Bone Marrow	D11	Pro-13	QPCR	Pro-77	Less than 2 µg of DNA analyzed	Pro-94	Less than 2 µg of DNA analyzed	-	-	Pro-94	e
1501	Bone Marrow	D11	Pro-13	QPCR	Pro-77	Less than 2 µg of DNA analyzed	Pro-94	Less than 2 µg of DNA analyzed	-	-	Pro-94	e
1502	Bone Marrow	D11	Pro-13	QPCR	Pro-77	Less than 2 µg of DNA analyzed	Pro-94	Less than 2 µg of DNA analyzed	-	-	Pro-94	e
1001	Blood	D11	Pro-13	QPCR	Pro-40	Repeated by error	-	-	-	-	Pro-13	f
1002	Blood	D11	Pro-13	QPCR	Pro-40	Repeated by error	Pro-77	Less than 2 µg of DNA analyzed	Pro-94	Less than 2 µg of DNA analyzed	Pro-94	e
1003	Blood	D11	Pro-13	QPCR	Pro-40	Repeated by error	Pro-77	Less than 2 µg of DNA analyzed	Pro-94	Less than 2 µg of DNA analyzed	Pro-94	e

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

Repeated Samples for the Quantitative Determination of Ad.26 (b) (4) vector DNA in New Zealand White Rabbits Tissue and Fluid Samples

Subject	Tissue Type	Study day	Initial Assay		Repeat #1		Repeat #2		Repeat #3		Reported Results	
			Assay ID	Assay type	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason
1501	Blood	D11	Pro-13	QPCR	Pro-40	Repeated by error	Pro-77	Less than 2 µg of DNA analyzed	Pro-94	Less than 2 µg of DNA analyzed	Pro-94	e
1502	Blood	D11	Pro-13	QPCR	Pro-40	Repeated by error	Pro-77	Less than 2 µg of DNA analyzed	Pro-94	Less than 2 µg of DNA analyzed	Pro-94	e
1503	Blood	D11	Pro-13	QPCR	Pro-40	Repeated by error	Pro-77	Less than 2 µg of DNA analyzed	Pro-94	Less than 2 µg of DNA analyzed	Pro-94	e
2003	Blood	D11	Pro-19	QPCR	Pro-84	Less than 2 µg of DNA analyzed	-	-	-	-	Pro-84	e
2004	Blood	D11	Pro-19	QPCR	Pro-84	Less than 2 µg of DNA analyzed	-	-	-	-	Pro-84	e
2502	Blood	D11	Pro-19	QPCR	Pro-84	Less than 2 µg of DNA analyzed	-	-	-	-	Pro-84	e
2503	Blood	D11	Pro-19	QPCR	Pro-84	Less than 2 µg of DNA analyzed	-	-	-	-	Pro-84	e
3501	Blood	D11	Pro-29	QPCR	Pro-84	Less than 2 µg of DNA analyzed	-	-	-	-	Pro-84	e
3503	Blood	D11	Pro-29	QPCR	Pro-84	Less than 2 µg of DNA analyzed	-	-	-	-	Pro-84	e
2501	Bone Marrow	D11	Pro-29	QPCR	Pro-84	Less than 2 µg of DNA analyzed	-	-	-	-	Pro-84	e
2502	Bone Marrow	D11	Pro-29	QPCR	Pro-84	Less than 2 µg of DNA analyzed	-	-	-	-	Pro-84	e

Appendix 6

Repeated Samples for the Quantitative Determination of Ad.26 (b) (4) vector DNA in New Zealand White Rabbits Tissue and Fluid Samples

Subject	Tissue Type	Study day	Initial Assay		Repeat #1		Repeat #2		Repeat #3		Reported Results	
			Assay ID	Assay type	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason for repeat	Assay ID	Reason
3003	Bone Marrow	D11	Pro-56	QPCR	Pro-84	Less than 2 µg of DNA analyzed	-	-	-	-	Pro-84	e
3501	Bone Marrow	D11	Pro-56	QPCR	Pro-84	Less than 2 µg of DNA analyzed	-	-	-	-	Pro-84	e

a: Sample with the highest DNA concentration used
b: Refer to deviation report
c: Wrong concentration used in qPCR analysis in Pro-64. DNA isolation and qPCR analysis repeated under Pro-95. Refer to the Deviation Report
d: Original results reported. Repeat # 1 performed for confirmation of the qPCR results obtained from the first portion of the sample
e: Sample with the highest DNA concentration used
f: Original Results reported
g: DNA concentration lower than target. Repeated results in Pro-24 lower than original in Pro-04

Appendix 6

Appendix 1
Tissue and Fluid Preparation Procedure

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

ANALYTICAL PROCEDURE

(b) (4), (b) (6)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

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Table.1: Tissue Sample Volume Determination

Tissue Weight Range (mg)	Volume of Lysis Buffer to be used (µL)	Type of tube to use as applicable	Comments
1-110.4	500	15 mL	All tissue type
110.5-220.4	1000	15 mL	All tissue type
220.5-320.4	1500	15 mL	All tissue type
320.5-420.4	2000	15 mL	All tissue type
420.5-520.4	2500	15 mL	All tissue type
520.5-620.4	3000	15 mL	All tissue type
620.5-720.4	3500	15 mL	Muscle only
720.5-820.4	4000	15 mL	Muscle only
820.5-920.4	4500	15 mL	Muscle only
920.5-1020.4	5000	15 mL	Muscle only
1020.5-1120.4	5500	50 mL	Muscle only
1120.5-1220.4	6000	50 mL	Muscle only
1220.5-1320.4	6500	50 mL	Muscle only
1320.5-1420.4	7000	50 mL	Muscle only
1420.5-1520.4	7500	50 mL	Muscle only
1520.5-1620.4	8000	50 mL	Muscle only
1620.5-1720.4	8500	50 mL	Muscle only
1720.5-1820.4	9000	50 mL	Muscle only
1820.5-1920.4	9500	50 mL	Muscle only
1920.5-2020.4	10000	50 mL	Muscle only
2020.5-2120.4	10500	50 mL	Muscle only
2120.5-2220.4	11000	50 mL	Muscle only
2220.5-2320.4	11500	50 mL	Muscle only
2320.5-2420.4	12000	50 mL	Muscle only
2420.5-2520.4	12500	50 mL	Muscle only
2520.5-2620.4	13000	50 mL	Muscle only
2620.5-2720.4	13500	50 mL	Muscle only
2720.5-2820.4	14000	50 mL	Muscle only
2820.5-2920.4	14500	50 mL	Muscle only
2920.5-3020.4	15000	50 mL	Muscle only
3020.5-3120.4	15500	50 mL	Muscle only
3120.5-3220.4	16000	50 mL	Muscle only
3220.5-3320.4	16500	50 mL	Muscle only
3320.5-3420.4	17000	50 mL	Muscle only
3420.5-3520.4	17500	50 mL	Muscle only
3520.5-3620.4	18000	50 mL	Muscle only
3620.5-3720.4	18500	50 mL	Muscle only
3720.5-3820.4	19000	50 mL	Muscle only
3820.5-3920.4	19500	50 mL	Muscle only
3920.5-4020.4	20000	50 mL	Muscle only

Appendix 6

(b) (4)

Table.2: Thymus Tissue Sample Volume Determination

Tissue Weight Range (mg)	Volume of Lysis Buffer to be used (µL)	Type of tube to use as applicable	Comments
1-110.4	1000	15 mL	Thymus only
110.5-220.4	2000	15 mL	Thymus only
220.5-320.4	3000	15 mL	Thymus only
320.5-420.4	4000	15 mL	Thymus only
420.5-520.4	5000	50 mL	Thymus only
520.5-620.4	6000	50 mL	Thymus only

6.0 Revision History

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

Tissue Weighing and Processing Information

Study/Reference No.: (b) (4) Species: New Zealand White Rabbit Assay ID.:

Sample ID and Sample weight verified by/Date: _____

Lysis buffer volume calculations verified by/Date: _____

Put tissue on Dry Ice for transportation (√)	Tissue ID (as per Watson pull list)	Tube ID	Tissue original weight (mg) or N/Ap ( ) if on collection sheet[1,3]	Tissue analysis weight (mg) or code "O" if same as original weight (mg)[3]	Volume of Lysis Buffer[2] to be added for tissue homogenization (µL)	Volume of tissue homogenate used for Proteinase K treatment (µL)	Volume of Proteinase K[2] to be added (µL)	Performed by/Date
( )								

ssue weight can be prefilled or be found on the necropsy frozen sample collection sheet.
olume of Lysis buffer and Proteinase K to be used are calculated using Table 1 of appropriate AP and Reagent information recorded on Appendix 2.
alance ID should be recorded on Appendix 2 if applicable.

›mments : _____

_____

_____

Reviewed by/Date: _____

(b) (4)

Appendix 6

Fluid Sample Measurement and Pooling

Study/Reference No.: (b) (4) Species: New Zealand White Rabbit Assay ID.:

Sample ID verified by/Date: _____

Lysis buffer adjustment volume calculations verified by/Date: _____

Put samples on Dry ice for transportation (√)	Fluid sample ID (as per Watson pull list)	Tube ID	If less than 300 µL of blood or 400µL of bone marrow is present in tube, refer to Table 1 to pool aliquots	Add 300µL of blood or 400 µL of bone marrow sample in a new incubation tube and record the volume (µL).[1,2]	Bring sample volume to 600 µL using Lysis buffer and record volume (µL)[2]	Performed By /Date
( )			( ) or N/Ap ( )			

1 Use the same Watson sample tube if pooling was needed and it is not possible to acquire the minimum sample volume into a new incubation tube.

Table 1: Sample Pooling or N/Ap ( )

Tube ID(s)	Pooling information[2]	If volume after pooling is still less than 300 µL for blood or 400µL for bone marrow , bring to these required volume with PBS 1X pH 7.2 and record volume (µL)[2]	Performed By /Date
	Total volume _____µL pooled in tube ID ____		
	Total volume _____µL pooled in tube ID ____		
	Total volume _____µL pooled in tube ID ____		
	Total volume _____µL pooled in tube ID ____		

2 Pipette IDs should be recorded on Appendix 2.

Comments : ***Reagent information will be recorded on Appendix 2.**

_____

_____

_____

Reviewed by/Date: _____

(b) (4)

Page 1 of 1

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

Tissue and Fluid Samples Processing Assay Sheet

Study/Reference No: (b) (4) Assay ID.:

REAGENTS

Name	*Batch / Lot #*	*Inventory #*	*Expiry Date*	*Completed by/ Date*
Matrix beads or N/Ap ( )				
PBS (1X) pH 7.2 or N/Ap ( )		IMR		
Lysis Buffer or N/Ap ( )		IMR		
Proteinase K or N/Ap ( )		IMR		

INSTRUMENTS

Name	*ID*	*Completed by/ Date*
Pipettes		
Balance ID or N/Ap ( )		
Geno Grinder		
Waterbath	Tox- or N/Ap ( )	
Microcentrifuge / Centrifuge	Tox-	

Comments: _____

_____

_____

(b) (4)

Appendix 6

Tissue and Fluid Samples Processing Assay Sheet

Study/Reference No: (b) (4) Assay ID.:

Tissue Sample Processing Steps or N/Ap ( )	*Performed (√)* Assay ID: _____	Assay ID: or N/Ap ( ) _____	Assay ID: or N/Ap ( ) _____	Assay ID: or N/Ap ( ) _____	*Performed by / Date*
(b) (4)	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( ) or N/Ap ( )	( ) or N/Ap ( )	( ) or N/Ap ( )	( ) or N/Ap ( )	
	( ) or N/Ap ( )	( ) or N/Ap ( )	( ) or N/Ap ( )	( ) or N/Ap ( )	
	( )	( )	( )	( )	
	Cycle 1: ( ) Cycle 2: ( ) Cycle 3: ( ) or N/Ap for Cycle 3 ( )	Cycle 1: ( ) Cycle 2: ( ) Cycle 3: ( ) or N/Ap for Cycle 3 ( )	Cycle 1: ( ) Cycle 2: ( ) Cycle 3: ( ) or N/Ap for Cycle 3 ( )	Cycle 1: ( ) Cycle 2: ( ) Cycle 3: ( ) or N/Ap for Cycle 3 ( )	
	( )	( )	( )	( )	
	( ) or N/Ap ( )	( ) or N/Ap ( )	( ) or N/Ap ( )	( ) or N/Ap ( )	
	( )	( )	( )	( )	
	( ) Start time:	( ) Start time:	( ) Start time:	( ) Start time:	
	End time :	End time :	End time :	End time :	
	( ) or N/Ap ( )	( ) or N/Ap ( )	( ) or N/Ap ( )	( ) or N/Ap ( )	

1 More than two cycles may be needed depending on the type of tissue. If more than 3 cycles need to be performed this should be footnoted on Appendix#2 and the scientist or his delegate should co-sign.

Comments: _____

_____

_____

(b) (4)

Appendix 6

Tissue and Fluid Samples Processing Assay Sheet

Study/Reference No: (b) (4) Assay ID.:

Fluid Sample Processing Steps or N/Ap ( )	*Performed (√)* Assay ID: _____	Assay ID: or N/Ap ( ) _____	Assay ID: or N/Ap ( ) _____	Assay ID: or N/Ap ( ) _____	*Performed by / Date*
(b) (4)	( )	( )	( )	( )	
	( ) Start time:	( ) Start time:	( ) Start time:	( ) Start time:	
	End time :	End time :	End time :	End time :	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( ) Start time:	( ) Start time:	( ) Start time:	( ) Start time:	
	End time :	End time :	End time :	End time :	
	( ) or N/Ap ( )	( ) or N/Ap ( )	( ) or N/Ap ( )	( ) or N/Ap ( )	

Comments: _____

All pages reviewed by/Date: _____

Appendix 6

Appendix 2
Tissue and Fluid DNA Isolation Assay Procedure

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4), (b) (6)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

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8.0 Revision History

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Appendix 6

TOTAL DNA ISOLATION USING THE MAXWELL 16 LEV BLOOD DNA KIT -ASSAY SHEET-

Study/Reference No: (b) (4) Assay ID.:

REAGENTS / WORKING SOLUTIONS

Name	*Batch / Lot #*	*Inventory #*	*Expiry Date*	*Completed by/ Date*
70% Ethanol	Batch:	N/Ap		
10% Bleach	Batch:	N/Ap		
Nuclease-free water	Lot:			
Maxwell 16 LEV Blood DNA Kit	Lot:			
Lysis Buffer	Lot: or N/Ap ( )			
Proteinase K	Lot:			
Elution Buffer	Lot:	Refer to the kit	Refer to the kit	

INSTRUMENTS

Name	*ID*	*Completed by/ Date*
Pipettes		
Maxwell 16	IM-	
Waterbath	Tox- or N/Ap ( )	
Microcentrifuge / Centrifuge	Tox-	

Comments: _____

_____

_____

(b) (4)

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Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

TOTAL DNA ISOLATION USING THE MAXWELL 16 LEV BLOOD DNA KIT
-ASSAY SHEET-

Study/Reference No: (b) (4)

ASSAY

Steps	*Performed (√)* Assay ID: _____	Assay ID: or N/Ap ( ) _____	Assay ID: or N/Ap ( ) _____	Assay ID: or N/Ap ( ) _____	*Performed by / Date*
Cleaning					
(b) (4)	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( )				
	N/Ap ☐				
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	N/Ap ☐				
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	

Comments: _____

Appendix 6

TOTAL DNA ISOLATION USING THE MAXWELL 16 LEV BLOOD DNA KIT
-ASSAY SHEET-

Study/Reference No: (b) (4)

ASSAY

Steps	*Performed (√)*				*Performed by / Date*
	Assay ID: ______	Assay ID: or N/Ap ( ) ___	Assay ID: or N/Ap ( ) ___	Assay ID: or N/Ap ( ) ___	
(b) (4)					
	( )	( )	( )	( )	
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	( )	( )	( )	( )	

Comments: ______________________________

Appendix 6

TOTAL DNA ISOLATION USING THE MAXWELL 16 LEV BLOOD DNA KIT
-ASSAY SHEET-

Study/Reference No: (b) (4)

ASSAY

Steps	*Performed (√)* Assay ID: _____	Assay ID: or N/Ap ( ) ___	Assay ID: or N/Ap ( ) ___	Assay ID: or N/Ap ( ) ___	*Performed by / Date*
(b) (4)					
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	( ) or N/Ap ☐	
	Freezer ID : _____or Sample Management ( ) or N/Ap ( )				
	Freezer ID : _____or Sample Management ( ) or N/Ap ( )				
	( )				
	( )				
	( )				
	( )				
	( )				

Comments: _____

_____

_____

All pages 1 to 4 reviewed by/date: _____

Appendix 6

Sample Loading Sheet for DNA Isolation

Study / Reference No: (b) (4) Assay ID:_____

Sample #/ID (Animal number)	Matrix (Tissue or fluid type)	Code (A)[1] or N/Ap ( )	Cartridge position (1 to 16)
		or N/Ap ( )	1
		or N/Ap ( )	2
		or N/Ap ( )	3
		or N/Ap ( )	4
		or N/Ap ( )	5
		or N/Ap ( )	6
		or N/Ap ( )	7
		or N/Ap ( )	8
		or N/Ap ( )	9
		or N/Ap ( )	10
		or N/Ap ( )	11
		or N/Ap ( )	12
		or N/Ap ( )	13
		or N/Ap ( )	14
		or N/Ap ( )	15
		or N/Ap ( )	16
Sample ID and Matrix verified by/Date :			
Loading performed by/Date:			

Record instruments and pipettes used on Appendix 1

[1] Applicable if a carryover of paramagnetic cellulose particles occur during the elution step. In this case, **100 µL** of elution buffer may be added to the elution tube, sample should be centrifuged at **10,000 x g for 2 minutes** at ambient room temperature and DNA should be transferred in to a new PCR clean tube. Centrifugation can be repeated if required. This procedure is recorded as Code A.

Comments:_____

Reviewed by/Date:_____

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

NEW ZEALAND WHITE RABBIT POOL GENOMIC DNA PREPARATION ASSAY SHEET

Study/Reference No: (b) (4)

Page: 1 of 2

Table 1: Instruments

Name	ID	Completed by / Date
Microcentrifuge		
Pipettes		

Table 2: New Zealand White Rabbit Pool Genomic DNA Preparation

Tissue Type/Matrix	Custom ID	DNA Isolation Assay ID	DNA Isolation date	DNA volume (µL)*	Tick when performed (√)	Performed by/Date
Thymus Genomic DNA					( )	
Mesenteric Lymph nodes Genomic DNA					( )	

Verified by/date: _____

Comments: _____

(b) (4)

Appendix 6

NEW ZEALAND WHITE RABBIT POOL GENOMIC DNA PREPARATION ASSAY SHEET

Study/Reference No: (b) (4)

Page: 2 of 2

Table 3: Preparation of New Zealand White Rabbit Pool Genomic DNA

Steps	Performed (√)	Performed by / Date
1. Place the samples on dry ice for transportation	( )	
2. If required, quickly thaw the genomic DNA samples on a bench at room temperature and then keep on wet ice once thawed.	( ) or N/Ap ( )	
3. Gently vortex and quick spin the samples in a centrifuge set to 10 000 x g for 10 seconds at room temperature	( )	
4. Pool the genomic DNA in an appropriate size of PCR clean tube	( )	
5. Gently vortex and quick spin the sample in a centrifuge set to 10 000 x g for 10 seconds at room temperature	( )	
6. Perform the spectrophotometry on the genomic DNA samples according (b) (4)	( )	
7. Aliquot the genomic DNA into 1000 µL (or other appropriate volume) in a freezer set to maintain -20°C	( ) Freezer ID:	

Table 4: New Zealand White Rabbit Pool Genomic DNA

Genomic DNA Name	Batch No. (Place label in area)	Expiry Date	Aliquots ID (Place an example of label in area)
New Zealand White Rabbit Pool Genomic DNA			No. of aliquots: ____

Comments: _____

_____

_____

_____

All pages reviewed by / Date: _____

(b) (4)

Appendix 6

Appendix 3
DNA Quantity Assessment Procedures

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4), (b) (6)

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

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(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

96-Well DNA Spectrophotometry Assay Sheet

Study/Reference No: (b) (4) Assay I.D.: _____

Page : 1 of 2

REAGENTS / WORKING SOLUTIONS

Name	*Batch / Lot #*	*Inventory #*	*Entered by/Date*
Diluent (Nuclease-free water)			
Reference Solution (elution buffer from Maxwell kit used to prepare blank)	or Same as Maxwell kit ( )	IMR-	
96-well UV Transparent Plate			

INSTRUMENTS

Name	*ID*	*Entered by/Date*
Spectrophotometer (M2 or M5)	or N/Ap ( )	
Microcentrifuge		
Refrigerator	or N/Ap ( )	
Pipettes and multichannel pipettes		

ASSAY

Steps	*Performed (√)*	*Performed by/Date*
If frozen, thaw samples on wet ice or in a refrigerator set to maintain 4°C.	On wet ice ( ) In a refrigerator set to maintain 4°C ( ) If not frozen: N/Ap ☐	
If frozen samples were thawed, mix gently and quick spin tubes.	( ) or N/Ap ☐	
Keep samples on wet ice or in a refrigerator set to maintain 4°C until use.	On wet ice ( ) In a refrigerator set to maintain 4°C ( )	

Comments _____

_____

_____

_____

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

96-Well RNA Spectrophotometry Assay Sheet

Study/Reference No: (b) (4) Assay I.D.: _____

Page : 2 of 2

Steps	*Performed (√)*			*Performed by/Date*
Sample Dilution or N/Ap ( )				
		Repeats #1: Or N/Ap ☐	Repeats #2: Or N/Ap ☐	
Samples: If required, dilute the samples. The dilution of samples should be documented using the appendix 4.	( )	( )	( )	
Reference blank: Prepare a reference blank control sample with the same dilution factor and elution buffer as the DNA samples as indicated in the procedure.	( )	( )	( )	
Sample Analysis or N/Ap ( )				
Referring to the Appendix 2, transfer 50 µL of the diluted samples to the appropriate well of the 96-well half-area microplate.	( )			
Open the DNA background calibration file located in the appropriate study folder corresponding to the 96-well plate lot and instrument. Record the plate blank values for both wavelengths.	Lm1: _____ Lm2: _____			
Open the DNA quantification protocol file located in the SoftMax Pro study folder corresponding to the 96-well plate lot and instrument. Record the plate blank values for both wavelengths.	Lm1: _____ Lm2: _____			
Verify the plate blank values from the background calibration for Lm1 and Lm2.	( )			
Select the appropriate wells as Blanks and Samples.	( )			
Analyze the plate.	( )			
Save the results in the Study Folder.	( )			

Comments: _____

_____

_____

_____

_____

Pages 1 and 2 Reviewed by/Date: _____

(b) (4)

Appendix 6

96-WELL PLATE SEQUENCE SHEET Page : __ of __

96-WELL PLATE LAYOUT* #1 Assay ID: _____ or N/Ap ( )

	1	2	3	4	5	6	7	8	9	10	11	12	
A	Blank												A
B	01	08	15	22	29								B
C	02	09	16	23	30								C
D	03	10	17	24									D
E	04	11	18	25									E
F	05	12	19	26									F
G	06	13	20	27									G
H	07	14	21	28									H
	1	2	3	4	5	6	7	8	9	10	11	12	

96-WELL PLATE LAYOUT* #2 Assay ID: _____ or N/Ap (√)

	1	2	3	4	5	6	7	8	9	10	11	12	
A													A
B													B
C													C
D													D
E													E
F													F
G													G
H													H
	1	2	3	4	5	6	7	8	9	10	11	12	

*Plate sequences to be updated as required.

Comments: _____

_____

_____

Reviewed by/Date: _____

(b) (4)

Appendix 6

96-Well Background Calibration – Assay Sheet

Study/Reference No: (b) (4) Assay I.D.: _____

REAGENTS / WORKING SOLUTIONS

Name	*Batch / Lot #*	*Inventory #*	*Entered by/Date*
Nuclease-free Water (NFW)			
96-well half-area UV transparent plate			

INSTRUMENTS

Name	*ID*	*Entered by/Date*
Spectramax Spectrophotometer	M2 ( ) / M5 ( ) or N/Ap ( )	
Pipettes		

PROCEDURE

Background Calibration of UV-transparent 96-well plates or N/Ap ( )		
Steps	*Performed (√)*	*Performed by/Date*
Add 50 µL (half-area plates) of NFW to each well of new 96-well half-area UV transparent microplate.	( )	
Open the background calibration protocol file 96NucleicAcid_background_XX.epr (where XX represents the version) located in \\labscience\immunology\SOFTMAX PRO DATA\MolecularBio and ensure the corrected wavelengths are selected.	Lm1: 260 nm ( ) Lm2: 280 nm ( )	
Analyze the plate containing NFW.	( )	
Record the plate blank values for both wavelengths.	Lm1: _____ Lm2: _____	
Save the results using an appropriate file name in the SoftMax Pro study folder.	( )	
Creation of DNA quantification protocol file in the SoftMax Pro study folder (to be performed by a scientist or delegate) or N/Ap ( )		
Steps	*Performed (√)*	*Performed by/Date*
Open the SoftMax Pro DNA quantification protocol file (template): 96NucleicAcid_DNA_XX.epr (where XX represents the version) Located in: \\labscience\immunology\SOFTMAX PRO DATA\MolecularBio	( )	
In >PLATE>SETTINGS>PATHCHECK, enter the plate blank values from the background calibration for Lm1 and Lm2	( )	
Save the DNA quantification protocol file in the SoftMax Pro study folder using the project number, "DNA", instrument ID, 96-well plate manufacturer, and lot number as the file name. Eg: (b) (4)DNA IV-194 Corning 123456789	( )	

Comments: _____

_____

Reviewed by/Date: _____

(b) (4)

Appendix 6

Spectrophotometry Dilution Sheet

Study/Reference No: (b) (4)

Assay I.D.: ____________

Page: ______ of ______

Reference Blank Spectrophotometry dilution or N/Ap ( )								
Sample ID	**Tube ID**	**Dilution Factor**	**Sample volume (μL)**	**Performed (√)**	**Diluent volume (μL)**	**Performed (√)**	**Repeat Required**	**Performed by /Date**
Reference Blank				( )		( )	N/Ap	

Sample Spectrophotometry dilution or N/Ap ( )								
Sample ID	**Tube ID**	**Dilution Factor**	**Sample volume (μL)**	**Performed (√)**	**Diluent volume (μL)**	**Performed (√)**	**Repeat Required (tick where applicable)**	**Performed by /Date**
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	
				( )		( )	Yes ( ) Code __ or No ( )	

Results and repeat codes Verified by/Date:	

Comments: *Appropriate elution buffer (same as the one used during the sample DNA isolation procedure)

Record buffer, pipettes, suppliers, lot numbers and expiry dates of reagents in Appendix 1.

Reviewed by/Date: ____________________

(b) (4)

Appendix 6

Appendix 4
QPCR Procedure

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4), (b) (6)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

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Appendix 6

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Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

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Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

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Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

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Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

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Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

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(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

(b) (4)

Appendix 6

qPCR ASSAY SHEET

Study/Reference No: (b) (4)

Assay I.D.: _____

Page: 1 of 5

Table 1: Reagents

Name	Batch / Lot #	Inventory #	Expiry date	Completed by / Date
Master Mix Solution		N/Ap		
SpC Master Mix Solution or N/Ap □		N/Ap		
Rabbit genomic DNA or N/Ap □				
1X TE or N/Ap □				
70% Ethanol				
10% Bleach				
Nuclease-free water				

Table 2: Quality Control Samples or N/Ap □

Name	Preparation Date	Prepared in Assay ID
STDS, QC's and NTC or N/Ap □		
SpC stock B or N/Ap □		

Table 3: Instruments

Name	ID	Completed by / Date
Laminar flow hood		
PCR workstation hood		
Centrifuge		
Microcentrifuge		
Pipettes		
Refrigerator		
QuantStudio™ 7 Flex Real-Time PCR System		

Comments: _____

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

qPCR ASSAY SHEET

Study/Reference No: (b) (4)

Assay I.D.: _____

Page: 2 of 5

Table 4: Assay Protocol

(b) (4)

Performed (√)				*Performed by / Date*
Assay ID: or N/Ap □ _____	**Assay ID: or N/Ap □** _____	**Assay ID: or N/Ap □** _____	**Assay ID: or N/Ap □** _____	
( )	( )	( )	( )	
( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	
( )	( )	( )	( )	
( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	
( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	
( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	
( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	
( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	
( )	( )	( )	( )	

Comments: _____

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

qPCR ASSAY SHEET

Study/Reference No: (b) (4)

Assay I.D.: _____

Page: 3 of 5

Table 5: Assay Protocol

(b) (4)

	Performed (√)				*Performed by / Date*
	Assay ID: _____ or N/Ap □	Assay ID: _____ or N/Ap □	Assay ID: _____ or N/Ap □	Assay ID: _____ or N/Ap □	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	( ) or N/Ap □	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( )	( )	( )	( )	
	( )	( )	( )	( )	

Comments: _____

(b) (4)

Appendix 6

qPCR ASSAY SHEET

Study/Reference No: (b) (4)

Assay I.D.: _____

Page: 4 of 5

Table 6: Assay Data Review

DATA REVIEW Review performed by Analyst, TL or Scientist Initial/Date :	Assay ID: _____ or N/Ap ☐	Assay ID: _____ or N/Ap ☐	Assay ID: _____ or N/Ap ☐	Assay ID: _____ or N/Ap ☐
No template control (NTC):				
Mean BCC value of NTC < value selected as LOD (5 copies/reaction), or no signal (e.g. Undetermined in SDS software or a value of 40 in SoftMax Pro)	/ 3	/ 3	/ 3	/ 3
Spiked Control Master Mix No Template Control or N/Ap ☐				
SpC NTC replicates %CV is ≤30%	Yes / No	Yes / No	Yes / No	Yes / No
Number of replicates used to calculate and %CV	/3	/3	/3	/3
Calibration Curve:				
$R^2 \geq 0.99$	Yes / No	Yes / No	Yes / No	Yes / No
Slope is between -3.1 to -3.6	Yes / No	Yes / No	Yes / No	Yes / No
Number of standards within ±30% of nominal and %CV is ≤30%	/8	/8	/8	/8
Run Quality Control Samples (Run QCs)				
Number of Run QC 1 that are within ±30% of nominal and %CV is ≤30%	/2	/2	/2	/2
Number of Run QC 2 that are within ±30% of nominal and %CV is ≤30%	/2	/2	/2	/2
Number of Run QC 3 that are within ±30% of nominal and %CV is ≤30%	/2	/2	/2	/2
Total number of Run QCs that are within ±30% of nominal and %CV is ≤30%	/ 6	/ 6	/ 6	/ 6
Assay is acceptable:	Yes / No	Yes / No	Yes / No	Yes / No

Comments: _____

(b) (4)

Appendix 6

qPCR ASSAY SHEET

Study/Reference No: (b) (4)

Assay I.D.: _____

Page: 5 of 5

Table 7: Assay Scientific Review

SCIENTIFIC REVIEW

Performed Initial/Date :

	Assay ID: _____	Assay ID: _____ or N/Ap □	Assay ID: _____ or N/Ap □	Assay ID: _____ or N/Ap □
QuanStudio 7 data analysis settings were correct:	Yes / No	Yes / No	Yes / No	Yes / No
If no then appropriate corrections made	Yes / N/Ap	Yes / N/Ap	Yes / N/Ap	Yes / N/Ap
SoftMax Pro template and formulas were correct:	Yes / No	Yes / No	Yes / No	Yes / No
If no then appropriate corrections made	Yes / N/Ap	Yes / N/Ap	Yes / N/Ap	Yes / N/Ap
Negative controls passed all acceptance criteria:	Yes / No	Yes / No	Yes / No	Yes / No
Standards passed all acceptance criteria:	Yes / No	Yes / No	Yes / No	Yes / No
Run QCs passed all acceptance criteria:	Yes / No	Yes / No	Yes / No	Yes / No
Samples passed all acceptance criteria:	Yes / No / N/Ap	Yes / No / N/Ap	Yes / No / N/Ap	Yes / No / N/Ap
Samples to be repeated are flagged	Yes / N/Ap	Yes / N/Ap	Yes / N/Ap	Yes / N/Ap
Assay is acceptable:	Yes / No	Yes / No	Yes / No	Yes / No
If no, out of acceptance criteria (OAC) form completed?	Yes / N/Ap	Yes / N/Ap	Yes / N/Ap	Yes / N/Ap

All pages reviewed by / Date: _____

Comments: _____

(b) (4)

Appendix 6

Standards and QCs Spiking Sheet

Study No: (b) (4)

Assay ID: _____

Name: Ad26 (b) (4) DP

Stock ID: Stock 2

Lot/Batch no: _____ or N/AP

Concentration*: 2.00E+06 copies/µL

Anchem no: From IM-

Aliquot/Container no: _____

Expiry date: _____

Preparation date: _____

Approved by/Date: _____

Remove AD26 (b) (4) DP plasmid DNA stock solution aliquot from storage in a freezer set to maintain -80°C and equilibrate to RT before use ( )

Table 1. Preparation of Rabbit Genomic DNA Working Solution in Nuclease-free Water Preparation Date: _____

Working Solution ID	Target Concentration (µg/µL)	Stock ID	Stock Concentration* (µg/µL)	Volume Total (µL)	Stock Volume (µL)	Stock Performed (Y)	Nuclease-Free Water Volume (µL)	Nuclease-Free Water Performed (Y)	Final Calc. Concentration (µg/µL)
Pooled Rabbit gDNA (0.14 µg/µL)	0.14	Pooled Rabbit gDNA Stock	1.111	1428	180	( )	1248	( )	0.14

Table 2. Preparation of AD26 (b) (4) DP Standard and QC Working Solutions in Rabbit Genomic DNA Working Solution

Working Solution ID	Target Concentration (copies/µL)	Stock ID	Stock Concentration (copies/µL)	Volume Total (µL)	Stock Volume (µL)	Stock Performed (Y)	Pooled Rabbit gDNA (0.14 µg/µL) Volume (µL)	Pooled Rabbit gDNA (0.14 µg/µL) Performed (Y)	Final Calc. Concentration (copies/rxn)**
NTC (Std 0)	0	N/Ap	N/Ap	80	N/Ap	N/Ap	80	( )	0
STD 1 (ULOQ)	200 000.0	Ad26 (b) (4) DP Stock 2*	2 000 000.0	100	10	( )	90	( )	1 000 000.0
STD 2	20 000.0	STD 1 (ULOQ)	200 000.0	100	10	( )	90	( )	100 000.0
STD 3	2 000.0	STD 2	20 000.0	100	10	( )	90	( )	10 000.0
STD 4	200.0	STD 3	2 000.0	100	10	( )	90	( )	1 000.0
STD 5	50.0	STD 4	200.0	200	50	( )	150	( )	250.0
STD 6	25.0	STD 5	50.0	100	50	( )	50	( )	125.0
STD 7	7.0	STD 6	25.0	182	51	( )	131	( )	35.0
STD 8 LLOQ	4.0	STD 7	7.0	140	80	( )	60	( )	20.0
STD 9 (Acc STD)	2.0	STD 8 LLOQ	4.0	40	20	( )	20	( )	10.0
Stock 4	200 000.0	Ad26 (b) (4) DP Stock 2*	2 000 000.0	100	10	( )	90	( )	1 000 000.0
QC 1	50 000.0	Stock 4	200 000.0	200	50	( )	150	( )	250 000.0
Stock 5	10 000.0	QC 1	50 000.0	100	20	( )	80	( )	50 000.0
QC 2	1 000.0	Stock 5	10 000.0	200	20	( )	180	( )	5 000.0
Stock 6	200.0	QC 2	1 000.0	100	20	( )	80	( )	1 000.0
Stock 7	100.0	Stock 6	200.0	100	50	( )	50	( )	500.0
Stock 8	40.0	Stock 7	100.0	200	80	( )	120	( )	200.0
QC 3	12.0	Stock 8	40.0	200	60	( )	140	( )	60.0

Comments: Pipet ID should be recorded on Appendix #1A (Assay Sheet).

**Final Cal Concentration (copies/rxn) = Target Concentration (copies/µL) X Sample volume (5 µL) loaded in each PCR well (Formula not applicable if sample is not loaded)

Nuclease-free water lot no. / expiry date should be recorded on Appendix #1A (Assay Sheet).

Rabbit gDNA Stock lot no. / expiry date should be recorded on Appendix #1A (Assay Sheet).

Aliquots of 60 µL of STD1 to STD9 prepared ( ) or N/AP ( )

Aliquots of 100 µL of NTC and QC1 to QC3 prepared ( ) or N/AP ( )

*Stock concentration may change according to lot number or stock ID being used

Calculations verified by: _____ Date: _____

Prepared by: _____ Date: _____

Reviewed by: _____ Date: _____

(b) (4)

Page 1 of 1

Appendix 6

AD26 (b) (4) DP Dilution Sheet

Study No: (b) (4)

Assay ID: _____

Name: Ad26 (b) (4) DP

Lot/Batch no: _____

Concentration*: 1.9E+08 copies/µL

Anchem no: From IM-

Aliquot/Container no: _____

Expiry date: _____

Stock ID: _____ or N/Ap

Lot/Batch no: _____

Concentration*: _____ copies/µL

Anchem no: _____

Aliquot/Container no: _____

Expiry date: _____

Preparation date: _____

Approved by/Date: _____

Remove AD26 (b) (4) DP plasmid DNA stock solution aliquot from storage in a freezer set to maintain -80°C and equilibrate to RT before use ( )

Table 1. Preparation of AD26 (b) (4) DP Intermediate Stock Solutions in 1X TE ☐ N/Ap

Working Solution ID	Target Concentration (copies/µL)	Stock ID	Stock Concentration (copies/µL)	Volume Total (µL)	Stock Volume (µL)	Stock Performed (√)	1X TE Volume (µL)	1X TE Performed (√)	Final Calc. Concentration (copies/µL)
Ad26 (b) (4) DP Stock 1	2.00E+07	Ad26 (b) (4) DP	1.9E+08	95	10	( )	85	( )	2.0E+07

Table 2. Preparation of AD26 (b) (4) DP Intermediate Stock Solutions in Nuclease-free Water ☐ N/Ap

Working Solution ID	Target Concentration (copies/µL)	Stock ID	Stock Concentration (copies/µL)	Volume Total (µL)	Stock Volume (µL)	Stock Performed (√)	Nuclease-Free Water Volume (µL)	Nuclease-Free Water Performed (√)	Final Calc. Concentration (copies/µL)**
Ad26 (b) (4) DP Stock 2	2.00E+06	Ad26 (b) (4) DP Stock 1	2.0E+07	500	50	( )	450	( )	2.0E+06

Table 3. Preparation of AD26 (b) (4) DP stock in Nuclease-free Water for Spiked Master Mix Preparation ☐ N/Ap

Working Solution ID	Target Concentration (copies/µL)	Stock ID	Stock Concentration (copies/µL)	Volume Total (µL)	Stock Volume (µL)	Stock Performed (√)	Nuclease-Free Water Volume (µL)	Nuclease-Free Water Performed (√)	Final Calc. Concentration (copies/rxn)**
SpC Stock 1	2.5E+05	Ad26 (b) (4) DP Stock 2*	2.0E+06	80	10	( )	70	( )	2.5E+05
SpC Stock 2	2.5E+04	SpC Stock 1	2.5E+05	200	20	( )	180	( )	2.5E+04
SpC Stock 3	2.5E+03	SpC Stock 2	2.5E+04	200	20	( )	180	( )	2.5E+03
SpC Stock 4	2.0E+02	SpC Stock 3	2.5E+03	1500	120	( )	1380	( )	2.0E+02
SpC Stock A	1.0E+02	SpC Stock 4	2.0E+02	2400	1200	( )	1200	( )	1.0E+02
SpC Stock B	3.0E+01	SpC Stock A	1.0E+02	4000	1200	( )	2800	( )	6.0E+01

Comments: Pipet ID should be recorded on Appendix #1A (Assay Sheet).

1X TE lot no. / expiry date should be recorded on Appendix #1A (Assay Sheet).

Nuclease-free water lot no. / expiry date should be recorded on Appendix #1A (Assay Sheet).

**Final Cal Concentration (copies/rxn) = Target Concentration (copies/µL) X Stock volume (2µL/reaction) used to spike the Master Mix

Aliquots of 400 µL of Stock B prepared ( ) or N/AP ( )

*Stock concentration may change according to lot number or stock ID being used

Calculations verified by: _____ Date: _____

Prepared by: _____ Date: _____

Reviewed by: _____ Date: _____

(b) (4)

Page 1 of 1

Appendix 6

Sample Preparation Sheet

Study No: (b) (4)

Assay ID: _____

Approved by/Date: _____

Table 1. **Preparation of Rabbit Total DNA Samples (UnSpC)**

Working Solution ID	Target Concentration (µg/µL)	Stock ID			Stock Concentration (µg/µL)	Volume Total (µL)	Stock		Nuclease-Free Water		Final Calc. Concentration (µg/µL)
							Volume (µL)	Performed (√)	Volume (µL)	Performed (√)	
S01	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S02	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S03	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S04	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S05	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S06	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S07	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S08	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S09	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S10	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S11	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S12	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S13	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S14	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S15	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S16	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S17	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S18	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S19	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S20	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S21	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S22	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S23	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S24	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S25	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S26	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S27	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S28	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S29	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14
S30	0.14	1001	Brain	D11	0.6580	47.0	10	( )	37.0	( )	0.14

Comments: Pipet ID should be recorded on Appendix #1 (Assay Sheet).

Nuclease-free water lot no. / expiry date should be recorded on Appendix #1 (Assay Sheet).

Use fresh on the day of preparation and discard after use

Calculations verified by: _____ Date: _____

Prepared by: _____ Date: _____

Reviewed by: _____ Date: _____

(b) (4)

Appendix 6

100 µM PRIMER STOCK PREPARATION ASSAY SHEET

Study/Reference No: (b) (4)

Page: 1 of 2

Table 1: Reagents

Reagent name	Batch / Lot #	Inventory #	Expiry Date	Completed by / Date
TE buffer				

Table 2: Instruments

Name	ID	Completed by / Date
Microcentrifuge		
Pipettes		

Table 3: Volume of TE Buffer Used to Dissolve Lyophilized Primers

Oligo Name	Mfg. ID	Ref. No.	Inventory no.	TE Buffer Volume for 100 µM Solution (µL)*	Tick when performed (√)	Performed by/Date
CMV-FP					( )	
CMV-RP					( )	

Mfg. ID, Ref. No.and TE Buffer Volume Verified by/date: _____

*Primers reconstitution volume can be calculated using the resuspension calculator from https://www.idtdna.com/Calc/resuspension/ (10uL TE Buffer should be used per nmol of lypholized primer to obtain 100 uM final concentration)

Comments: _____

(b) (4)

Appendix 6

100 µM PRIMER STOCK PREPARATION ASSAY SHEET

Study/Reference No: (b) (4)

Page: 2 of 2

Table 4: Preparation of 100 µM Primer Stock

Steps	Performed (√)	Performed by / Date
1. Quick spin the tubes/vials (centrifuge set at 10 000 x g for 10 seconds).	( )	
2. Add the appropriate volume of TE Buffer to the lyophilized primers to achieve 100 µM solutions. Refer to volumes in **Table 3**.	( )	
3. Change pipette tips before adding TE Buffer to each lyophilized primer.	( )	
4. Mix tubes by gentle vortexing for approximately 3 to 5 seconds and quick spin the tubes/vials.	( )	
5. Incubate the tubes/vials at ambient room temperature for approximately 30 minutes.	Start:	
	End:	
6. Mix tubes/vials by gentle vortexing for approximately 3 to 5 seconds and quick spin the tubes/vials.	( )	
7. Aliquot dissolved primers into 20 µL (or other appropriate volume) and store in a freezer set to maintain -20°C for up to 6 months.	( )	

Table 5: 100 µM Primer Solution

Primer Name	Batch No. (Place label in area)	Expiry Date	Aliquots ID (Place an example of label in area)
100 µM CMV-FP			No. of aliquots: ____
100 µM CMV-RP			No. of aliquots: ____

Comments: _____

_____

_____

All pages reviewed by / Date: _____

(b) (4)

Appendix 6

Solution ID: ______________________ From Container ID: ______________

Batch ID: ______________________ From Anchem no. ______________

Total number of aliquots prepared : __________

Aliquot IDs: ________ to __________

Volume per aliquot: __________

Leftover (if applicable) : __________

Aliquoting performed by/Date: ______________

Pipettes, Repeaters ID : ____________________

Aliquoted under Study number: ______________

AP or SOP used : ________________

Storage ID: __________________

Place aliquot label here

Study / Reference Number	Aliquots ID	Aliquots Verified by/Date	Pooled in (if applicable)	Volume used	Volume remaining	Empty Aliquots Discarded (if applicable) (√)	Performed by/Date	Entries verified by/Date*
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					
			Approx total volume pooled __________ in aliquot ID__________					

*Entries to be verified by a Team Leader (TL) or a Scientist once the assay is performed.

Comments: ____

Reviewed by/Date: ______________

Page ______ of ______

Appendix 6

Appendix 5

Certificate of Analysis Ad26 (b) (4) DP DRM (b) (4)

(b) (4)

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

Technical Document - Technical Document Statement	
Owner Group: Leiden Vaccines (JVL)	**Effective Date:** 27-Feb-2018 08:29:17 EST
Document Title: Certificate of analysis Ad26 (b) (4) DP DRM (b) (4) (b) (4)	

(b) (4)

Printed On	02-May-2018 16:18:23 EDT(-0400)	**Confidential**	PAGE : 1 of 4

Appendix 6

Technical Document - Technical Document Statement	
Owner Group: Leiden Vaccines (JVL)	**Effective Date:** 27-Feb-2018 08:29:17 EST
Document Title: Certificate of analysis Ad26 (b) (4) DP DRM (b) (4) (b) (4) (b) (4)	

Statement

This material has been tested according to current GMP requirements.
All data conform specifications.
This certificate has been approved by Scientist Reference Materials and Head of QC. For electronic signature see end of this document.

*****END OF DOCUMENT*****

Appendix 6

Technical Document - Technical Document Statement	
Owner Group: Leiden Vaccines (JVL)	**Effective Date:** 27-Feb-2018 08:29:17 EST
Document Title: Certificate of analysis Ad26 (b) (4) DP DRM (b) (4) (b) (4)	

(b) (4)

Document Revision History

Version Number	Section	Description of Change	Justification of Change
2.0	All	Revised to report 12 months re-qualification	12 months re-qualification results available

Appendix 6

Technical Document - Technical Document Statement	
Owner Group: Leiden Vaccines (JVL)	**Effective Date:** 27-Feb-2018 08:29:17 EST
Document Title: Certificate of analysis Ad26 (b) (4) DP DRM (b) (4)	
Document Number: (b) (4)	**Version:** 2.0

APPROVAL PAGE

Approver Name	Justification	Date
(b) (6)	Department Approval	27-Feb-2018 08:18 38 EST
	Author Approval	27-Feb-2018 08:29:07 EST

Printed On 02-May-2018 16:18:23 EDT(-0400)	Confidential	PAGE : 4 of 4

Appendix 6

Technical Document - Technical Document Memo	
Owner Group: Leiden Vaccines (JVL)	**Effective Date:** 24-Jul-2018 05:24:15 EDT
Document Title: Memo on relation between VP concentration and viral DNA copy number	
Document Number: (b) (4)	**Version:** 1 0

Memo

1. Purpose

The purpose of the memo is to explain the relation between virus particle concentration and viral DNA copy number concentration in adenovector-based drug products.

2. Scope of memo

In scope of this memo is the relation between virus particle concentration and viral DNA copy number concentration in all adenovector-based drug products.

3. Statement

Virus particle concentration as stated on the Certificate of Analysis (CoA) of any adenovector-based drug product can be directly translated to viral DNA copy number concentration. The concentration reported in VP/ml is equal to viral DNA copy number/ml.

4. Statement assessment information

Virus particle concentration of adenovector-based drug substance (DS) and drug product (DP) is determined by VP qPCR methods (b) (4) (b) (4) The VP-qPCR method is used to determine the amount of virus particles, or vector concentration in the test article. This method is a real-time qPCR-based method that uses probes specifically designed to amplify (b) (4) (b) (4) in the genome of the virus particles. The DNA amplification in each test article, standard, or control is directly related to a VP concentration by way of a cal bration curve generated from a reference material. The reference material is derived from a purified Ad26 virus. The virus particle content by VP-qPCR has been linked to that by OD260 measurement. One viral DNA copy is present in one VP, therefore concentration reported in VP/ml is equal to viral DNA copy number/ml.

END OF DOCUMENT

Printed On 24-Jul-2018 05:47:59 EDT	Confidential	PAGE : 1 of 3

Appendix 6

Technical Document - Technical Document Memo	
Owner Group: Leiden Vaccines (JVL)	**Effective Date:** 24-Jul-2018 05:24:15 EDT
Document Title: Memo on relation between VP concentration and viral DNA copy number	
Document Number: (b) (4)	**Version:** 1 0

Document Revision History			
Version Number	**Section**	**Description of Change**	**Justification of Change**
1.0	N/A	New document	New document

Printed On	24-Jul-2018 05:47:59 EDT	**Confidential**	PAGE : 2 of 3

Appendix 6

Technical Document - Technical Document Memo	
Owner Group: Leiden Vaccines (JVL)	**Effective Date:** 24-Jul-2018 05:24:15 EDT
Document Title: Memo on relation between VP concentration and viral DNA copy number	
Document Number: (b) (4)	**Version:**

APPROVAL PAGE

Approver Name	Justification	Date
(b) (6)	Department Approval	24-Jul-2018 04:20:35 EDT
	Author Approval	24-Jul-2018 05:24:05 EDT

Printed On 24-Jul-2018 05:47:59 EDT	**Confidential**	PAGE : 3 of 3

Appendix 6

(b) (4)

Note de Service 02
Memorandum 02

DATE:	(b) (4), (b) (6)
FROM / DE:	
SUBJECT / SUJET:	Preparation of certificate of analysis for the pooled genomic DNA extracted from New Zealand White Rabbits Thymus and Mesenteric Lymph Nodes used as gDNA background in qPCR assays

PRODUCT NAME:	Pool of New Zealand White Rabbit Genomic DNA
DESCRIPTION:	Genomic DNA was extracted from harvested New Zealand White Rabbit Thymus and Mesenteric Lymph nodes using Maxwell 16 LEV method. This DNA is suitable for qPCR assays under validation study (b) (4) and linked sample analysis study (b) (4)
MEAN CONCENTRATION:	1154.6 µg/mL in Elution Buffer
CONCENTRATION % CV:	1.0
SPONSOR:	Janssen Research & Development
STUDY NUMBER:	(b) (4)
BATCH NUMBER:	
ALIQUOT VOLUME:	1 mL
NUMBER OF ALIQUOT:	9
STORAGE CONDITIONS:	Kept in a freezer set to maintain -20°C
SHELF LIFE:	One year from the date of preparation under proper storage condition, the stability will be monitored and deemed acceptable based on the assay's performance.
EXPERIMENTAL START DATE:	29 Aug 2018
EXPERIMENTAL COMPLETION DATE:	06 Sep 2018
DATE OF ISSUE:	07 Sep 2018

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 6

Test	Method	Acceptance Criteria	Result
DNA Isolation	(b) (4) HOM.01 (using Genogrinder) and (b) (4) DNA.01 (using Maxwell 16)	a) Report Result	a) Not Applicable
DNA Quantification	(b) (4) (Using a Ultrospec 3100)	b) Absorbance at A_{260} should be between 0.15 and 1.0	b) Absorbance at A_{260}: Sample 1: 0.583 Sample 2: 0.578 Sample 3: 0.571 Conform
		c) Absorbance at A_{280}: N/Ap	c) Absorbance at A_{280}: Sample 1: 0.331 Sample 2: 0.330 Sample 3: 0.325
		d) A_{260}/A_{280} ratio $\geq$ 1.7	d) A_{260}/A_{280} ratio: Sample 1: 1.760 Sample 2: 1.755 Sample 3: 1.755 Mean: 1.757 Conform
		e) The target minimum required DNA concentration is 140 µg/mL	e) Concentration (µg/mL): Sample 1: 1166 µg/mL Sample 2: 1156 µg/mL Sample 3: 1142 µg/mL Mean Concentration: 1154.7 Conform

This Product is for in vitro laboratory use only and not intended for human or animal diagnostic or therapeutic uses.

Prepared by/Date: (b) (6)

Approved by/Date: (b) (6)

Appendix 6

Appendix 6
Method Validation Summary

Appendix 6

METHOD VALIDATION SUMMARY
Version #5

Study/Reference Number: (b) (4)
Sponsor Name: Janssen
Analyte: Ad.26 (b) (4) DP RM
Assay Type: Quantitative Polymerase Chain Reaction (qPCR)
Matrix: New Zealand White Rabbit Tissue and Fluid
Instrument: QuantStudio™ 7 Flex Real-time PCR System; 384-well block
Regression Type: Semi-logarithmic

Parameter: DNA Extraction

Acceptance Criteria:

No acceptance criteria, results for samples from at least 10 animals (5 animals/gonads) used as a qualitative assessment of the extraction procedure for each sample type and reported for informational purposes only.

Results

Matrix	Concentration Range (µg/µL)	A260/A280 Ratio	Conclusion	Reference (Assay ID)
Blood	0.0619 – 0.0989	1.3 – 1.8	Acceptable	Val-10
Bone marrow (femur)	0.0866 – 2.4619	1.7 – 2.0	Acceptable	Val-10
Brain (forebrain)	0.3246 – 0.6592	2.1 – 2.2	Acceptable	Val-02
Brain (visual cortex)	0.2476 – 0.6563	2.0 – 2.2	Acceptable	Val-10
Heart	0.3540 – 0.8068	1.7 – 2.2	Acceptable	Val-02
Iliac lymph nodes	0.0150 – 1.8656	1.2 – 2.1	Acceptable	Val-02
Inguinal lymph nodes	0.0093 – 3.1084	1.2 – 2.1	Acceptable	Val-03 and Val-07
Mesenteric lymph nodes	0.2581 – 2.3572	1.9 – 2.0	Acceptable	Val-03
Kidney	2.5900 – 4.2852	2.0 – 2.2	Acceptable	Val-03
Liver	0.1066 – 2.3805	1.5 – 2.2	Acceptable	Val-04
Lung	0.2528 – 2.1431	1.7 – 2.2	Acceptable	Val-04
Muscle (Biceps femoris)	0.3277 – 0.4810	1.6 – 2.1	Acceptable	Val-04
Ovary	1.8423 – 3.6472	1.9 – 2.1	Acceptable	Val-05
Popliteal lymph nodes	1.1447 – 2.5032	1.9 – 2.1	Acceptable	Val-05
Skin with subcutis	0.3465 – 1.5146	2.0 – 2.1	Acceptable	Val-05
Spleen	1.1690 – 1.3683	2.1 – 2.2	Acceptable	Val-07
Testis	1.0742 – 3.4542	2.1 – 2.2	Acceptable	Val-07
Thymus	0.1287 – 3.4249	1.2 – 2.0	Acceptable	Val-07

Appendix 6

METHOD VALIDATION SUMMARY
Version #5

Parameter: qPCR Range of Response			
Acceptance Criteria: The back-calculated concentrations of the standards should be within ± 30% of their nominal concentrations. The precision should be ≤ 30% at each concentration level. The slope of the calibration curve should be between -3.1 and -3.6. The coefficient of determination (R^2) should be ≥ 0.99.			
Range of assessment	**Results**	**Conclusion**	**Reference (Assay ID)**
STD 1: 1000000 copies/reaction (ULOQ)	**Pass**	**Accepted**	Val-06
STD 2: 100000 copies/reaction	23/23 (100.0%) occasions meeting acceptance criteria		Val-08
STD 3: 10000 copies/reaction			Val-09
STD 4: 1000 copies/reaction			Val-12
STD 5: 250 copies/reaction			Val-13
STD 6: 125 copies/reaction			Val-15
STD 7: 35 copies/reaction (LLOQ)			Val-17
STD 8: 20 copies/reaction (LLOQ)			Val-18
STD 9: 10 copies/reaction (accessory)			Val-19
			Val-21
			Val-23
			Val-25
			Val-26
			Val-28
			Val-30
			Val-31
			Val-32
			Val-33
			Val-34
			Val-35
			Val-36
			Val-37
			Val-38

Appendix 6

METHOD VALIDATION SUMMARY
Version #5

Parameter: qPCR Intra- and Inter-assay precision and accuracy			
Acceptance Criteria: Mean back-calculated concentration within ±30% of theoretical concentration and %CV ≤30% at each concentration level. At least two out of three (or 67%) replicates for each QC acceptable for each occasion. At least 6 separate occasions and at least 67% of all occasions should meet acceptance criteria			
Results			
Level	**Results**	**Conclusion**	**Reference (Assay ID)**
ULOQ 1000000 copies/reaction	**Pass** 6/6 (100.0%) occassions meeting intra-assay acceptance criteria Global %CV: 4.3 Global %Nominal: 98.7	LLOQ-2 (20 copies/reaction) is selected as the LLOQ of the method since it met all acceptance criteria. The corresponding selected QC3 level is QC3-2 (60 copies/reaction).	Val-06 Val-08 Val-09 Val-12 Val-13 Val-18 Val-37
QC1 250000 copies/reaction	**Pass** 6/6 (100.0%) occassions meeting intra-assay acceptance criteria Global %CV: 4.8 Global %Nominal: 99.8		
QC2 5000 copies/reaction	**Pass** 6/6 (100.0%) occassions meeting intra-assay acceptance criteria Global %CV: 4.4 Global %Nominal: 102.7		
QC3-1 200 copies/reaction	**Pass** 6/6 (100.0%) occassions meeting intra-assay acceptance criteria Global %CV: 5.7 Global %Nominal: 105.0		
QC3-2 60 copies/reaction	**Pass** 6/6 (100.0%) occassions meeting intra-assay acceptance criteria Global %CV: 5.9 Global %Nominal: 108.0		
LLOQ1 35 copies/reaction	**Pass** 6/6 (100.0%) occassions meeting intra-assay acceptance criteria Global %CV: 5.5 Global %Nominal: 104.3		
LLOQ2 20 copies/reaction	**Pass** 6/7 (85.7%) occassions meeting intra-assay acceptance criteria Global %CV: 8.2 Global %Nominal: 104.0		

Appendix 6

METHOD VALIDATION SUMMARY
Version #5

Parameter: qPCR Specificity and Selectivity
Acceptance Criteria: **Specificity:** 100% of the unspiked lots analyzed neat or diluted to the target DNA concentration of 140 µg/mL for each matrix should be below the limit of detection (LOD). **Selectivity:** The majority (at least 80%) of the New Zealand White Rabbit DNA samples analyzed neat or diluted to the target DNA concentration of 140 µg/mL for each matrix and spiked with Ad.26 (b) (4) DP RM at the QC 3 level (60 copies/reaction) have mean back-calculated concentrations ≥ 50% of their nominal concentration (also referred to the PCR efficiency) and a CV ≤ 30% at each concentration level.

Results

Matrix	Results	Conclusion	Reference (Assay ID)
Blood	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-15 Val-21
Bone marrow (femur)	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-15 Val-21
Brain (forebrain)	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-12 Val-23
Brain (Visual cortex)	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 9/10 (90%) lots met acceptance criteria	**Accepted**	Val-15 Val-21
Heart	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 9/10 (90%) lots met acceptance criteria	**Accepted**	Val-12 Val-23
Iliac lymph node	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 9/10 (90%) lots met acceptance criteria	**Accepted**	Val-17 Val-21
Inguinal lymph node	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-17 Val-21
Mesenteric lymph node	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-13 Val-23
Kidney	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-13 Val-23
Liver	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-17 Val-21
Lung	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-12 Val-23
Muscle (Biceps femoris)	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-13 Val-23

Appendix 6

METHOD VALIDATION SUMMARY
Version #5

Parameter: qPCR Specificity and Selectivity (continued)			
Acceptance Criteria: **Specificity:** 100% of the unspiked lots analyzed neat or diluted to the target DNA concentration of 140 µg/mL for each matrix should be below the limit of detection (LOD). **Selectivity:** The majority (at least 80%) of the New Zealand White Rabbit DNA samples analyzed neat or diluted to the target DNA concentration of 140 µg/mL for each matrix and spiked with Ad.26 (b) (4) DP RM at the QC 3 level (60 copies/reaction) have mean back-calculated concentrations ≥ 50% of their nominal concentration (also referred to the PCR efficiency) and a CV ≤ 30% at each concentration level.			
Results			
Matrix	**Results**	**Conclusion**	**Reference (Assay ID)**
Ovary	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-15 Val-21
Popliteal lymph node	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-18 Val-23
Skin	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 9/10 (90%) lots met acceptance criteria	**Accepted**	Val-18 Val-23
Spleen	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-15 Val-21
Testis	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-15 Val-21
Thymus	**Pass** **Specificity:** 10/10 (100%) lots met acceptance criteria **Selectivity:** 10/10 (100%) lots met acceptance criteria	**Accepted**	Val-15 Val-23

Parameter: qPCR Limit of detection			
Acceptance Criteria: Lowest detectable concentration producing a positive signal in > 95% of replicates tested.			
Results			
Level	**Results**	**Conclusion**	**Reference (Assay ID)**
LOD-1 5 copies/reaction	**Pass** n = 9 positive = 9 % n positive = 100.0%	**Validated LOD**	Val-06 Val-08 Val-09
LOD-2 2 copies/reaction	**Fail** n = 9 positive = 5 % n positive = 55.6%	**Rejected**	
LOD-3 1 copies/reaction	**Fail** n = 9 positive = 2 % n positive = 22.2%	**Rejected**	

Appendix 6

METHOD VALIDATION SUMMARY
Version #5

Parameter: Linearity of dilutions			
Acceptance Criteria: The linearity of dilution will be considered acceptable if the mean back-calculated concentration of each diluted sample fall within ± 30% of the nominal concentration and the %CV is ≤ 30% at each concentration level.			
Results			
Matrix	**Results**	**Conclusion**	**Reference (Assay ID)**
Muscle	**Pass** Mean BCC: Within ± 30% of the nominal concentration CV: ≤ 30% at each dilution fold	**Validated dilution range:** **1:2000 to 1: 20000000**	Val-19
Skin	**Pass** Mean BCC: Within ± 30% of the nominal concentration CV: ≤ 30% at each dilution fold	**Validated dilution range:** **1:2000 to 1: 20000000**	
Illiac Lymph Node	**Pass** Mean BCC: Within ± 30% of the nominal concentration CV: ≤ 30% at each dilution fold	**Validated dilution range:** **1:2000 to 1: 20000000**	
Mesenteric Lymph Node	**Pass** Mean BCC: Within ± 30% of the nominal concentration CV: ≤ 30% at each dilution fold	**Validated dilution range:** **1:2000 to 1: 20000000**	
Inguinal Lymph Node	**Pass** Mean BCC: Within ± 30% of the nominal concentration CV: ≤ 30% at each dilution fold	**Validated dilution range:** **1:2000 to 1: 20000000**	
Popliteal Lymph Node	**Pass** Mean BCC: Within ± 30% of the nominal concentration CV: ≤ 30% at each dilution fold	**Validated dilution range:** **1:2000 to 1: 20000000**	

Appendix 6

METHOD VALIDATION SUMMARY
Version #5

Parameter: DNA Stability at the QC 1 and QC3 levels

Acceptance Criteria:

Reference samples: The replicate CV should be ≤ 30% for each aliquot and at least two out of three (or 67%) aliquot at each concentration level should be considered acceptable. In addition, the overall CV of the sample replicates for the reference aliquots should be ≤ 30% at each level.

Stability samples: Stability will be considered acceptable if the % difference between the experimental quantities for each aliquot is within ± 30% of the overall mean quantity of the reference samples. In addition, the replicate CV should be ≤ 30% for each aliquot and at least two out of three (or 67%) aliquot should be considered acceptable at each level.

Passed for at least 67% of the stability samples for the following conditions :

QC1= 250 000 copies/reaction/ QC3= 60 copies/reaction

Matrix	Level	Freeze/Thaw	Bench Top Time: hh:mm	Long Term (Days)
Blood	QC1	4	23:08	30
	QC3	4	22:58	
Bone marrow (femur)	QC1	4	23:08	
	QC3	4	22:58	
Brain (forebrain)	QC1	4	23:08	
	QC3	4	22:58	
Brain (visual cortex)	QC1	4	23:08	
	QC3	4	22:58	
Heart	QC1	4	23:08	
	QC3	4	22:58	
Iliac lymph nodes	QC1	4	23:08	155
	QC3	3*	12:22*	
Inguinal lymph nodes	QC1	4	23:08	30
	QC3	3**	12:22**	
Mesenteric lymph nodes	QC1	4	23:08	
	QC3	4	22:58	
Kidney	QC1	4	23:08	
	QC3	4	22:58	
Liver	QC1	4	23:08	
	QC3	4	22:58	
Lung	QC1	4	23:08	
	QC3	4	22:58	
Muscle (Biceps femoris)	QC1	4	23:08	
	QC3	3	12:22	
Ovary	QC1	4	23:08	
	QC3	4	22:58	
Popliteal lymph nodes	QC1	4	23:08	
	QC3	3	12:22	
Skin with subcutis	QC1	4	23:08	
	QC3	4	22:58	
Spleen	QC1	4	23:08	
	QC3	4	22:58	
Testis	QC1	4	23:08	
	QC3	4	22:58	
Thymus	QC1	4	23:08	
	QC3	4	22:58	

* Accepted in deviation. Refer to the conclusion section

** Assessment failed to meet acceptance criteria. Please refer to the Conclusion section.

Appendix 6

METHOD VALIDATION SUMMARY
Version #5

Remaining Parameters to be Performed and/or Limitations
• Some blood, bone marrow, iliac and inguinal lymph nodes, liver and thymus samples yielded results below the target DNA concentration of 140 µg/mL or below the target ratio of 1.7. For the blood and the bone marrow, this is considered acceptable due to the nature of the samples. However for the other tissues, if the DNA yield is below the target concentration in the linked biodistribution study, DNA isolation will be repeated (if samples are available) using either the back-up tissue sample or the leftover tissue homogenate. However the amount of tissue DNA loaded in the Maxwell can be adjusted in order to obtain a higher DNA yield. In the eventuality where study samples have a DNA concentration ≤ 140 µg/mL, they will be processed neat in the appropriate number of PCR wells to achieve a total quantity of at least 2 µg of DNA analyzed, where possible, and flagged as such in the results table in the linked sample analysis study. Where possible, DNA isolation will be repeated for study tissue samples with a ratio < 1.7. However if the ratio is still < 1.7 after the repeated DNA isolation assay, sample will be analyzed in the linked sample analysis study but flagged as such in the results table.

Conclusion
• DNA was isolated from at least 10 animals (exept for testis and ovary for which 5 animals each were used) using tissue homogenization and DNA isolation procedures that provided acceptable results. Study samples collected under Study No. (b) (4) can be processed for DNA isolation using these procedures. All qPCR parameters met acceptance criteria. The overall assay failure rate was 0.0% (not taking into account the DNA isolation assays). Therefore, (b) (4) DNA samples can be analyzed by qPCR as per validated paramters.
• Stability assessments met all the acceptance criteria. However, it should be noted that for the Iliac lymph node at the QC3 level only (60 copies/reaction), the combined freeze/thaw and bench-top stability was accepted in deviation due a the %CV between replicates not meeting the acceptance criteria for 4 out of 7 aliquots (or 57 %). Therefore, individual qPCR wells for each aliquot with %CV > 30% were compared to the overall mean quantity of the reference aliquot. 2 out of 3 replicates for each aliquots were found to be within ±30% of the overall mean quantity of the reference aliquot indicating that the sample was stable following stability assessment. Therefore the iliac lymph node was considered stable up to 3 free/thaw cycles and for 12 h 22 minutes when left on the bench at room temperature.
• The combined freeze/thaw and bench-top stability did not meet the acceptance criteria for the inguinal lymph node at the QC3 level only (60 copies/reaction) due to a %CV between replicates and/or a % difference out of the acceptance criteria for 4 out of 7 aliquots (or 57 %). The combined freeze-thaw and bench top stability was not repeated given that this matrix was not collected in the linked sample analysis study (b) (4) Therefore the stability assessment was not required.

Appendix 6

METHOD VALIDATION SUMMARY
Version #5

Reasons for update:

Version	Date	Reason for Revision
05	Signature of MVS	• QC3 added in the DNA stability heading to reflect the stability assessments performed.
04	04-Feb-2019	• Additional Range of Response Assays covering the whole validation were included on page 2 of 9. • Additional Long Term Stability assement was included for the Iliac lymph node on page 7 of 9.
03	23-Jan-2019	• Additional range of response assessment Assay ID included • Additional Precision and Accuracy assessment occasion added in order to have at least six separate occasions meeting acceptance criteria to define the Assay LLOQ. • Linearity of dilutions section updated to indicate that dilution folds 2000 to 20 000 000 were validated instead of 20 to 20 000 000 given that the mean back-calculated results for dilutions folds 20 and 200 were not within the curve range of response. • Stability section updated to indicate that the inguinal lymph node spiked at the QC3 level for the combined freeze/thaw and bench-top stability failed to meet acceptance criteria and the reason of this matrix not being repeated was indicated in the conclusion section.
02	26-Oct-2018	• To include the Stability summary. • Remaining Parameters to be Performed and/or Limitations section updated to add clarifications for the DNA isolation for tissues.
01	30-Aug-2018	New MVS

Prepared by: (b) (6) Date: 15 Feb 2019

Approved by: Date: 15 Feb 2019

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

(b) (4)

FINAL REPORT

Study Phase: Pathology

Test Facility Study No. (b) (4)

Sponsor Reference No. (b) (4)

TEST FACILITY:
(b) (4)

Appendix 7

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1. INTRODUCTION

This report presents the pathology findings in rabbits assigned to Study No. (b) (4). The objective of this study was to evalutate the biodistribution properties and persistence of a single dose of Ad26 (b) (4) a replication incompetent non-pathogenic Adenovirus Serotype 26 vector expressing the (b) (4) when given by single intramuscular injection (with or without co-administration with the (b) (4)) to rabbits followed by an observation period of up to 180 days.

2. MATERIALS AND METHODS

Experimental procedures applicable to pathology investigations are summarized in Text Table 1.

Text Table 1
Experimental Design

Group No.	Test Material	Dose Level	Dose Volume (mL)	Necropsy Day	No. of Study Animals per Necropsy Day	
					Males	Females
1	Reference Item	0	1	11,90,120,180	3	3
2	Ad26 (b) (4)	1×10^{11} vp	0.5		5	5
3	Ad26 (b) (4) (b) (4)	1×10^{11} vp + 150µg	1 (of mixture)		5	5

Following terminal euthanasia on Day 11, 90, 120 or 180, a complete gross pathological examination was performed on all animals, as specified in the Study Plan.

2.1. Computerized System

Critical computerized system used in this study phase is listed in Text Table 2.

Text Table 2
Computerized System

System Name	Version No.	Description of Data Collected and/or Analyzed
Provantis	10	Gross pathology.

Appendix 7

3. RESULTS AND DISCUSSIONS

3.1. Mortality

There were no unscheduled deaths during the course of this study.

3.2. Gross Pathology – Terminal Euthanasia (Days 11, 90, 120 and 180)

(Table 1 and Appendix 1)

Following a single intramuscular injection of Ad26 (b) (4) and an observation period of up to 180 days, there were no test item-related gross findings. Even though they were not always present in a concurrent control animal, the gross findings observed in treated animals were isolated (i.e. not more than 1 out of 5 animals) and without any trend (i.e. no dose- or timepoint-relationship). Therefore, all gross findings observed were considered incidental, of the nature commonly observed in this strain and age of rabbits, and unrelated to administration of Ad26 (b) (4)

Appendix 7

4. CONCLUSIONS

Following a single intramuscular injection of Ad26 (b) (4) and an observation period of up to 180 days, there were no test item-related gross findings.

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

5. REPORT APPROVAL

DocuSigned by:
(b) (4), (b) (6)

(b) (4), (b) (6)
Diplomate ECVP
Study Pathologist

Appendix 7

Table 1
Incidence of Necropsy Findings by Organ/Group/Sex

Appendix 7

Incidence of Necropsy Findings by Organ/Group/Sex Explanation Page

Abbreviation	Description
GALT	Gut Associated Lymphoid Tissue

Note: This is a comprehensive list of abbreviations. All of the abbreviations listed may not be applicable to this report.

Dosing Information

Dosing information is abbreviated on various data outputs; the following represents the dosing information for this study:

Group No.	Test Material	Dose Level
1	Reference Item	0
2	Ad26 (b) (4)	1×10^{11} vp
3	Ad26 (b) (4) (b) (4)	1×10^{11} vp + 150µg

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Incidence of Necropsy Findings by Organ/Group/Sex: Day 11

(b) (4)

Removal Reason(s): TERMINAL EUTHANASIA	Male			Female		
	0 Group 1	1x10E11 vp Group 2	1x10E11 vp+150 ug Group 3	0 Group 1	1x10E11 vp Group 2	1x10E11 vp+150 ug Group 3
Number of Animals:	3	5	5	3	5	5
LYMPH NODE						
Enlargement	.	.	.	.	.	1
MUSCLE, SKELETAL						
Focus; dark	1	.	.	.	.	.
OVARY						
Small	.	.	.	.	.	1
OVIDUCT						
Cyst; pale	.	.	.	.	1	.
SITE, INJECTION						
Focus; dark	.	1	1	1	1	.
SUBCUTIS						
Focus; dark	.	.	.	.	.	1
THYMUS						
Focus; dark	1	.	.	.	.	.
WHOLE ANIMAL						
No Visible Lesions	1	4	4	2	3	1

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Incidence of Necropsy Findings by Organ/Group/Sex: Day 90

(b) (4)

Removal Reason(s): TERMINAL EUTHANASIA	Male			Female		
	0 Group 1	1x10E11 vp Group 2	1x10E11 vp+150 ug Group 3	0 Group 1	1x10E11 vp Group 2	1x10E11 vp+150 ug Group 3
Number of Animals:	3	5	5	3	5	5
LYMPH NODE, MESENTERIC						
Focus; dark	.	.	.	.	1	.
SKIN						
Abrasion; dark	.	.	.	.	.	1
WHOLE ANIMAL						
No Visible Lesions	3	5	5	3	4	4

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Incidence of Necropsy Findings by Organ/Group/Sex: Day 120

(b) (4)

Removal Reason(s): TERMINAL EUTHANASIA	Male			Female		
	0 Group 1	1x10E11 vp Group 2	1x10E11 vp+150 ug Group 3	0 Group 1	1x10E11 vp Group 2	1x10E11 vp+150 ug Group 3
Number of Animals:	3	5	5	3	5	5
LYMPH NODE						
Discoloration; dark	.	.	1	.	0	.
Small	.	.	0	.	1	.
SITE, INJECTION						
Focus; dark	.	.	1	.	.	.
WHOLE ANIMAL						
No Visible Lesions	3	5	3	3	4	5

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Incidence of Necropsy Findings by Organ/Group/Sex: Day 180

(b) (4)

Removal Reason(s): TERMINAL EUTHANASIA	Male			Female		
	0 Group 1	1x10E11 vp Group 2	1x10E11 vp+150 ug Group 3	0 Group 1	1x10E11 vp Group 2	1x10E11 vp+150 ug Group 3
Number of Animals:	3	5	5	3	5	5
GLAND, ADRENAL						
Enlargement	.	1	1	.	.	.
GLAND, SEMINAL VESICLE						
Enlargement	.	.	1	.	.	.
KIDNEY						
Adhesion	.	.	.	1	.	0
Discoloration; pale	.	.	.	0	.	1
LIVER						
Small	.	.	.	.	1	.
THYMUS						
Focus; dark	.	1	.	.	.	0
Small	.	0	.	.	.	1
UTERUS						
Mass	.	.	.	1	.	.
WHOLE ANIMAL						
No Visible Lesions	3	4	3	2	4	3

Appendix 7

Appendix 1
Individual Gross Pathological Findings

Appendix 7

Individual Gross Pathological Findings Explanation Page

Abbreviation	Description
(G)	Gross Pathology
(H)	Histopathology
(TGL)	Trackable Gross Lesion
< or >	Value outside the validation rule range in Provantis
Cass	Cassette
GALT	Gut associated lymphoid tissue
ID	Identification
LN	Lymph Node
LT	Left
RT	Right
SS	Special Stain

Note: This is a comprehensive list of abbreviations. All of the abbreviations listed may not be applicable to this report.

Dosing Information

Dosing information is abbreviated on various data outputs; the following represents the dosing information for this study:

Group No.	Test Material	Dose Level
1	Reference Item	0
2	Ad26 (b) (4)	1 x 10^{11} vp
3	Ad26 (b) (4) (b) (4)	1 x 10^{11} vp + 150µg

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1001 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

THYMUS;
Focus; dark: 2, left.

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1002 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

MUSCLE, SKELETAL;
Focus; dark: 2, quadriceps femoris right.

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1003 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1004 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1005 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1006 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1007 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1008 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1009 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1010 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1011 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1012 Group: 1 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1501 Group: 1 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

SITE, INJECTION;
Focus; dark: 3, biceps femoris right

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1502 Group: 1 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1503 Group: 1 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1504 Group: 1 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

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Animal Ref.: 1505            Group: 1            Sex: Female         Species: Rabbit     Strain: New Zealand White

Test Material: Test Item not supplied   Dose: 0   Route: Intramuscular, Injection         Study Type: DISTRIBUTION
Date of Death   : 12SEP2018   Study Day No. (Week): 90 (13)           Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018   ** NECROPSY COMPLETE **
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Gross Pathology Observations:
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Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions
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Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1506 Group: 1 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1507 Group: 1 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1508 Group: 1 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1509 Group: 1 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

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Animal Ref.: 1510            Group: 1            Sex: Female         Species: Rabbit     Strain: New Zealand White

Test Material: Test Item not supplied   Dose: 0   Route: Intramuscular, Injection         Study Type: DISTRIBUTION
Date of Death   : 11DEC2018   Study Day No. (Week): 180 (26)          Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018   ** NECROPSY COMPLETE **
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Gross Pathology Observations:
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Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

KIDNEY;
   Adhesion: right to capsule

UTERUS;
   Right horn found not continuous.
   Mass; [a]: 170x80x50mm, pale, soft, cystic, cut surface: fluid
      pale, clear, location not recorded
```

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1511 Group: 1 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 1512 Group: 1 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Test Item not supplied Dose: 0 Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2001 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2002 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

SITE, INJECTION;
Focus; dark: 3, biceps femoris, right.

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2003 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2004 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2005 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2006 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2007 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2008 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2009 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2010 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2011 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2012 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2013 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2014 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2015 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2016 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2017 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2018 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2019 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2020 Group: 2 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

GLAND, ADRENAL;
Enlargement: bilateral

THYMUS;
Focus; dark: >10

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2501 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

SITE, INJECTION;
Focus; dark: >10, biceps femoris right , extending into quadri-
ceps femoris right

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2502 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2503 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2504 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2505 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

OVIDUCT;
Cyst; pale: 1, left

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2506 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

LYMPH NODE, MESENTERIC;
Focus; dark: 3

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2507 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2508 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2509 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2510 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2511 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2512 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

LYMPH NODE;
Small: popliteal left

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2513 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2514 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2515 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2516 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

LIVER;
Small: left lateral

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2517 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2518 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2519 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 2520 Group: 2 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp Route: Intramuscular, Injection Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3001 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3002 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

SITE, INJECTION;
Focus; dark: >10, biceps femoris right, extending into quadriceps femoris right.

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3003 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4)

Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3004 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3005 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 24JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 24JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3006 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3007 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3008 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3009 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3010 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3011 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

SITE, INJECTION;
Focus; dark: 3

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3012 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3013 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3014 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

LYMPH NODE;
Discoloration; dark: mediastinal.

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3015 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3016 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

GLAND, SEMINAL VESICLE;
Enlargement

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3017 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

GLAND, ADRENAL;
Enlargement: left

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3018 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3019 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3020 Group: 3 Sex: Male Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 10DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 10DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3501 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

LYMPH NODE;
Enlargement: Iliac right

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3502 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

OVARY;
Small: Bilateral

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3503 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3504 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

GALLBLADDER;
Not found

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3505 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 25JUN2018 Study Day No. (Week): 11 (2) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 25JUN2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

SUBCUTIS;
Focus; dark: 1, hindlimb right, overlying injection site

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3506 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3507 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3508 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3509 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

SKIN;
Abrasion; dark: ventral cervical

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3510 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 12SEP2018 Study Day No. (Week): 90 (13) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12SEP2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3511 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3512 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3513 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3514 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3515 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 12OCT2018 Study Day No. (Week): 120 (18) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 12OCT2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3516 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3517 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

KIDNEY;
Discoloration; pale: bilateral

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3518 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions

Sponsor Reference No. (b) (4) Test Facility Study No. (b) (4)

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3519 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

THYMUS;
Small

Appendix 7

Individual Gross Pathological Findings

(b) (4)

Animal Ref.: 3520 Group: 3 Sex: Female Species: Rabbit Strain: New Zealand White

Test Material: Ad26 (b) (4) Dose: 1x10E11 vp+150 Route: Intramuscular, Injection
Study Type: DISTRIBUTION
Date of Death : 11DEC2018 Study Day No. (Week): 180 (26) Mode of Death: TERMINAL EUTHANASIA
Date of Necropsy: 11DEC2018 ** NECROPSY COMPLETE **

Gross Pathology Observations:

Complete gross examination was performed.
EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Any remaining study plan required tissues, which have been examined, have no visible lesions