From: LeDuc, James W.

Sent: Sunday, February 9, 2020 4:15 PM

To:Yuan ZhimingCc:Shi, Pei yongSubject:Suggestions

Attachments: Questions on nCoV in Wuhan lab.docx

Dear Zhiming,

I am devastated to see the evolving nCoV epidemic unfolding in Wuhan and I just hope that you, your family and the larger Institute colleagues are well and surviving this very difficult time.

I want to suggest that you conduct a thorough review of the laboratory activities associated with research on coronaviruses so that you are fully prepared to answer questions dealing with the origin of the virus. I'm sure that you have considered this already, but attached are some areas where you may wish to investigate and be prepared to address. You might even consider preparing a manuscript that addresses these topics in an effort to be transparent and proactive. I would be pleased to work with you on such a paper if you think that would be helpful.

I raise these issues since I am receiving questions along these lines more and more frequently. Initially they came from social media and other "alternate information sources" but in the last few days I have been approached by senior officials and major reputable newspapers. Most link the opening of the new BSL4 lab as a possible source of the virus. Clearly addressing this will be essential, with any kind of documentation you might have available used to back up your comments. (It's not clear to me where the coronavirus work was/is actually being conducted.)

I have the utmost respect and admiration for Dr Shi and I am in no way casting doubt on her or her colleagues. I just think that we need to aggressively address these rumors and presumably false accusations quickly and provide definitive, honest information to counter misinformation. If there are weaknesses in your program, now is the time to admit them and get them corrected.

I trust that you will take my suggestions in the spirit of one friend trying to help another during a very difficult time.

Jim

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Investigation into the possibility that the nCoV was the result of a release from the Wuhan Institute of Virology (main campus or new BSL3/BSL4 facilities).

The questions below deal with the period 1 October 2019 to the present:

Where is coronavirus research conducted?

What level of biocontainment?

How many different laboratories actually handle live virus?

Where are coronavirus stocks stored?

Is there an inventory record of each isolate of each coronavirus kept? If so, are there any discrepancies between the record and actual current inventory number (i.e., is there evidence to suggest that virus stocks may have been stolen or used without proper record?)

Physical Security

Is there controlled access to the laboratories and freezers where coronavirus stocks are held? (Locked doors; card-key access; biometric readers; others?) Were any breaches in security noted/access to the facility by unauthorized individuals?

Is the laboratory constantly monitored by security personnel (24/7)? If not, you could briefly summarize your physical security program during the period in question.

Is there any evidence to suggest a mechanical failure in biocontainment during the time in question?

- -were biological safety cabinets used and appropriately certified?
- -Exhaust air filtration systems working correctly?
- -Autoclaves and waste stream disinfection systems working properly?
- -Animal husbandry and management?
- -Waste stream integrity (think of FMD leak in UK a few years ago)

Virus Stocks (You may wish to explain that many novel coronaviruses are known only from their sequence and are not able to replicate in culture)

When was the nCoV first handled in your laboratory?

What was the source of that virus? (patient specimen or field collected animal or other?)

During the period in question, what other coronaviruses (that replicate in culture) are stored/handled in your laboratories?

What are the coronaviruses in your possession that are most closely related to nCoV based on genetic sequences and are able to replicate in culture?

Is anyone on your team conducting gain of function studies, recombination studies or any other studies that may have resulted in the creation of the nCoV?

Personnel

How many people have access to the coronavirus stocks and laboratory?

Senior investigators? Junior investigators? Technical support staff? Post-docs? Students? Animal handlers? Janitors and other cleaning staff? Building support personnel? Others?

Is there any evidence to suggest that a disgruntled employee may have had access to the coronavirus stocks? (Recently fired or reprimanded individual(s), for example.)

Does the Institute have an occupational health clinic where employees and students can go to seek medical care? If so, was there any indication of unusual illness similar to that seen for nCoV among Institute staff? If yes, when were cases first seen relative to the nCoV outbreak.

Does a serum bank exist for staff and students working on infectious agents? If yes, could a current serum and the most recent banked sera be serologically tested for antibody to nCoV in an effort to document seroconversion? (If positive, this would not be able to differentiate between community acquired and occupational acquired infection, but absence of evidence of infection would be helpful in ruling out the lab as a source of infection.)

Have any of individuals working at the Wuhan Institute of Virology (main campus or BSL4 campus) been infected with the nCoV? Family members of employees?

If yes, when was the date of onset of illness for the first case recognized? (How does this date compare with the progress of the epidemic; that is, was this among the first cases recognized or later after the outbreak was well underway? How does this compare to the first recognition of nCoV in the greater Wuhan community?)

Where the individuals infected involved in coronavirus research?

Geography

(These questions deal with any association between the physical location of the lab(s) and the districts in Wuhan where the illness was first seen. The assumption is that someone suffering an occupational exposure would go to their local hospital for treatment.)

Where and when were the first Wuhan (or Hubei Province) residents infected with the nCoV first identified (hospital or clinic name/date of earliest cases)?

Do staff members of the Institute reside in the district serviced by this (these) hospital/clinic (s)?

Were any Institute staff members seen for clinical illness at this/these hospital (s) during the time in question?

Do staff members of the Wuhan Institute of Virology frequent the sea food/live market first associated with the nCoV outbreak?

Did any staff member visit the market in the weeks prior to it being closed?

If so, how many staff frequent the market? How often would they visit the market during the period of interest? Have any become infected with nCoV?