The Biomedical Research Institute of Southern California

Animal Welfare Assurance for Domestic Institutions

I, **Sally Sarawar** as named Institutional Official for animal care and use at the Biomedical Research Institute of Southern California, provide assurance that this Institution will comply with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (Policy).

I. Applicability of Assurance

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, DHHS, and/or NSF (if applicable). This Assurance covers only those facilities and components listed below.

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

The Biomedical Research Institute of Southern California located at 1692 Ord Way, Oceanside, CA 92056

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

None

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."

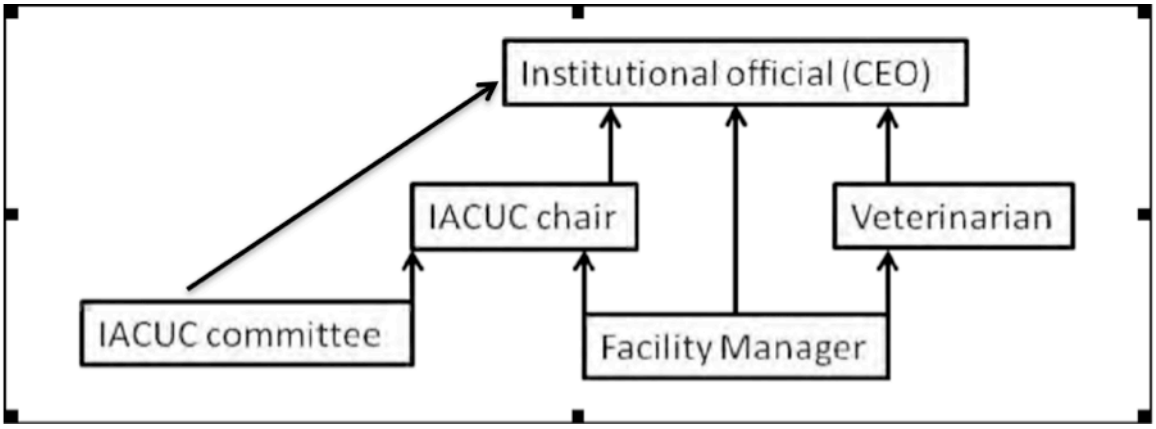
C. This Institution acknowledges and accepts responsibility for the care and use of animals involved in activities covered by this Assurance. As partial fulfillment of this responsibility, this Institution will ensure that all individuals involved in the care and use of laboratory animals understand their individual and collective responsibilities for compliance with this Assurance, and 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 according to 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 (subaward) 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 the PHS Policy are as follows:



The principal investigator for each project submits protocols for review by the IACUC committee to the IACUC chair. The protocols are reviewed at full meetings of the IACUC committee. When a protocol is approved a notice is sent to the Institutional Official (who is currently also the CEO) and Facility Manager. Animals can then be ordered by the Facility Manager and vendors approved by the veterinarian and IACUC. The veterinarian is responsible for ensuring that the policies and procedures for animal husbandry meet or exceed standards for animal husbandry. Random inspections may be performed by the Veterinarian at any time without notice. The Facility Manager will consult with the Veterinarian regarding treatment of any ill animals or unexpected complications during an experiment. These may be observed by the Facility Manager/animal care staff and reported to Principal Investigators or their personnel (listed in the approved protocol). Both the IACUC Chair and the Veterinarian report directly to the Institutional Official (IO). All members of the IACUC also have an open and direct line of communication with the IO. The IACUC chair and the Veterinarian have the authority to temporarily halt any protocol for violations reported by any person. The IACUC will consider the temporary halt at the next meeting and upon majority vote implement the appropriate action, which may include a warning letter, termination of the protocol or removal of animal facility privileges.

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

1) Name: Dr. Mari Bray
   Qualifications
   - Degrees: DVM, DACLAM
   - Training or experience in laboratory animal medicine or in the use of the species at the institution:
     Dr. Bray completed a three year post-doctoral residency in laboratory animal medicine at Yale University from 1989-1992 and has been practicing in this field since that time.

   Authority: Dr. Bray has delegated program authority and responsibility for the Institution's animal care and use program including access to all animals. She has the authority and responsibility to implement the PHS policy and the recommendations of the guide.

Responsibilities:

Dr. Bray has the responsibility of monitoring the operation of the animal facility. As the consulting veterinarian she provides professional services and expertise in maintaining research animals in optimal health, treating animals in emergency situations, periodic inspection of animals, animal quarters and facility to ensure continued compliance with the Animal Welfare Act and other established guidelines and programs for sanitation and maintenance, in general oversight of operations and practices and procedures of the animal facility and consults with scientists in the selection and utilization of animal models, protocols and procedures. She is responsible for providing guidance and recommendations in order to assure that the institutional animal care and use program meets or exceeds the requirements of the Animal Welfare Act, USDA regulations, the PHS policy, the NRC Guide for the Care and Use of Laboratory Animals and other applicable federal, state and local statutes and regulations relating to laboratory animals. She is on call 24 hours per day every day of the year including weekends and holidays. She is responsible for providing backup veterinary care for animal medical emergencies if she is unavailable due to illness or vacation.

Time contributed to the program:

Dr. Bray is present at the Institution an average of approximately 2-3 hrs every 6 months. 100% of this time is devoted to the Animal Care and Use program. In addition, Dr. Bray contributes an average of 1-2 hrs per month to the program while off-site reviewing protocols and providing consultation on various topics.

(b) (6)

(b) (6)

C. The IACUC at this Institution is properly appointed according to 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 5 members, and its membership meets the composition requirements of PHS Policy 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.

Please see attached Table (Part VII).

D. The IACUC will:

1) Review at least once every 6 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:

A quorum of at least 3 members of the committee shall be present for all program reviews, which will be scheduled to be done in combination with the facilities inspection. These will be scheduled to be done at least one month in advance and all members of the committee will be invited to attend.
Each portion of the program, including IACUC functions, veterinary care, personnel qualifications and training, occupational health and emergency and disaster plans will be thoroughly reviewed using the OLAW Semiannual Program Review and Facility Inspection checklist at least once every 6 months. Each member will be provided with a copy of the check-list.
Any program deficiencies will be noted along with a correction schedule and deadline for the corrections to be made. It will be noted whether a deficiency is minor or major. Minority views on all aspects will be incorporated into the review.

The results of the program review will be reported to the Institutional Official within 30 days of the review.

2) Inspect at least once every 6 months all of the Institution's animal facilities, including satellite facilities and animal surgical sites, using the *Guide* as a basis for evaluation. The IACUC procedures for conducting semiannual facility inspections are as follows:

Every animal room, procedure room, the cage washing facility, the feed storage area and other animal use facilities as applicable are thoroughly inspected using the criteria outlined in the OLAW Semiannual Program Review and Facility Inspection checklist at least once every 6 months. A quorum of at least 3 members of the committee shall be present for all inspections and all members of the committee are invited to attend. These inspections are scheduled to be performed concomitantly with the program review.
Any departures from the Guide will be noted along with a correction schedule and deadline for the corrections to be made. It will be noted whether the departure indicates a minor or major deficiency. Minority views on all aspects will be incorporated into the review.

The results of the facility inspection will be reported to the Institutional Official within 30 days of the inspection.

3) Prepare reports of the IACUC evaluations according to 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:

The check-list provides the guide for the members of the IACUC for the program review and facilities inspection. Individual IACUC members will convey their observations to the IACUC Chairperson who in turn will draft the reports using the sample OLAW Semiannual report format from the OLAW website.
The reports will contain a description of the nature and extent of the institutions adherence to the Guide and PHS Policy, identify specifically any departures from the provisions of the Guide and PHS Policy, and state the reasons for each departure. The reports will distinguish significant from minor deficiencies. If program or facilities deficiencies are identified, the reports will contain a reasonable and specific plan and schedule for correcting each deficiency. This will be monitored by a designated member of the IACUC or an appointee thereof and the changes reported to and reviewed by the IACUC.

Any concerns noted by a member of the IACUC or by individuals within or outside the Institution, whether during program review or facilities inspection will be noted. Copies of the draft reports will be reviewed, revised as appropriate and approved by the IACUC. The final reports will be approved by a majority of the IACUC members and will include any minority opinions. If there are no minority opinions, this will be noted on the report.

The completed reports will be submitted to the Institutional Official within 30 days of the evaluation. In addition, the IACUC chairperson will notify the IO when all deficiencies have been corrected.

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

Any individual may report concerns to the IO or to any member of the IACUC.

There is 'Whistle-blowing' Policy whereby deficiencies in animal care and treatment may be reported by individuals within or outside BRISC without discrimination for reporting violations of the standards under the Guide. Any of the members of the IACUC may be contacted in confidence by any method, including anonymous reports on the form designated for such use. Personnel shall be protected against reprisal by the Institute or persons within the Institute.

Notices are posted in the animal facility advising individuals how and where to report animal welfare concerns and stating that anyone who reports a concern will be protected against reprisals according to the 'Whistleblower' policy.

Any reported deficiency whether valid or not will be included in the report to the Institutional Official. A full investigation will then ensue by members of the IACUC designated by the chairperson (an unaffiliated member will always be present in the committee performing the investigation). The investigation can consist of interviewing personnel, reviewing data and other research documents and any other lawful investigative methods deemed necessary by the subcommittee.

The results of the investigation will be presented to the full committee for review and they will make a decision as to whether there is a deficiency. The committee will then determine whether punitive action is warranted up to and including dismissal of an employee or suspension of an animal use protocol. Reported concerns and all associated IACUC actions will be recorded in the meeting minutes.

The concerns and decision of the committee including a plan to correct any deficiencies will be reported to the Institutional Official. A plan to review the deficiency will also be included as

described in the section above. The IO will make a report in writing to OLAW if it is determined that there is a serious or continuing deficiency.

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:

Recommendations to the IO are discussed and developed by the IACUC. The discussion and recommendations are included in the IACUC meeting minutes.

The IACUC completes the template for the report to the Institutional Official developed by the NIH. Specifically, any deficiencies in the program and facilities are noted in the report. Written recommendations can be made to the Institutional Official regarding any aspect of the institution's animal program, facilities or personnel training. These recommendations may be formulated during the 6-monthly program reviews and facility inspections or can be formulated during any other IACUC meeting in which there is a quorum present and the majority of the quorum vote to make a recommendation and/or implement these changes. The meeting minutes and the report including the recommendations are forwarded to the Institutional Official.

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

The Principal Investigators of BRISC submit their proposed research to the IACUC chairperson using a defined template. The IACUC research proposal is then forwarded, by email to all other members of the IACUC committee. This is done well in advance of the IACUC meeting to enable the committee members to conduct a thorough review. The Principal Investigator works with the Veterinarian on development of the protocol and procedures prior to the IACUC review.

Any member of the IACUC may raise concerns about the protocol. In order to approve the protocol, the IACUC will conduct a review of those components related to the care and use of animals and will determine whether the research project will be in accordance with the Guide in so far as it applies to the research project, unless acceptable justification for departure from the Guide is presented.

The submitted research protocols are then reviewed by a convened meeting of the full committee. A quorum (a majority of the voting members which is 3/5) of the IACUC must be present throughout the meeting. Protocols are approved by a vote of a simple majority (51%) of the members present. This procedure is termed 'full committee review' or 'FCR'. Specifically the committee examines the written responses to an application for animal research, which is designed to conform to the standards of the Guide. These questions determine the identity and qualifications of all animal handlers, funding, summary in lay terms of the proposal, justification of the choice, strain, number and length of use of animals, criteria for detecting discomfort, proposed measures to avoid pain and suffering, methods of euthanasia, presence of biohazards, special needs and related topics. In addition, the committee confirms that the Principal Investigator has signed the Project Directors assurance of compliance with the Guide.

Further, the IACUC will determine whether the research project conforms with the institution's assurance and meets the following requirements: a) Procedures with animals will avoid or minimize discomfort, distress, and pain to animals, consistent with sound research design; b) Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with the appropriate sedation, analgesia or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator; c) Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly sacrificed at the end of the procedure or, if appropriate during the procedure; d) The living conditions of animals will be appropriate for their species and contribute to their health and comfort. The housing, feeding, and nonmedical care of the animals will be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied; e) Medical care for animals will

be available and provided as necessary by a qualified veterinarian; f) Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures; g) Methods of euthanasia used will be consistent with the current recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia, unless a deviation is justified for scientific reasons in writing by the investigator.

Following discussion by the committee, applications are approved by oral vote or show of hands. The possible outcomes of a Full Committee Review of a protocol are a) Approval; b) Require modifications to secure approval; c) Withhold approval.

If modifications are required to secure approval, the following procedures are used:

1. If all members of the IACUC are present at a meeting, a list of queries are written by each reviewer and/or compiled by the IACUC chair, and delivered to the investigator so he/she can address each one of these queries in a revised version of the protocol. The IACUC chairperson emails the revised protocol to all members, together with the original list of queries, so each member has the opportunity to read if their own questions as well as other reviewer's questions have been addressed, before expressing their opinion in moving Approval of the revised protocol. If more questions are raised, or if the investigator has not addressed all original questions, this same process happens until the protocol is revised to the satisfaction of all IACUC members. Alternatively, by unanimous vote at the meeting the committee may decide to have the modifications reviewed by Designated Member Review (DMR - see below). Voting and queries are centralized by the IACUC chair, who writes emails to the group with the revised protocol version(s) and the list of queries. All these emails and lists of questions/requests as well as the different versions of the protocol up to the final approved format are archived by the IACUC chairperson.

2. If all members of the IACUC are not present at a meeting, the committee may use DMR subsequent to FCR with the following stipulation: All IACUC members must agree in advance in writing that the quorum of members present at a convened meeting may decide by unanimous vote to use DMR subsequent to FCR when modification is needed to secure approval. However, any member of the IACUC may, at any time, request to see the revised protocol and/or request FCR of the protocol.

3. If all members are not present and the IACUC lacks written standard procedures as described above, the committee has the option to vote to return the protocol for FCR at a convened meeting or to employ DMR. All members, including the members not present at the meeting, must have the revised research protocol available to them and must have the opportunity to call for FCR. A DMR may be conducted only if all members of the committee have had the opportunity to request FCR and none have done so.

If an IACUC uses DMR, the approval date is the date that the designated member(s) approve the study.

An alternative procedure for review is 'designated member review' or 'DMR'. In this type of review, prior to review all members are provided with complete copies of the protocols. Each member has the opportunity to request full committee review. Polling of members after receipt of all materials is the mechanism used for providing all IACUC members with the opportunity to call for full committee review. Polling in this instance is not an approval vote on the proposed research. Records of such polling will be maintained to document that the opportunity for members to request a full committee review meeting has been provided. Polling is mainly done by email but could also be done by mail, or by phone contact with the IACUC chairperson. If no member calls for full committee review, then the IACUC chairperson will designate one or more qualified IACUC members to review the protocol. The possible outcomes of a Designated Member Review of a protocol are a) Approval; b) Require modifications to secure approval or c) Request a full committee review of the research project. If the DMR(s) does not Approve the protocol as is, the member(s) performing the review will send all comments and questions usually by email to the investigator and the IACUC chairperson. All queries should be addressed by the investigator, and a revised protocol is presented to the DMR(s) and IACUC chair (by email). This process continues until all queries are properly addressed for protocol approval. If a protocol is assigned to more than one designated reviewer, the reviewers must be

unanimous in any decision. They must all review identical versions of the protocol and if modifications are requested bay any one of the reviewers then the other reviewers must be aware of and agree to the modifications. Designated reviewers are not allowed to withhold approval - full committee review is required in this case. The application template form is the same as for full committee review. If the designated members reviewing the protocol cannot agree on whether to approve it, a full committee review is required.

If FCR is requested, approval of the protocol may be granted only after review at a convened meeting of a quorum of the IACUC and with approval of a majority of the quorum present.

After all required modifications have been made, a final revised protocol ie an identical document with all the modifications required by all the reviewers is submitted to all designated reviewers for review and approval.

If multiple designated reviewers are used, their decision must be unanimous, otherwise the protocol will be referred for FCR.

For both FCR and DMR, in compliance with the Guide, no IACUC member can review or vote on a protocol with which he or she has a conflict of interest. An alternate member of the IACUC with no conflict of interest may replace the conflicted member who will be asked to leave the room during the protocol review. IACUC members who recuse themselves due to a conflict of interest do not count towards the quorum and a quorum of unconflicted members must be maintained throughout the entire meeting for a Full Committee Review.

No study can begin before the protocol has been reviewed and approved by the IACUC.

Approved applications are assigned a serial number and applicants are notified of the decision in writing.

All the above documents, including related correspondence will be dated, kept on file and made available to regulatory inspectors.

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 according to PHS Policy IV.C. The IACUC procedures for reviewing proposed significant changes in ongoing research projects are as follows:

Significant changes to an IACUC-approved protocol must be reviewed and approved by the IACUC before they occur to determine whether the research project will be in accordance with the Guide. BRISC interprets significant changes to mean those that have the potential to impact substantially and directly on the health and well-being of the experimental animals. Examples of significant changes include, but are not limited to, changes: a) in the objectives of a study; b) from non-survival to survival surgery; c) resulting in greater discomfort or a greater degree of invasiveness; d) in the species or in approximate number of animals used; e) in the Principal Investigator; f) in anesthetic agent(s) or the use or withholding of analgesics; g) in the method of euthanasia; and h) in the duration, frequency, or number of procedures performed on an animal. The investigator is required to provide an amendment, which specifically addresses the items of the application, noting how altered circumstances or procedures satisfy the original questions.

Proposed significant changes to ongoing procedures are submitted for IACUC review by the Principal Investigator for the project. They are then reviewed and approved by either FCR or DMR using the same procedures and criteria as for review of new protocols described above in Section III.D.6).

No significant changes can be implemented before they have been reviewed and approved by the IACUC.

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 according to PHS Policy IV.C.4. The IACUC procedures to notify investigators and the Institution of its decisions regarding protocol review are as follows:

After review, the IACUC will notify its investigators and the Institute in writing of its decision to approve or withhold approval of the protocol or of any modifications required to secure IACUC approval. Required modifications, once made must be reviewed by the IACUC using the procedures described in Section III.D.6 above. If the IACUC decides to withhold approval of an activity, the correspondence must include a statement of the reasons for its decision and the investigator is given an opportunity to respond either in writing or in person.

The IACUC notifies the Institution 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 by providing the Institutional Official with a copy of the IACUC meeting minutes. If the IACUC decides to withhold approval of an activity, the meeting minutes must include a statement of the reasons for its decision. Written communication between the IACUC and investigators is the responsibility of the IACUC chair and copies of all correspondence are maintained by the IACUC chair. Communication for significant changes to protocols is the same as for protocols (see above).

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 at least once every 3 years according to PHS Policy IV.C.1.-5. The IACUC procedures for conducting continuing reviews are as follows:

After approval of a protocol the IACUC conducts post-approval monitoring and continuing review of protocols.

Post approval monitoring.
The IACUC conducts semiannual program and facility reviews as described above in Section III.D.2. During the reviews IACUC members monitor animal health and conditions and that procedures are compliant. They may also work with facilities management staff to monitor any necessary repairs or upgrades. The veterinarian may also make periodic checks on the animals or may visit at the request of animal care or research staff. The IACUC reviews documented training records for individuals who work with animals to ensure that they are appropriately trained. All animals are monitored daily by the animal care staff and any unexpected outcomes, illnesses or other adverse events or concerns are reported to the Principal Investigator and the Veterinarian. Any unexpected outcomes are recorded and reviewed by the IACUC, together with any suggested refinements of procedures. Any non-compliance is reported to the IACUC chair who will then convene a subcommittee to review and investigate the potential non-compliance. The findings will be presented and reviewed at a convened meeting of a quorum of the IACUC who may vote to suspend the activity if non-compliance is confirmed (see below). The IACUC also review any reported concerns involving the care and use of animals as described in Section III.D.4. and review any reports of incidents involving occupational health and safety.
At present BRISC personnel do not perform any surgery on live animals or use any controlled substances, but the IACUC will implement monitoring strategies such as examination of surgical areas, including anesthetic equipment, use of appropriate aseptic technique, and handling and use of controlled substances if the need arises for future projects.

Continuing review of protocols
All approved protocols are reviewed annually by the IACUC. A request is made to the Principal Investigator to attest to the current accuracy of the protocol (for example that there have been no changes in procedures, personnel or animal usage). Any significant changes must be reviewed and approved by the IACUC before initiation as described above. The IACUC conducts a complete and new review of all protocols utilizing all of the criteria mandated for the initial review at least once

every three years. Before the third anniversary of the protocol, the investigator must resubmit the protocol for re-review by the IACUC, who use the same criteria and procedures used for reviewing a new protocol to assess the resubmitted protocol by FCR or DMR as described in Section III.D.6 above. The review and approval must be conducted prior to the expiration date. The results of all IACUC reviews, including annual renewals are recorded in the IACUC meeting minutes.

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

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 (6.b above).

The IACUC may suspend an activity only after review of the matter at a convened meeting of a quorum of the IACUC and after the majority of the quorum present have voted in favor of suspension.

If the IACUC suspends an activity involving animals, or any other institutional intervention results in the temporary or permanent suspension of an activity due to noncompliance with the Policy, Animal Welfare Act, the *Guide*, or the institution's Assurance, the Institutional Official in consultation with the IACUC shall review the reasons for suspension, take appropriate corrective action, and report that action with a full explanation, in writing, to OLAW and to any funding agency. Initial/preliminary reports to OLAW may be made telephonically.

Suspensions, whether temporary or permanent, will be reported to OLAW in accordance with NIH Notice of February 24, 2005, NOT-OD-05-034 Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals

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

The BRISC Occupational Health and Safety program is designed to promote a safe work environment by minimizing the risk of illness or injury associated with working with or around research animals and research-related hazard. The program covers all individuals who work with animals (or animal waste) directly as well as those who may be exposed indirectly to animals or their by-products. These include not only animal caretakers, technicians, students, volunteers, investigators, and veterinarians, but facility maintenance engineers, housekeeping staff, security and other staff.

BRISC Safety Officer conducts annual Health and Safety training sessions for employees. In addition, BRISC contracts with two companies, (b) (4) and (b) (4) for assistance in maintaining compliance with all federal, state and local, HIPAA regulations regarding Occupational health and safety and for assistance with Occupational Health and Safety Training for employees. BRISC uses (b) (4) Occupational Health Specialists to help with planning and monitoring as well as a medical provider for the Occupational Health services. BRISC Occupational Health and Safety Program includes, but is not limited to, the following:

Control and Prevention Strategies from BRISC and in collaboration with (b) (4) Occupational Health Specialists ((b) (4))

1. *Health history and evaluation.* Prospective and existing employees who work directly with animals are sent to (b) (4) for a job-related medical evaluation that complies with all federal, state and local HIPAA regulations. BRISC personnel including the Principal Investigator and Safety Officer provide information on the specific hazards that the employee may encounter to (b) (4) , who may also visit BRISC facilities to further evaluate risks. At (b) (4) **,** employees have a medical history taken to determine their health status and whether they have special needs such as immunosuppression or animal allergies that

may require specific accommodations. Depending on their specific job requirements and medical history, they may also have a medical exam, that determines if employee may be cleared for work, with or without specific accommodations. In the unlikely event that an employee is deemed unable to fulfill job requirements due to a medical condition, he/she may seek a second opinion. No medical information is revealed to BRISC; only the accommodations required to enable the employee to fulfill job requirements without compromising their health.

2. *Hazard identification and risk assessment*. The identification and assessment will be performed by the Principal Investigator or Supervisor and the Safety officer and possibly other experts including the Veterinarian. As mentioned above the risk assessment is based on job tasks, the species exposed to (only mice are used at BRISC), the hazards that are evident, the periods of exposure and possibly best practices. (b) (4) uses this information, the health status of the individual and special conditions such as a history of allergies or immunosuppression in risk assessment.
3. *Procedures to alleviate hazards and minimize risks*. All personnel entering the animal facility will be trained by the institution's Safety Officer regarding safety issues (including potential biohazards) in the facility. This training is offered to all employees who work with animals directly as well as those who may be exposed indirectly to animals or their by-products. This includes staff working in maintenance, safety, security and housekeeping, summer students and visiting faculty who may enter the animal facility or other areas where animals or their products are present. Training will include proper handling disposal, emergency procedures for each hazard. Material safety data sheets are on file in a convenient location for all chemicals used. Education for employees regarding allergies zoonoses, personal hygiene and handling hazardous agents will be provided prior to engaging in work involving these hazards. Depending on the assessed risk, additional training may be required before the individual may start work. Refresher education regarding zoonoses and personal hygiene will be offered by the Safety Officer annually. This training is documented and training documentation is retained by the Safety Officer. Per the Institutional Chemical Hygiene plan, various controls (engineering, administrative and personal protective equipment) are in place to address exposure hazards. All personnel are trained in the use of personal protective equipment (PPE) such as gloves, masks, head covers (bouffant caps), safety glasses, disposable gowns and shoe covers. Facilities are mopped regularly with disinfectant and surfaces are wiped down with disinfectant after use. Facilities equipment and procedures are designed, selected and developed to reduce the possibility of physical injury and health risk to personnel. All personnel are trained in good personnel hygiene practices, prohibiting eating and drinking, use of tobacco products and application of cosmetics and/or contact lenses in animal rooms and laboratories.
   BRISC does not provide Occupational HealthCare services or training for contractors who may enter the animal facility, for example to certify biosafety cabinets. For contractors, we confirm that the contracting company is responsible for the health and safety of its workers and that adequate training is provided. BRISC staff advise the contractors of the hazards and risks present in the worksite and of rules and procedures for working safely. The contractors have the opportunity to request additional information. BRISC staff provide all necessary PPE and monitor contractors on the job to ensure that they are working safely.
4. *Immunizations.* Immunizations are offered to employees based on risk assessment. For example, animal care staff and laboratory staff working with animals are offered tetanus vaccinations. Other vaccinations may be offered depending on the specific biohazards that the individual may be exposed to. Records of vaccinations received and opt-in status are maintained the Safety Officer. Immunizations are administered by, and in consultation with (b) (4)
5. *Precautions taken during pregnancy, illness or decreased immunocompetence.* Animal care staff or researchers will receive education and training regarding risks specific for their work. As part of this training, information will be given regarding risks for those with special circumstances or conditions such as pregnancy, animal allergies or immunodeficiency. The training will include the increased risk for development of infectious disease in immunocompromised individuals and will be given to both personnel who work directly with animals, in addition to those who may be exposed indirectly to animals or their by-products.

6. *Animal/Allergy Medical Surveillance.* All BRISC employees who work directly with animals, or who may be exposed indirectly to animals or their by-products are given the opportunity to opt-in the BRISC Animal/ Allergy Medical Surveillance program. This program enables them to consult with (b) (4) about specific health risks and preventative measures and to receive periodic medical evaluations to monitor work-related conditions such as allergies. An employee can opt to participate at any time. No medical information is disclosed to the employer (BRISC), although the need for specific accommodations is communicated to the Safety Officer and Principal Investigator, as well as to the employee. (b) (4) maintains all medical records of employees in this program and procedures are in place to transfer the medical records if the need to use a different medical provider arises.
   Offers of employment for employees who work with animals are contingent upon them undergoing a fit-for-work medical evaluation, as described in Section III.E.1, which is used for risk assessment. All individuals working in the animal facility are trained in all hazards that may be encountered including: the types of hazard present, proper handling and disposal of hazardous substances, emergency procedures, allergies, zoonoses, vaccinations, personal hygiene, use of PPE and how to enroll in the Animal/Allergy Medical Surveillance Program. All individuals who enter the animal facility are offered the chance to opt in the Animal/Allergy Medical Surveillance Program. Individuals who work with animals or their by-products or bedding /cages are strongly encouraged to opt-in. All training and acceptance of enrollment in the Animal/Allergy Medical Surveillance Program are documented and records are maintained by the Safety Officer. An employee can request to be sent to (b) (4) for a 'Fit-for-Work' evaluation. (b) (4) may suggest additional accommodations that may enable the employee to meet job requirements or may suggest that they are re-assigned to work outside of the animal facility. As mentioned above, all personnel entering the animal facility receive comprehensive training on the risks associated with the use of animals, including signs and symptoms to be aware of. This training, in addition to safeguards that are already in place should prevent any illness or injury from occurring as a result of working in the animal facility. These safeguards include wearing PPE including masks/respirators, personal hygiene, working with animals and changing cages in biosafety cabinets, control or airflow and exhausts, physical barriers in the facility and waste disposal procedures.

7. *Availability and procedures for treatment of bites, scratches, illness or injuries.* Staff will be trained in safe animal handling procedures and the use of personal protective equipment to minimize the risk of bites and scratches. However if any injuries do occur, they should be reported immediately to the immediate supervisor who will then contact the Safety Officer to determine the need for minor first aid vs. an appointment with (b) (4) or emergency care. (b) (4) have a 24 hr helpline that provides advice on work-related injuries occurring outside of normal business hours and provides guidance on whether emergency care is needed. The injured person may also elect to go directly for emergency care or other medical treatment. Information about procedures for treatment of bites, scratches illness or injuries is posted in the Animal facility. If any injuries and illnesses do occur, they should be immediately reported the Facility Supervisor and the Biosafety Officer, who will keep record of the injury and the procedures that followed to remediate that.
8. *Animals are purchased from approved vendors only.* Only mice are used. Vendor health information is reviewed by the consulting veterinarian to determine whether any zoonoses are present and this information is discussed at the IACUC meeting. The IACUC committee vote to approve specific vendors. The vendors send email alerts if zoonoses (or other health concerns) are subsequently found in shipped and received animals.
9. *Health insurance program*. Full-time and some part-time BRISC employees are eligible for a health program that covers preventative, non-emergency and emergency care. The health insurance program is the primary source of medical care for employees, whereas (b) (4) the Occupational Health Service medical provider provides treatment and preventative measures for work-related conditions and injuries only.
10. *Monitoring*. The BRISC Safety Committee monitors the Occupational Health program with the help of (b) (4) medical-trained professionals. The Safety Committee comprises the BRISC Safety Officer, the Institutional Official and the IACUC chair and may include, or seek guidance from, (b) (4) staff, the Veterinarian, Human Resources/workers comp program administrators and Facilities Management staff. The BRISC Safety Officer maintains

records of training, risk assessments and vaccination records for all staff. The Institutional Official is responsible for implementation of the program.

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

Please see Facility and Species Inventory in Section X. BRISC has separate animal rooms for uninfected stock mice (b) (4) and mice infected with pathogenic agents (b) (4). Each room is approximately 170 square feet in size, including service areas. Mice are the only species that we work with. Our average daily inventory in (b) (4) is 10 cages (30 mice) and in (b) (4) 20 cages (60 mice). We use microisolator cages containing 2-4 mice per cage. Cages in (b) (4) are placed in a Hepa-filtered ventilated unit.

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

IACUC members are provided with online links to the PHS Policy for the Humane Care and Use of Laboratory Animals and the National Research Council (NRC) Guide for the Care and Use of Laboratory Animals. They will also be given a copy of this Assurance.
In addition IACUC members complete online training from the AALAS Learning library. This includes training modules 'IACUC Essentials' and 'Working with the IACUC'.
Continuing education is also provided by the Veterinarian at IACUC meetings.

Researchers, animal care staff and other personnel involved in animal care or use. All personnel who wish to work in the Animal Care facility must first complete a form documenting their experience and training. The form documents experience in specific procedures as well as training on animal care and use that includes minimizing numbers of animals required to obtain valid results and limiting pain and distress. Both the staff member and the Principal Investigator sign the form. A copy is also provided to the IACUC to document the persons experience. This forms part of the protocol review during which IACUC members review the experience of individuals working on the protocol to ensure that they have the expertise to perform the procedures listed in the protocol. Animal facility staff receives practical training in all procedures related to animal husbandry and sanitation of facilities, in addition to the Occupational Health and safety training described above, which is provided to all personnel who use the animal facility.

All new personnel are provided online links to the PHS Policy for the Humane Care and Use of Laboratory Animals and the National Research Council (NRC) Guide for the Care and Use of Laboratory Animals. They will also be given a copy of this Assurance and final copies of any IACUC approved protocols that they are named on. They are provided with thorough instruction by experienced personnel who are familiar with the care and use of laboratory animals and are highly experienced in all the procedure required for the research. All personnel are also required to complete online training provided on the AALAS website including the modules 'Introduction to mice', 'Working with laboratory mice', 'IACUC essentials' and 'Working with the IACUC'. This training includes information on how to handle mice safely to minimize the risk of injury to the researcher or the animal subject, humane practices in animal care and use, minimizing the numbers of animals required to obtain valid results and limiting a pain or distress, including the proper use of anesthetics and analgesics. The training references the three R's of humane animal experimentation (reduction, refinement and replacement). The training also covers methods whereby deficiencies in animal care and treatment are reported including those reported by members of staff and the fact that no individual can be discriminated against or subject to reprisal for reporting concerns about animal care and use. In addition the concept of alternatives to animals in research, and avoiding unnecessary duplication of experiments is covered. Continuing education is provided to reinforce initial training and to provide updates on changes in legislation or policy. This animal care and use refresher training is completed at least once every 3 years, while the Health and safety training is completed annually.

All training is documented and documentation of training is retained for at least 3 years by the IACUC chair.

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 6 months and will be reevaluated by the IACUC at least once every 6 months according to PHS Policy IV.B.1.-2. Reports have been and will continue to be prepared according to 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 PHS Policy and 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 2 — not 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. The report of the most recent evaluations (program review and facility inspection) is attached.

V. Recordkeeping Requirements

A. This Institution will maintain for at least 3 years:
   1. A copy of this Assurance and any modifications made to it, 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 granted or withheld
   4. Records of semiannual IACUC reports and recommendations (including minority views) as forwarded to the Institutional Official, Dr. Sally Sarawar.
   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 3 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. The Institutional reporting period is the calendar year (January 1 – December 31). The IACUC, through the Institutional Official, will submit an annual report to OLAW by January 31 of each year. The annual 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)
   2. Any change in the description of the Institution's program for animal care and use as described in this Assurance
   3. Any change in the IACUC membership

4. 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, Dr Sally Sarawar.
5. Any minority views filed by members of the IACUC

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 VI.A. and VI.B. above should include any minority views filed by members of the IACUC.

VII. Institutional Endorsement and PHS Approval

A. Authorized Institutional Official

Name: Sally Sarawar

Title: President and CEO

Name of Institution: Biomedical Research Institute of Southern California

Address:
Physical Location:
1692 Ord Way,
Oceanside, CA 92056.

Mailing address:
4225-H Oceanside Blvd
(b) (4)
Oceanside CA 92056

Phone: (b) (6) Fax: (b) (6)

E-mail: ssarawar@bri-sc.org

Acting officially in an authorized capacity on behalf of this Institution and with an understanding of the Institution's responsibilities under this Assurance, I assure the humane care and use of animals as specified above.

Signature: (b) (6) Date: May 9th 2018

B. PHS Approving Official *(to be completed by OLAW)*

Dr. Venita B. Thornton - Senior Assurance Officer
Office of Laboratory Animal Welfare
National Institutes of Health
6705 Rockledge Drive
RKL1, Suite 360, MSC 7982
Bethesda, MD 20892-7982

Signature: (b) (6) Date: May 10, 2018

Assurance Number: D16-00895 (A4703-01)

Effective Date: 5/10/2018 Expiration Date: April 30, 2022

VIII. Membership of the IACUC

Date: December 5th , 2017	
Name of Institution: Biomedical Research Institute of Southern California	
Assurance Number: #A4703-01	
IACUC Chairperson	
Name*: Claudia Gabaglia	
Title*: Assistant Professor	Degree/Credentials*: M.D. Ph.D.
Address*: 4225-H Oceanside Blvd (b) (4) Oceanside CA 92056	
E-mail*: cgabaglia@bri-sc.org	
Phone*: (b) (6)	Fax: (b) (6)

IACUC Roster

Name of Member/ Code**	Degree/ Credentials	Position Title***	PHS Policy Membership Requirements****
Claudia Gabaglia	M.D. Ph.D.	Chairperson	Scientist; affiliated
Mari Bray	DVM	Veterinarian	Veterinarian; affiliated
(b) (6)			Scientist; affiliated
			Nonscientist; unaffiliated
			Nonscientist; affiliated
			Scientist (alternate); affiliated

* 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.

*** List specific position titles for all members, including nonaffiliated (e.g., banker, teacher, volunteer fireman; not "community member" or "retired").

**** PHS Policy Membership Requirements:

Veterinarian	veterinarian with training or experience in laboratory animal science and medicine or in the use of the species at the institution, who has direct or delegated program authority and responsibility for activities involving animals at the institution.
Scientist	practicing scientist experienced in research involving animals.
Nonscientist	member whose primary concerns are in a nonscientific area (e.g., ethicist, lawyer, member of the clergy).
Nonaffiliated	individual who is not affiliated with the institution in any way other than as a member of the IACUC, and is not a member of the immediate family of a person who is affiliated with the institution. This member is expected to represent general community interests in the proper care and use of animals and should not be a laboratory animal user. A consulting veterinarian may not be considered nonaffiliated.

[*Note: all members must be appointed by the CEO (or individual with specific written delegation to appoint members) and must be voting members. Non-voting members and alternate members must be so identified.*]

IX. Other Key Contacts (optional)

If there are other individuals within the Institution who may be contacted regarding this Assurance, please provide information below.

Contact #1	
Name: Claudia Gabaglia	
Title: Chairperson IACUC committee	
Phone: (b) (6)	E-mail: cgabaglia@bri-sc.org
Contact #2	
Name: Sally Sarawar	
Title: Institutional Official	
Phone: (b) (6)	E-mail: ssarawar@bri-sc.org

X. Facility and Species Inventory

Date: 9/21/17			
Name of Institution: Biomedical Research Institute of Southern California			
Assurance Number:			
Laboratory, Unit, or Building*	Gross Square Feet [*include service areas*]	Species Housed [*use common names, e.g., mouse, rat, rhesus, baboon, zebrafish, African clawed frog*]	Approximate Average Daily Inventory
(b) (4)	170	Mouse	10 cages
	170	Mouse	20 cages

*Institutions may identify animal areas (buildings/rooms) by a number or symbol in this submission to OLAW. However, the name and location must be provided to OLAW upon request.