PMI
A-3367-01

ANIMAL WELFARE ASSURANCE
in accordance with the PHS Policy for
Humane Care and Use of Laboratory Animals

I, **Jorge L. Garcia, DVM** has named Institutional Official for animal care and use at **PMI**, hereinafter referred to as Institution, by means of this document, provide assurance that this Institution will comply with the Public Health Service Policy on Humane Care and Use of Laboratory Animals, hereinafter referred to as PHS Policy.

I. APPLICABILITY OF ASSURANCE

A. The following are branches and components over which this Institution has legal authority, included are those that operate under a different name:

PMI As the primary institution, PMI is included in this section.

B. The following are other institution(s), or branches and components of another institution:

None

This Assurance applies whenever this Institution conducts the following activities: all research, research training, experimentation, biological testing, and related activities involving live vertebrate animals supported by the PHS. This Assurance covers only those facilities and components listed below.

II. INSTITUTIONAL COMMITMENT

A. This Institution will comply with all applicable provisions of the Animal Welfare Act and other Federal statutes and regulations relating to animals.

B. This Institution is guided by the "U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training."

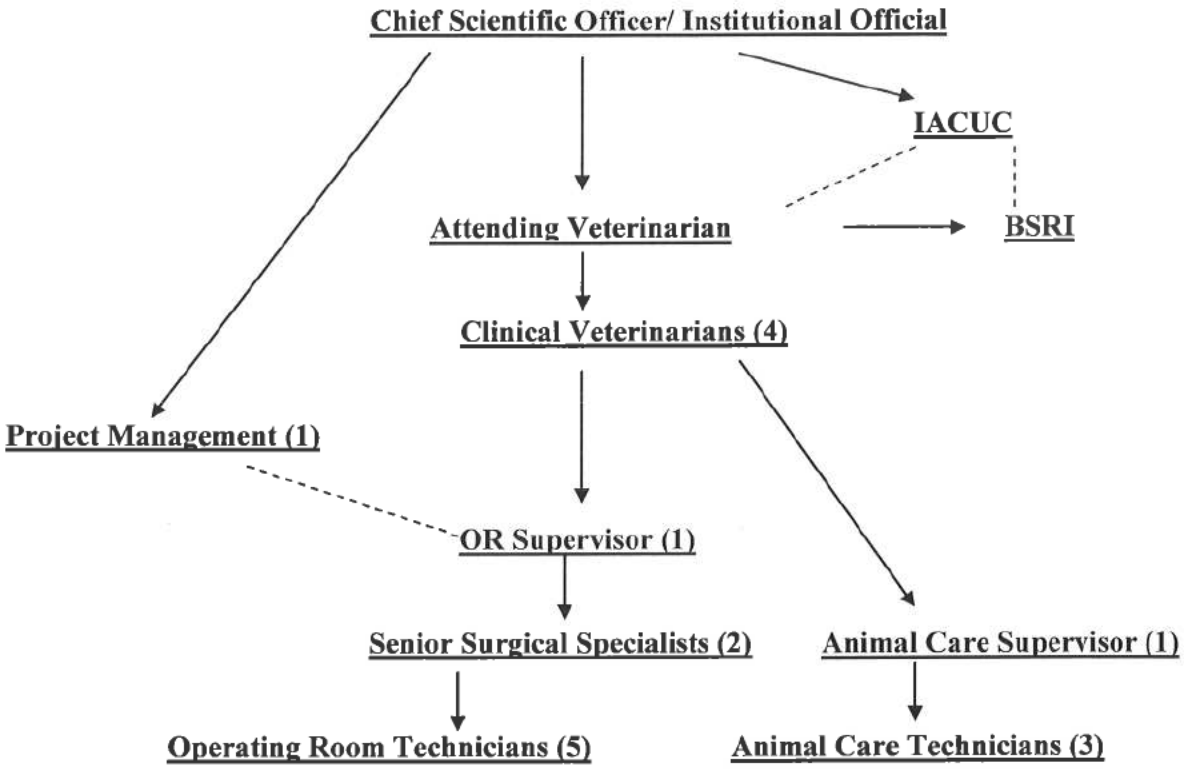
C. This Institution acknowledges and accepts responsibility for the care and use of animals involved in activities covered by this Assurance. As partial fulfillment of this responsibility, this Institution will ensure that all individuals involved in the care and use of laboratory animals understand their individual and collective responsibilities for compliance with this Assurance, as well as all other applicable laws and regulations pertaining to animal care and use.

D. This Institution has established and will maintain a program for activities involving animals in accordance with the "Guide for the Care and Use of Laboratory Animals" ("Guide").

E. This Institution agrees to ensure that all performance sites engaged in activities involving live vertebrate animals under consortium (sub award) or subcontract agreements have an Animal Welfare Assurance and that the activities have Institutional Animal Care and Use Committee (IACUC) approval.

III. INSTITUTIONAL PROGRAM FOR ANIMAL CARE AND USE

A. The lines of authority and responsibility for administering the program and ensuring compliance with this Policy are as follows:



The Institutional Official and IACUC have the authority and responsibility for Blood Systems Research Institute's (BSRI) animal care and use program. Dr. Currie has overall authority as described in page 4 of 26 of the Assurance application.

B. The qualifications, authority, and percent of time contributed by the veterinarian(s) who will participate in the program are as follows:

PMI

SARAH CURRIE, DVM, Senior Clinical Veterinarian
Interim Attending Veterinarian

Qualifications:

- Dr. Currie is a graduate of School of Veterinary Medicine, Oklahoma State University. Dr. Currie serves as the Attending Veterinarian. In this role, she is directly responsible for the overall care of animals. She leads and supervises a diverse range of studies for medical device research, reviews and approves protocols, manages the flow of operating rooms and provides consultation and expertise to clients.

- Dr. Currie has been in a private practice prior to joining the PMI veterinary team and has excellent surgical expertise in a wide variety of animals.

Authority: Dr. Currie has the overall direct program authority and responsibility for the Institution's animal care and use program which include management of OR technicians and research projects and serves as a study director on multiple protocols. If she serves as a Study Director, (b) (6) assumes the role of acting attending veterinarian. At PMI, Dr. Currie provides surgical and technical expertise and training for investigative clientele. She shares primary responsibility for clinical and surgical services, as well as supervisory responsibilities and training for the technical and animal care staff. Dr. Currie has access to all animals in the program. Dr. Currie has the same authority as an employee of the Institution, therefore, has delegated authority by virtue of position.

Time Contributed to Program: Employee, 50%

(b) (6)

(b) (6)

C. The Institutional Animal Care and Use Committee (IACUC) at this Institution is properly appointed in accordance with the PHS Policy IV.A.3.a and is qualified through the experience and expertise of its members to oversee the Institution's animal care and use program and facilities. The IACUC consists of at least five members, and its membership meets the composition requirements set forth in the PHS Policy, Section IV.A.3.b. Attached is a list of the chairperson and members of the IACUC and their names, degrees, profession, titles or specialties, and institutional affiliations.

PMI has an active IACUC committee comprised of members with extensive experience. Please see attached IACUC Roster as of October 31, 2015.

D. The IACUC will:

1. Review at least once every six months the Institution's program for humane care and use of animals, using the "Guide" as a basis for evaluation. The IACUC procedures for conducting semiannual program reviews are as follows:

Every six months the IACUC conducts their programmatic review of the animal care and use program. All IACUC members are invited to participate in the semiannual program inspections including the outside members as part of the subset. The non-affiliated and non-scientist members are strongly encouraged to attend. Invitations are sent out by the IACUC Secretary to all members.

The program evaluation is completed at the convening of the IACUC during the regular monthly meeting (July and January) using a local form based on the "Guide". As the evaluation is carried out, the committee members confer regarding the program aspects under review. If clarification or documentation is necessary, the IACUC Secretary would obtain these for the committee at the time of the evaluation. Findings resulting from the program evaluation are recorded and compiled by the IACUC secretary in a final report which is distributed at the next month's meeting. Depending on the nature of the finding, concerns raised about the program evaluation are either corrected at the time of the finding or addressed at a later date through weekly management meetings attended by veterinary staff, Animal Care, and operations personnel. The action items are distributed to the appropriate management departments with deadlines. Once all items are addressed, the final report is submitted to the IACUC for review at their next meeting. After their review of the final report, the IACUC signs the document and the signed forms are forwarded to the IO for his review and acknowledgement signature.

2. Inspect at least once every six months all of the Institution's animal facilities, including satellite facilities, using the "Guide" as a basis for evaluation. The IACUC procedures for conducting semiannual facility inspections are as follows:

Every six months the IACUC conducts their programmatic review of the animal care and use program. All IACUC members are invited to participate in the semiannual program inspections including the outside members as part of the subset that participates in the facility inspections. The non-affiliated and non-scientist members are strongly encouraged to attend. Invitations are sent out by the IACUC Secretary to all members.

The facility inspection is completed during the regular IACUC monthly meeting (July and January) using a local form based on the "Guide". The Attending Veterinarian or designee is available to respond to any committee questions and/or to clarify current practice. The IACUC Secretary records comments made by the IACUC inspectors and any responses from Animal Care and/or the Attending Veterinarian. An inspection of all areas including animal holding, feed and bedding, surgical prep, ORs, necropsy room and a review of the documentation associated with the standard operating procedures related to these areas are completed. Findings resulting from the facility inspection are recorded and compiled by the IACUC Secretary in a final report which is distributed at the next month's meeting. Depending on the nature of the finding, concerns raised about the facility inspection are either corrected at the time of the finding or addressed at a later date through weekly management meetings attended by veterinary staff, Animal Care, and operations personnel. The action items are distributed to the appropriate management departments with deadlines. Once all items are addressed, the final report is submitted to the IACUC for review at their next meeting. After their review of the final report, the IACUC signs the document and the signed forms are forwarded to the IO for his review and acknowledgement signature.

3. Prepare reports of the IACUC evaluations as set forth in the PHS Policy IV.B.3 and submit the reports to the Institutional Official. The IACUC procedures for developing reports and submitting them to the Institutional Official are as follows:

A semi-annual report of the IACUC evaluations is compiled by the IACUC Secretary. The report includes program evaluations and departures from the Guide with reasons for each departure, if any, facility inspections including findings and corrective actions, minority views, and any recommendations or concerns regarding the animal care program. Deficiencies noted are categorized by minor or significant with a reasonable plan and schedule for correcting each deficiency. Minor is corrected on the spot or within 2 weeks. Significant is reviewed by the committee and IO and is given between 2 weeks to 3-6 months for major infrastructure. After reviewing the report during the monthly IACUC meeting, a majority of the IACUC members signs the final document acknowledging their review of the report. The report is then sent to the IO for review and acknowledgement. All documents are on file with the IACUC Secretary.

4. Review concerns involving the care and use of animals at the Institution. The IACUC procedures for reviewing concerns are as follows:

Within PMI, reporting of concerns, questions, or complaints regarding animal welfare and noncompliance may be done anonymously through the use of an internal document entitled, "Animal Welfare Reporting Form" which is located or posted around the facility. Reporting can be completed on the written form or by calling the phone numbers posted around the facility. Concerns may also be reported directly to the appropriate party such as the IO, Attending Veterinarian, IACUC Chairperson, and/or Study Director. In the case of personnel for whom English is a second language, an Interpreter is assigned and the IACUC Secretary transcribes the incident in the reporting form and immediately informs the appropriate personnel. Depending on the nature of the concern, activities involving the animal may be immediately placed on temporary hold by the veterinarian

until a full assessment has been made on whether there is an impact on animal welfare. This may also be applicable to deficiencies in animal care and use program. The complaint or concern would be discussed further with the IO, representatives from management, veterinary staff and other appropriate personnel to determine whether at a local level the concern can be addressed or whether a full investigation of the concern is warranted. The IACUC is notified either way. They are also notified regarding any follow-up or investigation. Conclusions and/or corrective action plans resulting from the follow-up or investigation will be considered by the IACUC. It is the IACUC that decides the best means to address the complaint which may include training or disciplinary action. The discussion occurs at the monthly meeting or *ad hoc* and is recorded in the minutes then forwarded to the IO.

In the case of a community or public complaint, the complaint is forwarded to the IO, management representatives, veterinary staff, and the IACUC Secretary who records and informs the committee. An investigation is immediately initiated to determine the cause and rectify the problem. If local regulatory authorities are involved, PMI will observe any recommendations they make to address the complaint.

5. Make written recommendations to the Institutional Official regarding any aspect of the Institution's animal program, facilities, or personnel training. The procedures for making recommendations to the Institutional Official are as follows:

IACUC members can make recommendations to Institutional Official at any time. Members have the opportunity monthly to raise comments they have regarding any aspect of the institution's animal program, facilities, or personnel training. The semiannual inspection and program evaluation provide an additional avenue for the committee to make recommendations regarding the animal care and use program. Finally, weekly management meetings allow for continuing dialogue between the veterinary, surgical, technical, and operations personnel, providing another means for addressing any issues with the animal care and use program, such as protocol conduct, animal welfare, and facility improvements. All discussion related to the animal care and use program is recorded then forwarded to the IO.

6. In accord with the PHS Policy IV.C.1-3, the IACUC shall review and approve, require modifications in (to secure approval), or withhold approval of PHS-supported activities related to the care and use of animals. The IACUC procedures for protocol review are as follows:

All research proposals must be reviewed and approved before the study can be initiated. Due to the volume of protocols submitted, the IACUC utilizes the Designated Member Review (DMR) format. All DMR's are appointed by the IACUC Chairperson. The potential outcomes of DMR are: approve, require modifications to secure approval, or call for a full committee review. All DMR's must be unanimous in any decision. DMR may be utilized only after all IACUC members have been provided the opportunity to call for full committee review. Prior to initiating the DMR process, the IACUC Secretary sends an email to all IACUC members with a list of the protocols to be reviewed. IACUC members have 24 hours to respond to the email to request full committee review of a

project. No response is considered approval to conduct the review by DMR. To conduct research procedures, the following procedures are required:

- The Principal Investigator (PI) completes the required forms "Justification for Use of Experimental Animals" and "Animal Studies Protocol".

- The IACUC Secretary prepares the documents, draft versions of protocol and justification forms, and if necessary, the PI is contacted at this step to further clarify minor administrative items.

- Once administrative review is completed, the protocol and justification forms are routed to veterinarians for review. If it is a GLP study, the forms are submitted to the QA Unit for QA review. The review is conducted to address any potential veterinary issues and/or any technical concerns in the conduct of the study, focusing on procedures that have the potential to cause pain and/or distress. The IACUC utilizes guidelines regarding monitoring endpoint and humane termination. Any concerns regarding procedures that might cause pain and/or distress to the animals are discussed with the client, such as species selection, PMI standard practices, alternative searches, and animal numbers. If serious concerns or questions are raised during the veterinary review, these must be addressed sufficiently before the protocol is forwarded to the committee. All questions raised are submitted to the Sponsor and/or Principal Investigator (PI) through the IACUC Secretary. Responses to these questions are then incorporated into the protocol and the revised protocol is then submitted to the IACUC.

- If there is no request for full committee review, the IACUC Chair selects the Designated Member Reviewers who are notified by the IACUC Secretary. The Designated Member Reviewers consists of 3 members to include one Clinical Veterinarian, and 2 other members or a non-scientific member regardless of the GLP status. They review the protocol and justification forms and if modifications are requested by one of the reviewers, the other reviewers are informed and must agree to the modifications. Any requests for clarification by the Designated Member Reviewers are submitted to the IACUC Secretary who notifies the PI. Further discussion may continue until the response to the reviewer's requests is adequate. These responses from the PI are incorporated into the final version of the protocol and the committee is updated by the IACUC Secretary. Once all questions are clarified and resolved, the Designated Member Reviewers approve the protocol. Whatever the recommendation maybe, the PI is notified in writing. Once approved, the finalized protocol is signed by the appropriate study personnel. All final and signed documentation are filed in the RA/QA office in the IACUC Approval binder.

- If there is a request for full committee review, the IACUC Secretary will arrange the convened meeting. They review the protocol and justification forms and if modifications are requested by one of the reviewers, they are handled as described below regarding Full Committee Review (FCR). Any requests for clarification by the Full Committee Reviewers are submitted to the IACUC Secretary who notifies the PI. Further discussion may continue until the response is adequate. These responses from the PI are incorporated into the final version of the protocol. Once all questions are clarified and resolved, the protocol is approved as described below regarding

FCR. Whatever the recommendation maybe, the PI is notified in writing. Once approved, the finalized protocol is signed by the appropriate study Sponsor representative and Study Director. All final and signed documentation are filed in the RA/QA office in the IACUC Approval binder.

- During the monthly convened meetings, the IACUC reviews all protocols approved by DMR the previous month using the approved protocol summary form. This form summarizes all protocols submitted and approved by DMR since the last meeting. This provides the committee with the opportunity to receive updates from the veterinary and OR staff, or to discuss quality of reviews of approved studies. All DMR recommendations stand as the final decision and do not require additional committee review. The feedback from the veterinarians during the monthly convened meeting is helpful to provide updates on the study only.

- The IACUC may invite consultants (e.g., bio-statisticians) to assist in the review of complex issues. Consultants offer only their opinions on complex issues and do not vote with the IACUC. The IACUC may also invite the PI to clarify protocol issues or concerns.

- All approved minutes are forwarded to the IO monthly for his review.

  a) If any IACUC Committee member requests Full Committee Review (FCR) of a protocol or if the DMR recommends FCR then the following procedures are followed: The IACUC Secretary notifies PI that the protocol and justification will be reviewed by FCR.
  b) A convened meeting is scheduled and a quorum of members must be present during the FCR review.
  c) FCR of a protocol can result in approval, modifications required in (to secure approval), or approval withheld. FCR outcomes require a majority vote of the quorum present.
  d) The IACUC Secretary records the recommendation and IACUC Chair notifies IO.
  e) IACUC Secretary records the FCR's recommendation and all documents are retained by the RA/QA department.

Conflicts of interest are avoided because animal welfare is the first priority for all IACUC members. Furthermore, IACUC is independent from the Principal Investigator (sponsor or client) which is not a committee member. As any institution that conducts PHS funded studies, most members work with the institution.

The outside member provides an unbiased opinion for the IACUC. No principal investigators, sponsors or personnel who may benefit from the studies whether monetary or in kind are on the committee. If it is perceived that a member has a conflict of interest with a study, they will not participate in the IACUC review or approval of that specific project except to provide information to the committee.

7. Review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing activities as set forth in the PHS Policy IV.C. The IACUC procedures for reviewing proposed significant changes in ongoing research projects are as follows:

Any changes made to an approved protocol shall be done by filing an amendment form and obtaining approval prior to initiation. Minor amendments may be approved by the veterinarians. Examples of what the IACUC considers a minor change to the study are listed below:

a) Change in personnel other than the Principal Investigator.
b) Change in minor administrative information (i.e. contact information)
c) Change in sex of test model
d) Request for mice and rats (no more than 10% of the original number approved)

The process for minor amendment review is as follows:

a) The Principal Investigator or Study Director requests an amendment for the previously approved protocol.
b) PI completes the Amendment Form and submits to the IACUC Secretary.
c) Amendment is reviewed by the veterinarian or, if the veterinarian is the Study Director, another designated IACUC member.
d) If the proposed amendment is minor and in sufficient detail, then the amendment is approved.
e) The original copy is retained by the RA/QA department and a copy is given to the PI and the surgical team.

Significant changes to a protocol must be reviewed either by FCR or by DMR and follow the same procedures at those listed in Part III. D. 6. Examples of changes that are considered significant include:

a) Increase >10% for rats and mice.
b) Any increase in the total numbers of animals requested for USDA regulated species, such as guinea pigs, hamsters, dogs, pigs, etc. and other vertebrate species.
c) Changes in the objectives of a study.
d) Changes in the Principal Investigator.
e) Changes in anesthetic agents or the use or withholding of analgesics.
f) Change from acute to chronic procedure.
g) Changes in the method of euthanasia.
h) Change or addition of new species (test system)
i) Change in pain category (involving painful procedures; degree of invasiveness)
j) Changes in the duration, frequency, or number of procedures performed in an animal.
k) Addition of new test article other than the approved test article
l) Change in the design of the test article and its components
m) Any changes that may impact personnel safety.

All amendments must be approved prior to initiation.

Some of the changes may or may not fall within these categories; therefore, the IACUC has granted authority to the attending clinical veterinarian to oversee all pre- and post-operative care of all animals, including but not limited to: pain relief/analgesia, antibiotic therapies, the use of anesthetic agents, and any surgical and medical care required. Veterinary discretion is exercised over all veterinary and surgical procedures. However, any significant change made by the veterinarian during the conduct of the study must be reviewed and approved by the IACUC prior to future work if the change(s) implemented will be used for all future research animals on that particular study.

8. Notify investigators and the Institution in writing of its decision to approve or withhold approval of those activities related to the care and use of animals, or of modifications required to secure IACUC approval as set forth in the PHS Policy IV.C.4. The IACUC procedures to notify investigators and the Institution of its decisions regarding protocol review are as follows:

> For approved protocols, an approval letter is issued containing the approval date, approved IACUC number (IAC#) and study number (ANS#). For withheld approval, the Principal Investigator is notified by the IACUC Secretary regarding the status of the protocol and the issues raised. The PI is notified in writing of the outcome of protocol review. If approval is withheld by the IACUC, then the IACUC Secretary notifies the PI in writing of the outcome and what questions were raised. The PI may be requested or elect to attend the next IACUC meeting to address the specific concerns raised by the committee. Until these issues are addressed to the committee's satisfaction, no further action will be taken towards study initiation. The reviews are recorded in the meeting minutes which are forwarded to the Institutional Official.

9. Conduct continuing review of each previously approved, ongoing activity covered by PHS Policy at appropriate intervals as determined by the IACUC, including a complete review in accordance with the PHS Policy IV.C.1-4 at least once every three years. The IACUC procedures for conducting continuing reviews are as follows:

> The Institution has been conducting post approval monitoring since 1984. We do routine post approval monitoring of studies during the daily clinical veterinary rounds and supported by QAU's quarterly unannounced audits.
>
> All protocols are approved for a maximum of 3 years, the initial year plus two annual updates. All USDA covered species protocol are reviewed annually by the DMR based on their date of approval. The Principal Investigator is contacted by the IACUC Secretary when the anniversary date of the original approval occurs and the PI is provided with an "Annual Progress Report". The Principal Investigator is asked to document any changes to the protocol or to the personnel. This documentation is forwarded to the IACUC and is reviewed during their regularly scheduled monthly meetings. At the completion of the third year, if the PI should decide to continue the study, she/he must submit a renewal for committee review and approval. The DMR or FCR must review and approve the *de novo* submission of the protocol in order for the study to continue. In addition, post approval monitoring is done during the monthly convened meeting. The Veterinarian who is also an IACUC member reports or updates conditions of studies conducted. The Veterinarian also makes recommendations for studies involving long term care and updates the committee of its activities. In the event of critical issues that falls prior to the convened meeting, the IACUC Secretary will disseminate information through email.

10. Be authorized to suspend an activity involving animals as set forth in the PHS Policy IV.C.6. The IACUC procedures for suspending an ongoing activity are as follows:

The IACUC is authorized to suspend an activity involving animals. A suspension of a protocol means no work can continue under that protocol until further notice from the IACUC. Suspension of the protocol and its ongoing activities are serious and necessitates quick response and thorough investigation. Depending on the nature of the concern, activities involving the animal may be immediately placed on temporary hold by the veterinarian until a full assessment has been made, focusing on the impact on animal welfare. If necessary, the Veterinarian, as a member of the IACUC, and the Chairperson may intervene prior to the convening of the IACUC. Some factors discussed with the PI at this time include the nature of the finding, impact on the animal, confidentiality issues, whether training and/or education might be helpful to rectify the problem, and consequence of non-compliance. In addition, the IO is informed during this process. The grounds for suspension may include but are not limited to:

a) Significant impact on animal welfare
b) Expired protocol
c) Problems identified as non-compliance of 21 CFR Part 58-GLPs, the PHS Policy or USDA Animal Welfare Regulations.

The IACUC may suspend an activity that it previously approved if it determines that the activity is not being conducted in accordance with applicable provisions of the Animal Welfare Act, the Guide, the Institution's Assurance or IV.C.1.a-g of the PHS Policy. The IACUC may suspend an activity only after review of the matter at a convened meeting of a quorum of the IACUC and with the suspension vote of a majority of the quorum present. If the IACUC suspends an activity involving animals, the Institutional Official in consultation with the IACUC shall review the reasons for suspension, take appropriate corrective action, and report that action with the full explanation to OLAW.

E. The occupational health and safety program for personnel working in laboratory animal facilities or have frequent contact with animals is as follows:

The Employee Health & Safety Committee in coordination with (b) (4) is responsible for reviewing the program and providing guidance to and monitoring all personnel working with hazardous agents. In addition, the IACUC and the requirements of local and state regulatory agencies monitor the program. Provisions for First-Aid, injury, illness or emergencies are defined in our Employee and Health Safety SOPs. All work related injuries or accidents, no matter how minor, must be reported immediately to the supervisor or designee (Injury and Illness Reporting Form). First aid kits are located in all the laboratory area and in the room adjacent to the animal holding areas. Employees may seek medical attention from (b) (4) or current medical provider. In case of life and death, 911 is called.

To assess potential dangers of procedures that use hazardous biologic, chemical, and physical agents, PMI established the EH & S Committee. The committee which meets a minimum of semi-annual or as needed is composed of operational and technical staff representatives, veterinarian, and the animal care supervisor.

Hazards can be identified through Material Safety & Data Sheets (MSDS) for new substances; news bulletin from the Toxic Management Department (TMD) and

Environmental Protection Agency (EPA); during EH&S semi-annual inspections; and Sharps and Injury Reports. Hazards can also be indentified during protocol review. Once an agent has been identified as hazardous during IACUC protocol review, it falls under the purview of the EH&S Committee to determine if any training is necessary, any precautions with regards special handling or disposal are required, notices, special requirements such as additional PPE, etc. Any EH&S Committee recommendations are forwarded to the IACUC Secretary and incorporated into the protocol. If necessary, the EH&S Committee will monitor studies until they are conducted properly as per regulatory requirements. The IACUC must conduct a review and grant an approval for these protocols prior to study initiation.

In addition, EH&S Committee members conduct routine training sessions on the Occupational Health and Safety Program at PMI, the outline of which is listed below. At this time, personnel are reminded about the policies and procedures related to OHS and are provided the opportunity to discuss any concerns or questions they have with regards to their safety in the workplace. Finally, committee members raise and address other safety concerns that have been identified by PMI personnel during their semi-annual meeting.

As pre-employment, personnel are informed regarding the job requirements and health-related risks. This has been coordinated through (b) (4) A questionnaire is completed at the time of hire and assessed by a physician and/or staff nurse. All personnel are enrolled in the OH&S Program at the time of hire. Depending on the nature of the job, the hazards and risk assessments differ. For instance, if personnel will be working in the OR, they are informed about potential radiation exposure and proper ergonomics. Because of this, OR techs are provided radiation badges to monitor their exposure and are trained on lifting techniques. If personnel will be working in Animal Care, they are informed regarding noise levels, potential for slips and falls, animal bites, chemical cleaning agent hazards, allergens, and zoonoses. All Animal Care personnel are provided appropriate personal protective equipments (PPE) e.g. ear protection, non-skid boots, etc.

After the initial health risk assessment and if the employee is determined to be at risk or susceptible, they are required to maintain vaccinations, boosters, or may be required to use respirators (N95) whenever in contact with possible allergens. Depending in their condition, personnel may or may not be assigned certain responsibilities. All newly employed personnel are required to obtain the following:

- TB screening
- General Medical
- Tetanus toxoid (if booster hasn't been received within last 10 years), optional if allergic
- Physical examination including lab work (SMA-12, CBC, VDRL, UA), optional
- Additional testing as needed (allergies, etc.)

Employees are required to maintain their annual TB screening, tetanus booster if needed, and optional annual physical and/or lab work. Rabies vaccinations for OR and Animal Care Staff are provided if deemed necessary per protocol. Radiation badges are provided for employees who have access to ORs and are monitored through an outside provider. It

is the responsibility of the EH&S Committee to oversee and monitor this program with support from the Director or designated administrative agent.

Description of Educational Programs

All personnel must complete the following annual training of the Occupational Health and Safety Program:

- Standard Microbiological Practices: BSL 1 and BSL 2 agents
- Universal Precautions
- Bloodborne Pathogens
- Hazard Communication Program
- Environmental Health and Safety
- Precautions for Handling Human Tissue
- Radiation Safety
- Respiratory Protection Program
- Ergonomics
- Zoonotic Diseases
- Allergies to Laboratory Animal Allergens
- Illness and Injury Prevention Program
- Occupational Health & Safety Program identifies potential health risks for employees with immunocompromised health status, allergies and other potential risks.

For any study involving specific agents that have not yet been used at PMI, additional training is provided either by PMI Staff or the sponsor. All studies are overseen by the senior clinical veterinarians, with each veterinarian sitting on either the IACUC or EH&S committee. Any concerns raised would be immediately reported to the appropriate committee.

All topics are discussed in a lecture format with question and answer sessions. The training covers policies, SOPs, and any specific protocols that require attention. The format allows personnel to receive an annual refresher but most importantly to raise any concerns, questions, or issues encountered in the facility or either during the conduct of study, during a routine day. An outside service may be contacted to provide training but all training is conducted on site.

Personal Protection & Hygiene

All veterinary, OR, animal care personnel, and clients are provided with standard work clothes such as scrubs and uniforms whether or not their work involves the use of hazardous agents. In addition, other standard PPE are provided for all personnel working with animals such as caps, masks, face shields, gloves, and booties. Lead aprons and radiation badges are provided and required for study personnel if their studies require the use of the fluoroscopic units and/or they employ the use of a radionuclide. In addition, steel-toe boots are provided to animal care personnel when working with the colony. An outside service is contracted for laundering service of all work clothes.

Personnel and clients are advised regarding the standard requirements for gowning. Minimally, all personnel must wear close-toed shoes, shoe covers, scrubs or uniforms, and latex gloves when providing husbandry or veterinary care in animal holding rooms. During chronic procedures in surgical suites, all personnel must wear shoe covers, scrubs, hair bonnet, face mask and sterile latex gloves. Earplugs and/or muffs are provided for use in areas of high noise.

Provisions for hand washing/clothing policy

Change facilities are provided for all personnel. There is a women's locker room which contains the shower and lockers. The men's locker room contains the shower and lockers. 3 Restrooms are available to all personnel and clients. Surgical scrub sinks are located in the anterooms adjacent to the Operating Rooms. A sink is also available in the personnel lunch/ break room. Street clothes are not allowed in ORs. All personnel who enter the ORs are required to follow proper gowning procedures and PPE requirements. It is the policy of PMI that no work clothing be worn by staff members off premises. Work clothes are changed daily or more frequently if unduly soiled.

Provisions for Personnel Working with Non-Human Primates

We currently do not house Non-Human Primates but is available if needed. The Non-Human Primate SOPs will then be activated for strict compliance.

Eating, Drinking, and Smoking Policies

Eating, drinking, handling contact lenses, and applying cosmetics are restricted to the fore section of the facility, specifically to the break room, lobby, conference room, administrative offices or lavatories. Smoking is prohibited within any indoor environment at the facility.

F. The total gross number of square feet in each animal facility (including each satellite facility), the species of animals housed therein and the average daily inventory of animals, by species, in each facility is provided in the attached Facility and Species Inventory table.

Please see attachment – Facility and Species Inventory

G. The training or instruction available to scientists, animal technicians, and other personnel involved in animal care, treatment, or use is as follows:

The following lists the training or instruction mandatory to OR technicians and surgical specialists:

- Aseptic techniques
- Pain assessment and management emphasis on species-specific signs of pain and distress
- Standard operating room maintenance
- Radiation Safety
- Universal Precautions, Personal Protective Equipment (PPE) and Zoonoses
- Specific surgical techniques (as required by protocol)

- Blood collection
- Controlled Substance Program
- Pre- and post procedural care and record keeping; medical documentation
- IACUC – its role and its responsibilities
- Regulatory overview: USDA, GLP, and OLAW
- Animal Welfare
- AVMA Euthanasia Panel: Methods of humane termination; endpoint criteria

Species addressed include primarily large animals such as lagomorphs, canine, swine, caprine, ovine and bovine. All training is documented by an attendance sheet and appropriate training records or certificates are filed upon completion. The veterinary library maintains resources to facilitate investigator research and train staff as needed. The materials are also available for consultation by the staff. In-house training is provided as needed, specifically training based on investigator procedures is done and can range from training on restraint and handling, euthanasia, various blood collection techniques and surgical procedures, different animal models, anesthesia and analgesia. OR personnel received anesthesia training on parenteral agents during hands-on sessions. Information on dosing is provided and methods of monitoring anesthesia depth are reviewed and demonstrated. Individuals utilizing isoflurane anesthesia are provided specific training ad hoc. Instruction is given in proper animal handling and care, injection techniques, observation and dosage calculations.

In addition, a training protocol has been implemented to assist veterinarians, surgical specialists and clients in the refinement of procedures. This can result in the reduction of animals used in the R & D process. Clients are also encouraged to conduct pilot studies on bench top and cadaver models to improve techniques. IACUC members are also given opportunities to observe wet lab training.

For scientists and other sponsor personnel including Principal Investigators who will be involved in the direct handling of animals, training is provided prior to the initiation of the study. The study materials included topics such as:

1.Handling
2.Tranquilization
3.Immobilization
4.Anesthesia
5.Pre / Post procedural care
6.Analgesia, pain assessment
7.Euthanasia
8.Methods in which deficiencies in animal care and treatment are reported.
9.Humane methods of animal care
10.Minimizing distress

Records of training are kept on file and archived by the IACUC Secretary. CVs with a description of animal experience are also requested. In addition, for complicated studies, a pilot study is required in order to assess unanticipated results or adverse events. These wet-labs are participated in by both clients and staff.

Animal Care staff is trained on pain assessment with emphasis on species-specific signs of pain and distress; Universal Precautions, Personal Protective Equipment (PPE) and zoonoses; IACUC – its role and its responsibilities; regulatory overview: USDA, GLP, OLAW, and animal welfare, care and maintenance of various species, and standard husbandry practices. Training may be conducted via SOP review, lecture with Q & A, attendance of local conference, and participation in in-house training sessions provided by management and veterinary staff. Included in the animal care staff training is the role of the IACUC, which includes research and testing methods to minimize the animal numbers required to obtain valid results, alleviate or limit pain and distress. The animal care staff is also empowered to go directly to the veterinarian for any health related issues. They also are encouraged to have direct contact with the IACUC. The IACUC is also encouraged to interact with the animal care staff.

Investigator training is provided as needed. Prior to handling animals for their studies, all investigators are required to submit a CV for review by the IACUC. If it is deemed necessary for the PI to receive training, this will be provided by the management. The type of training will be dependent on the PI's experience and the protocol requirements. In addition, the comprehensive veterinary review serves to provide a venue for veterinarians to advise and educate investigators about conducting research, such as pain and distress, justification of animal numbers, requirements for alternative via literature searches, assignment of pain categories, animal species selection, etc. This is a critical portion of the protocol review process.

Training records are maintained in individual training files by our RA/QA department.

IACUC provides training to its members as mentioned above and educates them regarding their responsibilities. The IACUC Secretary informs new IACUC members of the IACUC library and provides access to a number of useful written materials including the following:

- The USDA Animal Welfare Act Regulations and related Animal Care Policies
- The Guide for the Care and Use of Laboratory Animals
- The ARENA Institutional Animal Care and Use Committee Guidebook
- The OLAW PHS Policy on Humane Care and Use of Laboratory Animals, and
- AVMA Panel on Euthanasia
- Applicable SOP and policies adopted by PMI
- AALAS website for training references
- PMI Animal Welfare Assurance
- Any other useful websites (iacuc.org; AWIC, etc.)

As part of their continuing education, IACUC members are required to attend various conferences, training seminars, and symposiums offered locally and paid for by management. The local AALAS Chapter, NCB-AALAS, holds periodic training through labs, lectures, etc. which IACUC members are required to attend. In addition, updates to regulatory policies are discussed as necessary with members during the IACUC meetings.

PMI has a training program that involves review of SOPs, annual recurrent training on the following topics which cover personnel pregnancy and illness. Training is also provided as-needed on these topics:

SOP 8000 Occupational Health and Safety Program: the objective is to alert employees to potential hazards. This informs employees that if they have potential health risks (allergies, pregnancy, immunocompromised, etc.), they are required to report these to the Occupational Health Provider and HR and appropriate measures taken. This also includes information such as zoonotic diseases.

Additional SOPs below cover other topics that the personnel are required to know and for which they receive training.

SOP 8001 Accident Prevention Program
SOP 8002 Hazardous Agents
SOP 8003 Hazard Communication Program
SOP 8004 Emergency Action Plan (EAP)
SOP 8005 Injury and Illness Prevention Program – includes blood borne pathogens
SOP 8006 Universal Precautions
SOP 8007 Use of Personal Protective Equipment (PPE)
SOP 8010 Sharps Management Program and Injury Log
SOP 8011 Medical Waste Management Program
SOP 8012 Respiratory Protection Program
SOP 8013 Radiation Program: this SOP addresses practices for all personnel, including pregnant personnel.
SOP 8017 Animal Bites and Scratches

GLP Training, Subpart B, 58.29 (f) "Any individual found at any time to have an illness that may adversely affect the quality and integrity of the nonclinical laboratory study shall be excluded from direct contact with test systems, test and control articles and any other operation or function that may adversely affect the study until the condition is corrected. All personnel shall be instructed to report to their immediate supervisor any health or medical conditions that may reasonably be considered to have adverse effect on a nonclinical laboratory study.

IV. INSTITUTIONAL PROGRAM EVALUATION AND ACCREDITATION

All of this Institution's programs and facilities (including satellite facilities) for activities involving animals have been evaluated by the IACUC within the past six months and will be re-evaluated by the IACUC at least once every six months thereafter, in accord with the PHS Policy IV.B.1-2. Reports have been and will continue to be prepared in accord with the PHS Policy IV.B.3. All IACUC semiannual reports will include a description of the nature and extent of this Institution's adherence to the "Guide." Any departures from the "Guide" will be identified specifically and reasons for each departure will be stated. Reports will distinguish significant deficiencies from minor deficiencies. Where program or facility deficiencies are noted, reports will contain a reasonable and specific plan and schedule for correcting each deficiency. Semiannual reports of the IACUC's evaluations will be submitted to the Institutional Official. Semiannual reports of IACUC evaluations will be maintained by this Institution and made available to the OLAW upon request.

This Institution is Category One (1)—accredited by the Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC). As noted above, reports of the IACUC's semiannual evaluations (program reviews and facility inspections) will be made available upon request.

V. RECORDKEEPING REQUIREMENTS

A. This Institution will maintain for at least three years:
1. A copy of this Assurance and any modifications thereto, as approved by the PHS.
2. Minutes of IACUC meetings, including records of attendance, activities of the committee, and committee deliberations.
3. Records of applications, proposals, and proposed significant changes in the care and use of animals and whether IACUC approval was given or withheld.
4. Records of semiannual IACUC reports and recommendations (including minority views) as forwarded to the Institutional Official, **Jorge L. Garcia, DVM**.
5. Records of accrediting body determinations.

B. This Institution will maintain records that relate directly to applications, proposals, and proposed changes in ongoing activities reviewed and approved by the IACUC for the duration of the activity and for an additional three years after completion of the activity.

C. All records shall be accessible for inspection and copying by authorized OLAW or other PHS representatives at reasonable times and in a reasonable manner.

VI. REPORTING REQUIREMENTS

A. This Institution's reporting period is **January 1 – December 31.** The IACUC, through the Institutional Official, will submit an annual report to OLAW on **the last day of the month following the end of the reporting period** of each year. The report will include:

1. Any change in the accreditation status of the Institution (e.g. if the Institution obtains accreditation by AAALAC or AAALAC accreditation is revoked), any change in the description of the Institution's program for animal care and use as described in this Assurance, or any change in the IACUC membership. If there are no changes to report, this Institution will provide written notification that there are no changes.
2. Notification of the dates that the IACUC conducted its semiannual evaluations of the Institution's program and facilities (including satellite facilities) and submitted the evaluations to the Institutional Official, **Jorge L. Garcia, DVM.**

B. The IACUC, through the Institutional Official, will promptly provide OLAW with a full explanation of the circumstances and actions taken with respect to:

1. Any serious or continuing noncompliance with the PHS Policy.
2. Any serious deviations from the provisions of the "Guide."
3. Any suspension of an activity by the IACUC.

C. Reports filed under sections VI.A. and VI.B. of this document shall include any minority views filed by members of the IACUC.

VII. INSTITUTIONAL ENDORSEMENT AND PHS APPROVAL

A. Authorized Institutional Official

Name: Jorge L. Garcia

Title: Founder & Chief Scientific Officer

Name of Institution: PMI

Address: 1031 Bing St, San Carlos, CA 94070

Phone: (b) (6)

Fax: (b) (6)

E-mail: j.garcia@pmipreclinical.com

Signature (b) (6)

Date: 3/29/2016

B. PHS Approving Official

Doreen H. Barlett-Senior Assurance Officer
Division of Assurances-Office of Laboratory Animal Welfare
National Institutes of Health
bartletd@mail.nih.gov
Phone: 301-402-4325
Fax: 301-451-5672

Signature (b) (6)

Date: 3/30/16

C. Effective Date of Assurance: 3/28/16

D. Expiration Date of Assurance: 3/31/20

MEMBERSHIP OF THE INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE

DATE: October 31, 2015
NAME OF INSTITUTION: PMI
ASSURANCE NUMBER: A-3367-01

Chairperson Name, Title, and Degree/Credentials	Business Address, Phone, Fax, and Email of Chairperson
Name*: Crystal Lala	Address*: 1031 Bing St. San Carlos, CA 94070
Title*: Senior Project Manager	

Degree/credentials*:	Phone*:	Fax*:	Email*:
Bachelor of Science	(b) (6)	(b) (6)	c.lala@pmipreclinical.com

Name of Member/Code**	Degree/Credentials	Position Title	PHS Policy Requirements***
Sarah Currie, DVM (b) (6)	Veterinarian	Clinical Veterinarian	V, S
		Surgical Specialist	S
		OR Technician	S
		Teacher	NS, NA

*This information is mandatory.
**Names of members, other than the chairperson and veterinarian, may be represented by a number or symbol in this submission to OLAW. Sufficient information to determine that all appointees are appropriately qualified must be provided and the identity of each member must be readily ascertainable by the Institution and available to authorized OLAW or other PHS representatives upon request.
***PHS Policy Requirements - identify which IACUC members meet the four criteria below:

- Veterinarian (V) - a veterinarian with direct or delegated program responsibility.
- Scientist (S) - a practicing scientist experienced in research involving animals.
- Nonscientist (NS) - a member whose primary concerns are in non-scientific areas (e.g. ethicist, lawyer, member of the clergy).
- Nonaffiliated (NA) - a member who is not affiliated with the Institution in any way other than as a member of the IACUC, and who is not a member of the immediate family of a person who is affiliated. This member is expected to represent the interests of the general community in the proper care and use of animals and should not be a laboratory animal user. A consulting attending veterinarian may not be considered nonaffiliated.

Notes:

1. All members must be appointed by the CEO (or individual with specific written delegation to appoint members) and must be voting members. Ad hoc or nonvoting members may be listed and identified as such, but are not considered members for the purpose of the PHS Policy, and do not contribute to a quorum.
2. If Alternate members are listed, identify for whom (by name or code number, not specialty) they will serve as Alternates.

OTHER KEY CONTACTS (OPTIONAL)
If there are other individuals within the Institution who may be contacted regarding this Assurance, please provide information below.

(b) (6)

FACILITY AND SPECIES INVENTORY

DATE: October 31, 2015
NAME OF INSTITUTION: PMI
ASSURANCE NUMBER: A-3367-01

Laboratory, Unit, or Building*	Gross Square Feet (including service areas)	Species Housed in Unit (use complete common names)	Approx. Average Daily Inventory
	PMI – 22,000 ft² (Gross)		
(b) (6)	390 ft²	Quarantine Room - Canine	12
	750 ft²	Sheep	10
	860 ft²	Canine	33
	1836 ft²	Pigs	8
		Goats	2
		Ovine	2
	448 ft²	Cows	2
	390 ft²	Rabbits	7
	231 ft²	Rats	3
		Mice	51
	BSRI (The BSRI Rodent Vivarium (room 25)		
	~600 ft²	Mice	3006
	~50 ft²	Mice	0

*Institutions may identify animal areas in any manner, e.g., initials, ID number, etc. However, the name and location must be provided to OLAW upon request.