The New York City
Uncontrolled Donation after Cardiac Death Protocol

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Subject to change dependent upon legal and or regulatory changes requested from the New York State Department of Health

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for the NYC UDCD Study Group

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INTRODUCTION

Thousands of individuals have had their lives extended as recipients of transplanted kidneys, hearts, pancreata, livers, and other solid organs in the United States. Although the number of transplant recipients is growing arithmetically, the number of transplant candidates is growing exponentially thus creating an ever widening gap between number of individuals on waiting lists and the supply of transplantable organs. One reason for this deepening gulf between life and death is that currently there are only three ways of retrieving organs: in the hospital following neurological death [brain death], in the hospital following cardiac death [CDCD—Controlled Donation after Cardiac Death] and live donation.

The recent IOM report *Organ Donation: Opportunities for Action* (Childress et al., 2006) emphasized the substantial potential to expand organ donation if opportunities for retrieving organs were permitted following a sudden cardiac death that occurred outside of the hospital. Cardiac deaths are, at present, classified according to whether the death is controlled, for example, when a patient or family chooses to discontinue life support for a terminally ill patients in anticipation of donation, or uncontrolled, where the death is unanticipated. Uncontrolled cardiac deaths may also occur in or out of hospital settings. In the hospital setting, controlled donation after cardiac death (CDCD) requires a multi-layered process beginning with the decision to forego treatment and permit death. Only after that decision is reached is the discussion of donation initiated. Whereas obtaining consent for organ donation following neurologic death ("brain death") has long-standing clearly defined protocols and policies, protocols for obtaining consent for donation following controlled cardiac death have only recently been required by the Joint Commission and are not yet the norm in some areas of the United States. Even if widely accepted, however, CDCD in the hospital will generate relatively

few organs, as even in the hospital most cardiac deaths are unanticipated [referred to as uncontrolled donations after cardiac death (UDCD)].

Realizing the potential for uncontrolled donations after cardiac death (UDCD) as a reliable source for solid organs requires gaining acceptance of the concept both within medicine and in the larger community and establishing protocols to actualize possible opportunities. Most recently, a pilot program in Pittsburgh is investigating how such a protocol might be implemented for cardiac arrests presenting to the emergency department (ED). Some protocols permit retrieving organs from patients in intensive care units. These in-hospital programs, however, neglect to provide access to organs for those cardiac deaths that occur outside the hospital and are declared in the field. Studies in Spain, (Alvarez et al., 1997, 2000; Gomez et al., 1993; Sanchez-Fructuoso et al., 2006) elsewhere in Europe and the U. S. (Light et al., 1997) have shown that well-integrated Emergency Medical Services (EMS), emergency departments, and procurement services can effectively employ structured out of hospital UDCD protocols to dramatically increase organ donation. These investigations demonstrated that model centers-of-excellence could be developed to identify and address institutional, professional and community barriers to out of hospital UDCD.

The Health Resources and Services Administration (HRSA) recently funded our consortium of investigators from Bellevue Hospital Center, the Fire Department of New York City (FDNY), and the New York Organ Donor Network (NYODN) to develop an out of hospital UDCD pilot program in New York City. While the intent of the new program is to demonstrate how an UDCD program might ultimately supply enough organs to those in need so that the waiting list becomes obsolete, understanding, support and public perception of the program is essential for its inception and acceptance. Previous experience in the U.S. (Light et al., 1997) demonstrated that professional, political, and community leaders were able to galvanize community

acceptance and successfully implement an out of hospital UDCD donation program in Washington D.C; unfortunately, the program fell prey to a lack of continued funding.

UDCD Protocol Context in Terms of Current Organ Donation Practice

One way to evaluate the ethical acceptability of a UDCD protocol is to compare the elements of this protocol to current organ donation practice (Figure 1). Presently accepted practice in hospitals in regard to donation after neurologic death or under CDCD hold that a potential donor is only identified once the determination of neurologic death occurs [according to accepted guidelines] or once the decision has been made to permit cardiac death by removing a ventilator. In almost all of the hospitals in the donor service area in which this pilot program is being conducted, neurologic death is confirmed by two physical examinations by two independent physicians performed six hours apart and by the documentation of a failed apnea test. The official time of death is determined at the time of the second examination. Following the determination of death the hospital and OPO together assess suitability and maintain organ perfusion to preserve the option of donation. Measures to assess and preserve the potential donor include maintaining mechanical ventilation, insertion of central venous and arterial lines, administration of vasoactive and antidiuretic medications as needed, and testing for infectious diseases. The family is then approached for donation; if the family declines, the preservation measures are withdrawn, and cardiac arrest ensues shortly thereafter. If the family consents to donation, the preservation measures continue, the organs are procured and allocated according to UNOS criteria.

This experience with donation after neurologic death provides the template for developing practice and process for donation after uncontrolled cardiac death. Donation after uncontrolled cardiac death will respect the very same elements:

1. Prominence for the "dead donor rule"—only donors who were dead according to the determination of death by irreversible cardiac arrest would be acceptable as donors;
2. Sequencing of discussions requiring the determination of death to precede any discussion with the family regarding donation;
3. Instituting preservation to preserve the rights of the family to donate;
4. An absolute separation of the process of determination of death and the discussion of possible donation;
5. Full empowerment of the family to decide whether or not to donate;
6. Respect for the family's decision and the avoidance of coercion in family contacts;
7. Respect for altruism and rejection of commodification compensation, payment, gift or token of regard for the family.

In the UDCD program, EMS paramedics would respond to an out-of-hospital cardiac arrest and perform all appropriate efforts at resuscitation. The paramedics consult with an online medical control physician to manage the resuscitation. The online medical control physician may terminate the resuscitation of the patient in the field according to current guidelines. This EMS crew and OLMC physician will be blinded to the response of the organ preservation crew. Only after termination of resuscitation will the organ preservation crew approach the potential donor and family member(s). After receiving permission from a LNOK/SIFM or in cases where donor status is confirmed through legally accepted documentation (e.g. the registry of intent/consent), potential donor screening and organ preservation measures ensue for those eligible. Such measures include testing for infectious diseases, laboratory specimens, and neurologic assessments to screen donors for eligibility, and preservation measures including placing of intravenous and intra-arterial groin catheters and anticoagulant medication administration (including heparin and thrombolytic) to preserve the option of donation for the family. The

LNOK is then approached; if the donation is declined, the preservation measures are withdrawn. If the LNOK consents, then organ preservation continues, and organ recovery proceeds according to standard approaches.

In cases involving CDCD, the LNOK has a substantial amount of time to conceptualize and integrate the upcoming death that his or her loved one is facing prior to being approached for organ donation. In UDCD this is not the case. This is the key element of difference that this protocol will be testing for acceptability; query: is it possible to approach a loved one or next of kin at this moment of death and proceed to stage the decision in a way that is respectful to the grieving person? When all of the protocols and procedures are in place this is the key question of ethical acceptability that the protocol is designed to explore. In both ND and UDCD, permission for preservation and consent for organ donation must be obtained in a culturally sensitive and ethically responsible manner, but in UDCD, this must occur in a vastly compressed time frame that ensues immediately following the death of a loved one.

By its structure, its insistence on the dead donor rule, its insistence on separate resources for preservation activities vs. life-saving activities, its separation of the life-saving care team from the organ preservation team with its own Organ Preservation Vehicle, its scrupulous support of family choice and its careful and skillful preservation of organs, this pilot project fulfills both the public health mandate to save lives and the basic ethical precept of do-no-harm. It stands solidly within accepted ethical precept and practice.

METHODS

Participatory action research methods (Stringer, 2007) and the SEED-SCALE process for social change (Taylor-IDE & Taylor, 2002) guided the development of the NYC UDCD protocol. The

SEED-SCALE process for social change has brought about significant and sustained community reforms in the international and domestic arenas. In the first three steps of the process, evidence based approaches are used to build community capacity for social reform. The first step establishes a coordinating committee, the second identifies the successes of each community and the third initiates the study of outside communities. In the specific case of the UDCD program, the principal investigator (LG) established a planning committee to identify all key stakeholders to approach for collaborative UDCD protocol development and for raising public support for its introduction. The committee included experts in health program evaluation and organ donation procedures, pre-hospital, emergency medicine, and transplant providers, NYC government officials and their legal counsels, and a bioethicist. The committee discussed the organ donation shortage, current UDCD issues as described in the recent IOM report (Childress and Liverman 2006) and suggested ideas about how an out of hospital UDCD program could be implemented in the NYC demographic area. Step two proceeded with a review of UDCD options advocated by the IOM Committee (Childress & Liverman, 2006). The NYC UDCD program would build on the success of a pilot program in Washington D.C. that showed the potential to recruit UDCD kidney donors using cold perfusion techniques (Light et al, 1997), a program that was discontinued primarily due to financial considerations. The most promising options for out of hospital UDCD identified were recent protocols established in Spain that employed cardiopulmonary support after death determination; such programs have potential to procure livers in addition to kidneys, with improved outcomes when compared to the Washington D.C. program *(Sánchez-Fructuoso, Marques, Prats D, et al, 2006; Sánchez-Fructuoso, Prats, Torrente, et al, 2000; Sanchez-Fructuoso, de Miguel Marques, Prats, & Barrientos, 2003; González-Segura, Castelao AM, Torras J, et al, 1998).*

Steps four and five encompass the SEED process. SEED stands for "Self-Evaluation for Effective Decision making." Step four involves self-evaluation though the gathering of

community specific information pertaining to resources and needs. In the case of the NYC UDCD program such data were collected though the collaborative efforts of the New York Organ Donor Network, which identified the need for solid organs in New York City as well as the specific concerns of stakeholders who may be affected by the implementation of the NYC UDCD protocol.

Step five advocates for effective decision making through collaborative discussions such that all stakeholders share in development and implementation. A guiding principle of the SEED-SCALE process is that a three-way partnership between government, experts, and the community at large be established to ensure program acceptance and sustainability. In the UDCD program, the planning committee identified a coalition of officials, experts, and communities that would be necessary to achieve support for the program (Figure 2). Internal stakeholders were defined as entities that would be charged with out of hospital UDCD program implementation and hence would need to adopt new protocols that might impact their traditional patient and deceased care responsibilities; these organizations included the providers at Bellevue Hospital, FDNY EMS, the NYODN, and the Office of the Medical Examiner as key stakeholders.

Other New York City and State agencies also participated in planning and identified legal and regulatory barriers that needed to be addressed. Government officials necessary to grant approval for initiating the out of hospital UDCD program included the President of the New York City Health and Hospitals Corporation, the NY State and City Health Commissioners, NY State and City EMS officials, and the Chief Medical Examiner for NYC. Legal representatives from FDNY, the NYPD, the NY State Department of Health, the NYODN, the NYC HHC, and the NY Task Force for Life and the Law negotiated whether current NY State and NYC law allowed for the NYC UDCD program implementation and drafted memoranda of understanding where

appropriate; the ethics of the program were evaluated under consultations from the NY Task Force for Life and the Law and the NYS Department of Health legal representatives. External stakeholders included civic, community, and religious organizations that might be engaged in town hall style meetings to assist with program planning and acceptance from the general public. Market research was conducted with a public relations firm (Ogilvy Public Relations Worldwide) to formulate a plan to engage the general public through media and educational campaigns.

Data Collection

Officials, experts, and the community were engaged in layers including informal consultations, expert panels, stakeholder meetings, and engagement of community members through town hall style meetings. Ethnographic data in the form of meeting minutes, digital video data, and quantitative surveys were collected in all stages of the process. Accounts of progress were posted on a Wiki (www.organdonation.pbwiki.com) and the protocol was designed with internet-based diagramming software (www.gliffy.com). Team members had editing access to these collaborative environments so that they could discuss and edit the content as appropriate.

Data Analysis

Data from meetings, media, and surveying were organized in the Wiki by source and the protocol was parsed into sections amenable for collaborative editing. Study team members edited and discussed content in weekly meetings and on the Wiki (akin to an internet chat room). Qualitative data were analyzed and summarized using a coding scheme reflective of the conceptual model for organ donation behavior (Wall et al, unublished). Quantitative data were presented with summary statistics and graphical presentations using Microsoft Excel. An action

research matrix was established in the Wiki summarizing all data collected and was used to track progress of the protocol development and acceptance. Hypertext links were established between the primary source materials, the summary, and research matrix to justify the findings. When progress was made and protocol changes accepted unanimously by team members (as evidenced by approvals posted in the Wiki), the protocol was updated in the collaborative diagramming software. This iterative process continued until the protocol sections were finalized and agreed upon by all study team members.

RESULTS

In New York City, patients who have cardiac arrests undergo resuscitation per predefined protocols. After all measures are exhausted, if return to spontaneous circulation is not achieved, then the EMS online medical control physician may terminate the resuscitation attempts in the field. This practice is customary in many EMS systems nationwide. When a death pronouncement occurs, the paramedics discontinue their resuscitation protocols, inform the family of the death declaration (if family is available), and notify the New York City Police Department (NYPD) who notifies the Office of the Chief Medical Examiner of the outcome. At this moment, the deceased is transferred to the jurisdiction of the NYPD and subsequently to the Office of the Chief Medical Examiner. If no family members are present, the NYPD notifies the family through its institutional protocols.

The participants universally agreed that the new protocol should not interfere in any way with the existing EMS resuscitation protocols. Such an approach would ensure that the EMS providers would take every necessary step to resuscitate the patient, and a separate team would arrive to consider the newly deceased as a potential organ donor. The following provides

a brief summary of the most recent version of the NYC UDCD protocol as agreed upon by the stakeholders who are to be affected by its implementation.

Pre-Hospital Protocol

The EMS protocol as conceived is depicted in Figures 3a-c. The protocol was envisioned to follow a clinical guideline approach with coordinated services among FDNY EMS, the NYODN, the Bellevue Emergency Department and Trauma Services, the NYU Langone Medical Center Transplant team, the NYPD and the Office of the Chief Medical Examiner. Calls to 911 for medical complaints are transferred to FDNY's Emergency Medical Dispatch where an initial call-type is determined (Figure 3a number 1). A specially trained organ preservation crew consisting of two emergency medical technicians (EMTs), an emergency medicine physician (attending or resident having undergone at least 2 years of training), and an organ donation family services specialist (FSS), in a specially equipped vehicle, the Organ Preservation Vehicle (OPV), will monitor the selected dispatch radio frequencies (3), and if a job with a call-type of 'arrest' is transmitted (2), the OPV crew will initiate a response to the job location (5) if it is within the catchment area (4).

Sometimes an EMS crew may find a patient to be in cardiac arrest even though the initial call-type was not designated as such (6,7,8). In this case, the EMS crew will transmit this information (confirmed arrest) to the borough dispatcher (9). The borough dispatcher then announces all confirmed arrests on the dispatch frequency, which is monitored by the Emergency Medical Dispatch, who then routes the call to the Online Medical Control (OLMC) facility (10) and upgrades the call to an 'arrest' (12). The OPV crew will initiate a response (5) to the job assignment upon hearing this transmission (3) if not already en route to the job location, and if it is within the catchment area (4).

Should the OPV crew not hear these transmissions (e.g., in a radio dead zone), a redundant mechanism by which the OPV crew may identify an appropriate job will occur in the following manner. Upon hearing the transmission of a confirmed 'arrest,' the radio dispatcher routes the job to the OLMC facility (10). OLMC team members consist of two OLMC paramedics and an OLMC physician who provides real-time medical orders for the paramedics, including for cardiac arrest cases. The OLMC physician and paramedic work in proximity to each other separated by cubicle dividers. The OLMC physician will initiate care decisions, as is standard protocol, and will be blinded to OPV crew availability. The designated OLMC paramedic, immediately after learning of the cardiac arrest (11) will confirm whether the OPV crew was aware of the cardiac arrest via telephone landline to cellular transmission (3).

If two appropriate assignments (i.e., patients in cardiac arrest within catchment area) are occurring simultaneously, the OPV crew will review the computer aided dispatch (CAD) job text for each, review patient specific information (e.g, age, comorbidities, etc.) if available, and respond to the location of the apparent best candidate for UDCD. If the 911 call results in a 'non-arrest' situation, then standard EMS procedures dictate the care of the patient (12).

Upon identifying an appropriate assignment, the OPV crew will inform the OLMC paramedic via cellular telephone (Figure 3b number 13). The OLMC paramedic will create a new computer-aided dispatch (CAD) assignment for the OPV with the appropriate destination. At the discretion of its crew, the OPV may respond to an assignment location in emergency mode (i.e., using lights and sirens), but will cease when within a one block distance of the lamppost location so as not to upstage the treating EMS providers. If the OPV crew is responding because the initial call-type was a "cardiac arrest", the OPV crew will continue to monitor the radio for confirmation by EMS (14). At this time, the OPV FSS may check the organ donor registry to

see if the name of the patient is a member by contacting the NYDON call center. When the treating EMS teams arrive on scene, if the patient is determined to have obvious signs of prolonged death (15), such as rigor mortis, dependent lividity, decapitation, etc., the OPV call will be cancelled (22), and standard procedures for handling the deceased will ensue. If EMS transmits information that the patient is not in cardiac arrest (16), then EMS will transport the patient to the closest hospital and the OPV crew will close out their assignment to become available for the next appropriate call (22).

The OPV will arrive at the lamppost location after the treating EMS providers (17). Once there, the OPV crew transmits an "on scene" signal (18) via its mobile data terminal (MDT). If according to standard protocols, after ventricular fibrillation is eliminated, an advanced airway device is placed, oxygenation and ventilation are achieved, interventions are sustained for greater than 30 minutes, and appropriate resuscitative medications are administered, then the OLMC physician may order termination of the resuscitation, and will document the time of the order (REMAC Guideline; Kern et al, 2001). The physician will notify the OLMC paramedic of all field termination of resuscitations. If the OPV crew was responding to the job for which a pronouncement was given, then the OLMC paramedic will notify the OPV crew of the time via telephone (19). Only when the OPV crew receives confirmation of pronouncement from the OLMC paramedic via telephone or MDT message, will they be allowed to proceed to the scene of the cardiac arrest (23). If this occurs while the OPV crew is still responding to an arrest, then the OPV crew should immediately proceed to the patient location if arrival is expected to occur within the time allotted to obtain permissions for organ preservation.

If no report of termination of resuscitation has been given by OLMC, then the EMS crew will inquire whether the EMS team is on scene or has transported the patient to a 911 receiving hospital (20). If the treating EMS crew has already initiated transport of the patient to the

hospital, then the OPV crew will close out their assignment (22). Otherwise, if EMS is still on scene, then the OPV crew will remain in the vehicle near the lamppost location (21) waiting for the patient to be transported by EMS or for termination of resuscitation orders from the OLMC physician (19) so they may proceed to the scene of the cardiac arrest (23). If at any point the patient is transported by EMS to the hospital (if there is a return to spontaneous circulation or the OLMC physician perceives the patient would benefit from prolonged resuscitation in an emergency department, for example, for hypothermia cases), the OPV crew closes out their assignment (22).

Upon OPV crew activation (Figure 3c) the OPV Family Services Specialist (FSS) will notify the NYODN call center that a potential UDCD case is under evaluation (24). At this time, the OPV physician will call the Bellevue Hospital ED and establish an estimated time of arrival for the deceased to prepare for preservation measures should the deceased meet screening criteria and the OPV crew receives permission for preservation. Such measures include mobilizing equipment for ECMO (26) and trauma team activation (27). The NYODN call center will notify the on call perfusionist to prepare for ECMO (28), so that the perfusionist may potentially arrive at the Bellevue Hospital ED at nearly the same time as the deceased (29). The NYODN call center will also notify the on call transplant coordinator and organ preservationist to prepare for a possible UDCD case.

After notifying the appropriate personnel about the potential UDCD case, the OPV crew will proceed to the scene of the cardiac arrest to screen the deceased for inclusion into the UDCD protocol (30). Once at the scene of the cardiac arrest, the OPV crew including the two EMTs and the FSS will approach the treating EMS team to learn more about the specifics of the deceased, the cardiac arrest, and to identify any potential family. The OPV crew as a unit will screen the potential donor for inclusion according to modified Madrid Criteria (Gomez, 1993;

Alvarez 1997, 2000, 2002). Our modified Madrid criteria accept only cases where the arrest time is known, or where the initial rhythm is ventricular tachycardia or ventricular fibrillation (suggesting a recent arrest). The OPV crew will then check our screening criteria and confirm that the deceased is under 60 years of age, has no obvious evidence of renal failure (such as dialysis access), no evidence of liver disease such as jaundice or ascites, no evidence of injection drug use, no evidence of foul play, no major trauma to the body, and no limb amputations (suggesting severe vascular disease). These questions are designed as a quick screen and will take no more than a few minutes. A more complete evaluation will occur once the body has been transported to Bellevue (including removal of garments for a more careful physical inspection). If the candidate is excluded, then the deceased will be handled according to standard NYPD protocols and the FSS will counsel the family as to what transpired and whom to contact for additional assistance. The FSS will also provide additional information to the family using the guide titled, *After Death Has Occurred*, which may be kept by the family as a reference. The OPV crew will then end their assignment (43).

If the deceased meets UDCD inclusion criteria then the OPV FSS will attempt to locate preferably a legal next of kin (LNOK) or in the absence of one, a self identified family member at the scene (32). Attempts will also be made to confirm whether the deceased is on an organ donor registry of intent or consent (33), and if documentation of the patient's name and date of birth are immediately available. A LNOK or SIFM, if available, will be asked for verbal permission to proceed with organ preservation measures to afford the individual(s) time to consider donation as an option for their loved one (34). The permissions requested at this time include additional physical examinations to determine UDCD program eligibility, the administration of heparin and thrombolytic medications, and then one minute of manual chest compressions to circulate the heparin and thrombolytic medications. If the LNOK/SIFM agrees, or if the deceased has expressed his or her wish to donate such as on a registry of intent,

consent, or with a driver's license, then the preservation maneuvers may proceed. If at anytime it is determined that permission will not be granted or the period of discussion exceeds 20 minutes from the time of death pronouncement, then attempts to obtain permission for preservation will cease. The deceased will be handled according to standard NYPD protocols and the OPV crew will end their assignment (43). In cases where a LNOK/SIFM may only be contacted by telephone, such an attempt will be made by the OPV FSS to obtain verbal permission for preservation over the phone within the 20 minute time as described. OPV crew members may serve as a witness for the verbal permissions. If the deceased is on a registry of intent or consent, then preservation measures may proceed without LNOK/SIFM permission unless there are objections from family or bystanders at the scene. In the case of objections by a bystander, the OPV FSS will request LNOK/SIFM information from the bystander and make it clear to the bystander that in expressing this objection, the individual is not allowing the LNOK/SIFM the opportunity to make a donation decision. If a LNOK/SIFM cannot be contacted and the deceased is not on a registry, then the OPV crew will end their assignment (43) after counseling the family.

The OPV crew will only approach the deceased after family permissions are obtained for preservation. The OPV physician will first perform the final UDCD program screening measures: a focused neurological assessment to assess brainstem function prior to reinitiating cardiopulmonary support and confirmation or establishment of peripheral intravenous access. The neurological assessment will include observing for evidence of brainstem function by assessing:

a. Pupils (e.g. response to bright light)
b. Ocular movement (e.g. vestibulo-ocular reflex)
c. Facial sensation and facial motor response (e.g. corneal reflex)
d. Pharyngeal reflex (e.g. response after stimulation of the posterior oropharynx)

To perform the neurologic assessments, administer medications, and supervise the cardiopulmonary support, the OPV team will include an emergency medicine resident physician or an attending physician to perform these duties. If residents are recruited, they will be second year level or greater (≥ PGY-2) who have been trained in intubation and cardiac arrest management; the residents will be recruited from the NYU/Bellevue and Long Island Jewish Emergency Medicine Residency Programs and paid as moonlighters ensuring that there is no conflict with mandatory ACGME guidelines for hours of service during a day or a week. Emergency medicine attending physicians will be recruited from the NYU/Bellevue physician group.

Residents or faculty who are to join the OPV team will undergo a training course to refresh their skills on assessing brainstem function, with competency evaluations to occur at the end of the refresher course. Such courses are offered throughout the year at Bellevue Hospital Center where certification to perform neurological death determination is awarded upon completion of the course.

If brainstem function is determined to be absent, the OPV physician will determine if adequate intravenous access exists, as evidenced by a 10 mL saline lock infusion; if the IV is deemed inadequate, the physician will attempt to place a new peripheral IV or if unable to secure such access, then alternatively, an intra-osseous line will be established. If for some unanticipated reason, the OPV physician is unable to obtain peripheral IV or IO access, the OPV crew will end their assignment (43). A "hands off" period whereby the deceased is left alone will have occurred during the UDCD screening process and as the NYPD transfers the care of the deceased to the OPV team. During this time, the family may begin to process their loved one's demise. It is likely that the hands off period will have exceeded 2 minutes; however, for eligible

cases where the family grants permission immediately or there is proof of organ donor registration (either in a registry of consent or intent) in the absence of the legal next of kin (LNOK) or self identified family member (SIFM) objection, preservation measures may proceed immediately. Consent for organ donation from the LNOK will proceed in a more protracted fashion so that there is a clear understanding of facts and options, the application of values and history to the situation and alternatives, and the communication of clear directives are delivered and understood. Such criteria for informed consent would only be achieved after the LNOK is afforded time to process his or her loss.

After peripheral IV or IO access is confirmed, the OPV crew will proceed with the initial preservation measures (36). The OPV physician will administer the heparin and thrombolytic medications, and the EMTs will perform one minute of manual chest compressions to circulate the medications. Following the circulation of the medications, the OPV crew will transport the deceased to the OPV (37). If deemed necessary by the OPV crew, the NYPD officers and or treating FDNY EMS personnel may be requested to assist with the transport of the deceased to the OPV. Once the deceased is secured in the OPV, the OPV physician will assess the airway (38). If a secure endotracheal airway is present, a portable ventilation unit will be applied to reinitiate ventilation (40). If no such airway exists, then a definitive one will be established or alternatively a laryngeal mask airway (LMA) will be placed at the discretion of the OPV physician (39) and ventilations will be reinitiated soon thereafter (40). The OPV crew EMTs will then apply an automated chest compression device (the LUCAS device) to maintain circulation for organ preservation (41) and then proceed to transfer the patient to the UDCD receiving ED at Bellevue Hospital (42).

During the initial preservation measures, the OPV FSS role will be to counsel family as to what is transpiring, obtain permission for ECMO (if not already granted), and when appropriate,

attempt to identify the legal next of kin (LNOK) to discuss organ donation. *The UDCD Approach to Family of the Deceased* section describes in detail the approach the OPV FSS will follow when discussing the organ preservation and donation considerations with family. At the discretion of the OPV FSS, the SIFM may be approached for ECMO permission at this time or defer the conversation until the SIFM is willing and able to have it (e.g. while the deceased is en route to the receiving hospital). If the legal next of kin is present, organ donation consent may be discussed immediately following the perfusion permissions.

In Hospital UDCD Protocol

The in hospital UDCD protocol begins upon arrival to the Bellevue ED (Figure 4). Upon arrival (44), the ED clerical team will generate a rapid hospital identification number establishing the NYODN as the guarantor for the deceased. Prior to continuing with the UDCD protocol, the OPV physician will conduct a second brainstem evaluation to assess whether the reinstitution of cardiopulmonary support in the cardiac deceased has impaired the natural progression to brain death in the newly deceased. In the highly unlikely situation that residual brainstem function is observed at any point, the potential donor would no longer be considered a candidate for donation, cardiopulmonary support would be discontinued, and the deceased will be transferred to the OCME. HRSA will be notified of the occurrence immediately so as to determine whether it is ethical to proceed with the OPV program or discontinue the program; the data safety monitoring board established to monitor public perception of the UDCD program and transplant outcomes, and the NYS Department of Health will also be notified of this unlikely event.

Once brainstem function is assessed and confirmed to be absent, the ED team will reassess the airway (45), establishing a definitive one when appropriate (e.g. if an LMA was used or if the airway was dislodged), and activate the trauma team. The trauma team in coordination with the

ED team will screen the potential donor for exclusion criteria (46); the ED nurses will have the criteria available on rapid assessment sheets so that the ED and trauma teams adhere to the UDCD guidelines. In coordination with the organ preservation FSS, the trauma team will then verify that verbal permission from the LNOK/SIFM (47) has been obtained or that the deceased expressed a wish to donate with a registry of intent, consent, or a driver's license to proceed with measures necessary to establish ECMO (in the absence of LNOK/SIFM objection). If permission for ECMO has not been obtained before the potential donor arrives at the Bellevue Hospital ED, then the UDCD protocol will be discontinued and the deceased will be handled according to Bellevue Hospital's standard protocols. In the case that the LNOK/SIFM grants permission (or the deceased has expressed his or her wish to donate on a registry of intent or consent or has such indication on a driver's license in the absence of LNOK/SIFM objection), the trauma team will immediately establish catheter access for ECMO (48). If the ECMO machine is available and ready for use, it will be immediately applied; otherwise, the catheters will be infused with heparin to prevent clotting while the ECMO device is being prepared. The ECMO machine will be primed so that it may be immediately initiated when appropriate; a primed ECMO machine maintains its sterility for three weeks, and the perfusionists will maintain the primed machine so that the machine is readily available for use. The LUCAS chest compression device will be discontinued during this procedure. The trauma team will insert an occlusion balloon on the contra-lateral side of the ECMO catheters so as to prevent circulation to organs above the diaphragm. Placement of the occlusion balloon improves circulation to the abdominal organs including the liver, kidneys, and pancreas and ensures that ECMO does not produce an artificial perfusion of cardiac or cerebral vessels after such a declaration of death. A radiograph will be taken to ensure that the occluding balloon is appropriately inflated and placed just above the diaphragm. Concurrent with the activities of the trauma team, the on call perfusionist will confirm that the perfusion machinery is primed for use.

During catheter placement, blood will be drawn for ABO and HLA typing, serologies including HIV, Hepatitis B and C, AST, ALT, and bilirubin profiles (49). OCME laboratory specimens will also be sent when appropriate. Nucleic Acid Amplification Testing (NAT) specimens will be sent to an outside laboratory contracted by the NYODN for HBV, HCV, and HIV testing and also HTLV testing as is current NYODN practice. After the balloon is confirmed to be in place, ECMO will be initiated (50). Mechanical ventilation will be discontinued and the deceased will be perfused with normothermic autologous blood and THAM based solution. To monitor the potential viability of the liver and kidneys, serial arterial blood gases, chemistries, renal and liver function tests will be sent and recorded every 30 minutes (51). Urine output will also be monitored during ECMO. Organ suitability (52) will be assessed using standard NYODN criteria as the rapid lab results become known (e.g. if HCV or HIV results are positive).

While preservation measures are being conducted, the organ preservation FSS will discuss organ donation options with the LNOK (53). If within 4 hours after ECMO is initiated, no LNOK is identified, or the LNOK does not give written informed consent for the donation to proceed, or the deceased is not confirmed to be on a registry of consent, preservation measures will cease and the deceased will be handled according to standard Bellevue Hospital protocols. If the organs are not suitable for donation per the NYODN protocols, the organ preservation FSS will inform the family and the preservation efforts will cease. If the LNOK provides written informed consent for the donation to proceed, or in the absence of a LNOK, the potential donor is confirmed to be on a registry of consent, the transplant team will be notified and organ procurement and allocation will ensue according to standard NYODN DCD protocols; the latter assumes the New York State Registry of Consent is operational, if not, then written informed consent from the LNOK will be required for all donations to proceed. Despite being on a registry of intent, written informed consent must be obtained prior to organ donation. ECMO will continue for at least four hours prior to organ procurement to afford an opportunity to assess

improvement in liver function (with serial enzyme testing) and receive additional serologic reports (e.g. NAT tests for HIV) (54). The deceased will be brought to the operating room for organ procurement within 4 hours of establishing ECMO.

UDCD Program Outcome Assessment

This program evaluation is comprised of two concurrent studies. The first study design is a one arm interventional trial with a convenience sample of patients following cardiac arrest who are declared dead outside the hospital setting and their families. The intervention is the new UDCD protocol as described with the goal of obtaining permission to preserve organ function for recently deceased patients following cardiac arrest so that an organ donation decision can be made by a family member (Figure 5). The second trial assesses the viability of the organs procured through the new UDCD program (Figure 6). Mixed methods will be used to evaluate the impact of the new UDCD program on organ donation, transplantations, and the outcomes of transplant recipients who receive the UDCD organs.

UDCD Community Recruitment

Organ preservation crew will collect clinical data pertaining to the deceased and will keep an online journal describing an account of interactions with the treating EMS team, NYPD, and the family of the deceased. The organ preservation crew EMTs will document clinical data on EMS run sheets and will also write ethnographic notes describing the family and EMS treating team responses to their presence at the scene. The FSS will collect study specific data and will also record an independent assessment of their interactions with family and the treating EMS team. All notes will be transcribed into a secure Internet environment for subsequent analysis.

Organ preservation crew will contact family who interface with the organ preservation crew two weeks after the day of death for a follow up telephone survey. Verbal consent for survey data collection will be obtained from participants. An organ preservation crew member (either FSS or EMT who did not have contact with the family) will ask semi structured qualitative questions about participant opinion of the organ preservation program and reaction to the organ preservation crew presence at the scene of the cardiac arrest.

Proposed questions include:

1) How would you describe the care your family member received from EMS?
2) How did you feel about being approached for organ preservation at that time?
3) Describe how the Organ Preservation Team treated you.
4) What is your opinion of the new Organ Preservation Program?
5) How might the new Organ Preservation Program be improved?
6) Please tell us anything else you would like to add about the new program?

Please tell us how much you agree with the following statements
(Disagree, Disagree Somewhat, Agree Somewhat, Agree):

7) I am satisfied with the care my family member received from EMS.
8) The organ preservation team respected my family.
9) The organ preservation team treated my loved one's body with respect.
10) I am satisfied with the new organ preservation program.
11) The new organ preservation program should continue.

Data from these conversations will be recorded using the online environment in the form of

journal notes, without any identifying information. Using standard qualitative analysis software, journal data will be organized into themes, theoretical constructs, and a thematic table will be presented to establish participant reaction to the new program. Likert scale data from the satisfaction questions will be presented in a frequency table. After each interaction with a potential donor family, an independent committee of experts will review the qualitative and quantitative responses and an overall impression of family reaction to the program will be coded as "unacceptable" or "acceptable" (see Data Safety Monitoring section). The UDCD study team members will also monitor secondary outcomes including any formal complaints issued to New York City agencies as well as press reports that cite interviews with family approached by the organ preservation crew.

Transplant Recipient Outcomes

We will track both immediate outcomes from transplantation of these UDCD grafts as well as long-term surrogates. The organ preservation crew will prospectively record data regarding total warm ischemic time, as well as hepatic function as measured by AST, ALT, and bilirubin concentrations (total and direct) at 30-minute intervals during the organ preservation process. We will also collect data on serum creatinine and urine output during this time period. Clinical outcome data for the UDCD organ recipients will be collected by the clinical transplant teams at the local centers, and be reported as de-identified data to the study group.

The immediate outcome data for kidney transplants will include the rate of primary non-function (defined as the requirement for dialysis at 90 days post-transplant), and delayed graft function (defined as the requirement for dialysis post-transplant). We will also collect serial serum creatinine concentrations at 1 week, 1 month, 3 months, 6 months, 9 months, and 1 year post-transplant, and report rates of biopsy proven acute rejection. We will also report patient and

graft survival rates at 1 year.

For the liver grafts, our primary endpoints will be rates of delayed graft function defined as any graft with an initial AST > 2,500 following transplantation. Primary non-function will be defined as those patients re-listed for a liver within 1 week post-transplant and who either receive a liver or die while awaiting re-transplantation. In addition we will collect data on AST, ALT, and total and direct bilirubin at 1 day, 1 week, 2 weeks, and 4 weeks post-transplant. We will also report overall graft and patient survival at 1 year. Finally, since biliary complications are recognized following DCD liver transplants, we will ask centers to report all biliary complications including, but not limited to, biliary (anastomotic) strictures, bile leaks, cholangitis, and ischemic cholangiopathy defined as diffuse intrahepatic strictures on cholangiography within 120 days of transplantation in the absence of vascular occlusion (Chan et al 2008). The clinical data will all be collected as part of standard post-transplant follow-up. No additional laboratory data will be collected solely for research purposes.

Data Safety Monitoring

The data safety monitoring board (DSMB) has been established and is comprised of an impartial committee of experts to monitor the UDCD pilot program. The committee includes experts from biostatistics and data safety monitoring, emergency medicine, transplant surgery, bioethics, and clergy disciplines (See Appendix B for a complete description of the DSMB proposal). An initial face-to-face meeting with the UDCD research team will occur to establish the monitoring process. Recruited experts will have no prior relationship with the UDCD investigative team. Experts will have experience with DSMB activities. Data will be evaluated for safety of the transplant recipients (clinical) as well as the psychosocial impact on family who interface with the organ preservation crew.

The clinical evaluation will proceed using the standard approaches of the OPOs and transplant community for transplant outcome assessment (e.g. rate of primary non-function, rejection short term, long term, and etc.). UDCD transplant recipient outcomes will be compared to randomly selected age, sex, and organ matched controls from the population of organ transplant recipients in the NYC demographic area. Two controls will prospectively be selected for each case, one receiving a CDCD organ and the other receiving an ND donor. Organs of interest will be kidneys and livers.

The psychosocial evaluation will proceed in the following manner. Organ preservation crew members will supply their journal notes and impressions of interactions with family at the scene of the cardiac arrest to the DSMB. The UDCD program also includes follow up phone calls to those approached and interfacing with the organ preservation crew for quality assurance monitoring. After two weeks, an organ preservation crew member (who did not have contact with the family) will contact the family to ask semi-qualitative questions about their opinions of the organ preservation program and their reaction to their presence at the scene of the cardiac arrest. For each interaction, the DSMB will review the data from the organ preservation crew journal notes and data obtained from these questions to provide a qualitative assessment as to whether the interaction was "unacceptable" or "acceptable." Decisions will be made after reviewing all the data from the survey as well as secondary outcomes including any formal complaints issued to city agencies as well as negative press that cite interviews with family approached by the organ preservation crew. A Bayesian stop rule will be used for quantitative evaluation of the qualitative data, with the quantitative score ("acceptable" or "unacceptable") as the coding scheme.

Data will be sent after each case to the data safety monitoring board for qualitative and

quantitative assessments. The online environment will notify DSMB members of any changes to the journal so that they will be informed immediately after the data are entered. The independent assessment will occur in a blinded fashion so that study team members have no influence over the assessment of their interactions and clinical outcomes.

Evidence Based Justification for Protocol Design

This protocol, as conceived by the stakeholders, aims to expand the pool of potential organ donors to include patients who die from sudden death outside of the traditional hospital setting. The protocol extrapolates what are tested practices of donation after cardiac death (DCD), preservation in the prehospital setting, and normothermic extracorporeal membrane oxygenation (ECMO) to continue organ preservation in the ED setting.

All of the above practices are employed for kidney transplantation. DCD organs have been used among the transplant community since 1996, and each year, their use grows steadily. (Punch, et al 2007). In 2005, 6.5% of all kidney transplants were performed with DCD organs. DCD organs are characterized by the Maastricht classification system which is based on the site of donor death. Maastricht class III refers to a timed withdrawal of support following cardiac death in a hospital setting. Because the timing of the withdrawal of support is determined by the physician, it has been termed "controlled" DCD (or CDCD) and was the first type of DCD used for transplantation. Over time, centers have begun to use Maastricht class II (patients who suffer cardiac death following unsuccessful resuscitation in the hospital) and class IV (those who suffer cardiac arrest after brain death) donors. Because these classes reflect unplanned cessation of cardiac function, they have been termed "uncontrolled" DCD (or UDCD), and yet in all of the above cases, the death occurs in a hospital setting. Maastricht class I donors are those who suffer a cardiac death outside of the hospital.

DCD kidneys, from the time of their initial use, were noted to have higher rates of delayed graft function (DGF) and primary non-function (PNF). Both of these outcomes are thought to result from increasing degrees of ischemia/reperfusion injury. When CDCD kidneys are perfused with preservation solution at 4C°, 60% of transplant recipients exhibit DGF and 2% of them havePNF (Farney et al, 2008). Recipients of UDCD kidneys show similar DGF rates but PNF rates have been reported as high as 22% (Valero et al, 2000).

The high DGF and PNF rates have already spurred research into alternative methods of preservation to reduce this ischemia/reperfusion injury. Specifically, the preservation of the organs with cold oxygenated blood via ECMO and most recently 37C° (normothermic) ECMO are already studied. In particular, several centers have reported that normothermic ECMO has dramatically improved both DGF and PNF rates (down to 0% for PNF and 9% for DGF) under both CDCD and UDCD conditions (Valero et al, 2000; Farney et al, 2008; Magliocca et al, 2005).

Prehospital donation has been previously attempted as well. Light et al (1997) reported the results of the Washington D.C. experience with Maastricht class I uncontrolled DCD kidneys preserved with cold preservation using abdominal perfusion in a manner similar to peritoneal dialysis. The study group transplanted 23 kidneys from these donors noting high rates of DGF (76.2%) and PNF (8.7%) with these kidneys, but comparable serum creatinine concentrations at 1 year - an established surrogate for long-term graft survival (Light, et al 1997). More recently, the Hospital Clinico San Carlos in Madrid, Spain reported the results of a more extensive program for DCD donors. Among the 342 DCD kidneys transplanted at this center, as of 2004, 273 kidneys were from Maastricht class I donors. The organs were preserved using cold ECMO perfusion (Sanchez-Fructuoso et al, 2006). Their reported DGF rate was 60.9% with a PNF rate

of 4.4%. The complication rates from both Light et al. and Sanchez-Fructuoso et al. are noteworthy in that they are comparable to rates reported at centers using more conventional DCD strategies (Maastricht class II, III, and IV donors) despite using inferior perfusion methods (Valero et al, 2000; Koyama et al, 1997; Ko et al, 2000; Lee et al, 2005).

With this empirical evidence, our experts suggested that the protocol combine the use of normothermic ECMO, which has yielded the lowest complication rates, with the use of Maastricht class I donors in order to improve preservation success and expand the donor pool to fill the growing need for kidneys. Based on the above studies, our study design is expected to yield similar rates of DGF and PNF to those centers that have employed normothermic ECMO on in-hospital UDCD donors.

Liver transplantation has been slower to embrace the use of DCD organs for transplantation. DCD livers make up a smaller percentage of total organs transplanted than do DCD kidneys (Selck et al, 2008). They have demonstrated similar problems related to ischemia/reperfusion injury (Foley et al, 2005). In liver transplants, these ischemic complications manifest themselves as increased rates of biliary complications, hepatic artery thrombosis, and primary non-function. In particular, the risk of ischemic cholangiopathy has been significantly higher (13.7% vs 1%) in a single center evaluation (Chan et al, 2008). Evaluating the overall impact on graft and patient survival has been more difficult. While some studies have shown similar graft survival rates despite increased complications (Chan et al, 2008), there is increasing evidence showing that patients' long term survival is lower (57%) with DCD livers than patients who receive standard ND livers (74%) (Selck et al, 2008).

Nevertheless, DCD livers continue to be used in this country in limited cases. In an effort to ameliorate the reported complications, the use of normothermic ECMO for liver transplantation

is now under investigation although the data is more limited than the experience with kidneys. Normothermic ECMO has been used on a small scale at the University of Michigan, with no PNF reported among 8 grafts transplanted (Magliocca et al, 2005). In Spain, Fondevila and his colleagues reported similar results using DCD livers preserved with normothermic ECMO. ECMO is not only used for its preservative properties, it also enables serial measurement of aminotransferase concentrations to better assess the viability of livers prior to organ transplantation. By setting strict criteria for aminotransferase concentrations (both baseline and percent change), Fondevila et al (2007) identified 10 of 40 livers that were acceptable for transplantation. While the number of acceptable grafts has been reduced, results have shown only 1 of 10 grafts with PNF and similarly only 1 of 10 grafts having biliary complications. Long term survival was 70% for normothermic ECMO DCD liver patients and 2 year graft survival was 50%, much higher than the 16% graft survival reported with prior attempts at DCD liver transplantation that did not use normothermic ECMO (Fondevila et al, 2007).

APPENDIX A - Approach to Family of the Deceased

Upon entering the scene, the organ preservation crew will introduce themselves to the NYPD personnel (if present) and the treating EMS providers, explaining their roles and how their assistance may be needed. The treating EMS providers will briefly provide the organ preservation crew with all of the following available information: the deceased's name, time of death, next-of-kin family (or SIFM) information and family dynamics. In addition, the treating EMS providers will answer specific clinical screening questions developed to ascertain initial medical suitability of the potential donor. The treating EMS providers will remain at the scene and wait for the outcome of the discussion between the organ preservation crew and the LNOK/SIFM, which will not exceed 20 minutes from the time of pronouncement. If permission for preservation is obtained, the treating EMS providers may assist with transporting the deceased to the OPV if required; the organ preservation FSS priorities are to obtain permissions for preservation, communicate with the Bellevue Hospital ED, and coordinate with the NYODN personnel including the activation of the on call perfusionist. The organ preservation FSS will not assist with transport of the deceased to the OPV. As soon as the name and identifying information of the deceased are acquired, the organ preservation FSS will send the information via electronic message to the NYODN Donor Center to ascertain donor registry status.

FSS Introduction/Assessment

The organ preservation FSS will introduce him/herself to family or another appropriate person at the scene by presenting the FSS title and association with the NYODN. The FSS will then offer condolences. The following sample script will be used.

"Mrs. Smith, I am very sorry for your loss and want to extend my deepest, sincerest condolences to you."

The FSS will then ask the person at the scene if he/she is a family member of the deceased. If the person at scene is a Legal Next of Kin (LNOK) or Self-Identified Family Member (SIFM), then the FSS will reaffirm that the LNOK/SIFM understands what has occurred. The FSS will ask the LNOK/SIFM if there are any questions about the situation, acknowledging that this is a difficult time for the LNOK/SIFM. When appropriate, the FSS will explain that the deceased may have the opportunity to save a life through organ donation. The FSS will request permission from the LNOK/SIFM to proceed with steps for initial preservation procedures at the scene, in the OPV, and for the transport to the Bellevue Hospital ED to allow the LNOK time to consider donation.

If the LNOK/SIFM agrees, the FSS will thank the LNOK/SIFM reiterating the individual's agreement to ensure that the verbal permission for preservation is witnessed. The FSS will explain the preservation procedures. The FSS will continue to support the LNOK/SIFM and complete the preliminary medical/social history questionnaire to determine initial suitability. The FSS will provide continuous support to the family and LNOK/SIFM on-site, on the way to, and at the receiving hospital, as necessary and appropriate. The FSS will attempt to obtain permission for ECMO (femoral cannulation) from the LNOK/SIFM and later, for written informed consent for donation by the LNOK.

If the LNOK/SIFM does not initially grant permission, the FSS will re-approach the LNOK/SIFM when appropriate, to ensure understanding of this unique opportunity and restate that granting permission for preservation does not mean that the LNOK/SIFM is agreeing to organ donation. The FSS will reinforce that the decision to preserve the organs can be discontinued at any time.

The FSS will clarify that for organ donation to take place, the LNOK must sign a consent form. The FSS may also clarify any misconceptions or concerns about organ donation (e.g., unfairness of the allocation process, religious concerns, disfigurement, lack of trust, and etc.). In the case of evidence of consent to donation by the potential donor, the FSS will ensure that the LNOK/SIFM understands that the deceased had previously expressed the wish to donate. If the LNOK/SIFM continues to refuse permission, the FSS will respect this wish and acknowledge the LNOK/SIFM's decision. The FSS will offer a pamphlet with practical guidance on what things need to be done when someone dies (the *After Death Has Occurred* brochure).

If the person at the scene is an unrelated bystander, the FSS will ascertain the bystander's relationship to patient, identify him/herself as being from the NYODN, and request contact information for the deceased underscoring the importance of reaching the family as soon as possible. When the bystander provides contact information, the FSS will work with the NYPD to assist with the contact and facilitate the NYPD effort to inform the family/LNOK of the death and will proceed with the approach for obtaining permission for preservation. The FSS will not be the person informing the family of the death; such notification will remain the role of the NYPD. In the case of evidenced prior consent to donation by the deceased (e.g. registry of consent or intent confirmation), the FSS will inform the bystander of the deceased's wish to donate and, if appropriate, will explain the function of initial preservation. If the bystander objects to providing contact information, the FSS will explain the importance and consequence of the bystander's decision. The FSS will state that the patient is dead and the family is entitled to be offered the opportunity to preserve the organs so that the LNOK can make a decision about donation. The bystander will be told that lives that can be saved by giving the LNOK the opportunity to make the decision that the LNOK is legally entitled to make. The bystander must be informed that time is of the essence, and that the decision to obstruct the preservation measures will deprive the family of the opportunity to consider donating the deceased's organs, if so desired.

In cases where there is a bystander present, if the LNOK/SIFM may only be contacted by telephone, the FSS will work with the NYPD personnel on site for notification of the death. Once the person contacted is identified as a family member, the NYPD officers at the scene will inform the LNOK/SIFM of the death. The FSS will have provided the police department with the appropriate language for introducing the FSS. The FSS will provide the same information as outlined in the *Preservation Process Explanation* section. When the LNOK/SIFM grants permission for preservation, the FSS will inform the LNOK/SIFM that his/her agreement to preservation will be documented and will then ask permission for the initial steps for preservation. If the LNOK is not present at the scene and permission for preservation is not obtained from the LNOK/SIFM, the FSS will request LNOK contact information. The FSS will work with the NYPD to contact and inform the LNOK of the death. The LNOK will be appropriately introduced by the NYPD officers at the scene to the FSS, who will inform the LNOK of the approach to organ preservation, and how this act will preserve the LNOK's opportunity to donate. The FSS will record the telephonic consent or arrange to meet the LNOK at Bellevue Hospital, as appropriate.

If the cardiac arrest occurs without any bystander or family present, the FSS will investigate if the deceased had expressed his or her wish to donate. The FSS will review the driver's license of the deceased to see if the desire to donate is indicated on it and will use the name and date of birth to search the New York State Organ Donor Registry of Consent and Intent. In the case of evidenced consent to donation by the deceased, the FSS will work with the NYPD to locate and notify family while preservation commences. When family is not available at the time of death and the FSS has not found any evidence that the individual has consented to organ donation, no attempt at organ preservation will be initiated, and the usual protocol for those who

die outside the hospital is initiated. In this case, care of the deceased is transferred to the NYPD.

Preservation Process Explanation

The FSS will first explain the human need for organs, this unique opportunity to donate, and the time constraints inherent in the UDCD process. The following is sample language for the FSS to use.

> *Mrs. Smith, again I am so sorry for your loss and for what may seem like a rushed process, but in a situation like this we don't have lots of time. When someone has a cardiac arrest, there is a limited amount of time during which the organs can be used for transplantation. I wonder if you and your [deceased's relationship to person, e.g. husband] ever discussed the idea of donating organs at the time of death? I know that often this is not a conversation that families have and previously, individuals who died outside the hospital, like your loved one, were not able to donate their organs, but there are over 100,000 people on the organ recipient list who are waiting for a donated organ. Everyday people die because there are not enough organs to go around. In this part of NYC alone there are _____ (get current stats for the day for area zip code) people waiting for organs. You and your [e.g. husband] have a unique opportunity to save lives that many families do not.*

If there is evidence that the potential donor has consented to donation either by reviewing a driver's license or by FSS confirmation that the deceased is on the NY State Organ Donor Registry (of intent/consent), the LNOK/SIFM will be informed of the patient's decision followed

by the *Preservation Process* explanation. A notification form will also be presented for signature, as well as a medical/social history questionnaire (if the SIFM is an appropriate source and in the absence of a LNOK). The LNOK/SIFM will be offered the opportunity to travel to the hospital as outlined in the *Preservation Process Explanation* section. The following is sample language for this instance.

> *Mrs. Smith, your [e.g. husband] wanted to save lives. We know this because [e.g. Mr. Smith] consented to donation on (provide date when patient registered). On that day [Mr. Smith] signed up with the state donor registry. I'm here to help you carry out your [husband's] wish to save lives.*

The FSS will then explain the benefits of donation to donor families, that preservation may be discontinued at any time, but allows time to make a definitive decision. The FSS will also inform the family that the deceased will be transported to the Bellevue Hospital ED, and offers support. The following is sample language.

> *Organ donation has helped thousands of families during their grief...to know that something positive can result from your loss. I realize this may not be something you wish to discuss right now in your period of grief but to preserve this opportunity and to allow you to consider it a bit later, the organ preservation team will need to take necessary measures to assure that your [husband's] organs are preserved in case you choose to donate them later.*

The FSS will then explain what would take place during preservation. The following is sample language.

We would like to give you some time to think and grieve so with your permission, the Preservation Team would like to do two things that will allow the organs in your [husband's] body to be preserved until you can think about this a little more and make a thoughtful decision. To preserve your opportunity and have the time to consider donation, we will need to again artificially administer oxygen to your loved one's body and into his organs.

Here, we will do basic things:

1. *To protect the organs, we administer heparin, a drug that prevents blood clots from forming inside vessels, and a thrombolytic medication that breaks up existing blood clots.*
2. *We will do manual chest compressions to circulate the heparin and thrombolytic medications.*
3. *We will transport your loved one's body to the vehicle, and with your permission, we will apply a device which will administer chest compressions to circulate the blood throughout the organs and tissues to keep them in good condition.*
4. *We will also attach a ventilator machine to the tube in his throat to give oxygen to the organs.*
5. *We will then transport your loved one's body to the Bellevue Hospital Emergency Department to continue the preservation.*

We are very sorry that nothing we can do will restore life to your loved one. These efforts are solely intended to preserve the organs in his/her body for a time, so you will have the choice of donating if you so choose or to realize your

[husband's] previous wish if that was [his] and or your desire. May we begin to preserve this opportunity for you? No organs will be removed until you (if speaking to the LNOK) agree and sign consent. These measures can be stopped at any time, but not beginning now means this opportunity will be lost.

After the LNOK/SIFM provides explicit permission for the initial preservation measures, the FSS will obtain explicit permission for the placement of the large groin intravenous and intraarterial catheters and initiation of ECMO upon arriving at the Bellevue Hospital ED. The following is sample language.

Thank you for giving us permission to preserve your [husband's] organs and for the opportunity to save lives. As I mentioned before, [Mr. Smith's] body will be taken to the Bellevue Hospital Emergency Department in the Organ Preservation Vehicle. As promised, we will not be moving forward with organ donation until you (if the LNOK or the LNOK) give us written informed consent. At this time, however, we need your approval to continue organ preservation. To do this, we will put two large intravenous and intraarterial catheters into your [husband's] groin, so that we may connect his or her body to a machine to keep oxygenated blood circulating through the body; in this way, the function of the organs can be maintained for up to six hours while you make your decision and we determine that your Gift of Life will be able to be used by someone through transplantation.

Do we have your permission to connect [Mr. Smith's] body to this machine upon arrival to Bellevue Hospital?

After the LNOK/SIFM provides explicit permission for ECMO, the FSS provides guidance on the next steps. The following is sample language.

Mrs. Smith, again, I'm so sorry for your loss. I thank you for allowing me the time to present you with this unique opportunity and your willingness to consider saving a life. I invite you to travel with us to Bellevue Hospital so we can complete the consent forms and medical/social history while the Organ Preservation Team continues preservation of the organs. Mrs. Smith, your permission for preservation may be withdrawn at any time. I know this seems rushed, and I apologize for that, but you (if the LNOK) have five hours to make the decision that can save lives.

Consent for Donation Process

Once the LNOK has agreed to donation, the FSS obtains written informed consent and completes the medical/social history questionnaire. The following is sample language.

Mrs. Smith, thank you for thinking of others at such a tragic time. We will do everything in our power to make sure that [Mr. Smith's] gift is able to save a life. To proceed, I will need to read you the consent form and have you sign it. I (or my colleague) will have to also ask you a series of questions related to [Mr. Smith's] medical and social history. This will allow us to better assess the suitability of the organs for transplantation. We will not be able to proceed with donation until this paperwork is completed. Mrs. Smith, thank you for your generosity. Let's begin with the consent form.

The FSS will then read the consent form to the LNOK and obtain the signature. The medical/social history questionnaire may be completed at this time. Note that the medical/social history questionnaire may be completed prior to obtaining written informed consent for donation.

The FSS will then explain to the LNOK the next steps, outlining the possible time frame, that the procurement will take place in the operating room, establishing how the progress will be communicated, and offering guidance and/or assistance with funeral arrangements. The FSS will also provide appropriate literature and information on NYODN Donor Family Services that support family of donors, as well as a "memory box" to the family, as is customary for all deceased donations.

APPENDIX B - Structure and Function of an Independent Data and Safety Monitoring Board (DSMB) to Oversee the New York City Protocol for Uncontrolled Donation after Cardiac Death (UDCD)

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Introduction

The New York City protocol for uncontrolled donation after cardiac death (UDCD) is intended to increase the opportunities for the preservation and ultimate transplantation of organs from patients who had suffered out-of-hospital cardiac arrest and died in the field. While the protocol raises a number of issues involving logistics, ethics, medical care, psychological impact, and public perception, it holds the prospect for saving a substantial number of lives and decreasing the ongoing suffering among those on waiting lists for organ transplantation.

The program will be evaluated using two concurrent substudies. The first substudy will assess the feasibility, success, and impact of obtaining permission to preserve organ function from the families of recently-deceased victims of cardiac arrest. The second substudy will assess the viability of transplanted organs procured through this process. Despite the soundness of the medical and scientific basis for the proposed protocol, there is a substantial risk associated with its implementation, including public misconception, the generation of ill will, and the creation of additional emotional distress among family members. Thus, the investigators involved in the design and implementation of the protocol have proposed the formation of an independent data and safety monitoring board (DSMB) to monitor the program. The DSMB will be charged with evaluating the medical effectiveness and safety of the associated transplants, as well as the psychological and social impact of the program on involved families.

Addressing the clinical effectiveness of the program is relatively straightforward, as there are established measures of success rates and benchmarks for organ transplantation. Optimal methods for assessing the psychological and social impact of the program are less clear. Family members will be interviewed at a suitable time after interaction with the organ preservation vehicle (OPV) teams and will be asked to rate their interactions and experiences. Family members will also be asked about the effects of the program on their experience with their family member's death.

While the DSMB will be given substantial latitude in interpreting the accumulating clinical, psychological, and other data, a Bayesian analysis will be used to guide DSMB deliberations, providing an ongoing assessment of the probability that the fraction of family members experiencing unacceptable interactions or subsequent negative reactions to the protocol exceed a predetermined threshold. The specifics of the threshold used for the stopping boundary and the associated statistical characteristics of the stopping rule will be determined during collaborative meetings between DSMB members, including a statistical expert on the DSMB, and the protocol investigators.

In preparing a suggested DSMB structure and budget, it has been assumed the DSMB will include ethical, biostatistical, emergency medicine, and organ transplantation expertise; will

meet face-to-face annually with protocol investigators and in closed session; and that other interactions will occur by teleconference or electronic mail.

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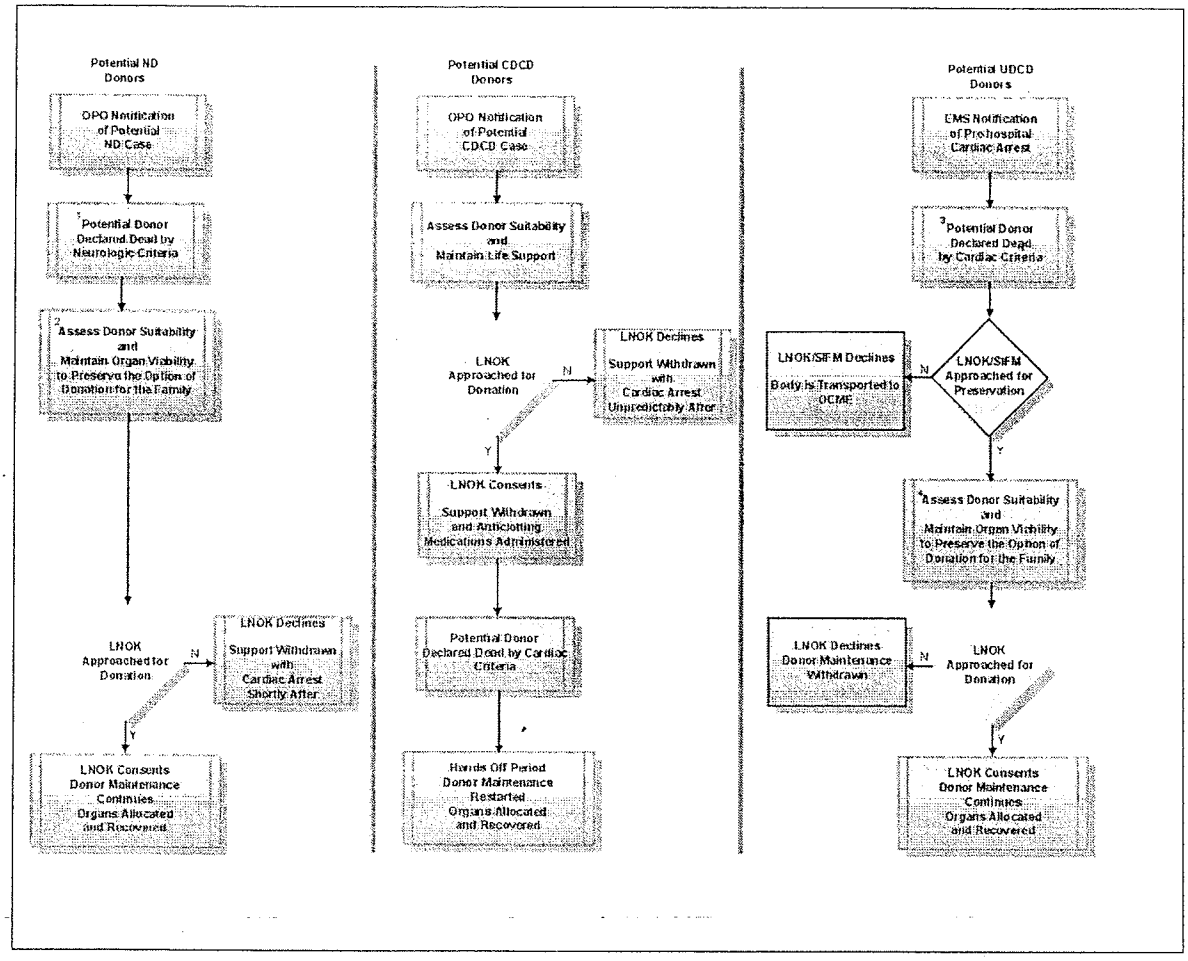
Figure 1 – Context of UDCD Program



Boxes with vertical borders indicate pre-defined processes. Boxes without vertical borders are new processes. Diamonds indicate decision points.

[1]Neurologic death indicates the cessation of all brain activity. This is generally confirmed with two independent and sequential physical examinations conducted by two physicians six hours apart and a failed apnea test. Official time of death is the time of the second examination.

[2]Measures to assess and maintain the donor include: 1) establishment of central venous and arterial lines, 2) administration of vasoactive and anti-diuretic medications as needed, 3) testing for Infectious diseases.

[3]EMS paramedics resuscitate until the OLMC physician establishes time of death according to pre-established protocols.

[4]After death is declared in the field, the treating EMS providers transfer the care of the deceased to the organ preservation crew. Measures to assess and maintain potential donor organs include: 1) Heparin and thrombolytic medication administration, 2) Establishment of large femoral venous and arterial cannulae appropriate for ECMO, 3) Placement of an occlusion balloon inserted through the femoral artery to be placed in the abdominal aorta just above the level of the diaphragm.

Figure 2 – Coalition of Partners for the UDCD Program

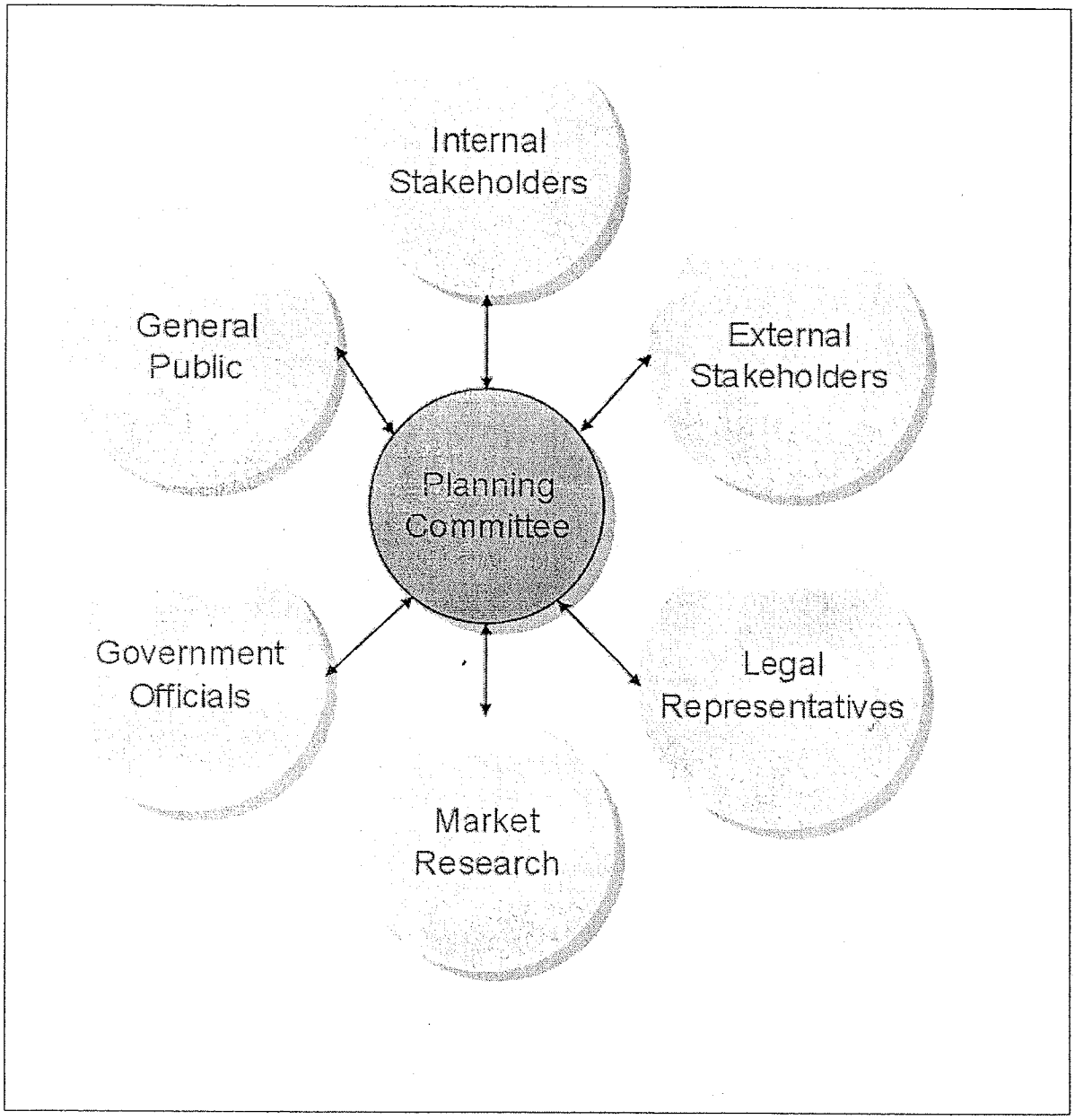
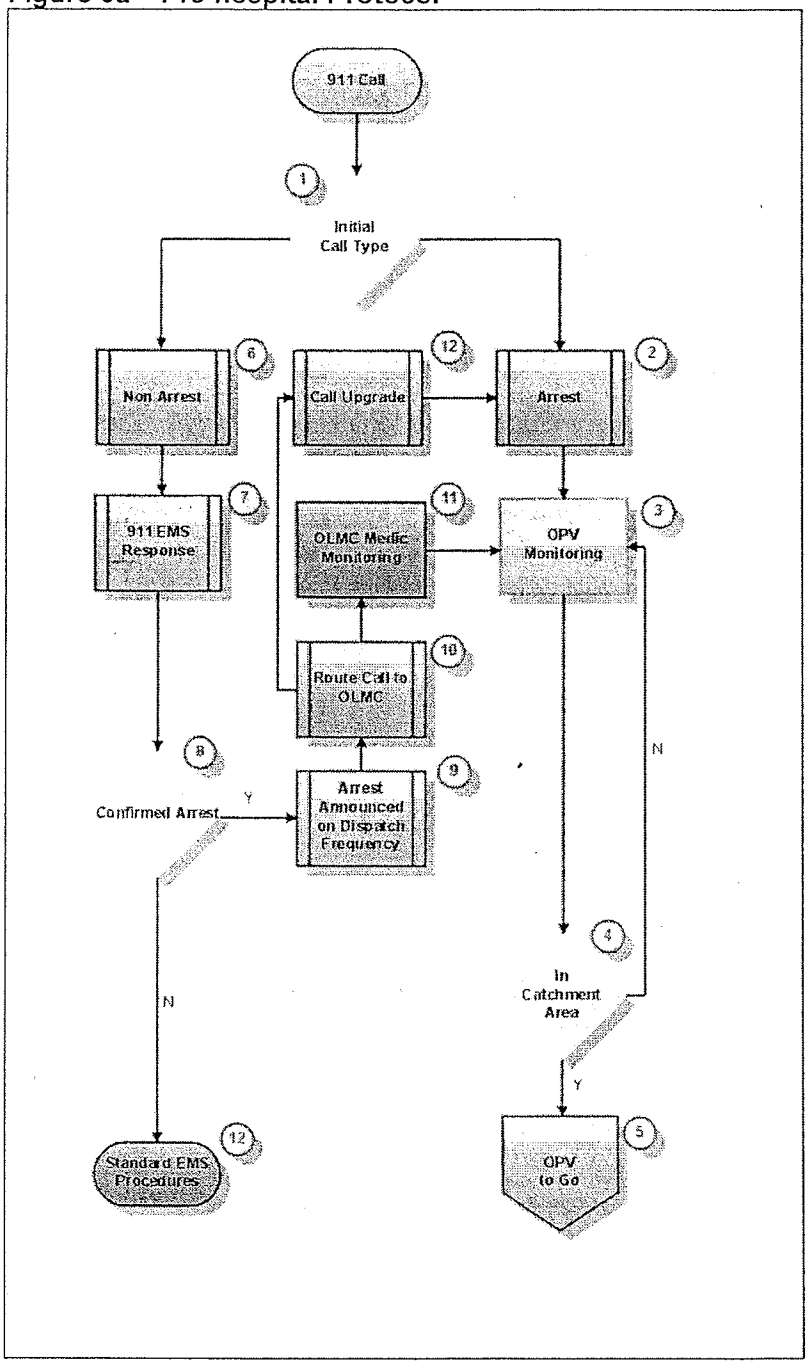
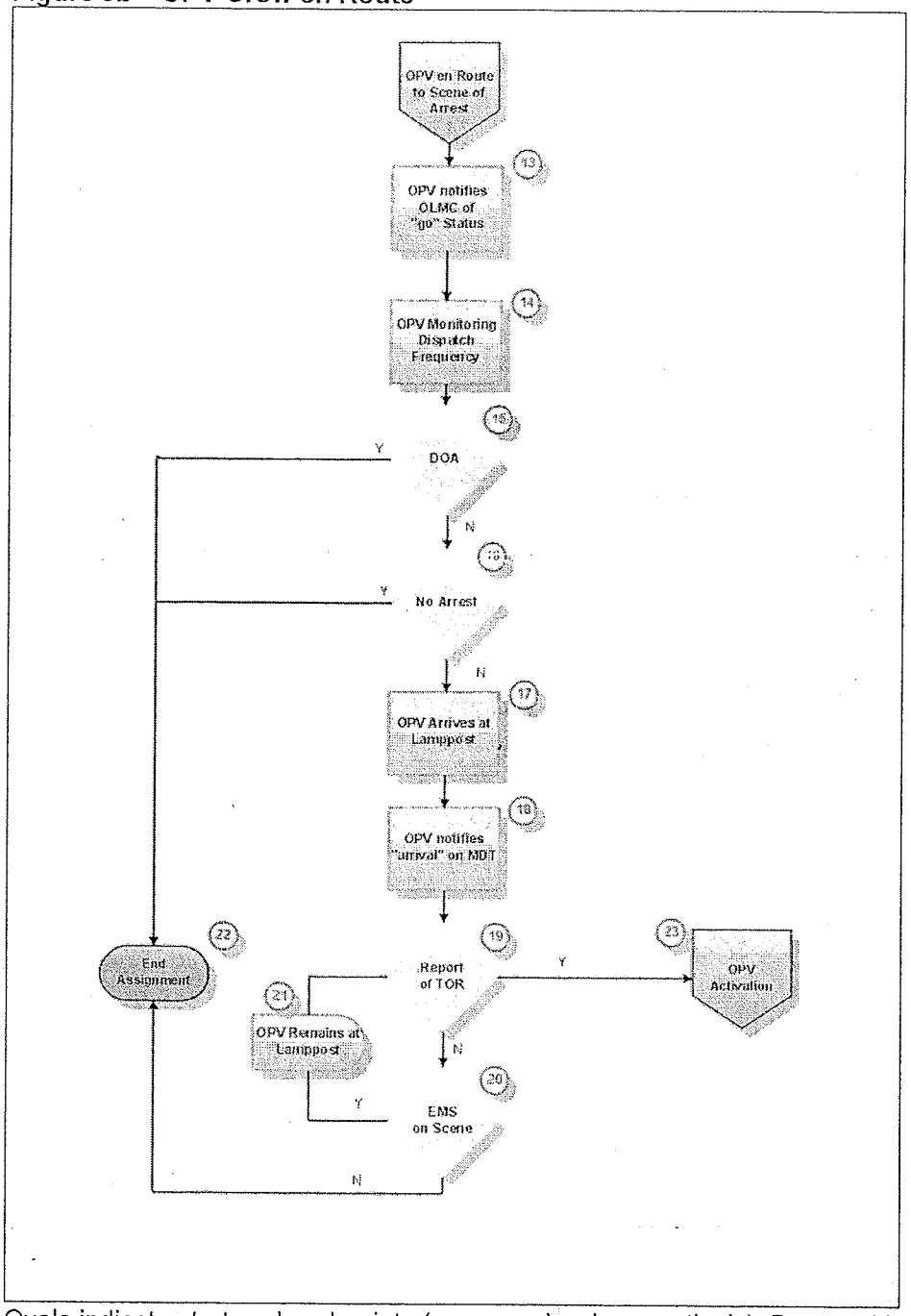


Figure 3a – Pre-hospital Protocol



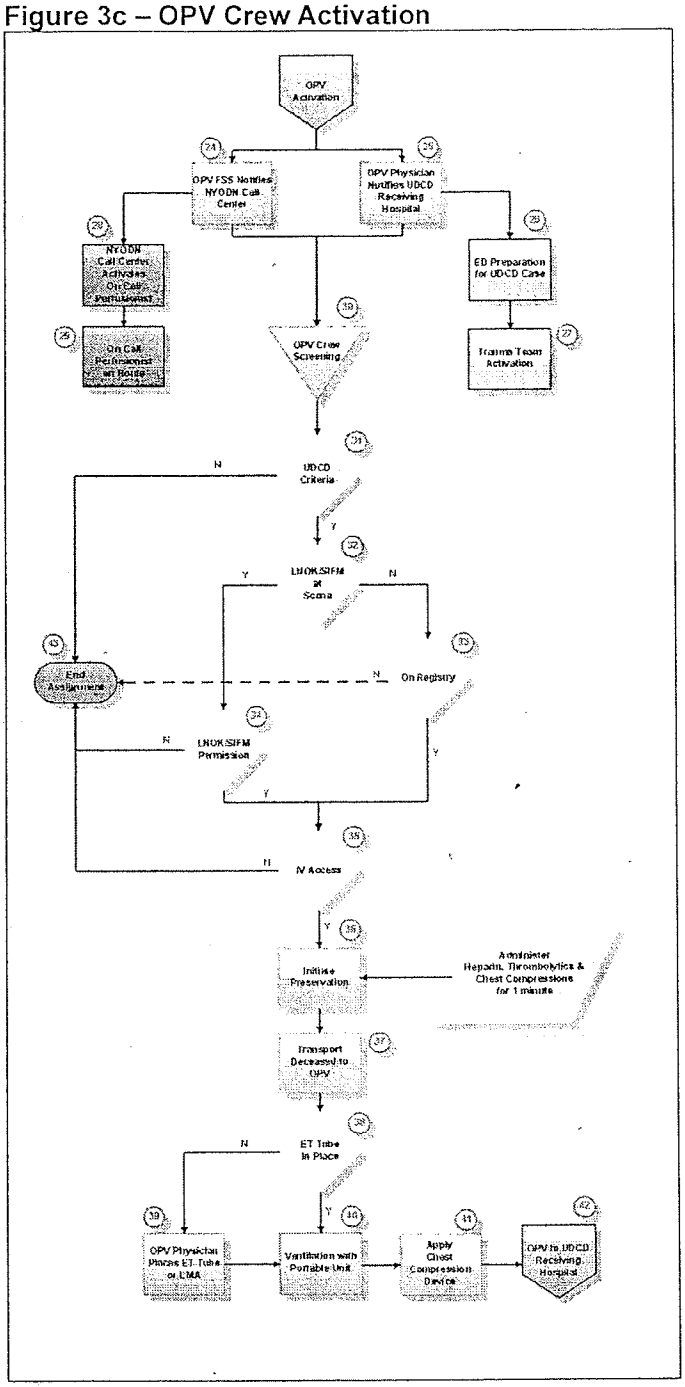
Ovals indicate start and end points (green and red respectively). Boxes with vertical borders indicate pre-defined processes. Boxes without vertical borders are new processes. Diamonds indicate decision points. A pentagon indicates a continuation to the next figure.
Pink indicates EMS dispatch, blue is for the treating EMS team, purple is for the OLMC, and orange is for the OPV crew.

Figure 3b – OPV Crew en Route



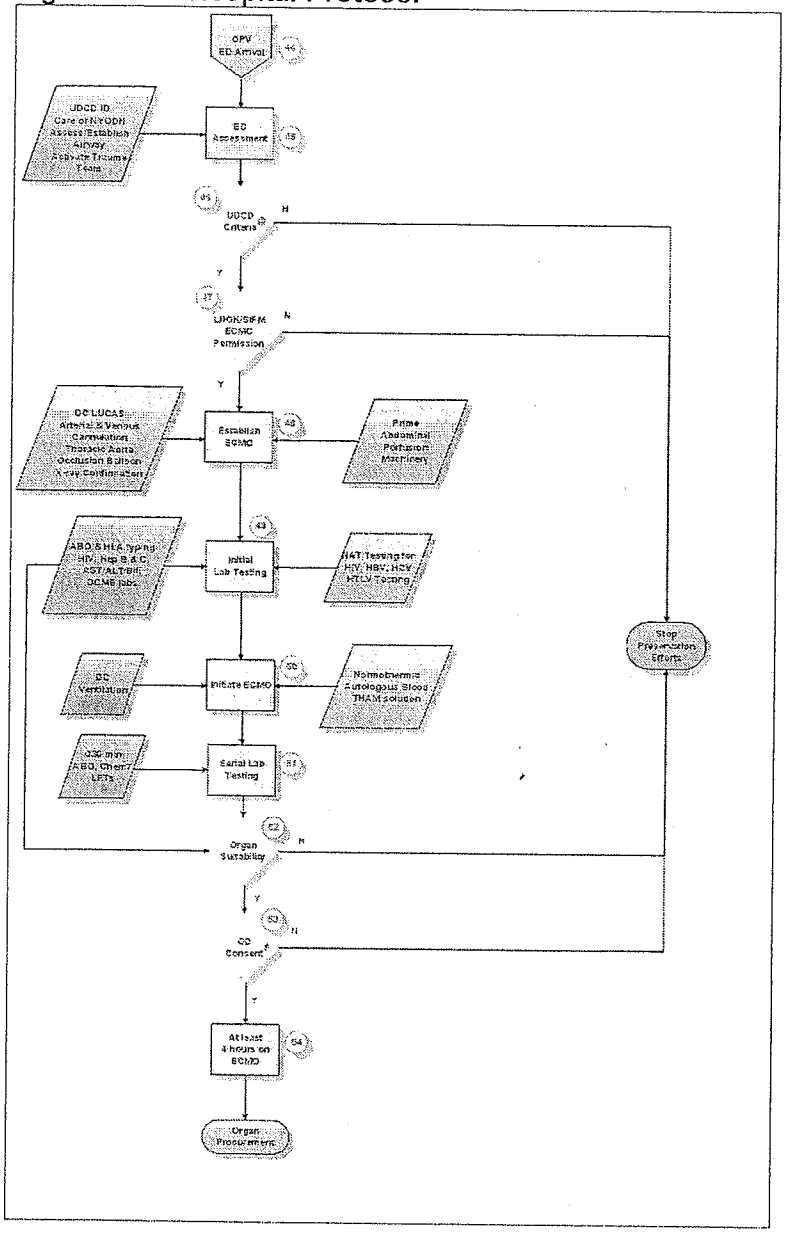
Ovals indicate start and end points (green and red respectively). Boxes with vertical borders indicate pre-defined processes. Boxes without vertical borders are new processes. Diamonds indicate decision points. A truncated oval indicates a planned delay. A pentagon indicates a continuation to the next figure.
Orange is for the OPV crew.

Figure 3c – OPV Crew Activation



Ovals indicate start and end points (green and red respectively). Boxes with vertical borders indicate pre-defined processes. Boxes without vertical borders are new processes. Diamonds indicate decision points. A triangle indicates a merge. A pentagon indicates a continuation from the previous figure or to the next figure (3a & 3c respectively). Brown indicates NYODN Call Center, grey is for the ED UDCD team, and orange is for the OPV crew.

Figure 4 – In Hospital Protocol



[@]UDCD Exclusion Criteria include: 1) Age > 60, 2) unknown downtime or initial rhythm of asystole, 3) CPR started > 15 mins from the CA, 4) evidence of foul play, IVDU, serious injury to chest or abdomen, limb amputations, jaundice, dialysis access, or 5) inadequate IV or IO access.

[#]OD Consent will be obtained from the LNOK or verified in a registry of consent within 4 hours of initiating ECMO.

Ovals indicate start and end points (green and red respectively). Boxes without vertical borders are new processes. Diamonds indicate decision points. A pentagon indicates a continuation from the previous figure (3b).

Magenta is for ED clerical staff, tan indicates NYODN perfusionist role, grey is for the processes occurring in the ED, and aqua is for the trauma team.

Figure 5 – UDCD Recruitment Quality Assurance Study

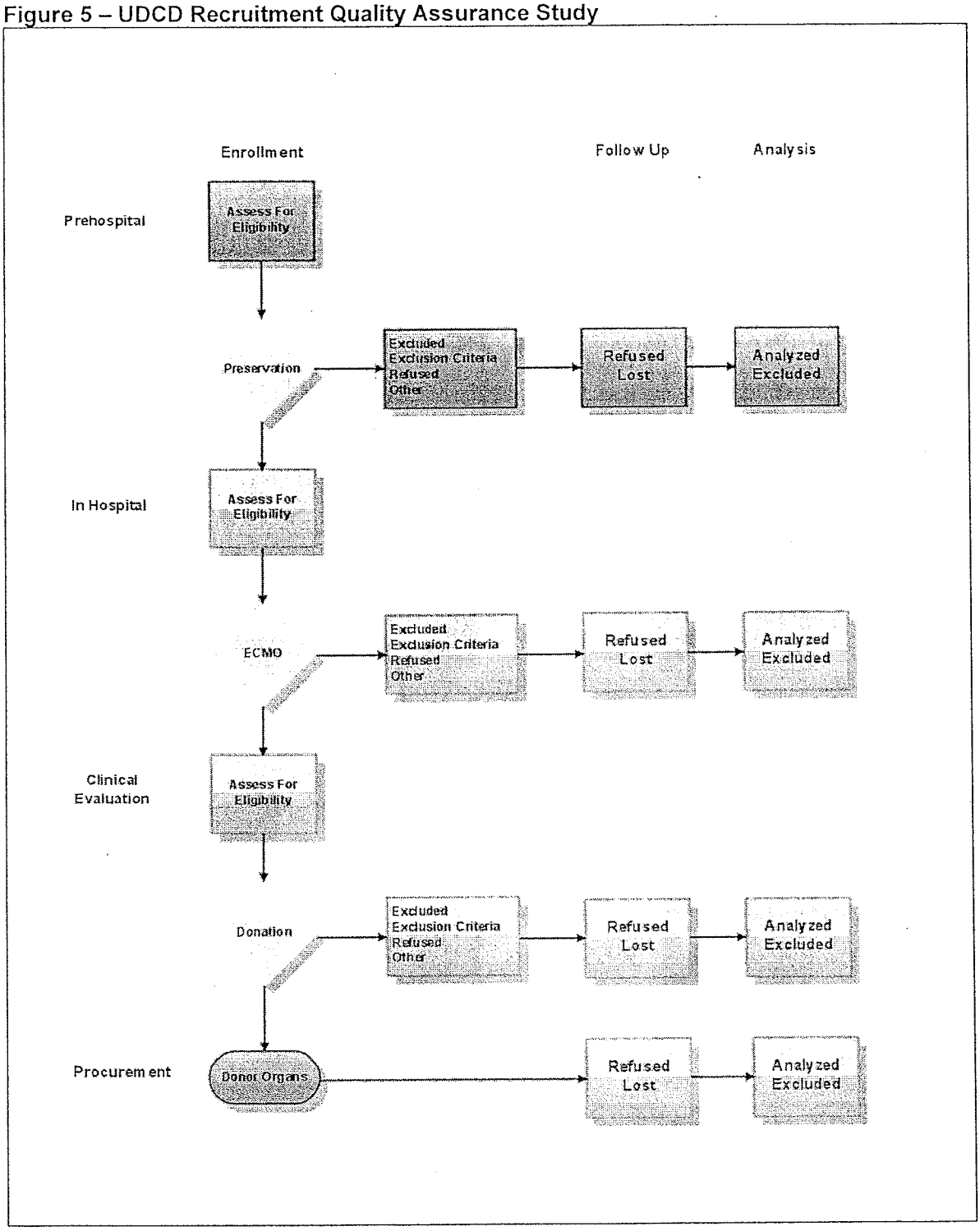


Figure 6 - UDCD Clinical Outcomes Study