INCIDENT RESPONSE PLAN

For [redacted] BSL3 Suite (rooms

And BSL3 buildings

Texas A&M University, College Station, TX 77843

to ensure compliance with

42 CFR Part 73.14 – Select Agents and Toxins

1. Purpose

1.1. General. This is the incident response plan for the possession and use of Brucella abortus, Brucella suis and Brucella melitensis at Texas A&M University main campus (College Station, TX). This incident response plan meets the requirements of 42 CFR Part 73 and 9 CFR Part 121. This plan covers the use of Brucella strains in the Veterinary Research Building at Texas A&M University, BSL-3 laboratory rooms and in buildings

1.2. This plan describe the entity's response procedures for the theft, loss, or release of a select agent or toxin, inventory discrepancies, security breaches (including information systems), severe weather and other natural disasters, workplace violence, bomb threats, suspicious packages, and emergencies such as fire, gas leak, explosion, power outage. This plan is coordinated with the University-wide incident response plans in place at TAMU.

2. Roles and Responsibilities

2.1. Principal Investigator. The principal investigator, Dr. Thomas A. Ficht has primary responsibility for the implementation of the select agent program within a particular laboratory or select agent work area. Where possible, all incidents covered in this plan must be reported directly to Dr. Ficht.

2.2. Oversight by Responsible Official and Alternate Responsible Official. Oversight of the select agent program is performed by the Responsible Official, the Alternate Responsible Official and the Biosafety Officer. Richard Ewing, Vice President for Research, is the Responsible Official at TAMU. The Alternate Responsible Officials is Angelia Raines. The Biosafety Officer is Brent Mattox. Dr. Ficht will report incidents, as required, to the Biosafety Officer and the Responsible Official or Alternate Responsible Official. Where required, the Responsible Official will report incidents to CDC.

2.3. Annual Program Review. The Responsible Official or Alternate Responsible Official will audit the incident response program on an annual basis. This review will include drills and exercises to ensure the effectiveness of the incident response plan. Based on the outcome of drills, exercises or reported incidents, this incident response plan may be updated.

2.4. Contact Information. The **Principal Investigator**, Thomas A. Ficht, may be contacted during business hours at (979) 845-4118, at home at and on his mobile phone at His email address is tficht@cvm.tamu.edu. The **Responsible Official**, Richard Ewing, may be contacted during normal business hours at (979) 845-8585 and at all other times at (979) . His email address is rewing@vprmail.tamu.edu. If the Responsible Official is unavailable, the **Alternate Responsible Official** Angelia Raines may be contacted

during normal business hours at (979) 847-9362 and at all other times at (979) . Her email address is araines@vprmail.tamu.edu. The **Biosafety Officer**, Brent Mattox can be reached at (979) 845-2132 during business hours, and after hours at (979) The mailing address for the Responsible Official, Alternate Responsible Official and Biosafety Officer is Environmental Health & Safety, xxxx TAMUs, College Station, TX, 77843. His email address is bsmattox@neo.tamu.edu.

3. **Description of Work**

This plan covers the following work.

	Work description	Unique features	Biological Use Authorization	Biosafety Level
	Storage of *Brucella abortus, B. suis, B. melitensis*	Locked freezer	0741	3
	Work with *Brucella abortus, B. suis, B. melitensis*	BSC	0741	3
	Storage of *Brucella*-infected animal carcasses	Locked freezer	0741	3
	Inoculation of mice with *Brucella* spp. and necropsy of infected animals	BSC	0741	3

Additional information concerning the laboratories and the select agent use is contained in the facility's CDC select agent application for registration on file at the CDC's Select Agent Program office. A copy is also securely stored at the entity's Office of Environmental Health and Safety.

4. **Response to theft, loss or release of *Brucella abortus, Brucella suis*, or *Brucella melitensis***

4.1. Determination of Loss or Theft. Possible loss or theft of the select agent will be reported to the Principal Investigator if any of the following have occurred:

4.1.1. The lock on the Select Agent storage area has been found open or appears to have been tampered with.

4.1.2. Evidence of forced entry into the laboratory or storage areas has been found.

4.1.3. A discrepancy in the Select Agent inventory has been identified.

4.1.4. An employee reports cultures or samples missing.

4.1.5. A package containing select agents fails to arrive in the laboratory at the time indicated on CDC Form 2.

4.1.6. A *Brucella* –infected mouse is missing from its microisolator cage.

4.2. Investigation of Loss or Theft by the Principal Investigator. Upon receiving a report of possible loss or theft of select agents, the Principal Investigator will immediately contact all personnel authorized for select agent access and call a meeting to determine whether the report of possible loss or theft can be explained by other means. For example, if an employee reports a malfunctioning lock, failure to note destruction of a strain in the inventory, or locates missing samples, the incident will be considered resolved, and no further report will be made.

4.2.1. Loss or Theft has not occurred: If the incident can be explained by means other than loss or theft (i.e. an employee reports having broken a lock or forgetting to record destruction of a culture, or has replaced the culture in the wrong

location), the incident will be considered resolved and internal laboratory report will be filed. Procedures will be reviewed with laboratory personnel to prevent re-occurrence of the incident.

4.2.2. Loss or Theft has occurred: If no alternative explanation for the possible loss or theft of select agent can be found, the Principal Investigator will notify the Responsible Official for assistance in filing CDC Form 3, Report of Loss or Theft of select agent.

4.3. Release of a Select Agent or Toxin. Possible release of *Brucella* will be reported if any of the following has occurred:

4.3.1. A package containing *Brucella* has been received, which has been damaged in transit, such that the primary containment vessel appears to have been compromised.

4.3.2. Simultaneous failure of the biosafety cabinet and negative pressure in the BSL-3 suite during work in the biosafety cabinet with open *Brucella* cultures.

4.3.3. Simultaneous spill of *Brucella* cultures outside the Biosafety cabinet and failure of negative pressure in the Biosafety Level 3 suite. In case of a spill, a spill kit containing absorbent material and disinfectant is located in a sealed container under the sink in room

4.3.3.1. Personnel are advised to immediately leave the lab after removing any contaminated clothing and to return in tyvek suits with full face respirators after the air has been scrubbed clean by air handlers (approx one hour).

4.3.4. In case release of *Brucella* outside the BSL-3 laboratory is suspected, the Principal Investigator will notify laboratories on the on the first floor of the as well as the Responsible Official.

4.4. Exposure of laboratory personnel to *Brucella* cultures. The following incidents may result in unintentional exposure to *Brucella* that can result in a laboratory-acquired infection. In any of these cases, personnel should report the exposure to the Principal Investigator and report to TAMU Occupational Health, where they will be given the option to initiate post-exposure prophylaxis. The exposure will be reported by the Principal Investigator to the Responsible Official, who will notify CDC of the exposure. A spill kit containing absorbent material and disinfectant is located in rooms

4.4.1. A spill of live *Brucella* culture outside the biosafety cabinet

4.4.2. Failure of the Biosafety Cabinet during work with *Brucella*

4.4.3. Needle stick or cut with sharps contaminated with *Brucella*

4.4.4. A bite from a *Brucella* infected animal, if the bite penetrates the double gloves and breaks the skin

4.4.5. A centrifuge accident that results in aerosolization of *Brucella*.

5. Security Breaches **A security breach will be determined to have occurred if any of the following are observed:**

5.1. The access control system has failed, leaving the BSL-3 suite accessible to unauthorized persons.

5.2. An unauthorized person is observed unaccompanied in the BSL-3 suite
A lost or stolen card was used to access the BSL-3 laboratory

5.3. An unauthorized person has accessed the computer used to control entry to the BSL-3 suite.

5.4. An unexpected or suspicious package arrives in the laboratory

If any of the above occurrences is observed, it must be reported immediately to the Principal Investigator. The Principal Investigator will then notify the Responsible Official of the security

breach and take steps to correct the problem. Within 24 hours, an inventory will be performed of all samples in the laboratory and in select agent storage. Any missing select agent samples will be reported to CDC using Form 3. Regardless of the outcome of the security breach, the Principal Investigator and the Responsible Official will review the incident to determine whether changes to the Security plan are required to avoid similar occurrences in the future.

6. Severe weather or natural disasters. **The most likely occurrences in this area are severe thunderstorms, floods or earthquakes.**

   6.1. If severe weather (thunderstorms or flooding) is predicted, experiments with select agents should be suspended until the severe weather has passed to avoid power outages during the work. All samples should be secured inside the locked -80°C freezer or the locked +4°C storage.

   6.2. If an earthquake is felt, workers should immediately leave the building--if possible, shedding gloves and lab coat on the way out of the BSL-3 suite. Cleanup, if necessary, can be performed once it is safe to re-enter the building.

   6.3. Power to the BSL-3 suite may be affected if the emergency generator is flooded. In this case, all samples should be secured inside the -80°C freezer. If the vivarium is threatened by flooding, animal cages should be fastened shut, put into secondary containers (biohazard bag or large Tupperware) and transported to (CMP) for secure holding until the threat of flooding has passed. If it becomes necessary to evacuate the College Station area, all animal experiments will be terminated before evacuation by euthanizing the animals and storing the carcasses in the secure select agent storage in room .

   6.4. In case of a power outage, if there is no immediate danger to the building, secure all infectious samples inside the -80°C freezer, the +4°C refrigerator, or the incubators. The Biosafety cabinets and air handling system of the BSL-3 suite are on emergency backup power, which will prevent exposure to infectious samples in case of a power outage. Follow standard procedures for leaving the laboratory and return once the power has been restored to resume work.

7. **Fire, Gas leak, Steam leak, Explosion, Bomb threat:**

   7.1. If work is being performed in the Biosafety cabinet, cap all samples, dispose of gloves and outer laboratory coat, and leave the laboratory immediately. If the fire is within the BSL-3 laboratory, and the worker feels (s)he can safely extinguish the fire, then the fire extinguisher located in the interior hall may be used. If a worker feels his or her safety threatened, (s)he should leave the laboratory immediately without stopping to decontaminate or secure any work, using the designated escape routes (through the locker rooms or the exterior "airlock" door on the west side of the building). Upon leaving the building, personnel should assemble outside the in the assigned spot (southern corner of corner of Parking) and report to the Lab Safety Officer for attendance.

   7.2. Notify the appropriate emergency responders: Fire 4-911 or 911 from mobile phones, the Principal Investigator and the Biosafety Officer. For steam and gas leaks, notify TAMU Operations and Maintenance at xxx-xxxx.

   7.3. In case a bomb threat is received by telephone, follow TAMU procedure to notify the University Police should be notified immediately by calling the emergency number, **9-1-1**. Also inform the Principal Investigator and Responsible Official. Always be sure to give the name of the building, room number, your name and telephone extension number.

      7.3.1. The University Police will assign personnel to investigate the call and take whatever police action may deemed necessary and reasonable for the safety of the campus community. The Police will conduct a search of the building, or of specific locations in or around the building. When judged prudent and feasible

to do so, the search will be conducted with the assistance and cooperation of the Principal Investigator and/or Responsible Official. After an evaluation/assessment of the content of the bomb threat, the decision to evacuate or close building shall be made jointly, whenever possible, by the Police and the Principal Investigator and/or Responsible Official.

7.3.2. Any unusual or suspicious object should be reported immediately to the University Police or to any immediate supervisor or administrative officer. Suspected objects or materials should **NOT** be touched or disturbed. Every bomb threat or incident of a suspected explosive device should be considered valid until all reasonable precautions for public safety have been taken or until the danger to life and property is terminated.

8. **Failure of Select Agent Storage Freezer:**

8.1. If the -80°C freezer in that is used to store *Brucella* strains fails, the strains will be moved to a temporary backup location, which is either the other -80°C Revco freezer located in room or in secure freezer in a locked BSL-2 laboratory. This freezer will be padlocked in order to limit access to personnel authorized to work with select agents.

9. **Workplace violence:**

9.1. Incidents of disruptive or threatening behavior on the part of an employee, student or visitor should be reported immediately to the Principal Investigator, who will report the incident to the Department Head, the Responsible Official and the Workplace Violence Response Team, as proscribed by the TAMU Personnel and Procedures manual section 290-09. If the individual accused of disruptive or threatening behavior is authorized for access to select agents, this person's access will be suspended pending the results of an investigation by the Workplace Violence Response Team. If an act of violence or a physical assault has occurred, or the threatening activity occurs within the BSL-3 laboratory, the person feeling threatened should call the police immediately to report the incident. If the person accused of violence has access to select agents, the person's access will be suspended pending the outcome of the investigation. Suspension of select agent access will be reported to the Responsible Official and a suspended individual's keycard access will be inactivated within 24 hours.

10. **Entry of emergency responders into the BSL-3 laboratory.**

10.1. In a case in which a life-threatening injury or medical condition (i.e. heart attack) occurs inside the BSL-3 laboratory, emergency responders will be allowed to enter the laboratory. If possible, upon feeling ill the laboratory worker should immediately exit the suite to facilitate treatment by emergency responders. An off-master key for emergency responders is located in the building's "Knox box" for Fire response. Personnel protective equipment, including Tyvek suits, N95 masks, HEPA-filtered respirators and gloves, are located inside the entrys (locker rooms) to the BSL-3 suite. A spill kit containing absorbent materials and disinfectant is located under the bench in each of the labs . A First Aid kit is located inside the locker rooms of the BSL-3 suite. If responders are required to enter an area where a spill has occurred, they will be referred to Scoot and White Clinic and offered post-exposure prophylaxis consisting of oral doxycycline.

10.1.1. Entry procedure for the BSL-3 laboratory: Don a Tyvek suit, gloves, shoe covers and respiratory protection (N95 mask) before entering laboratories

10.1.2. Providing first aid and emergency medical treatment in the BSL-3 laboratory: A person working inside the biosafety hood is not considered to be contagious unless a spill has occurred. The person's gloves may be contaminated, and

may be removed to facilitate treatment. If there is no space within the labs to put the person on the floor, move the person to the interior hallway to administer treatment.

10.1.3. Exit procedure from the BSL-3 laboratory: Emergency responders should remove Tyvek suit, mask, shoe covers and gloves before exiting and leave them behind in the BSL-3 laboratory. Hands should be washed immediately upon exit from the BSL-3 laboratory.

10.1.4. Decontamination procedures for medical equipment and clothing: Emergency responders should decontaminate equipment before leaving the laboratory by one of the following methods:

10.1.4.1. Autoclaving. Autoclaves are located within the BSL3 suite or on the of the

10.1.4.2. Wiping surfaces with 10% bleach, followed by 1% Virkon-S.

11. Incident Response Plan Testing

11.1. Drills or tabletop exercises will be conducted annually to test the effectiveness of the biosafety plan. The drills or exercises will be coordinated with the TAMU Police Department and will include, but not be limited to, the Principal Investigator or designee, EH&S Biosafety Officer, TAMU Fire Department representative and the Campus Emergency Planner.

11.2. The drill or exercise will include, but not be limited to, accessibility to restricted space, attempted or unauthorized entry into restricted spaces challenge, animal room security, staff knowledge of hazard/emergency protocols for their work location(s) and other situations that are deemed appropriate for each work location.

11.3. Following the drill or exercise, which will test the various components of the incident response plan for completeness, those involved will critique their findings for each drill/exercise location. The Principal Investigator working with the Responsible Official and Biosafety Officer will implement changes as necessary changes to the plan. Results of the drill or exercise will be reviewed by the Biological Safety Administrative Advisory Committee (Biosafety Committee).

12. Emergency Response Plans

12.1. The entity emergency response plan is contained in a separate document and is referenced in the individual laboratory emergency response plan.

12.2. Additional information concerning the laboratory emergency response plan is contained in the laboratory's CDC select agent application for registration on file at the CDC's Select Agent Program office. A copy is also securely stored at the entity's Office of Environmental Health & Safety.

12.3. The Responsible Official and Biosafety Officer should be contacted immediately in the case of any emergency in a select agent lab. The Responsible Official will coordinate access and information issues with campus police, fire, and emergency responders.

12.4. If necessary, the Responsible Official will coordinate the emergency relocation of select agents to another secure location.

13. Site security and Control **are described in detail in the Select Agent Security Plan**

13.1. The laboratories are secured by a card reader and key. Sharing of key cards with other personnel is not permitted.

13.2. Individuals not authorized for access to select agents must be accompanied by approved personnel at all times while in the BSL-3 or ABSL-3 suites.

13.3. Data that could enable access to select agents by unauthorized personnel should be located on password-protected computers.

13.4. If approved personnel are observed violating security or biosafety procedures, this observation should be reported immediately to the Principal Investigator. The Principal investigator will investigate the allegation and determine whether the violator should have his/her select agent access suspended or revoked. Suspension of select agent access will be reported to the Responsible Official and the individual's key card access will be terminated within 24 hours.

14. References

14.1. 42 CFR Part 73

14.2. 7 CFR Part 331

14.3. 9 CFR Part 121

14.4. Biosafety in Microbiological and Biomedical Laboratories, Centers for Disease Control and Prevention, National Institutes of Health, Fourth Edition, May 1999

14.5. Laboratory Security and Emergency Response Guidance for Laboratories Working with Select Agents (Revised BMBL, Appendix F), published in Morbidity and Mortality Weekly Report, December 6, 2002.

Appendix 1: Emergency Telephone Numbers

Thomas A. Ficht	Office: 845-4118
Emergency	9-911
University Police	(979) 845-2345
College Station Police	(979) 764-3600
College Statioin Fire	(979) 764-3700
Environmental Health & Safety	(979) 845-2132
TAMU Area Maintenance (HVAC failure, steam leak, gas leak)	(979) 845-5542
TAMU Maintenance (24 hours)	(979) 845-4311
Radiological Emergencies	(979) 862-1111
Responsible University Officials	RO-Richard Ewing (979) 845-8585 business ARO-Angelia Raines (979) 847-9362 business Biosafety Officer-Brent Mattox (979) 845-2132 business
Building manager	5-3194
	2-4778
	5-4185
Neighboring labs to notify in case of simultaneous containment breach and spill outside	
	8-3649
	5-9813
	x-xxxx
	5-9814

8-4057
5-2050

Appendix 2: Decontamination Procedures for Spills of *Brucella* Cultures

1. Signal others in the BL3 labs of any spill outside the biological safety cabinet. All personnel should change out of contaminated clothing and wash any exposed skin with a disinfectant, such as Purell. Clothes must be removed within the BL3 area and will be autoclaved by those cleaning up.
2. Put on a clean scrub suit and go to the shower on the first floor animal facility. Shower thoroughly with soap.
3. Return to the lab for cleanup: Put on a full face respirator and tyvek suit (contained in the SPILL KIT). Put on double gloves and shoe covers.
4. Use paper towels to cover the spill. Prevent creation of contaminated aerosols.
5. Saturate all materials with 10% bleach solution (see previous section for description).
6. Allow to soak 15 minutes while remaining in the room. Clean up debris and other contaminated materials and place in autoclave bags.
7. Disinfect all exposed surfaces using 1X Wexcide or 1% Virkon (surface disinfectant solution).
8. Wipe surface of full-face respirator with 1% Virkon or 1X Wexcide, being careful to avoid skin contact with Wexcide.
9. Remove all clothing and place in autoclave bag.
10. Remove full face respirator and spray off all surfaces in the lab with 1% Virkon or 1X Wexcide.
11. Make sure that all contaminated material is autoclaved, surface-disinfected or incinerated.
12. Inform others not to work in the lab until the air handling system is able to clear any residual organisms from the air (3h).
13. Return to the lab after 3 hours and perform another decontamination of all lab surfaces with 1% Virkon or 1X Wexcide.
14. Report accident to Dr. Thomas A. Ficht.

Contents of spill kit located in BL-3 labs

Full-face respirator, Tyvek suit, clean scrub suit, absorbent material, Purell skin disinfectant, towel, copy of decontamination procedures for spills.

5/17/07

STANDARD OPERATING PROCEDURES FOR BIOSAFETY LEVEL 3

Although these procedures have been written specifically for the BSL3 suite in Building room , they are applicable to experiments in building oom , except where explicitly indicated otherwise

Entry Procedures:

Sign up to use the BL3 by writing your name, date, and time of entry into the suite on the dry erase board located in Dr. Samuel's BL-2 laboratory, room Before entering the facility, the operator must first enter all details required in the log-in book outside the anteroom (name, date, time in).

Once inside the anteroom the operator dons a laboratory gown/coat and 2 pairs of gloves.

Biosafety Cabinet Use

Before working in the biosafety cabinet, the UV light is turned off, the fluorescent light is switched on, and a biohazard bag, a paper towel, a Wexide squeeze bottle and a fresh absorbent sheet (if needed) are placed in the cabinet.

All materials needed to complete the experiment are placed in the cabinet to limit the number of times hands pass through the air barrier. Equipment is not to be placed on the intake grills at the front of the cabinet, nor blocking the exhaust opening at the back of the cabinet.

The outer (second) pair of gloves is always removed before withdrawing hands from the biosafety cabinet. A new outer pair of gloves is then donned before proceeding with other work in the BL-3.

A biohazard bag should be present in the cabinet. Absorbent material (such as paper towels) is placed in the bottom of the biohazard bag. This bag is used for discarding solid waste (gloves, plastic waste, pipette tips). Once the bag is full, it is closed, wiped with Wexide and taken out of the cabinet to be collected into a larger covered waste container next to the cabinet.

Liquid waste should be put into a special container inside the biosafety cabinet with sufficient concentrated hypochlorite bleach to achieve a final concentration of not less than 10% and allowed to react overnight before disposal. Wipe the outside of the container with Wexide or 10% chlorine bleach before removing it from the cabinet. The liquids are then disposed of down the sink using large amounts of water.

Contaminated pipettes and plastic inoculating loops should be submerged in a container filled with the appropriate concentration of Wexide solution. The contaminated pipette tray must remain in the hood until the operator is ready to autoclave it.

Anything removed from the BSC during the work session is to be decontaminated by wiping with Wexide while still in the BSC. Ethanol (70%) is then used to remove the Wexide.
At the end of each work session, culture tubes, DNA tubes, racks and other material to be removed from the cabinet are decontaminated by wiping with Wexide while still within the cabinet. Ethanol (70%) is then used to remove the Wexide.

The absorbent sheet and other absorbent materials used during cleaning along with the gloves are placed into a biohazard bag while still within the cabinet. The bag is closed with autoclave tape while still in the cabinet. Wipe the outside of the bag with Wexide. Do not twist or tie the bag as it will blow open in the autoclave. Place the bag into a larger covered waste container next to the cabinet.

A fresh pair of gloves is donned and the hood is now wiped down completely with Wexide followed by 70% ethanol (the ethanol serves to remove the Wexide). Nothing should be left in the Biosafety cabinet when leaving the facility.

All tissue or cell culture related materials should be disposable whenever possible. Only disposable plastic pipettes and plastic inoculating loops are to be used in the BSL3 lab.

Exiting Procedures

If autoclaving is necessary, the operator is to follow autoclaving procedures detailed below.

Once done with working outer gloves are removed and put in the general biohazard container. Enter changing room and remove gloves outside to inside. Finally, you must wash and dry your hands with microbicidal soap before exiting the anteroom.

The operator exits through the outer door and notes his/her time out in the log book. Wash hands in Rm . for hygiene to remove residue from microbidical soap.

Decontamination Procedures

All waste material leaving the BSL3 facility must first be autoclaved for at least an hour except for the liquids decontaminated with bleach as noted above.

A double-door autoclave is located in the laboratory next to the anteroom.

Do not autoclave materials containing chlorine bleach, volatile chemicals or radioactive materials.

Monthly Wex-cide 128 (1 gal) poured down floor drains to ensure periodic decontamination. Log of activity maintained by facilities manager.

Decontamination Procedures for Spills

- Allow aerosols to settle in the room
- Dress in protective clothing (e.g., lab coat, gloves)
- Gently cover spill with paper towels and apply wex-cide, starting at perimeter and working towards the center
- Allow sufficient contact time (30-60 min) before clean up
- Decontaminate all wastes before disposal: atuoclave
- Spill procedure notice displayed in suite

AEROSOL CHALLENGES

1 Intra-entity transfer forms must be filled out at least one day prior to performance of any transfer between buildings.

2 *Coxiella* suspensions used for inoculations are prepared and loaded into conical tubes in rooms of building in the biological safety cabinets.

3 Inoculum containing viable organisms is transported from the facility in generalized "triple" packaging (primary receptacle, water tight secondary packaging, durable outer packaging) required for a biological agent of human disease.
3.1 The outer packaging is left in the locker room and the inner packaging is brought into room
3.2 This packaging requires the "Infectious Substance" label on the outside of the package. This packaging must be certified to meet rigorous performance tests as outlined in the DOT, USPS, PHS, and IATA regulations.
3.3 Such samples are transported through the men's or women's locker rooms at the CMP facility under constant supervision from approved persons.

4 At the CMP facility, personnel will change from street clothes into appropriate wardrobe
4.1 In the outer locker room, street clothes are removed and scrubs put on.
4.2 In the inner changing room, two pairs of gloves, facemask, tyvek suits and powered air-purifying respirators (PAPRs) are put on before entry into the main hallway.

5 At the CMP facility, animals will be transported to room 143 in microisolater cages and removed in the biological safety cabinets and loaded into cages for challenges.

5.1 Make certain that the room airflow indicator is working and that the air is flowing from outside the room to inside at a safe level.

6 Madison Chamber preparation and use (building room)
6.1 Plug cord from control box into the wall socket. Check the light on the control box. Connect the source of compressed air (e.g., building; tank) through the small flow meter to the nebulizer. Make sure that the compressed air regulator reads at least 30 psig. When the main switch is on, the vacuum pump, fans, and timer should be operating.
6.2 Carefully unscrew the glass jar from the nebulizer and place about 10 ml of challenge suspension in the jar or 2ml in a precious fluid chamber. Attach the jar to the nebulizer unit and adjust the vertical stainless steel tube so that the lower (intake) end is about half an inch below the level of fluid in the jar.
6.3 Load the animal basket into the chamber, being careful to center it so that it doesn't touch the fan blades. Close the door and turn on the main switch, activating the vacuum pump, fans, and timer.
6.4 Check the main (room) air flow meter (the larger meter on the right). The center of the float (ball) should run about "21".
6.5 Nebulizer jars are filled with inoculum under the safety cabinet.
6.6 Turn on the compressed air and simultaneously start the timer. The air flow rate through the compressed air flow meter should read about 5 psig. Check visually to be certain that the challenge inoculum is being nebulized.
6.7 After exactly 300 seconds (5 min), the compressed air supply to the nebulizer should be shut off and the nebulization process will stop. Flow through the small meter will drop to zero, and visual inspection of the nebulizer will show no activity. The timer should continue to run.
6.8 After an additional 600 seconds (10 min) or 900 seconds (15 min) total on the timer, turn off the main switch, stopping the vacuum pump, fans, and timer.
6.9 Open the chamber door and remove the animal basket.
9.1 Personnel handling the animals need to take extreme care and spray their gloves with Wexcide. After the transfer is complete, the outer pair of gloves are removed and immediately replaced.
6.10 Remove the glass nebulizer jar, and decant the challenge suspension back into the original tube for transfer back to the originating lab. The jar is decontaminated with bleach and is either reloaded with a different strain or thoroughly decontaminated and loaded with 70% ethanol for decontamination cycle.

7 Post run decontamination.
7.1 Place each individual housing cage back in the rack, then place the rack back into the chamber. Seal chamber door using the attached latching system.
7.2 Place 15ml of 70% ethanol into the nebulizer reservoir, and re-attach the jar to the chamber and run the chamber for 15 min.
7.3 Once the cycle has been completed (green light turns on), open the

chamber, and spray all external surfaces of the cage, rack and internal housing cages with Wexcide, covering all surfaces.
7.4 The cages/ rack should then be extensively rinsed out with water to remove Wexcide residue, wipe dry.
7.5 Spray internal surfaces of the chamber with Wexcide and soak for 10 minutes. Wipe dry, and spray with 70% ethanol to remove disinfectant residue. **WARNING: Be sure to spray ethanol after the Wexcide treatment as the residue may damage the chamber.**
7.6 All personnel decontaminate each other in room using disinfectant prior to leaving the lab, wexcide, diluted according to maufacturer's instructions are used for this purpose. Animal cages are similarly disinfected as is the rack that may be used to transport them into room143.5/17/07
7.7 The tyvek suits are removed in the hall outside room and placed in approved containers to be autoclaved by CMP personnel. The animal rack is transported back to the animal holding room.
7.8 Full-face respirators are removed last and surface decontaminated with 70% ethanol.

8 The inoculums and extracted tissues are returned to building in approved containers
8.1 Animals may either be sacrificed at CMP (building ...., or moved back to animal holding facilities in building by CMP personnel.
8.2 Tissues are harvested as early immediately post exposure to one week, and up to one-year post inoculation and homogenized in PBS.
2.1 Animal carcasses are autoclaved and sent to the incinerator by CMP personnel.
8.3 After thorough decontamination of container containing inoculums, containers are placed inside approved durable (leak-proof) transport container that is then closed, sealed, and disinfected as well.
8.4 Scrubs are removed in inner changing rooms and placed in containers to be autoclaved by CMP personnel. Facemasks and gloves are thrown away.
8.5 All personnel shower before entering the outer changing room.
8.6 Street clothes and personal belongings are collected before exiting BL-3 suite.
1.1 Outer packaging is used to transport the material back to the originating lab

Special Practices
All doors are kept locked.

Dr. Samuel controls access to the suite.

Laboratory personnel receive appropriate training and instruction on the potential hazards associated with work in the suite and necessary precautions.

As part of an Occupational Health Plan, workers with access to *C. burnetii* will participate in a periodic serologic analysis for response to *C. burnetii*. A serologic sample will be taken prior to work with virulent *C. burnetii* as a baseline sample. Scott and White Clinics, the Occupational Health Plan provider, will notify workers of reportable serologic responses. Personnel will be advise of the opportunity to consult with Scott and White clinicians about the relationship between serological titer, clinical disease, and treatment options. Personnel reporting to the PI with clinical symptoms consistent with acute Q fever will be advised of the opportunity to consult Scott and White clinicians.

All personnel working with *Coxiella burnetii* in the BL-3 have demonstrated proficiency in standard microbiological practices and techniques as well as practices specific to the suite.

OPERATING PROCEDURES FOR THE BIOSAFETY LABORATORY SUITE

, Building

THOMAS A. FICHT, PROFESSOR AND L. GARRY ADAMS, PROFESSOR
VETERINARY PATHOBIOLOGY

Although these procedures have been written specifically for the BSL3 suite in Building , they are applicable to experiments in building , and buildings except where explicitly indicated otherwise

May 30, 2007

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Acknowledgements

Biosafety Level 3 is applicable to clinical, diagnostic, teaching, research, or production facilities in which work is done with indigenous or exotic agents that may cause serious or potentially lethal disease as a result of exposure by the inhalation route. Laboratory personnel have specific training in handling pathogenic and potentially lethal agents, and are supervised by competent scientists who are experienced in working with these agents.

Personnel wearing appropriate personal protective clothing and equipment conduct all procedures involving the manipulation of infectious materials. Additionally, all procedures involving the manipulation of infectious materials are conducted within biological safety cabinets or other physical containment devices. The laboratory has special engineering and design features.

The following standard and special safety practices, equipment and facilities apply to the Biosafety Level 3 Laboratory Suite in the Veterinary Research Building. Disinfectants used include ethanol, 1% (w/v) Virkon-S and 10% (v/v) commercial bleach. Virkon-S is safe for use on human skin and is as effective as bleach at reducing *Brucella* viability. Ethanol is used for flame sterilization and may be used to clean surfaces, but is much less effective than either Virkon-S or bleach at inactivating *Brucella*.

1. ACCESS TO BSL3

1.1 Access is limited to areas working with SBAT is regulated by CDC/DOJ.

1.1 Access is limited to areas working with SBAT and is regulated by CDC/DOJ.

1.2 Personnel are issued a key and pass card when you have been assigned a CDC/DOJ approval number and successfully completed all training requirements under the direction of the PI or designee.

2.1 Passcards are not to be transferred between individuals or shared.

2.2 In order to maintain the accuracy of access logs cards may not be borrowed. In this event access may only be gained with the assistance of the PI.

1.2 Non-approved personnel must be escorted by approved personnel and are not permitted to work with or gain access to SBAT. "Access is defined as at any point in time in which has possession of the agent (example carries, uses or manipulates) or has the ability to gain possession of the select agent or toxin".

2.1 Baseline titers must be obtained from anyone entering the BSL3 suite.

2.2 Non-approved personnel must be escorted at all times in the BSL3 and sign a certificate of training to acknowledge the laws governing access to SBAT.

2.3 It is the responsibility of the escort to maintain contact with the trainee and to correctly and completely fill in the Facility Access Log.

2. GENERAL DESCRIPTION OF THE BSL3 SUITE

2.1 The rooms of the BSL3 suite are color-coded to indicate levels of risk of exposure. Each area requires that certain minimum levels of precaution be followed.

1.1 Signage on rooms have been updated to include contact names, telephone numbers, and entry requirements.

2.2 GREEN: The changing rooms and airlock are the only green areas in the BSL3 suite. In these rooms, personnel change out of street clothes before entering the suite and into street clothes before exiting the suite. Street clothes are not worn inside the BSL3 suite; scrub suits are not worn outside the BSL3 suite.

2.3 YELLOW: In these areas, risk of exposure is minimized by keeping all potentially contaminated items inside of double-containers. All personnel will be wearing a minimum of:

3.1 scrub suit,

3.2 clogs or shoe covers,

3.3 latex exam gloves (1 pair), and

3.4 0.1 micron particle masks are used when working with agent in biological safety cabinets. Any work with agent outside the cabinets requires the use of power-assisted personal respirators (PAPRs).

4.1 N95 or N100 masks may be used in place of the 0.1 micron masks, but require fit testing by EHSD.

2.4 Pink (Beige): The main labs are under negative pressure relative to the hallway to contain any accidental release of the agent. Culture flasks, tubes and plates may be transported between incubators and BSC in this area using secondary containers. Colonies may be counted on the plates after securing the lids.

4.1 No additional clothing is required at this point.

2.5 RED: All biosafety cabinets are potential sites of exposure. These are the only places where contaminated materials may be opened. In addition, the animal room is a site of high risk of exposure when animals are being housed. When actually working with contaminated items, clothing requirements include:

5.1 clothing required in the YELLOW zone,

5.2 wrap-around lab coat,

5.3 1 pair of Tyvek sleeves, and

5.4 latex exam gloves (2 pairs).

2.6 When working with animals, additional precautions are required, including the use of Tyvek coveralls and PAPRs as described below. Specific procedures for large animal work are outlined in Appendix 2. Entry Procedures

2.7 The entry doors from the outer hallway into the Men's and Women's changing rooms are kept locked at all times.

7.1 Before entering BSL3, make sure that someone else knows where you are.

7.2 Indicate your entry into the BSL3 suite on the marker board in the outer hallway. Upon entry, log your name, time of day and date, and the room in which you will be working in the logbooks present in the outer locker rooms.

7.3 Keys and cards are issued to individuals and are not shared.

7.4 When escorting individuals be sure to have the visitor fill in all the information requested. It is your responsibility to verify their ID.

2.8 The airlock area is used to make deliveries such as gas tanks and fresh mouse cages and is where the electronics for air handling is housed. It is separated from the main corridor of the BSL3 by a cipher-locked door. A

logbook is maintained in the "airlock" area to record entries of CMP/LARR personnel, gas tank deliveries, as well as maintenance.

2.9 In the Changing Rooms (Green):

9.1 OUTER CHANGING ROOM

1.1 Change out of street clothes. Store street clothes in a locker.

9.2 INNER CHANGING ROOM

2.1 Put on a scrub suit (shirt and pants).

2.2 Put on clogs or shoe covers.

2.3 Put on a face mask.

2.4 Put on 1 pair of latex exam gloves.

2.10 In the procedure laboratories:

10.1 Place signs on laboratory doors indicating the nature of the work performed.

1.1 Additional signage on rooms has been updated to include contact names, telephone numbers, and entry requirements.

10.2 Wrap-around lab coat are required over scrubs for procedures generating aerosols.

10.3 Put on 1 pair of Tyvek sleeves, covering both the exam gloves and the sleeves of the lab coat.

2.11 When working in the BIOSAFETY CABINET,

11.1 Put on a second pair of latex exam gloves.

11.2 When you move away from the BIOSAFETY CABINET:

2.1 Remove the outer gloves.

2.2 Disinfect the inner gloves with 70% ethanol.

3. PROCEDURES WHILE WORKING IN THE BSL3 SUITE

3.1 Follow all procedures outlined below under:

3.2 "Standard Microbiological Practices,"

3.3 "Special Practices: Biosafety Level 3," and

3.4 "Safety Equipment (Primary Barriers): Biosafety Level 3."

3.5 These sections are taken directly from "Biosafety in the Microbiological and Biomedical Laboratories."

3.6 The following specimens should be considered contaminated:

1.1 all items or liquids known to contain infectious agents;
1.2 any liquids or tissues of animal origin; and
1.3 any liquids containing cells or tissues of animal origin.
1.4 If there is any question about a substance, it should be considered contaminated.

3.7 All contaminated materials should be kept in double-containers when not inside a biosafety cabinet. The use of double-containers will protect against the possibility of a tube being cracked or incompletely sealed and against the possibility of breakage if dropped.

7.1 The tube, plate, dish, or zip-lock bag containing the contaminated material is the first (inner) container.
7.2 The second (outer) container may be:
2.1 a stainless steel container with lid (taped closed);
2.2 a plastic container with lid (taped or "locked" closed); or
2.3 a centrifuge carrier with plastic safety cover locked in place.
7.3 Exceptions to this include animals kept in Hepa filtered cages and plates containing bacterial colonies which are counted on the benchtop. The latter is transferred to the benchtop in sealed containers, but these are opened to visualize the colonies.

3.8 Handling sharp objects

8.1 Sharp objects include:
1.1 syringe needles,
1.2 glass Pasteur pipets (or any thin glass tubing),
1.3 broken glass,
1.4 knife (scalpel) blades, and
1.5 anything else that could puncture human skin.
8.2 Whenever possible, avoid the use of sharp objects and glass objects. Substitute plasticware for glassware.
8.3 Never re-cap bend, or break a hypodermic needle.
8.4 Never handle broken glass, use tweezers or tongs. Use a dustpan and broom to clean up broken glass.

3.9 When using the biological safety cabinets:

9.1 Minimize the number of items inside the biological safety cabinet. The only items should be those that are immediately required for the experiment. Too many items in the cabinet disrupt laminar airflow and reduce the level of protection provided by the cabinet.
9.2 Never obstruct the vents in the cabinet. These include:

2.1 the vent in the front of the cabinet (covered by the grill),
2.2 the vents on the left and right sides of the cabinet, and
2.3 the vent in the back of the cabinet.

9.3 Use plastic-backed absorbent paper for working with contaminated material.

3.10 Centrifugation of viable select agent (or any other BSL3 agent) may only be performed in sealed centrifuge cups. Signs to this effect must be placed on all centrifuges. Room are used for centrifugation and appropriate signage has been posted.

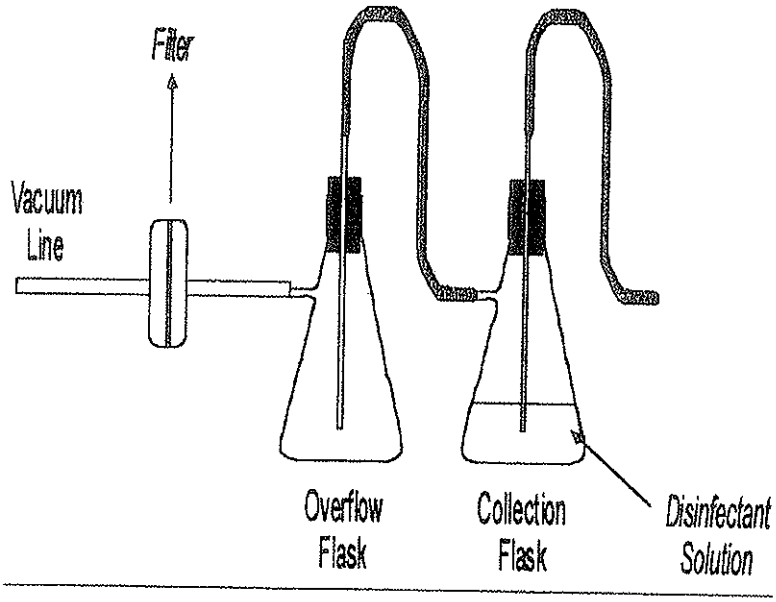

Fig. 1 Safety trap setup for use with in house vacuum line.

3.11 Spill procedures have been posted in rooms

3.12 To use the vacuum lines for aspirating biological fluids, use two large flasks in series with a microbiological filter (0.2 – 0.45 μm).

3.13 The telephones in the BSL3 suite are for emergency use only, to provide additional safety for you. Remember that you are holding potentially contaminated latex gloves very close to your face, that these gloves are touching the receiver, which is very close to your face and mouth, and that someone else will be using the receiver after you.

13.1 Remove the outer pair of latex exam gloves before picking up the receiver.

13.2 Decontaminate the receiver immediately after every use.

13.3 Do not give the BSL3 phone number to friends. They can leave a message, and you can return their calls when you leave the BSL3 suite. If there is an emergency, laboratory or office staff can transfer the call or come into the BSL3 suite to give you the message.

4. Routine Cleaning and Decontamination Procedures

4.1 Sharp objects

1.1 Whenever possible, avoid the use of sharp objects and glass objects. Substitute plasticware for glassware.

1.2 All sharp objects (section 3.8.1 above) are to be disposed of in the Isolyzer® bottles provided in each laboratory.

2.1 When the contents of the bottle reach the fill line (prior to expiration), add the catalysts according to directions on the bottle to encapsulate all sharp objects.

2.2 The outside of the isolyzer is decontaminated and it is disposed with trash (do not autoclave).

4.2 At the very minimum, all laboratory surfaces should be disinfected before and after work. The following disinfectants may be used:

2.1 70% ethanol or isopropyl alcohol

2.2 Wexcide® (diluted 1:256, or 15 ml per gallon of water)

2.3 10% household bleach (diluted 100 ml per liter of water)

2.4 Virkon-S (1% solution in water)

4.3 All material to be autoclaved are stored in leak proof pans

3.1 Glassware is kept in separate, stainless steel pans, from other disposables (tip boxes, etc) to minimize accidental injuries.

4.4 All other (non-sharp) waste and trash generated in the laboratories are placed in biosafety bags and autoclaved.

4.1 Decontamination

1.1 When a biohazard waste bag is approximately 2/3-full, it should be autoclaved.

1.2 Close the bag loosely with the rubber bands supplied.

1.3 Place autoclave tape over all occurrences of the word "Biohazard" on the bag.

1.4 Place the bag in a leak-proof pan before carrying the bag into the hallway (to prevent possible leakage of liquid onto the floor).

1.5 Autoclave using the "Gravity" program for trash (solid). Bacterial plates are autoclaved using the liquid cycle for spent media.

1.6 Test strips are also provided and at least one strip should be

inserted into the opening of a bag. The bags should not be sealed tightly to prevent bursting open during autoclaving.

1.7 When autoclave cycle is complete, place the bag in the utility bin provided in the "clean room" that is lined with a black plastic bag.

1.8 When the bin is full these bags are transferred to the general trash (dumpster).

1.9 All autoclave runs are recorded and the autoclaves are certified weekly using thermotolerant spores (commercial supplier).

1.10 Autoclaves are operated as described on the EHSD web page (http://finance.tamu.edu/ehsd/resources/biosafety.asp) using conditions recommended by NIH and described in the IBC application form.

4.5 Disposal of liquid waste:

5.1 Large volumes of liquid waste are kept in autoclaveable containers less than ¾ full, and autoclaved in pans to catch any spills.

1.1 Decontamination with appropriate dilution of bleach or Virkon-S may also be used (section 4.2 above).

5.2 Smaller cultures in disposable plasticware are placed inside biohazard bags and placed in autoclaveable pans (for double-containment) before autoclaving.

5.3 Liquid waste is autoclaved on the "Liquid" as described on the Environmental Health and Safety web page and the IBC application form.

5.4 When the cycle is complete, open the autoclave door about 2 inches and wait at least 10 minutes before removing the liquids. (Follow directions given by the messages on the autoclave).

5.5 After 10 minutes, take the bottles out of the autoclave. If the autoclaved waste contains no coagulated solids, it may be poured down the sink. Bottles with coagulated solids must be sealed and placed directly in the dumpster outside the building.

5.6 Liquids may also be decontaminated by adding an equal volume of 10N NaOH, undiluted sodium hypochlorite (household bleach) to a final concentration of 10%, or addition of 1% (w/v) solid Virkon-S.

4.6 All biological specimens removed from the BSL3 that cannot be autoclaved must be disinfected prior to transfer

6.1 Cages are currently autoclaved off-site due to the small size of the autoclave.

6.2 Animal carcasses are autoclaved prior to disposal (incineration or biodigestion) by CMP (building [redacted] as described in the IBC application form.

6.3 Any tissues containing viable organisms are transported from the facility in generalized "triple" packaging (primary receptacle, water tight

secondary packaging, durable outer packaging) required for a biological agent of human disease.[1]

3.1 This packaging requires the "Infectious Substance" label on the outside of the package. This packaging must be certified to meet rigorous performance tests as outlined in the DOT, USPS, PHS, and IATA regulations.

3.2 Tissues are placed in sterile specimen bags and the outside of each bag is sprayed with disinfectant solution. Specimen bags are then placed within a secondary container that is also sprayed with the disinfectant solution.

3.3 All other specimens are inactivated using a number of different methods (heating at 65°C for at least 1 hour, the addition of gentamycin or following nucleic acid extraction). The killing of these samples is verified by evaluating growth on solid media for extended times (≥2 weeks at 37°C).

3.4 Such samples are transported through the men's or women's locker rooms.

3.5 Secondary containers are placed inside a durable outer container that is not brought to the BSL3 lab.

6.4 Blood samples in glass or plastic tubes are placed in test tube racks and sprayed with bleach. They are then placed within a secondary container that is also sprayed with the disinfectant solution.

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[1] Examples of the kinds of material that may need to be removed from biohazard areas usually the buildings in the research park for analysis and or transfer without autoclaving to another BSL3 laboratory:

-placental samples from live birth or aborted fetus

-selected tissues from necropsied animals (lung, liver, spleen, lymph nodes, milk, etc)

-abomasal fluid sample in either a sterile swab container or fluid placed into an empty vacutainer

-blood samples: either heparanized or non-heparanized blood in vacutainers

-sheets from door with log entries, and euthanasia logs (they do not go into the animal room; they are on the "dirty" side next to the showers

-isolyzer containers

-boots

-animal carcasses

-respirators

Sample disinfection:

-log sheets are sprayed with bleach and removed

-boots are disinfected with bleach and scrubbed to remove clods before disinfection.

-isolyzers are activated (solidified) and outsides sprayed with bleach.

-respirators are sprayed with bleach before removal

Autoclaved items:

-all trash (including gloves, tyvek suits, masks), surgical utensils, empty feed bags, are bagged and sprayed with bleach before removal and transport to the autoclave. Animal carcasses are triple bagged (bleach sprayed between layers) and brought to the vet school incinerator. They are treated as infectious substances and incinerated together.

4.1 After thorough decontamination, containers are placed inside a durable (leak-proof) container such as stainless steel that is then closed, sealed, and disinfected as well.

4.2 The outer surface of all containers must be disinfected. A 1:10 dilution of commercial bleach is effective in inactivating even highly concentrated suspensions of Brucella (up to 10^{11} CFU/ml) immediately. This concentration greatly exceeds any dosage used in these buildings or that may contaminate the exterior of bags or other containers.

4.3 The addition of sera is known to reduce the effectiveness of sodium hypochlorite. To enhance effective decontamination the bags or containers containing tissues are decontaminated multiple times. However, suspensions of bacteria do not normally contain added sera.

4.7 Floors are mopped weekly with either:

7.1 Wexcide® or phenocide (as described above), or

7.2 Commercial bleach (1:10 dilution in water)

7.3 Virkon-S (1% w/v in water)

4.8 Caulk is used to fill any penetrations in walls and ceilings and corkboards replaced by dry erase board (laminated aluminum) from the facility.

5. Radioactive Waste Disposal

5.1 Liquid waste is maintained in leakproof carboys within a specifically designated and labeled area. This waste may be added to the regular radioactive waste stream after verifying that there is no threat of viable infectious agent.

1.1 Treatment of radioactive waste is usually performed by adjusting the liquid to a final concentration of 10% commercial bleach or 1% Virkon-S.

1.1 This liquid left up to one week and portions 100-1000 µl are tested for viability on tryptic soy agar plates in incubators. If the plates remain negative after one week of incubation at 37°C then the liquid is disposed of as radioactive waste.

1.2 If positive then the waste material is heated for 1 hour at 65°C and viability is checked again as described above.

1.3 The outside of the carboy is decontaminated with bleach and the liquid is added to the normal radioactive waste stream.

5.2 Solid waste (including test plates described above (section 5.1 above) is placed in biohazard bags and these are placed inside a second bag for chemical sterilization using ethylene oxide as described by the manufacturer.

2.1 After the prescribed treatment period the bag is unsealed and ethylene oxide is allowed to escape under a chemical fume hood.

8.7 All cultures, stocks, and other regulated wastes are decontaminated before disposal by an approved decontamination method, such as autoclaving. Materials to be decontaminated outside of the immediate laboratory are to be placed in a durable, leak proof container and closed for transport from the laboratory. Materials to be decontaminated at off-site from the laboratory are packaged in accordance with applicable local, state, and federal regulations, before removal from the facility.

8.8 An insect and rodent control program is in effect.

9. SPECIAL PRACTICES: BIOSAFETY LEVEL 3

9.1 Laboratory doors are kept closed when experiments are in progress.

9.2 The laboratory director controls access to the laboratory and restricts access to persons whose presence is required for program or support purposes. For example, persons who are immunocompromised or immunosuppressed or have breaks in their skin may be at risk of acquiring infections. Persons who are at increased risk of acquiring infection or for whom infection may be unusually hazardous are not allowed in the laboratory or animal rooms. The director has the final responsibility for assessing each circumstance and determining who may enter or work in the laboratory.

9.3 The laboratory director establishes policies and procedures whereby only persons who have been advised of the potential biohazard, who meet any specific entry requirements (e.g., immunization), and who comply with all entry and exit procedures, enter the laboratory or animal rooms.

9.4 When infectious materials or infected animals are present in the laboratory or containment module, a hazard warning sign, incorporating the universal biohazard symbol, is posted on all laboratory and animal room access doors. The hazard warning sign identifies the agent, lists the name and telephone number of the laboratory director or other responsible person(s), and indicates any special requirements for entering the laboratory, such as the need for immunizations, respirators, or other personal protective measures.

9.5 Laboratory personnel receive the appropriate immunizations or tests for the agents handled or potentially present in the laboratory (e.g., hepatitis B vaccine or TB skin testing).

9.6 Baseline serum samples are collected and stored for all laboratory and other at-risk personnel. Additional serum specimens may be collected periodically, depending on the agents handled or the function of the laboratory.

9.7 A biosafety manual is prepared or adopted. Personnel are advised of

1.1 The outside of the bag is decontaminated with bleach and the waste is added to the solid radioactive waste stream.

5.3 All radioactive work areas (or anything that may have come in contact) are surveyed using a Geiger counter and contaminated material is immediately removed. This material must not be left to expose co-workers. Even if shielded such material represents a potential source of harm. A swipe test should be performed weekly to better assess contaminatioin.

6. Decontamination Procedures for Spills

6.1 Immediately hold your breath. DON'T TAKE A DEEP BREATH!!

6.2 Signal others in the BSL3 labs of any spill outside Class IIa biological safety cabinet. All other personnel must exit and shower profusely with disinfectant soap and shampoo. Clothes must be removed within the BSL3 area and will be autoclaved by those cleaning up. Place a sign on the lab door to indicate unsafe condition.

6.3 Exit the lab and shower to remove any aerosol contamination.

6.4 Wait one hour to allow the room to evacuate any aerosol and put on a PAPRs and double gloves.

6.5 Use a polyzorb adsorbent pillow (one-liter) or paper towels to cover the spill. Prevent creation of contaminated aerosols.

6.6 Saturate all materials with disinfectant solution (see previous section for description).

6.7 Allow to soak 15 minutes while remaining in the room. Clean up debris and other contaminated materials and place in double autoclave bags.

6.8 Disinfect all exposed surfaces using any of the surface disinfecting agents (Wexcide, phenocide, bleach, Virkon-S) in aerosolizer. Virkon-S is the only disinfectant recommended for use on human skin.

6.9 Spray surface of PAPRs with disinfectant, being careful to avoid skin contact with disinfectant.

6.10 Remove all clothing and shoes and place in double autoclave bag. Have a bag outside the room to transfer all contaminated material from room.

6.11 Remove PAPRs and place in double plastic bag for autoclave sterilization.

6.12 Continue sterilization of BSL3 area using aerosolizer with 1X Wexcide.

6.13 Make sure that all contaminated material is autoclaved or ethylene oxide

sterilized.

6.14 Put on a clean wrap-around to go to locker room and shower profusely with disinfectant soap and shampoo.

7. PROCEDURE IN THE EVENT OF ACCIDENT

7.1 In the case of a spill proceed as described above and then report the accident to Dr. Thomas Ficht (979-845-4118 or r your immediate supervisor and departmental administrator (979-845-5941).

7.2 In the event that you have an accident that causes a break in the skin (broken glass, etc) be sure to disinfect the area carefully using VirKonS (Dupont).

7.1 Always be certain to disinfect yourself carefully before leaving the BSL3 lab.

7.3 Make an appointment to see your physician or the Occupational Health Program Physicians at Scott & White clinic (979-691-3072).

3.1 Follow the incident report and contact the biosafety officer (979-845-2132 or 979- University Police (979-845-9900 or 979 and the Office of Research Compliance (979-847-9382 or

3.2 Students (especially those on fellowship) should be sure to mention that this accident is covered by Occupational Health and not Workman's Compensation.

8. STANDARD MICROBIOLOGICAL PRACTICES

8.1 Access to laboratory is limited or restricted at the discretion of the laboratory director when experiments are in progress.

8.2 Persons wash their hands after handling infectious materials and animals, after removing gloves, and on leaving the laboratory.

8.3 Eating, drinking, smoking, dipping tobacco or snuff, handling contact lenses, and applying cosmetics are not permitted in the laboratory. Persons who wear contact lenses in laboratories should also wear safety glasses, goggles or a face shield. Food is stored outside the work area in cabinets or refrigerators designated for this purpose only.

8.4 Mouth pipetting is prohibited; mechanical pipetting devices are used.

8.5 All procedures are performed carefully to minimize the creation of aerosols.

8.6 Work surfaces are decontaminated at completion of any work and after any spill of viable material.

special hazards and are required to read and to follow instructions on practices and procedures.

9.8 Laboratory personnel receive appropriate training on the potential hazards associated with the work involved, the necessary precautions to prevent exposures, and the exposure evaluation procedures. Personnel receive annual updates, or additional training as necessary for procedural changes.

9.9 The laboratory director is responsible for ensuring that, before working with organisms at Biosafety Level 3, all personnel demonstrate proficiency in standard microbiological practices and techniques, and in the practices and operations specific to the laboratory facility. This might include prior experience in handling human pathogens or cell cultures, or a specific training program provided by the laboratory director or other competent scientist proficient in safe microbiological practices and techniques.

9.10 A high degree of precaution must always be taken with any contaminated sharp items, including needles and syringes, slides, pipettes, capillary tubes, and scalpels. Needles and syringes or other sharp instruments should be restricted in the laboratory for use only when there is no alternative, such as parenteral injection, phlebotomy, or aspiration of fluids from laboratory animals and diaphragm bottles. Plasticware should be substituted for glassware whenever possible.

10.1 Only needle-locking syringes or disposable syringe-needle units (i.e., needle is integral to the syringe) are used for injection or aspiration of infectious materials. Used disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal; rather, they must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal. Non-disposable sharps must be placed in a hard-walled container for transport to a processing area for decontamination, preferably by autoclaving.

10.2 Syringes which re-sheathe the needle, needle-less systems, and other safe devices should be used when appropriate.

10.3 Broken glassware must not be handled directly by hand, but must be removed by mechanical means such as a brush and dustpan, tongs, or forceps. Containers of contaminated needles, sharp equipment, and broken glass should be decontaminated before disposal, according to any local, state, or federal regulations.

9.11 All manipulations involving infectious materials are conducted in biological safety cabinets or other physical containment devices within the containment module. No work in open vessels is conducted on the open bench.

9.12 Laboratory equipment and work surfaces should be decontaminated with

an appropriate disinfectant on a routine basis, after work with infectious materials is finished, and especially after overt spills, splashes, or other contamination with infectious materials. Contaminated equipment should also be decontaminated before it is sent for repair or maintenance or package for transport in accordance with applicable local, state, or federal regulations, before removal from the facility. Plastic-backed paper toweling used on non-perforated work surfaces within biological safety cabinets facilitates clean-up.

9.13 Cultures, tissues, or specimens of body fluids are placed in a container that prevents leakage during collection, handling, processing, storage, transport, or shipping.

9.14 All potentially contaminated waste materials (e.g., gloves, lab coats, etc.) from laboratories or animal rooms are decontaminated before disposal or reuse.

9.15 Spills of infectious materials are decontaminated, contained and cleaned up by appropriate professional staff, or others properly trained and equipped to work with concentrated infectious material.

9.16 Spills and accidents that result in overt or potential exposures to infectious materials are immediately reported to the laboratory director. Appropriate medical evaluation, surveillance, and treatment are provided and written records are maintained.

9.17 Animals and plants not related to the work being conducted are not permitted in the laboratory.

10. SAFETY EQUIPMENT (PRIMARY BARRIERS): BIOSAFETY LEVEL 3

10.1 Properly maintained biological safety cabinets are used (Class II or III) for all manipulation of infectious materials.

10.2 Outside of a biological safety cabinet, appropriate combinations of personal protective equipment are used (e.g., special protective clothing, masks, gloves, face protection, or respirators), in combination with physical containment devices (e.g., centrifuge safety cups, sealed centrifuge rotors, or containment caging for animals).

10.3 This equipment must be used for manipulations of cultures and of those clinical or environmental materials which may be a source of infectious aerosols; the aerosol challenge of experimental animals; harvesting of tissues or fluids from infected animals and embryonated eggs, and necropsy of infected animals.

10.4 Face protection (goggles and mask, or faceshield) is worn for manipulations of infectious materials outside of a biological safety cabinet.

10.5 Respiratory protection is worn when aerosols cannot be safely contained (i.e., outside of a biological safety cabinet), and in rooms containing infected animals.

10.6 Protective laboratory clothing such as solid-front or wraparound gowns, scrub suits, or coveralls must be worn in, and not worn outside, the laboratory. Reusable laboratory clothing is to be decontaminated before being laundered.

10.7 Gloves must be worn when handling infected animals and when hands may contact infectious materials and contaminated surfaces or equipment. Disposable gloves should be discarded when contaminated, and never washed for reuse.

10.8 Working in the different labs warrants different levels of biocontainment. Any work within the biological safety cabinet (BSC) may be performed without any additional protective gear.

8.1 Work with infected animals outside the BSC requires the use of PAPRs.

11. EXIT PROCEDURES

11.1 Any time you move away from the biosafety cabinet:

1.1 Remove the outer pair of gloves.

1.2 Disinfect the inner pair of gloves with 1:10 dilution of bleach or 1% Virkon-S.

2.1 These are used beacuase they have been demonstrated to kill *Brucella* immedialtely even at high concentration while ethanol can take as long as 30 minutes at the same concentration.

11.2 Before leaving the Procedure Laboratories (Pink or Beige):

2.1 Decontaminate all surfaces with appropriate disinfectant.

2.2 Turn on the ultraviolet light in the biosafety cabinet.
Leave the fan motor running in the biosafety cabinet (it requires a minimum of 20 minutes fan operation to establish laminar flow conditions.)

2.3 Take off the outer pair of gloves and discard in waste in bio-safety cabinet.

2.4 Take off the Tyvek sleeves and discard in waste in bio-safety cabinet.

2.5 Take off the wrap-around lab coat.

2.6 Disinfect the inner pair of gloves.

11.3 In the Changing Rooms (Green):

3.1 INNER CHANGING ROOM:

1.1 Take off the facemask.

1.2 Remove the inner pair of latex gloves.

1.3 Remove scrub suit and clogs.

1.4 Wash hands in the sink or use the shower.

3.2 OUTER CHANGING ROOM:

2.1 Put on street clothes.

2.2 Hands may be washed again in the men's or women's rest room on the first floor opposite the BSL3 changing rooms.

12. STORAGE AND INVENTORY OF SELECT AGENT (*BRUCELLA*)

12.1 Room has been designated a storage space and all freezers (-20°C and -80°C) in room are kept locked and the key may only be obtained by personnel having access to rooms

12.2 A daily record of select agent access from the freezers is maintained. The originals are kept in room Freezer inventories are maintained in the office of the PI.

2.1 The use of select agent must be indicated on the log including box number and slot number within the box.

2.2 All additions to the inventory must be registered in the agent access log.

2.3 Be certain to include the strain designation, freezer, box and slot number.

2.4 Destruction or complete use of inventory must be recorded on the freezer inventory log. This is especially critical, since the absence of tubes may be construed as lost or stolen.

2.5 Personal inventory sheets should be immediately updated to record the destruction and emailed to the PI, who will adjust the master electronic inventory accordingly.

12.3 Using the daily record of select agent access (previous section) inventory reconciliation will be performed monthly and finalized during IBC/EHSD inspection in January shutdown, maintenance.

12.4 A log is maintained to monitor animal removal from room to reconcile with animal inventory.

12.5 When plates are struck out and additional plates prepared the number of plates should be indicated in your notebook.

5.1 Subsequent plate disposal should be reconciled with the plates struck out. This will be evaluated weekly by the PI or appointed personnel.

13. INTRAFACILITY TRANSFERS

13.1 SBAT is transferred from the BSL3 suite in building using IATA approved packaging described in section 4.6 above and is maintained in the possession of approved personnel (CDC/DOJ clearance) on university

property. In the event that public roads are taken a university police escort will be requested for a university vehicle.

1.1 The SBAT will only be handled within the interior BSL3 rooms of buildings [redacted] CMP) and may be preloaded into syringes prior to transport.

1.2 All material that is not injected into animals is returned to this packaging that is decontaminated and returned to the BSL3 suite in building [redacted]

1.3 The inoculant is re-titrated and the volume measured to verify return of the SBAT and the sample remaining is destroyed by autoclaving.

1.4 Tissues and other materials recovered from these animals is processed and once the bacterial burden is determined tissue samples and cultures are destroyed by autoclaving.

13.2 All intra-entity transfers must be recorded whether they involve different investigators or not.

14. EXPERIMENTAL PROTOCOLS

14.1 Centrifugation

1.1 All centrifugation is performed in sealed rotors or cups which are loaded and unloaded within biological safety cabinets.

1.1 This approach will ensure that spills from broken or leaky tubes, bottles or plates will be contained

14.2 Bacterial Growth

2.1 Agent stocks are removed from the -80°C and kept cold on frozen block. Strains are transported to procedure rooms 128-130 and opened only under the biological safety cabinet.

1.1 Removal of strains from the freezer must be properly recorded on the agent access log located on the freezer.

2.2 Agent is removed from the stock with a sterile inoculating loop and spread onto solid growth media. Plates are incubated for 1-5 days at 37°C.

2.1 Agent is transported back to the -80°C. Amount removed is properly recorded on the agent access log.

2.2 Bacteria may be spread on plates for confluence or isolation, depending upon application.

2.3 Inoculation of liquid media is performed by removing a single colony from solid media with a sterile inoculating loop or sterile toothpick and inoculating liquid media in a conical tube or nephalo flask.

3.1 Volume of liquid media may range from 1 ml to 500 ml.

2.4 Typical inoculation consists of growing a 5 ml culture for 48 hours at 37°C (stationary phase of growth) for a saturated culture. This culture can be used to inoculate a conical tube or larger nephlo culture (1:1000 dilution) that is used for experiments.

2.5 Liquid cultures are typically grown no longer than 72 hours.

2.6 Remove several colonies (10-30) using a flame sterilized, wire loop and inoculate 5-10 mls of appropriate liquid medium (we typically use TSB).

2.7 This culture is incubated for 48 hours with shaking at 37°C.

2.8 The 'overnight' culture is then used to inoculate the appropriate volume of fresh broth (1:1000 fold dilution).

2.9 This culture is grown as described above until saturation is achieved (48-72 hours). Growth can be monitored via optical density (turbidity). This is most easily achieved using nephalo flasks and a Klett meter.

9.1 Frozen stocks may be prepared from liquid cultures by removal of a portion of the culture to a cryovial or microcentrifuge tube. Addition of glycerol to a final concentration of 50% (v/v) to the culture and mixing before entry into the -80°C freezer is necessary.

2.10 Additions to the freezer inventory must be properly logged on the agent access log and reported to the PI.

2.11 The plates may be stored at 4°C for up to 4 weeks and used as described in the following steps.[2]

2.12 When growing cultures for stationary phase cells only (saturation) one can inoculate the appropriate amount of medium in step 3 above. However, there is less control of the cell quantity in the inoculant and cultures may grow differently.

2.13 The bacteria are pelleted by centrifugation at 5,000 x g and washed in PBS (phosphate buffered saline) prior to resuspension in PBS at the appropriate concentration.

2.14 The maximum number of plates that may be prepared in this fashion is 500 or 2 liters of liquid media.

14.3 Disposal of solid and liquid waste follows section 5 :"Routine cleaning and decontamination procedures".

14.4 Electroporation of *Brucella* and Knockout Construction

4.1 Grow 2 plates *Brucella* on solid media (confluent) for three days or a 50 ml overnight culture in a nephalo flask.

4.2 If grown on plates, resuspend each plate with 6 ml ice-cold water, and move suspension to a 50 ml conical tube. The contents from multiple plates should be combined into one tube to increase the cell density. Bring the total volume to 50 ml with ice cold water. If the liquid culture is grown, pellet the entire 50 ml overnight culture (preferably this culture should be cooled down on ice first). All samples must be kept on ice.

2. After four weeks the viability of these cultures is unreliable.

2.1 Centrifuge cups or rotors are brought to the biological safety cabinet and samples are loaded then sealed prior to transport to the centrifuge.

14.5 Cells are pelleted for 15 minutes at 4°C. After initial pelleting of cells, the supernatant is removed into a bleach waste cup (10% v/v). The cell pellet is washed three times at the same conditions.

14.6 After final wash, resuspend pellet in the minimum volume needed for your number of samples under the BSC.

6.1 All subsequent steps occur under the BSC only.

14.7 Plasmid DNA is added to individual samples. Samples are electroporated according to the manufacturer's directions and previously optimized conditions

14.8 The cuvette is removed and the cells are immediately resuspended in SOC-B media, then moved to a sterile microfuge tube (1 ml total volume).

8.1 The samples shake o/n in a bullet box at 37°C for 12-24 hours) prior to plating.

14.9 Marked deletion mutants are created in *Brucella* species by allelic exchange following electroporation of a plasmid containing segments of the genome upstream and downstream of the gene to be deleted, separated by a kanamycin cassette.

9.1 Following the overnight incubation in the last step of the electroporation protocol, the entire sample is plated onto TSA containing kanamycin. Arising colonies are then replica-plated onto TSA containing kanamycin and onto plates containing carbenicillin. Marked deletion mutants from allelic exchange should be kanamycin resistant (Km^R) and carbenicillin sensitive ($Carb^S$), indicating a double crossover event involving loss of the plasmid and gene of interest.

14.10 Unmarked gene deletions are created by electroporating a plasmid containing the *sacB* gene, and the upstream and downstream sequence of the deleted gene, into the marked deletion strain.

10.1 Following electroporation, cells are plated onto TSA containing carbenicillin to select for the first homologous recombination, i.e. a co-integration. Colonies are then replica-plated onto sucrose plates and to TSA containing carbenicillin. Colonies that grow on carbenicillin ($Carb^R$) but not sucrose (Suc^S) are co-integrates with a functional *sacB* gene. Resolution of co-integration occurs spontaneously and is selected for by inoculating 5 ml of sucrose and incubating for 24 hours with agitation at 37°C, with subsequent plating onto sucrose containing media. Colonies are replica plated onto TSA and TSA/Kan to look for the loss of the kanamycin resistance, and therefore the unmarked deletion mutant.

14.11 Conjugation and mutagenesis

11.1 *B. melitensis* 16M was grown on solid media up to 72 hours as described above.

11.2 *E. coli* β2155 with or without pSC189 is grown on TSA supplemented with DAP (50 µg/ml) for 24 hours on solid media and harvested into peptone saline.

11.3 The recipient *B. melitensis* 16M strain is grown on TSA for 72 hours and harvested into the same solution.

11.4 Donor and recipient bacteria on each of the plates are harvested in 5 ml of peptone-saline (1% (w/v) Bacto-peptone™ and 0.9% (w/v) NaCl) containing DAP.

11.5 Equal volumes (100 µl) of bacterial suspensions are mixed together to provide a donor to recipient ratio of approximately 1:100.

11.6 The suspension is plated on nitrocellulose filters placed on the surface of TSA plates supplemented with DAP (50 µg/ml) and incubated for no more than two hours at 37°C.

11.7 Serial dilutions of the conjugation mixtures are prepared in peptone saline and plated onto TSA plates supplemented with kanamycin (100 µg/ml) to evaluate *Brucella* transformation efficiency.

11.8 Using these conditions, growth of the donor *E. coli* strain β2155 strain is repressed by the absence of DAP, and no exconjugants were obtained in mixtures of *B. melitensis* 16M with *E. coli* β2155 lacking pSC189.

11.9 The remaining bacterial conjugation mixture is stored in peptone saline at 4°C. The transconjugants were plated on TSA containing 100µg/ml kanamycin and 50% (v/v) glycerol and isolated colonies are transferred to 96-well plates containing TSB supplemented with kanamycin and incubated for 48 hours at 37°C.

11.10 The bank consists of 18,709 mutants in 195 microplates and represents sixfold coverage of the genome (i.e., averages 6 insertions per gene) with greater than 99% assurance of covering the entire genome (Sambrook, 1989 #1377).

14.12 Intracellular survival.

12.1 *Brucella* are grown in TSB or TSB with appropriate antibiotic for approximately 24 hours.

12.2 J774.A1 macrophage at low passage are used to seed the wells of a 24 well plate at 2.5×10^5 per well in 0.5 ml DMEM.

12.3 Bacterial cultures are washed and diluted 5-fold with PBS prior to addition to each of four wells for each strain at a final MOI (multiplicity of infection) of 50 determined as described above.

12.4 The plates are centrifuged at 200 xg for 5 min at room temperature and then incubated at 37°C for 20 minutes.

12.5 The infected cell monolayers are washed with PBS (or peptone saline) three times, overlaid with 0.5 ml of DMEM containing 50 µg/ml gentamicin and incubated at 37°C for various times.

12.6 Following these incubations the media is replaced with 0.5 ml of solution containing 0.5% (v/v) Tween-20 to lyse the macrophage monolayer.

12.7 The cell lysate is pipetted vigorously to ensure cell lysis and serial dilutions were prepared in PBS and portions plated on TSA supplemented with antibiotic as necessary to evaluate bacterial survival.

12.8 The results are presented as the difference in replication for wild-type and mutant strains using the following formula: $\log_{10}$(CFU 16M at 48h/CFU 16M at 1h)] minus $\log_{10}$(CFU mutant at 48h/CFU mutant at 1h)].

12.9 The plates are incubated at 37°C until the colonies are large enough to count (>48 hours). The plates are counted on the benchtop using a colony counter. The values presented represent the means of at least three separate experiments.

14.13 Identification of attenuated mutants.

13.1 Based on the calculated transformation efficiency, conjugation mixtures were diluted and plated onto TSA supplemented with kanamycin.

13.2 Single colonies were visible within 72 hours and transferred from the TSA plates to individual wells of 96-well microtiter dishes containing TSB supplemented with kanamycin and incubated for 48 hours at 37°C.

13.3 These dishes were used to prepare duplicate dishes for storage at -80°C after adjusting the cell suspensions to 20% (v/v) with sterile glycerol and were also used to prepare fresh culture for macrophage infection following resuspension (1:20 dilution in 100µl) in fresh TSB supplemented with kanamycin and incubation at 37°C for 24 hours.

13.4 Murine macrophage-like J774.A1 cells were seeded in 96-well microtiter dishes at 5×10^5 cells/well and incubated for 18 hours at 37°C in atmosphere containing 5% (v/v) CO_2.

13.5 Infections were performed with the addition of 10µl of the 24-hour cultures of bacteria at a final multiplicity of infection (MOI) of approximately 50.

13.6 Bacteria were pelleted onto the cell monolayers by centrifugation for 5 minutes at 200 xg to synchronize uptake. Cultures were incubated at 37°C for 20 minutes prior to removal of extracellular bacteria by washing with peptone saline.

13.7 Incubation was continued at 37°C up to 48 hours following the addition of 200 µl complete DMEM supplemented with 40µg/ml gentamicin.

13.8 Following incubation, the media was removed and the monolayer fixed with 200µl of 3.7% (v/v) formaldehyde at room temperature for 30 at least minutes.

13.9 The fixed monolayers were washed three times with PBS [10mM sodium phosphate and 150 mM NaCl, pH 7.4], followed by incubation with 50µl of goat-anti-*B. melitensis 16M* serum diluted 1:500 in PBS-TT [PBS with 0.05% (w/v) Tween-20 and 0.05% (v/v) Triton X-100] prior to incubation for 1 hour at room temperature.

13.10 The primary antibody was removed and the plates washed three times

with 200 µl PBS-T (PBS with 0.05% (v/v) Tween 20).

13.11 Fifty µl of donkey anti-goat IgG-Alexa Fluor 488 diluted 1:500 in PBS-TT was then added to each well and incubation continued for 1 hour at room temperature in the dark.

13.12 The plates were washed again three times with PBS-T followed by PBS and evaluated via fluorescence microscopy (Olympus IX70) as described previously.

13.13 In contrast to infection by *B. melitensis* 16M that grows well and exhibits numerous cells full of bacteria, multiplication of attenuated mutants is greatly reduced in number and/or present in only a few macrophages.

14.14 Isolation of genomic DNA and identification of interrupted loci.

14.1 **Extraction**, preparation and subsequent DNA sequence analysis are all performed as previously described with the following specific changes warranted by the use of mariner transposon *Himar 1* (Hong, 2000 #11771).

14.2 First, genomic DNA from attenuated mutants is digested with HaeIII and self-ligated. Amplification of the interrupted loci utilized mariner-specific forward 5'-CAACACTCAACCCTATCTCG-3' and reverse primers 5'-CACTCAACCCTATCTCGGTC-3' under the following conditions: 95°C 4 min; 30X (95°C 30 sec, 57°C 30 sec, 72°C 90 sec); 72°C 7 min.

14.3 PCR products are purified from agarose gel using the QIAquick Gel Purification Kit (Qiagen, Valencia, CA). Sequencing is performed using the primer 5'-CACTCAACCCTATCTCGGTC-3' at the Gene Technologies Laboratory (GTL, Institute of Developmental and Molecular Biology, BSBW 437 Texas A&M University, College Station, TX 77843-3155).

14.15 Competitive *in vitro* growth.

15.1 *In vitro* and *in vivo* competitive growth and auxonography are performed, the competitive growth indices are calculated as described previously and reflect the median of at least three separate assays (Hong, 2000 #11771). Competitive growth ratios are reported (as described above) for survival in the mouse splenic clearance model and are representative of at least three separate experiments.

14.16 Tissue culture infection

16.1 This method used has been described extensively elsewhere (Per, 2003 #12428).

16.2 *Brucella* were grown in TSB or TSB with appropriate antibiotic for approximately 24 hours.

16.3 J774.A1 macrophage at low passage were used to seed the wells of a 24 well plate at 2.5×10^5 per well in 0.5 ml DMEM.

16.4 Bacterial cultures are washed and diluted 5- fold with PBS prior to addition to each of four wells for each strain at a final MOI (multiplicity of infection) of 50 determined as described above.

16.5 The plates were centrifuged at 1000 x g for 5 min at room temperature in cups with safety lids, opened under the biological safety cabinet and then incubated at 37°C for 20 minutes.

16.6 The infected cell monolayers were washed with PBS (or peptone saline) three times, overlaid with 0.5 ml of DMEM containing 50 µg/ml gentamicin and incubated at 37°C for various times.

16.7 Following these incubations the media was replaced with 0.5 ml of solution containing 0.5% (v/v) Tween 20 to lyse the macrophage monolayer.

16.8 The cell lysate is vigorously pipetted to ensure cell lysis and serial dilutions were prepared in PBS and portions plated on TSA supplemented with antibiotic as necessary to evaluate bacterial survival.

14.17 **Preparation of *Brucella*-loaded alginate-poly-L-lysine-alginate (APA) microcapsules.**

17.1 $5x10^8$ CFU of live *B. melitensis* mutant are re-suspended in 1 ml of MOPS buffer (10mM MOPS, 0.85% (w/v) NaCl, pH 7.4) and mixed with 5-10 ml of alginate solution (1.5% sodium alginate, 10mM MOPS, 0.85% (w/v) NaCl, pH 7.3).

1.1 Spheres are obtained by extruding the suspension through a 200 micron nozzle into a 100mM calcium chloride solution and stirred for 15 minutes using the Inotech encapsulator I-50 (Inotech Biosystems International, Rockville USA).

1.2 This is a completely enclosed system to protect against the generation of aerosol.

1.3 After extrusion of the bacteria-alginate mixture into the $CaCl_2$, the capsules are washed twice with MOPS for 5 minutes and further crosslinked with 0.05% poly-L-lysine (PLL, MW 22,000 Sigma, USA) or protein solution for 10 minutes.

1.4 Following two successive washes, the beads are stirred in a solution of 0.03% (w/v) alginate for 5 min to apply a final outer shell and washed twice with MOPS before storage at 4°C.

17.2 The viability of the organism within the spheres is not prolonged using this approach as determined by in vitro survival characteristics and recovery from vaccinated animals.

17.3 Microencapsulation enhances immunity through timed release of attenuated organism that is cleared too rapidly by the immune system to be effective when not encapsulated.

3.1 Delivery to animals is achieved through oral, subcutaneous, IP or intranasal routes. Microencapsulated vaccine (highly attenuated bacteria) may be preserved in a viable state for vaccine storage through lyophilization and through the use of additives such as trehalose.

14.18 Animal infection

18.1 Mouse infections are typically performed using one of five different

inoculation routes, i.p., oral, subcutaneous, intranasal or aerosol. The latter is described in a separate section.

18.2 Guinea pigs when used will be challenged via aerosol or intranasal and vaccinated either intranasally or orally.

18.3 The dose in either animal depends on the virulence of the strain evaluated. Wild-type strains of *B. melitensis* and *B. abortus* require 10^5 CFU to infect all the mice i.p., 10^{10} CFU orally, 10^4 CFU via subcutaneous and 10^6 to infect via intranasal. Higher doses may be required to observe colonization and clearance of attenuated mutants.

3.1 In some cases mixtures (1:1) of parental strain and mutant will be used in the same animal to compare clearance.

3.2 Following vaccination the organism is allowed to clear (time depends on the virulence of the strain) and is then challenged using one of the methods described above with an infectious dose of wild-type strain.

3.3 In some cases the organisms will be encapsulated in alginate beads that are delivered via IP or SQ inoculations or orally. These substances are natural products of low or no immunoreactivity. They do not prolong the life of the organism in vitro, but they do permit a gradual release in vivo that is thought to enhance immunity.

18.4 Brucella suspensions used for inoculations are prepared and loaded into syringes in rooms building in the biological safety cabinets.

18.5 The mice are brought to the individual labs in the microisolator cages and removed in the biological safety cabinets for injection. Alternatively, the mice are inoculated in the mouse room using the mobile cage changing station. In this latter case researchers wear tyvek suits and PAPRs and transport the loaded syringes in a sealed container.

15. AEROSOL CHALLENGES

15.1 Intra-entity transfer forms must be filled out at least one day prior to performance of any transfer between buildings.

15.2 *Brucella* suspensions used for inoculations are prepared and loaded into conical tubes in rooms of building in the biological safety cabinets prior to intra-entity transport to building

15.3 Inoculum containing viable organisms is transported from the facility in generalized "triple" packaging (primary receptacle, water tight secondary packaging, durable outer packaging) required for a biological agent of human disease.

3.1 The outer packaging is left in the locker room and the inner packaging is brought into room

3.2 This packaging requires the "Infectious Substance" label on the outside of the package. This packaging must be certified to meet rigorous

performance tests as outlined in the DOT, USPS, PHS, and IATA regulations.

3.3 Such samples are transported through the men's or women's locker rooms at the CMP facility under constant supervision from approved persons.

15.4 At the CMP facility, personnel will change from street clothes into appropriate wardrobe

4.1 In the outer locker room, street clothes are removed and scrubs put on.

4.2 In the inner changing room, two pairs of gloves, facemask, tyvek suits and powered air-purifying respirators (PAPRs) are put on before entry into the main hallway.

15.5 At the CMP facility, animals will be transported to room , in microisolater cages and removed in the biological safety cabinets and loaded into cages for challenges.

5.1 Make certain that the room airflow indicator is working and that the air is flowing from outside the room to inside at a safe level.

15.6 Madison Chamber preparation and use (building room

6.1 Plug cord from control box into the wall socket. Check the light on the control box. Connect the source of compressed air (e.g., building, tank) through the small flow meter to the nebulizer. Make sure that the compressed air regulator reads at least 30 psig. When the main switch is on, the vacuum pump, fans, and timer should be operating.

6.2 Carefully unscrew the glass jar from the nebulizer and place about 10 ml of challenge suspension in the jar. Attach the jar to the nebulizer unit and adjust the vertical stainless steel tube so that the lower (intake) end is about half an inch below the level of fluid in the jar.

6.3 Load the animal basket into the chamber, being careful to center it so that it doesn't touch the fan blades. Close the door and turn on the main switch, activating the vacuum pump, fans, and timer. Reset the timer to zero.

6.4 Check the main (room) air flow meter (the larger meter on the right). The center of the float (ball) should run about "21".

6.5 Nebulizer jars are filled with inoculum under the safety cabinet.

6.6 Turn on the compressed air and simultaneously start the timer. The air flow rate through the compressed air flow meter should read about 5 psig. Check visually to be certain that the challenge inoculum is being nebulized.

6.7 After exactly 300 seconds (5 min), the compressed air supply to the nebulizer should be shut off and the nebulization process will stop. Flow through the small meter will drop to zero, and visual inspection of the nebulizer will show no activity. The timer should continue to run.

6.4 After an additional 600 seconds (10 min) or 900 seconds (15 min) total on the timer, turn off the main switch, stopping the vacuum pump, fans, and timer.

6.9 Open the chamber door and remove the animal basket. To minimize this risk we use an approach in which a single individual handles the racks and animals with support personnel available to disinfect this individual and prevent spread of the organism or animal escape. Animal transfer is perform in a biological safety cabinet (class IIb).

6.9.1 Personnel handling the mice need to take extreme care and spray their gloves with Wexcide. After the transfer is complete, the outer pair of gloves are removed and immediately replaced.

6.10 Remove the glass nebulizer jar, and decant the challenge suspension back into the original tube for transfer back to the originating lab. The jar is decontaminated with 1:10 dilution of bleach and is either reloaded with a different strain or thoroughly decontaminated and loaded with 70% ethanol for decontamination cycle.

15.7 Post run decontamination.

7.1 Place each individual housing cage back in the rack, then place the rack back into the chamber. Seal chamber door using the attached latching system.

7.2 Place 15ml of 70% ethanol into the nebulizer reservoir and re-attach the jar to the chamber and run the chamber for 15 min.

7.3 Once the cycle has been completed (green light turns on), open the chamber and spray all external surfaces of the cage, rack and internal housing cages with Wexcide, covering all surfaces.

7.4 The soiled rack should then be extensively rinsed out with water to remove Wexcide residue, wipe dry.

7.5 Spray internal surfaces of the chamber with Wexcide and soak for 10 minutes. Wipe dry, and spray with 70% ethanol to remove disinfectant residue. **WARNING: Be sure to spray ethanol after the Wexcide treatment as the residue may damage the chamber.**

7.6 All personnel decontaminate each other in room [redacted] using disinfectant prior to leaving the lab. 1:10 dilution of household bleach, 1% (w/v) solution of virkon and wexcide diluted according to maufacturer's instructions are used for this purpose. Animal cages are similarly disinfected as is the rack that may be used to transport them into room 143.

7.7 The tyvek suits are removed in the hall outside room [redacted] and placed in approved containers to be autoclaved by CMP personnel. The mouse rack is transported back to room [redacted]

7.8 Full-face respirators are removed last and surface decontaminated with 70% ethanol.

15.8 The inoculums and extracted tissues are returned to building [redacted] in approved containers

8.1 Animals may either be sacrificed at CMP (building room or moved back to animal holding facilities in building by CMP personnel.

8.2 Tissues are harvested as early immediately post exposure to one week and up to one-year post inoculation and homogenized in PBS.

2.1 Animal carcasses are autoclaved and sent to the incinerator by CMP personnel.

8.3 After thorough decontamination of container containing inoculums, containers are placed inside approved durable (leak-proof) transport container that is then closed, sealed, and disinfected as well.

8.4 Scrubs are removed in inner changing rooms and placed in containers to be autoclaved by CMP personnel. Facemasks and gloves are thrown away.

8.5 All personnel shower before entering the outer changing room.

8.6 Street clothes and personal belongings are collected before exiting BL-3 suite.

1.1 Outer packaging is used to transport the material back to the originating lab

8.7 Serial dilutions were prepared and the bacterial recovery determined by plating on TSA and TSA supplemented with kanamycin (TSAK).

8.8 Wild-type and mutant will grow on TSA, while only marked mutants exhibit growth on TSAK.

8.9 The results are presented as the ratio of (CFU_{TSA}/CFU_{TSAK}) recovered to the ratio inoculated (CFU_{TSA}/CFU_{TSAK}) or the difference in log of these values and reflects the average of at least three separate assays.

15.9 Alternative routes of inoculation performed

9.1 Guinea pigs and mice will be hand restrained for less than one minute for IP or subcutaneous inoculations (0.1 ml).

9.2 Hand restraint for less than one minute is also used for oral (gavage) delivery (0.5 ml).

9.3 Intranasal inoculation is performed following anesthesia using isoflurane as described below. Ten ul of bacterial suspension is pipetted into each nare and the mouse recovers in less than one minute. We have used absorbent paper under the mouse to detect any leakage of the inoculant.

3.1 Personnel in Dr. Ficht's lab that have received anesthesia training from CMP including Jianwu Pei, Melissa Kahl-McDonagh, Tom Ficht, Angela Arenas, Xicheng Ding and Alfredo Wong-Gonzalez (5/11/2006).

3.2 Mice will be anesthetized prior to nasal exposure with *Brucella melitensis* to eliminate stress and the potential for aerosolization during inoculation. Two options are available for anesthesia. The first option, works best for our purposes, includes gas/inhalation anesthesia with isoflurane vaporized to the desired anesthetic

effect. Mice are anesthetized for only a couple of minutes with this method.

3.3 Delivery of isoflurane is performed using a closed container and a cotton ball containing a few drops of isoflurane. This step is performed within a class IIB biological safety cabinet and the animal is transferred to a second person to administer the inoculant. The status of the mouse is monitored based on breathing and reflex to stimulation (toe pinch) and will be monitored during recovery that takes only a few minutes.

3.4 The use of isoflurane in guinea pigs will require a precision vaporizer to deliver the correct amount of anesthetic and a scavenging system to prevent personnel exposure. **These experiments will only be initiated following specific training by CMP personnel and approval by the biosafety office to use in the appropriate facility.**

4.1 Following challenge the mice and guinea pigs are maintained for various periods depending on the experiment

3.5 In some cases we will monitor the clearance of vaccine strain over time between 1 and 16 weeks.

3.6 In other cases we will monitor the challenge that will typically be between 2-4 weeks but could be longer.

9.4 Post-infection:

9.5 Blood collection from the tail or lateral saphenous veins will require the use of a restraining device usually a 50 ml conical tube with a hole and typically takes 1-2 minutes to perform.

9.6 Guinea pigs will be hand restrained for blood collection from the lateral saphenous vein. Blood will be drawn (when necessary) from both animals at weekly intervals.

9.7 A small amount of blood (~100 µl) will be collected daily throughout the infection period from the lateral saphenous vein or the cephalic vein, not to exceed 10% of blood volume in a two week period without fluid replacement therapy.

9.8 Terminal blood collection will occur after Ketamine/Xylazine overdose.

9.9 The spleen will be removed and homogenized in PBS.

9.1 Serial dilutions will be prepared and bacterial burden determined by growth on plates with and without antiobiotic.

9.10 Since we are unable to keep incubators in building the spleens will have to be transported either to another facility where incubation may proceed or the animal will have to be transported to those facilities by CMP personnel.

10.1 Transport of the spleens will provide the smallest and most compact transport between sites and will be performed using appropriate IATA approved containers on university grounds.

Experimental Technique	Paragraph Number	1197	1228	1504	972
Autoclave	4		N**	Y	Y
Centrifugation	14.1		Y	Y	N
Bacterial Growth	14.2		Y	Y	N
Mutagenesis/ Electroporation	14.4		Y	Y	N
Mutagenesis/ Conjugation	14.11		Y	Y	N
Tissue culture	14.12		Y	Y	N
Nucleic acid extraction	14.14		Y	Y	N
Microencapsulation	14.17		Y	Y	N
Mouse inoculation (aerosol)	15		N	N	Y
Mouse inoculation (IP/SQ)	15.9		Y	N	Y
Mouse inoculation (Oral)	15.9		Y	N	Y
Mouse inoculation (intranasal)	15.9		Y	N	Y
Tissue extraction	15.8		Y	N	Y
Tissue homogenization	15.9		Y	Y	Y

**Transport trash triple bagged in leak-proof containers by CMP SR-approved personnel to building or to building room by Ficht lab SRA-approved personnel.

16. APPENDIX 1

The material on the following pages is taken from:

Biosafcty in Microbiological and Biomedical Laboratories

DEPT. HEALTH & HUMAN SERVICES PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH, AND THE CENTERS FOR DISEASE CONTROL AND PREVENTION

4TH EDITION; MAY, 1999.

16.1 Agent: Mycobacterium tuberculosis, M. bovis

Mycobacterium tuberculosis and M. bovis infections are a proven hazard to laboratory personnel as well as others who may be exposed to infectious aerosols in the laboratory. The incidence of tuberculosis in laboratory personnel working with M. tuberculosis has been reported to be three times higher than those not working with the agent. Naturally or experimentally infected nonhuman primates are a proven source of human infection (e.g., the annual tuberculin conversion rate in personnel working with infected nonhuman primates is about 70/10,000 compared with less than 3/10,000 in the general population). Experimentally infected guinea pigs or mice do not pose the same problem since droplet nuclei are not produced by coughing in these species; however, litter from infected animals may become contaminated and serve as a source of infectious aerosols.

Laboratory Hazards: Tubercle bacilli may be present in sputum, gastric lavage fluids, cerebrospinal fluid, urine, and in lesions from a variety of tissues. Exposure to laboratory-generated aerosols is the most important hazard encountered. Tubercle bacilli may survive in heat-fixed smears, and may be aerosolized in the preparation of frozen sections and during manipulation of liquid cultures. Because of the low infective dose of M. tuberculosis for humans (i.e., ID_{50} <10 bacilli) and in some laboratories a high rate of isolation of acid-fast organisms from clinical specimens (>10%), sputa and other clinical specimens from suspected or known cases of tuberculosis must be considered potentially infectious and handled with appropriate precautions.

Recommended Precautions: Biosafety Level 2 practices, containment equipment and facilities are required for activities at American Thoracic Society (ATS) laboratory level I, preparation of acid-fast smears, and culturing of sputa or other clinical specimens, provided that aerosol generating manipulations of such specimens are conducted in a Class I or II biological safety cabinet. Liquefaction and concentration of sputa for acid-fast staining may also be conducted safely on the open bench by first treating the specimen (in a Class I or II safety cabinet) with an equal volume of 5% sodium hypochlorite solution (undiluted household bleach) and waiting 15 minutes before centrifugation.

Biosafety Level 3 practices, containment equipment and facilities are required for laboratory activities of ATS levels II and III) in the propagation and manipulation of cultures of M. tuberculosis or M. bovis, and for animal studies utilizing nonhuman primates experimentally or naturally infected with M. tuberculosis or M. bovis. Animal studies utilizing guinea pigs or mice can be conducted at Animal Biosafety Level 2. Skin testing with purified protein derivative (PPD) of previously skin-tested-negative laboratory personnel can be used as a surveillance procedure. A licensed attenuated live vaccine (BCG) is available but is not routinely used in the United States for laboratory personnel.

16.2 Agent: Mycobacterium spp. other than *M. tuberculosis*, *M. bovis* or *M. leprae*

Pike reported 40 cases of nonpulmonary "tuberculosis" thought to be related to accidents or incidents in the laboratory or autopsy room. Presumably these infections were due to mycobacteria other than *M. tuberculosis* or *M. bovis*. A number of mycobacteria that are ubiquitous in nature are associated with diseases, other than tuberculosis or leprosy, in humans, domestic animals, and wildlife. Characteristically, these organisms are infectious but

not contagious. Clinically, the diseases associated with infections by these atypical-mycobacteria can be divided into three general categories:

- Pulmonary diseases resembling tuberculosis which may be associated with infection by *M. kansasii, M. avium* complex, and rarely, by *M. xenopi, M. malmoense, M. asiaticum, M. simiae* and *M. szulgai.*
- Lymphadenitis which may be associated with infection by *M. scrofulaceum, M. avium* complex, and rarely, by *M. fortuitum* and *M. kansasii.*
- Skin ulcers and soft tissue wound infections which may be associated with infection by *M. ulcerans, M. marinum, M. fortuitum,* and *M. chelonei.*

Laboratory Hazards: The agents may be present in sputa exudates from lesions, tissues, and in environmental samples (e.g., soil and water). Direct contact of skin or mucous membranes with infectious materials, ingestion, and accidental parenteral inoculation are the primary laboratory hazards associated with clinical materials and cultures. Infectious aerosols, created during the manipulation of broth cultures or tissue homogenates of these organisms associated with pulmonary disease, also pose a potential infection hazard to laboratory personnel.

Recommended Precautions: Biosafety Level 2 practices containment equipment and facilities are recommended for activities with clinical materials and cultures of *Mycobacterium* spp. other than *M. tuberculosis* or *M. bovis.* Animal Biosafety Level 2 practices, containment equipment and facilities are recommended for animal studies with mycobacteria other than *M. tuberculosis, M. bovis,* or *M. leprae.*

16.3 Agent: Brucella (B. abortus, B. canis, B. melitensis, B. suis)

B. abortus, B. canis, B. melitensis, and *B. suis* have all caused illness in laboratory personnel. Brucellosis is the most commonly reported laboratory-associated bacterial infection. Hypersensitivity to *Brucella* antigens is also a hazard to laboratory personnel. Occasional cases have been attributed to exposure to experimentally and naturally infected animals or their tissues.

Laboratory Hazards. The agent may be present in blood, cerebrospinal fluid, semen, and occasionally urine. Most laboratory-associated cases have occurred in research facilities and have involved exposure to *Brucella* organisms being grown in large quantities. Cases have also occurred in a clinical laboratory setting: direct skin contact with cultures or with infectious clinical specimens from animals (e.g., blood, uterine discharges) are commonly implicated in these cases. Aerosols generated during laboratory procedures have caused large outbreaks. Mouth pipetting, accidental parenteral inoculations, and sprays into eyes, nose and mouth have also resulted in infection.

Recommended Precautions: Biosafety Level 2 practices are recommended for activities with clinical specimens of human or animal origin containing or potentially containing pathogenic *Brucella* spp. Biosafety Level 3 and Animal Biosafety Level 3 practices, containment equipment and facilities are recommended, respectively, for all manipulations of cultures of the pathogenic *Brucella* spp. listed in this summary, and for experimental animal studies. Vaccines are not available for use in humans.

16.4 Principals of Biosafety

The term "containment" is used in describing safe methods for managing infectious agents in the laboratory environment where they are being handled or maintained. The purpose of containment is to reduce or eliminate exposure of laboratory workers, other persons, and the outside environment to potentially hazardous agents.

Primary containment, the protection of personnel and the immediate laboratory environment from exposure to infectious agents, is provided by both good microbiological technique and the use of appropriate safety equipment. The use of vaccines may provide an increased level of personal protection. Secondary containment, the protection of the environment external to the laboratory from exposure to infectious materials, is provided by a combination of facility design and operational practices. Therefore, the three elements of containment include laboratory practice and technique, safety equipment, and facility design. The risk assessment of the work to be done with a specific agent will determine the appropriate combination of these elements.

4.1 Laboratory Practice and Technique

The most important element of containment is strict adherence to standard microbiological practices and techniques. Persons working with infectious agents or potentially infected materials must be aware of potential hazards, and must be trained and proficient in the practices and techniques required for handling such material safely. The director or person in charge of the laboratory is responsible for providing or arranging for appropriate training of personnel.

Each laboratory should develop or adopt a biosafety or operations manual which identifies the hazards that will or may be encountered, and which specifies practices and procedures designed to minimize or eliminate risks. Personnel should be advised of special hazards and should be required to read and to follow the required practices and procedures. A scientist trained and knowledgeable in appropriate laboratory techniques safety procedures, and hazards associated with handling infectious agents must direct laboratory activities.

When standard laboratory practices are not sufficient to control the hazard associated with a particular agent or laboratory procedure, additional measures may be needed. The laboratory director is responsible for selecting additional safety practices, which must be in keeping with the hazard associated with the agent or procedure.

Laboratory personnel, safety practices, and techniques must be supplemented by appropriate facility design and engineering features, safety equipment, and management practices.

4.2 Safety Equipment (Primary Barriers)

Safety equipment includes biological safety cabinets (BSCs), enclosed containers, and other engineering controls designed to remove or minimize exposures to hazardous biological materials. The biological safety cabinet (BSC) is the principal device used to provide containment of infectious splashes or aerosols generated by many microbiological procedures. Three types of biological safety cabinets (Class I, II, III) used in microbiological laboratories are described and illustrated in Appendix A. Open-fronted Class I and Class II biological safety cabinets are primary barriers which offer significant levels of protection to laboratory personnel and to the environment when used with good microbiological techniques. The Class II biological safety cabinet also provides protection from external contamination of the materials (e.g., cell cultures, microbiological stocks) being manipulated inside the cabinet. The gas-tight Class III biological safety cabinet provides the highest attainable level of protection to personnel and the environment.

An example of another primary barrier is the safety centrifuge cup, an enclosed container designed to prevent aerosols from being released during centrifugation. To minimize this hazard, containment controls such as BSCs or centrifuge cups must be used for handling infectious agents that can be transmitted through the aerosol route of exposure.

Safety equipment also may include items for personal protection such as gloves, coats, gowns, shoe covers, boots, respirators, face shields, safety glasses, or goggles. Personal protective equipment is often used in combination with biological safety cabinets and other devices which contain the agents, animals, or materials being worked with. In some situations in which it is impractical to work in biological safety cabinets, personal protective equipment may form the primary barrier between personnel and the infectious materials. Examples include certain animal studies, animal necropsy, agent production activities, and activities relating to maintenance, service, or support of the laboratory facility.

4.3 Facility Design (Secondary Barriers)

The design of the facility is important in providing a barrier to protect persons working inside and outside of the laboratory within the facility, and to protect persons or animals in the community from infectious agents which may be accidentally released from the laboratory. Laboratory management is responsible for providing facilities commensurate with the laboratory's function and the recommended biosafety level for the agents being manipulated.

The recommended secondary barrier(s) will depend on the risk of transmission of specific agents. For example, the exposure risks for most laboratory work in Biosafety Level 1 and 2 facilities will be direct contact with the agents, or inadvertent contact exposures through contaminated work environments. Secondary barriers in these laboratories may include separation of the laboratory work area from public access, availability of a decontamination facility (e.g., autoclave), and handwashing facilities.

As the risk for aerosol transmission increases, higher levels of primary containment and multiple secondary barriers may become necessary to prevent infectious agents from escaping into the environment. Such design features could include specialized ventilation systems to assure directional air flow, air treatment systems to decontaminate or remove agents from exhaust air controlled access zones, airlocks as laboratory entrances, or separate buildings or modules for isolation of the laboratory. Design engineers for laboratories may refer to specific ventilation recommendations as found in the Applications Handbook for Heating, Ventilation, and Air-Conditioning (HVAC) published by the American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE).

4.4 Biosafety Levels

Four biosafety levels (BSLs) are described which consist of combinations of laboratory practices and techniques, safety equipment, and laboratory facilities. Each combination is specifically appropriate for the operations performed, the documented or suspected routes of transmission of the infectious agents, and for the laboratory function or activity.

The recommended biosafety level(s) for the organisms in Section VII (see "Agent Summary Statements" at end of manual) represent those conditions under which the agent can ordinarily be safely handled. The laboratory director is specifically and primarily responsible for assessing risks and for appropriately applying the recommended biosafety levels. Generally, work with known agents should be conducted at the biosafety level recommended in Section VII. When specific information is available to suggest that virulence, pathogenicity, antibiotic resistance

patterns, vaccine and treatment availability, or other factors are significantly altered, more (or less) stringent practices may be specified.

Biosafety Level 1 practices, safety equipment, and facilities are appropriate for undergraduate and secondary educational training and teaching laboratories, and for other facilities in which work is done with defined and characterized strains of viable microorganisms not known to cause disease in healthy adult humans. *Bacillus subtilis*, *Naegleria gruberi*, and infectious canine hepatitis virus are representative of those microorganisms meeting these criteria. Many agents not ordinarily associated with disease processes in humans are, however, opportunistic pathogens and may cause infection in the young, the aged, and immunodeficient or immunosuppressed individuals. Vaccine strains which have undergone multiple in vivo passages should not be considered avirulent simply because they are vaccine strains.

Biosafety Level 1 represents a basic level of containment that relies on standard microbiological practices with no special primary or secondary barriers recommended, other than a sink for handwashing.

Biosafety Level 2 practices, equipment, and facilities are applicable to clinical, diagnostic, teaching and other facilities in which work is done with the broad spectrum of indigenous moderate risk agents present in the community and associated with human disease of varying severity. With good microbiological techniques, these agents can be used safely in activities conducted on the open bench, provided the potential for producing splashes or aerosols is low. Hepatitis B virus the salmonellae, and *Toxoplasma* spp. are representative of microorganisms assigned to this containment level. Biosafety Level 2 is appropriate when work is done with any human-derived blood, body fluids, or tissues where the presence of an infectious agent may be unknown. (Laboratory personnel working with human-derived materials should refer to the *Bloodborne Pathogen Standards* for specific, required precautions).

Primary hazards to personnel working with these agents relate to accidental percutaneous or mucous membrane exposures, or ingestion of infectious materials. Extreme precaution with contaminated needles or sharp instruments must be emphasized. Even though organisms routinely manipulated at BSL2 are not known to be transmissible by the aerosol route, procedures with aerosol or high splash potential that may increase the risk of such personnel exposure must be conducted in primary containment equipment, or devices such as a BSC or safety centrifuge cups. Other primary barriers should be used as appropriate, such as splash shields, face protection, gowns, and gloves.

Secondary barriers such as handwashing and waste decontamination facilities must be available to reduce potential environmental contamination.

Biosafety Level 3 practices, safety equipment, and facilities are applicable to clinical, diagnostic, teaching, research, or production facilities in which work is done with indigenous or exotic agents with a potential for respiratory transmission, and which may cause serious and potentially lethal infection. *Mycobacterium tuberculosis*, St. Louis encephalitis virus, and

Coxiella burnetii are representative of microorganisms assigned to this level. Primary hazards to personnel working with these agents relate to autoinoculation, ingestion, and exposure to infectious aerosols.

At Biosafety Level 3, more emphasis is placed on primary and secondary barriers to protect personnel in contiguous areas, the community, and the environment from exposure to

potentially infectious aerosols. For example, all laboratory manipulations should be performed in a BSC or other enclosed equipment, such as a gas-tight aerosol generation chamber. Secondary barriers for this level include controlled access to the laboratory and a specialized ventilation system that minimizes the release of infectious aerosols from the laboratory.

Biosafety Level 4 practices, safety equipment, and facilities are applicable for work with dangerous and exotic agents, that pose a high individual risk of life-threatening disease, which may be transmitted via the aerosol route, and for which there is no available vaccine or therapy. Additionally, agents with a close or identical antigenic relationship to Biosafety Level 4 agents should also be handled at this level. When sufficient data are obtained, work with these agents may continue at this level or at a lower level. Viruses such as Marburg or Congo-Crimean hemorrhagic fever are manipulated at BL4.

The primary hazards to personnel working with Biosafety Level 4 agents are respiratory exposure to infectious aerosols, mucous membrane exposure to infectious droplets, and autoinoculation. All manipulations of potentially infectious diagnostic materials, isolates, and naturally or experimentally infected animals pose a high risk of exposure and infection to laboratory personnel, the community, and the environment.

The laboratory worker's complete isolation of aerosolized infectious materials is accomplished primarily by working in a Class III BSC or a full-body, air-supplied positive-pressure personnel suit. The Biosafety Level 4 facility itself is generally a separate building or completely isolated zone with complex, specialized ventilation and waste management systems to prevent release of viable agents to the environment.

The laboratory director is specifically and primarily responsible for the safe operation of the laboratory. His/her knowledge and judgment are critical in assessing risks and appropriately applying these recommendations. The recommended biosafety level represents those conditions under which the agent can ordinarily be safely handled. Special characteristics of the agents used, the training and experience of personnel, and the nature or function of the laboratory may further influence the director in applying these recommendations.

4.5 Animal Facilities

Four biosafety levels are also described for activities involving infectious disease work with experimental mammals. These four combinations of practices, safety equipment, and facilities are designated Animal Biosafety Levels 1, 2, 3, and 4, and provide increasing levels of protection to personnel and the environment.

4.6 Clinical Laboratories

Clinical laboratories, especially those in health care facilities, receive clinical specimens with requests for a variety of diagnostic and clinical support services. Typically, the infectious nature of clinical material is unknown, and specimens are often submitted with a broad request for microbiological examination for multiple agents (e.g., sputa submitted for "routine," acid-fast, and fungal cultures). It is the responsibility of the laboratory director to establish standard procedures in the laboratory which realistically address the issue of the infective hazard of clinical specimens.

Except in extraordinary circumstances (e.g., suspected hemorrhagic fever), the initial processing of clinical specimens and identification of isolates can be done safely at Biosafety Level 2, the recommended level for work with bloodborne pathogens such as hepatitis B virus

and HIV. The containment elements described in Biosafety Level 2 are consistent with the Occupational Exposure to Bloodborne Pathogens Standard 37 from the Occupational Safety and Health Administration (OSHA), that requires the use of specific precautions with all clinical specimens of blood or other potentially infectious material (Universal Precautions). Additionally, other recommendations specific for clinical laboratories may be obtained from the National Committee for Clinical Laboratory Standards.

Biosafety Level 2 recommendations and OSHA requirements focus on the prevention of percutaneous and mucous membrane exposures to clinical material. Primary barriers such as biological safety cabinets (Class I or II) should be used when performing procedures that might cause splashing, spraying, or splattering of droplets. Biological safety cabinets should also be used for the initial processing of clinical specimens when the nature of the test requested or other information is suggestive that an agent readily transmissible by infectious aerosols is likely to be present (e.g., *M. tuberculosis*), or when the use of a biological safety cabinet (Class II) is indicated to protect the integrity of the specimen.

The segregation of clinical laboratory functions and limiting or restricting access to such areas is the responsibility of the laboratory director. It is also the director's responsibility to establish standard, written procedures that address the potential hazards and the required precautions to be implemented.

Importation and Interstate Shipment of Certain Biomedical Materials.

The importation of etiologic agents and vectors of human diseases is subject to the requirements of the Public Health Service Foreign Quarantine regulations. Companion regulations of the Public Health Service and the Department of Transportation specify packaging, labeling, and shipping requirements for etiologic agents and diagnostic specimens shipped in interstate commerce (see Appendix D).

The USDA regulates the importation and interstate shipment of animal pathogens and prohibits the importation, possession, or use of certain exotic animal disease agents which pose a serious disease threat to domestic livestock and poultry (see Appendix E).

4.7 Laboratory Facilities (Secondary Barriers): Biosafety Level 3

7.1 The laboratory is separated from areas which are open to unrestricted traffic flow within the building. Passage through two sets of self-closing doors is the basic requirement for entry into the laboratory from access corridors or other contiguous areas. A clothes change room (shower optional) may be included in the passageway.

7.2 Each laboratory contains a sink for handwashing. The sink is foot, elbow, or automatically operated and is located near the laboratory exit door.

7.3 The interior surfaces of walls, floors, and ceilings are water resistant so that they can be easily cleaned. Penetrations in these surfaces are sealed or capable of being sealed to facilitate decontamination.

7.4 Bench tops are impervious to water and resistant to acids, alkalis, organic solvents, and moderate heat.

7.5 Laboratory furniture is sturdy, and spaces between benches,

cabinets, and equipment are accessible for cleaning.

7.6 Windows in the laboratory are closed and sealed.

7.7 A method for decontaminating all laboratory wastes is available, preferably within the laboratory (i.e., autoclave, chemical disinfection, incineration, or other approved decontamination method).

7.8 A ducted exhaust air ventilation system is provided. This system creates directional airflow that draws air from "clean" areas into the laboratory toward "contaminated" areas. The exhaust air is not recirculated to any other area of the building, and is discharged to the outside with filtration and other treatment optional. The outside exhaust must be dispersed away from occupied areas and air intakes. Laboratory personnel must verify that the direction of the airflow (into the laboratory) is proper.

7.9 The High Efficiency Particulate Air (HEPA)-filtered exhaust air from Class II or Class III biological safety cabinets is discharged directly to the outside or through the building exhaust system. If the HEPA-filtered exhaust air from Class II or III biological safety cabinets is to be discharged to the outside through the building exhaust air system, it is connected to this system in a manner (e.g., thimble unit connection) that avoids any interference with the air balance of the cabinets or building exhaust system. Exhaust air from Class II biological safety cabinets may be recirculated within the laboratory if the cabinet is tested and certified at least every twelve months.

7.10 Continuous flow centrifuges or other equipment that may produce aerosols are contained in devices that exhaust air through HEPA filters before discharge into the laboratory.

7.11 Vacuum lines are protected with liquid disinfectant traps and HEPA filters, or their equivalent, which are routinely maintained and replaced as needed.

7.12 An eyewash facility is readily available.

17. APPENDIX 2

17.1 Animal Biosafety:Standard Practices

1.1 Access to the animal facility is limited or restricted at the discretion of the laboratory or animal facility director and is secured using locked keypad access.

1.2 Personnel use double glove procedures as in the other laboratories and their inner gloves are washed after removing outer gloves, and before leaving the animal facility.

1.3 Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human use are not permitted in animal rooms. Persons who wear contact lenses in animal rooms should also wear goggles or a face shield.

1.4 All procedures are carefully performed to minimize the creation of aerosols.

1.5 Work surfaces are decontaminated after use or after any spill of viable materials.

1.6 Doors to animal rooms open inward, are self-closing and are kept closed when experimental animals are present.

1.7 All wastes from the animal room are appropriately decontaminated, preferably by autoclaving, before disposal. Infected animal carcasses are incinerated after being transported from the animal room in leakproof, covered containers.

1.8 An insect and rodent control program is in effect.

17.2 Animal Biosafety:Special Practices

2.1 The laboratory director or other responsible person restricts access to the animal room to personnel who have been advised of the potential hazard and who need to enter the room for program or service purposes when infected animals are present. Persons who are at increased risk of acquiring infection, or for whom infection might be unusually hazardous, are not allowed in the animal room. Persons at increased risk may include children, pregnant women, and persons who are immunodeficient or immunosuppressed. The supervisor has the final responsibility for assessing each circumstance and determining who may enter or work in the facility.

2.2 The laboratory director or other responsible person establishes policies and procedures whereby only persons who have been advised of the potential hazard and meet any specific requirements (e.g., for immunization) may enter the animal room.

2.3 When the infectious agent(s) in use in the animal room requires special entry provisions (e.g., the need for immunizations and respirators) a hazard warning sign, incorporating the universal biohazard symbol, is posted on the access door to the animal room. The hazard warning sign identifies the infectious agent(s) in use, lists the name and telephone number of the animal facility supervisor or other responsible person(s),

and indicates the special requirement(s) for entering the animal room.

2.4 Laboratory personnel receive appropriate immunizations or tests for the agents handled or potentially present in the laboratory (e.g., hepatitis B vaccine or TB skin testing).

2.5 Baseline serum samples from all personnel working in the facility and other at-risk personnel should be collected and stored. Additional serum samples may be collected periodically and stored. The serum surveillance program must take into account the availability of methods for the assessment of antibody to the agent(s) of concern. The program should provide for the testing of serum samples at each collection interval and the communication of results to the participants.

2.6 A biosafety manual is prepared or adopted. Personnel are advised of special hazards, and are required to read and to follow instructions on practices and procedures.

2.7 Laboratory personnel receive appropriate training on the potential hazards associated with the work involved, the necessary precautions to prevent exposures, and the exposure evaluation procedures. Personnel receive annual updates, or additional training as necessary for procedural or policy changes.

2.8 A high degree of precaution must always be taken with any contaminated sharp items, including needles and syringes, slides, pipettes, capillary tubes, and scalpels. Needles and syringes or other sharp instruments are restricted in the laboratory for use only when there is no alternative, such as for parenteral injection, blood collection, or aspiration of fluids from laboratory animals and diaphragm bottles. Plasticware should be substituted for glassware whenever possible.

8.1 Only needle-locking syringes or disposable syringe needle units (i.e., needle is integral to the syringe) are used for injection or aspiration of infectious materials. Used disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal; rather, they must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal. Non-disposable sharps must be placed in a hard-walled container, preferably containing a suitable disinfectant, for transport to a processing area for decontamination, preferably by autoclaving.

8.2 Syringes which re-sheathe the needle, needle-less systems, and other safe devices should be used when appropriate.

8.3 Broken glassware must not be handled directly by hand, but must be removed by mechanical means such as a brush and dustpan, tongs, or forceps. Containers of contaminated needles, sharp equipment, and broken glass should be decontaminated before disposal, according to any local, state, or federal regulations.

2.9 Cultures, tissues, or specimens of body fluids are placed in a container that prevents leakage during collection, handling, processing, storage, transport, or shipping.

2.10 Cages are autoclaved or thoroughly decontaminated before bedding is

removed or before they are cleaned and washed. Equipment and work surfaces should be decontaminated with an appropriate disinfectant on a routine basis, after work with infectious materials is finished, and especially after overt spills, splashes, or other contamination by infectious materials. Contaminated equipment must be decontaminated according to any local, state, or federal regulations before it is sent for repair or maintenance or packaged for transport in accordance with applicable local, state, or federal regulations, before removal from the facility.

2.11 Spills and accidents that result in overt exposures to infectious materials are immediately reported to the laboratory director. Medical evaluation, surveillance, and treatment are provided as appropriate and written records are maintained.

2.12 All wastes from the animal room are autoclaved before disposal. All animal carcasses are incinerated or biodigested. Dead animals are transported from the animal room after autoclaving to the incinerator/biodigestor in leakproof covered containers.

2.13 Animals not involved in the work being performed are not permitted in the lab.

17.3 Animal Biosafety: Equipment (Primary Barriers)

3.1 Personal protective equipment is used for all activities involving manipulations of infectious materials or infected animals.

1.1 Work in the animal room requires at a minimum additional wrap-around or solid-front gowns with shoe covers or Tyvek suits. Front-button laboratory coats are unsuitable. PAPRs are also available, but are considered unnecessary when working with the animals within a biological safety cabinet. All protective wear is appropriately contained within the animal room trash until decontamination or disposal.

1.2 Personnel wear extra gloves when handling infected animals. Gloves are removed aseptically and autoclaved with other animal room wastes before disposal.

1.3 Appropriate face/eye and respiratory protection is worn by all personnel entering animal rooms.

1.4 Boots, shoe covers, or other protective footwear, and disinfectant footbaths are available and used when indicated.

3.2 Physical containment devices and equipment appropriate for the animal species are used for all procedures and manipulations of infectious materials or infected animals.

3.3 The risk of infectious aerosols from infected animals or their bedding also can be reduced if animals are housed in partial containment caging systems, such as open cages placed in ventilated enclosures (e.g., laminar flow cabinets), solid wall and bottom cages covered with filter bonnets, or other equivalent primary containment systems.

17.4 Animal Biosafety:Facilities (Secondary Barriers)

4.1 The animal facility is designed and constructed to facilitate cleaning and housekeeping, and is separated from areas which are open to unrestricted personnel traffic within the building. Passage through two sets of doors is the basic requirement for entry into the animal room from access corridors or other contiguous areas. Physical separation of the animal room from access corridors or other activities may also be provided by a double-doored clothes change room (showers may be included), airlock, or other access facility which requires passage through two sets of doors before entering the animal room.

4.2 The interior surfaces of walls, floors, and ceilings are water resistant so that they may be easily cleaned. Penetrations in these surfaces are sealed or capable of being sealed to facilitate fumigation or space decontamination.

4.3 A foot, elbow, or automatically operated hand washing sink is provided in each animal room near the exit door.

4.4 If vacuum service (i.e., central or local) is provided, each service connection should be fitted with liquid disinfectant traps and a HEPA filter.

4.5 If floor drains are provided, they are protected with liquid traps that are always filled with water or disinfectant.

4.6 Windows in the animal room are non-operating and sealed.

4.7 Animal room doors are self-closing and are kept closed when infected animals are present.

4.8 An autoclave for decontaminating wastes is available, preferably within the animal facility. Materials are transferred to the autoclave in a covered leakproof container whose outer surface has been decontaminated.

4.9 A non-recirculating ventilation system is provided. The supply and exhaust components of the system are balanced to provide for directional flow of air into the animal room. The exhaust air is discharged directly to the outside and clear of occupied areas and air intakes. Exhaust air from the room can be discharged without filtration or other treatment. Personnel must periodically validate that proper directional airflow is maintained.

4.10 The HEPA filtered exhaust air from Class I or Class II biological safety cabinets or other primary containment devices is discharged directly to the outside or through the building exhaust system. Exhaust air from these primary containment devices may be recirculated within the animal room if the device is tested and certified at least every 12 months. If the HEPA filtered exhaust air from Class I or Class II biological safety cabinets is discharged to the outside through the building exhaust system, it is connected to this system in a manner (e.g., thimble unit connection) that avoids any interference with the performance of either the cabinet or building exhaust system.

18. TEST OF COMPREHENSION

Question

Answer (True or False)

- Street clothes may be worn in the BSL3 area under certain circumstances.
- Contaminated materials may be opened on the benchtop.
- When not inside a biosafety cabinet all contaminated materials must be kept in double-containers.
- All manipulations of contaminated material should be performed at least 6 inches inside the biological safety cabinets.
- Disinfect all work surfaces, door handles and any other materials which you may have come in contact with during your work.
- In the event of a spill, outer clothes must be left in the lab where the spill has occurred and the lab should be vacated for at least 1 hr.
- Spills should be covered with absorbent material and the site disinfected with bleach or other agent.
- Centrifuge rotors may be loaded and unloaded at the instrument.

I have read and understood the procedures manual, and I agree to follow all procedures outlined herein.	
I understand that violation of any of these procedures will result in disciplinary action against me:	
First violation	Warning
Second violation	Probation and 2-month prohibition from working in the BSL3 suite
Third violation	Dismissal from the TAMU payroll
Employee	**Date**
I have checked this employee's test answers and we have discussed the BSL3 procedures.	
Employer	**Date**

TEXAS A&M UNIVERSITY

Center for Disease Control (CDC) Select Agent Program

INSTITUTIONAL POLICIES
And
STANDARD OPERATING PROCEDURES

Office of Research Compliance
Centeq Building
Ste. B 150
1500 Research Parkway
College Station, Texas 77843-1186

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Introduction

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (The Act) requires entities to register with the U. S. Departments of Health and Human Services (HHS) or Agriculture (USDA) if they possess, use, or transfer select biological agents or toxins that could pose a severe threat to public health and safety or to animal or plant health or animal or plant products. In addition, the act requires:

- Maintenance of a comprehensive national database of select agents and toxins.
- Monitoring and enforcement of laboratory compliance with safe handling procedures.
- Increased security measures including controlled access to select agents and toxins and the screening of entities and personnel.
- Criminal and civil penalties for the inappropriate use of threat agents including specific viruses, bacteria, fungi, and toxins.

In support of this Act, CDC has primary responsibility for regulating the possession, use, and transfer of 39 biological agents and toxins that have the potential to pose a severe threat to public health and safety. The CDC Select Agent Program oversees these activities and registers all laboratories and other entities in the United States that possess, use, or transfer a select agent or toxin.

Under the authorities granted in the Act, the Select Agent Program performs specific functions to ensure the safe and secure handling and transfer of select agents and toxins. These functions include:

- Promulgation of an interim final rule on December 13, 2002 (42 C.F.R. Part 73) implementing the Act.
- Evaluation and approval of requests to possess, use, and transfer select agents and toxins.
- Registration of laboratories that possess select agents and toxins.
- Approval of transfer of select agents and toxins among registered laboratories.
- Inspection of laboratories to ensure appropriate safety and security measures are being followed.
- Maintenance of a national database of registered laboratories.

There are currently 318 entities registered with the Select Agent Program. The Select Agent Program has conducted over 380 inspections since February 7, 2003, when the regulations became effective. All registered entities have been inspected at least once. Regulated entities include: academic institutions; biomedical centers; commercial manufacturing (e.g., the pharmaceutical industry) or distribution facilities; federal, state, and local laboratories (including clinical and diagnostic laboratories); and research facilities.

In accordance with the Act, implementing regulations detailing the requirements for possession, use, and transfer for select agents and toxins were published by HHS (42 CFR part 73) and by USDA (9 CFR part 121 and 7 CFR part 331) .

Registration of an entity requires that an "Application for Laboratory Registration for Possession, Use, and Transfer of Select Agents and Toxins" (APHIS/CDC Form 1) should be completed and submitted to either HHS Centers for Disease Control and Prevention (CDC) or to USDA Animal Plant Health Inspection Service (APHIS). Registration also requires that the U.S. Department of Justice (DOJ) complete a security risk assessment (SRA) for the facility, its owners, and the designated responsible official. Before registration is granted, the facility must also meet Biosafety requirements that are commensurate with the risk that the select agent or toxin poses and must establish security measures that provide graded protection in accordance with the threat that the agent or toxin poses.
An entity that needs to register in order to possess, use, or transfer a select agent or toxin must submit its registration information to either APHIS or CDC, but is not required to submit the application to both APHIS and CDC.

In accordance with the final rule (42 C.F.R. Part 73) and (9 C.F.R. Part 121 & 7 C.F.R. Part 331), the IBC has the authority to review, approve, require modifications in, or disapprove all research activities that fall within its jurisdiction. The Texas A&M University's Institutional Biosafety Program (IBSP) policies and procedures provide guidance and responsibility, just as well as these policies.

The Texas A&M Select Agent Program SOPs apply to all the oversight of the IBC and the methods of reporting. These SOPs are reviewed periodically to ensure that they are up-to-date, that new legislation or regulations are reflected in the policies and that daily activities are being performed as described in the SOPs.

Persons subject to this policy

(1) All research and other activities involving select agents that are conducted by or under the direction of any full-time or part-time employee, trainee, or agent of Texas A&M University or designated affiliate shall be subject to review and approval by the IBC, regardless of the funding source if any, and regardless of the site at which the research is performed.

Purpose and Scope

The purpose and scope of regulations pertaining specifically to the use of select agents are found in 42 CFR § 73.2. This section simply states:

"This part implements the provisions of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 setting forth the requirements for possession, use, and transfer of select agents and toxins. The biological agents and toxins listed in this part have the potential to pose a severe threat to public health and safety, to animal health, or to animal products. Overlap select agents and toxins are subject to regulation by both CDC and APHIS."

IBC REVIEW OF RESEARCH POLICY

All research involving the use of recombinant DNA and/or other infectious materials and all other activities, which even in part involve such research, regardless of sponsorship, must be reviewed and approved by the Texas A&M University IBC. In addition, all research involving select agents must be reviewed and approved by the Institution's IBC and the Biological Safety Officer (BSO). No intervention or interaction with select agents in research may begin until the IBC has reviewed and approved the research protocol, and an Amendment to modify the Select Agent Registration with the CDC has been filed and approved. Research may not be initiated until the IBC has reviewed and approved the research protocol. Upon approval, researchers will receive an approval letter and a completed laboratory permit. Specific determinations of the biological safety level of each approved laboratory are made by the IBC.

The IBC's purpose and responsibility is to protect the human health and environment within laboratory settings. The IBC reviews and oversees such research to ensure that it meets well established ethical principles and that it complies with NIH Guidelines and federal regulations 42 CFR Part 72, 73, 1003, as it pertains to the Select Agent Program.

To approve research protocols, the IBC shall determine that all of the following requirements are satisfied:

1. Risks to subjects are minimized (this is an essential condition for approval) by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and, when appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes. This process consists of the completion of a Risk Assessment, and consultation with the Institutional BioSafety Officer (BSO).
2. The research protocol makes adequate provision for keeping the IBC informed of any modifications in the laboratory, such as new material, personnel, procedure, etc. to ensure laboratory safety.

The determination of a risk assessment may be found in Section II of the *NIH Guidelines*, along with the application of sound professional judgment as it relates to the agents/organisms to be used in the research activities in question.

1. The IBC will carefully weigh the relative risks and benefits of the research procedures to be applied to the subject.

2. The IBC will carefully consider the degree of risk involved in any activity should never exceed the humanitarian importance of the problems to be solved by that activity. Likewise, compensation to volunteers should never be such as to constitute an undue inducement to the subject.

3. There is a wide range of medical, social and behavioral research projects and activities in which no immediate physical risk to the subject is involved; e.g., those

utilizing personality inventories, interviews, questionnaires, or the use of observation, photographs, taped records, or stored data. However, some of these procedures may involve varying degrees of discomfort, harassment, or invasion of privacy which may constitute a risk.

4. There are also medical and biomedical projects concerned solely with organs, tissues, body fluids, and other materials obtained in the course of the routine performance of medical services such as diagnosis, treatment and care, or at autopsy. The use of these materials obviously involves no element of physical risk to the subject. However, their use for research, training, and service purposes may present psychological, sociological, or legal risks to the subjects or their relatives. In these instances, application of the policy requires IBC review to determine that the circumstances under which the materials are to be procured are appropriate and, if the subject is deemed to be at risk, that adequate and appropriate consent will or can be obtained for the use of these materials for research purposes.

5. Similarly, some studies depend upon stored data or information that was often obtained for quite different purposes. Here, the IBC will determine whether the use of these materials is within the scope of the original consent, or whether consent should be obtained or waived.

3. .

The determination of when an individual is at risk is a matter of the application of common sense and sound professional judgment as it relates to the circumstances of the research activity in question.

6. The IRB will carefully weigh the relative risks and benefits of the research procedures to be applied to the subject.

7. Research activities designed to yield fruitful results for the benefit of individual subjects or society, in general, may incur risks to the subjects provided such risks are outweighed by the benefit to be derived from activities.

8. The degree of risk involved in any activity should never exceed the humanitarian importance of the problems to be solved by that activity. Likewise, compensation to volunteers should never be such as to constitute an undue inducement to the subject.

9. There is a wide range of medical, social and behavioral research projects and activities in which no immediate physical risk to the subject is involved; e.g., those utilizing personality inventories, interviews, questionnaires, or the use of observation, photographs, taped records, or stored data. However, some of these procedures may involve varying degrees of discomfort, harassment, or invasion of privacy which may constitute a risk.

10. There are also medical and biomedical projects concerned solely with organs, tissues, body fluids, and other materials obtained in the course of the routine performance of medical services such as diagnosis, treatment and care, or at autopsy. The use of

these materials obviously involves no element of physical risk to the subject. However, their use for research, training, and service purposes may present psychological, sociological, or legal risks to the subjects or their relatives. In these instances, application of the policy requires IRB review to determine that the circumstances under which the materials are to be procured are appropriate and, if the subject is deemed to be at risk, that adequate and appropriate consent will or can be obtained for the use of these materials for research purposes.

11. Similarly, some studies depend upon stored data or information that was often obtained for quite different purposes. Here, the IRB will determine whether the use of these materials is within the scope of the original consent, or whether consent should be obtained or waived.

If the proposed activity involves an investigational drug, biological material, or device, it is the policy of the TAMU IRB that before these test articles may be tested on humans, or before an FDA-approved drug can be used for unapproved indications, the sponsor must obtain a Food and Drug Administration Exemption (Investigational New Drug (IND) or Investigational Device Exemption (IDE)) before the activity will be approved by the IRB.

Any activity involving the use of radiological, biological, or chemical materials must have approval of the Institutional Biosafety Committee before it can receive final approval by the IRB. This is part of Texas A&M University's System policy #15.01.03.M1.

Compliance with this policy or the procedures set forth herein will in no way render inapplicable pertinent laws of the State of Texas, any local law which may bear upon the proposed activity or the Rules and Regulations of Texas A&M University. In other words, all applicable state and federal rules must be followed in addition to the policies and procedures set forth by Texas A&M University regarding the use of human subjects in research.

Failure to Submit a Project for IRB Review

The implications of engaging in activities that qualify as research that is subject to IRB review without obtaining such review are significant. Results from such studies may not be published unless IRB approval had been obtained prior to collecting the data. To do so is in violation of Institutional policy. It is also against Institutional policy to use those data to satisfy thesis or dissertation requirements. If an Investigator begins a project and later finds that the data gathered could contribute to the existing knowledge base or that he or she may wish to publish the results, the Investigator should submit a protocol to the IRB for review as soon as possible. If the IRB does not approve the research, data collected cannot be used as part of a thesis or dissertation, and/or the results of the research cannot be published. Furthermore, FDA may reject such data if it is submitted in support of a marketing application.

GENERAL ADMINISTRATION

100

100 – GENERAL ADMINISTRATION	
101. Policies And Procedures Maintenance	
Policy: **Effective Date:** **Reviewed by:**	**Revised Date:** **Approved By:**

1. POLICY

Following regulations and guidance of OHRP, FDA, and the International Conference on Harmonization (ICH), supported by institutional policies, ensures that the rights and welfare of the human subjects of such research will be overseen and protected in a uniform manner, regardless of changes in personnel.

Written procedures must be in place to ensure the highest quality and integrity of the review and oversight of research involving human subjects and for the adequate documentation of such oversight.

Standard operating policies and procedures (SOPs) provide the framework for the ethical and scientifically sound conduct of human research.

Specific Policies

1.1 Review, Revision, Approval of Policies & Procedures

1.1.1 Changes to regulations, federal guidelines, or research practice as well as the policies and procedures of Texas A&M University may require a new SOP or a revision to a previously issued SOP.

1.1.2 Policies will be reviewed by the appropriate IRB Administrator at 1 year intervals.

1.1.3 Approval of new or revised SOPs is required prior to issuance.

1.1.4 Documentation of review and approval is required by signature of the responsible and authorized individuals.

1.2 SOP Dissemination and Training

1.2.1 When new or revised SOPs are approved, they will be disseminated to appropriate individuals and departments.

1.2.2 Training will be provided to all members of the IRB and IRB Compliance Staff on any new or revised policy and/or procedure. Evidence of training must be documented and filed with the Director of the Office of Research Compliance (or Program Coordinator).

1.2.3 Each new IRB member or staff employee must review all applicable SOPs prior to undertaking any responsibilities at the IRB. Evidence of training must be documented and filed with the Director of the Office of Research Compliance (or Program Coordinator).

1.3 Forms

Forms are used to: 1) ensure that policies are integrated into the daily operations of research and review throughout the Texas A&M University system, and 2) enable IRB Compliance Staff to manage review, tracking, and notification functions consistently. Forms are either controlled or non-controlled.

1.3.1 **Controlled forms** are regulatory documents that become part of the permanent record of IRB review and determination. Therefore, they must be reviewed and approved as described in sections 1.1 and 1.2.

1.3.2 **Non-controlled forms** are management tools that are not subject to the standards of control cited in sections 1.1 and 1.2.

2. SCOPE

These policies and procedures apply to all IRB Compliance Staff.

3. RESPONSIBILITY

The Director of the Office of Research Compliance (or designee) is responsible for establishing and periodically reviewing and modifying (as appropriate) IRB standard operating policies and procedures.

The IRB Committees through the IRB Executive Committee are responsible for review and approval of new and modified policies and/or SOPs. Each committee as a whole may appoint several reviewers, separate from the IRB professional staff, to act as reviewers on behalf of the committee.

The Institutional Official (Texas A&M Executive Vice President for Research) is responsible for granting final approval (as appropriate) to new and revised IRB policies. Changes that impact the university rules related to human subject research will be noted and the Director of the Office of Research Compliance will submit rule changes to the University Rules Committee.

4. APPLICATION REGULATIONS AND GUIDELINES

45 CFR 46.108 , 46.109
21 CFR 56.108, 56.109, 56.113
TAMU 15.99.01M1,15.99.01,01.01.01.M2, 15.01.01.M3,15.01,15.01.01

5. REFERENCES TO OTHER APPLICABLE SOPS

This SOP affects all other SOPs.

6. ATTACHMENTS

IRB Executive Committee Overview
SOP Revision Log
Forms Revision Log
Notification of SOP Change

7. PROCESS OVERVIEW

The Texas A&M University IRB will maintain and follow up-to-date policies and procedures that adhere to regulatory mandates and ethical principles.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Program Coordinator	Using SOP Revision Worksheet, monitor appropriate sources and contacts for policy updates, note policies that may need revisions and indicate priority.	SOP Revision Worksheet
IRB Program Coordinator	On pre-determined schedule, meet regarding changes to SOPs.	IRB Executive Committee /SOP Review Meeting
Director of the Office of Research Compliance (or Program Coordinator) *IRB Compliance Staff*	Discuss changes and determine if additional procedures are required or if forms need revisions.	
IRB Program Coordinator	Revise policies and/or procedures. Revise forms if needed. Track changes.	SOP Revision Log Forms Revision Log
IRB Program Coordinator	Update policy and archive hard copies of previous policy.	
IRB Program Coordinator	Notify IRB computer staff to make changes on web-electronic system and to archive previous version.	
	Replace & destroy paper copies of obsolete sections if any.	
IRB Program Coordinator	Notify research community & distribute new SOPs & forms as needed.	Notification of SOP Change email

100 – GENERAL ADMINISTRATION	
102. Training And Education	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Training of IRB Compliance Staff and members is critical if the IRB is to fulfill its mandate to protect the rights and welfare of research subjects in a consistent manner throughout the Texas A&M University research community.

IRB members, staff and others charged with responsibility for reviewing, approving, and overseeing human subject research should receive detailed training in the regulations, guidelines, ethics and policies applicable to human subjects research.

The IRB office will provide training opportunities for IRB members, Compliance staff and investigators at Texas A&M University.

Specific Policies

1.1 Training

1.1.1. Management level staff and members of any IRB who are overseeing research on human subjects, as defined in 45 CFR 46.102 (f) and/or 21 CFR 56.102(e), that is managed, funded, or taking place in an entity under the jurisdiction of Texas A&M University will receive initial and ongoing training regarding the responsible review and oversight of research and these policies and accompanying procedures.

1.1.2. The Director of the Office of Research Compliance (or Program Coordinator) establishes the educational and training requirements for the research community, IRB members and staff who review behavioral research involving human subjects at this institution and who perform related administrative duties. Texas A&M University has joined over 100 other University, Private and Government IRBs in using The Collaborative IRB Training Initiative (CITI) Program in the Protection of Human Subjects in Research maintained by the University of Miami. The CITI Human Subjects Research Education Program is a web-based program that consists of courses for Biomedical Researchers (14 modules) and courses for Social Behavioral Researchers (11 Modules) each focused on a different aspect of bio-ethics and human subjects research. Initial and ongoing training is provided and documented by this institution through the CITI PROGRAM. All research personnel listed on the IRB submission, regardless of their position, must complete the entire CITI program. Research personnel include principal investigators, co-investigators, research coordinators, and any other research team members who have contact with research participants and/or their

research data and identifiers. In addition, all IRB members and IRB Compliance Staff will be required to complete all modules.

1.1.3. Members of the IRB will participate in initial and continuing training in areas germane to their responsibilities.

1.1.4. Chairpersons will receive additional training in areas germane to their additional responsibilities or as needed.

1.1.5. IRB Compliance Staff will receive initial and continuing training in the areas germane to their responsibilities, including all Standard Operating Policies and Procedures (SOP).

1.1.6. IRB members and staff will be encouraged to attend workshops and other educational opportunities focused on IRB functions. Texas A&M University will support such activities to the extent possible and as appropriate to the responsibilities of members and staff.

1.2 Documentation

Training and continuing education shall be documented and added to the records of the IRB as described in these policies and procedures.

1.3 Training Resources

The IRB office provides educational resources and training opportunities for those involved in human subjects research.

1.3.1 **Online Web-Based Training: CITI** - The program offers a series of short training modules that are designed to provide training for either social/behavioral research or biomedical research. These modules meet the federal guidelines for human subjects training and can be completed at the pace of the individual. The site can be accessed at: http://www.citiprogram.org/default.asp.

1.3.2 **Brown Bag** - Informational sessions provided to the research community to discuss the IRB process, special topics related to human subjects' research. Offered twice per semester. They are very general, informal and scheduled during the lunch hour.

1.3.3 **Conferences and seminars** – Regional/national conferences such as Applied Research Ethics National Association (ARENA) and Public Responsibility in Medicine and Research(PRIM&R)

1.3.4 **Class Presentations** - Faculty can arrange for class presentations to discuss the IRB process. To schedule a presentation, please contact the IRB office at (979) 458-4067.

1.4 Community Outreach

The IRB in its attempt to enhance understanding of human research by participants, prospective participants and the community provides the following activities:

- Upon request IRB staff is available for presentations to various organizations
- Pamphlets on being research volunteers are available upon request
- IRB informational sessions are available to the public

The IRB will evaluate its outreach activities annually and make changes when appropriate.

2. SCOPE

These policies and procedures apply to all IRB members and staff.

3. RESPONSIBILITY

Director of the Office of Research Compliance (or Program Coordinator) is responsible for establishing, conducting and/or supervising all relevant training programs for IRB members and staff.

IRB Chairperson (or designee) is responsible for guiding the development of IRB member training programs, in collaboration with the Director of the Office of Research Compliance (or Program Coordinator).

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.107
45 CFR 46.107
TAMU 15.01.01(2)
OHRP IRB Guidebook
NIH NOTICE: OD-00-039 Required Education in the Protection of Human Research Participants

5. REFERENCES TO OTHER APPLICABLE SOPS

This SOP affects all other SOPs.

6. ATTACHMENTS

Brown Bag Registration Form
CITI Registration Directions
Training Checklist and Documentation – IRB Members
Training Checklist and Documentation – IRB Compliance Staff

7. PROCESS OVERVIEW

IRB members as well as all members of the research community will be required to complete CITI or other training requirements as determined by the IRB. IRB members will be given the opportunity to attend educational conferences and seminars in a effort to maintain the highest quality of human subject research review and protection.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
Director of the Office of Research Compliance (or Program Coordinator)	Establish training and educational requirements and content for IRB members and staff. Set annual training budget.	
Director of the Office of Research Compliance (or Program Coordinator)	Based on requirements and budget, determine training & education schedule. Schedule speakers, acquire outside publications, schedule attendance at PRIM&R and seminars as budget allows.	
Program Coordinator	Notify members of each IRB as to available training materials & schedule. Send reminders as needed.	Training Checklist and Documentation – IRB Members
Program Coordinator	Maintain documentation of all training and education completed.	Training Checklist and Documentation – Compliance Staff

100 – GENERAL ADMINISTRATION	
103. Management Of IRB Personnel	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

IRB Compliance Staff provides consistency, expertise, and administrative support to the IRBs, and serve as a daily link between the IRB and the research community. Thus, the IRB Compliance Staff is the most vital component in the effective operation of Texas A&M University's human subjects protection program. Therefore, the highest level of professionalism and integrity on the part of IRB Compliance Staff is expected.

Specific Policies

1.1 Job Descriptions and Performance Evaluations

Members of the IRB Compliance Staff should have a description of the responsibilities expected of their positions. The performance of IRB Compliance Staff will be reviewed according to current Texas A&M University policy.

1.2 Staff Positions

Staffing levels and function allocation will be determined according to Texas A&M University policy, management assessment of support requirements and budget constraints.

1.3 Hiring and Terminating IRB Compliance Staff

The human resource policies of Texas A&M University determine the policies for recruiting and hiring staff.

1.4 Delegation of Authority or Responsibility

Delegation of specific functions, authorities, or responsibilities by the Chairperson to a staff member must be documented in writing.

1.5 Documentation

The policies of Texas A&M University's Department of Human Resources determine the means of identifying, documenting and retaining formal staff interactions (such as performance reviews, termination procedures).

2. SCOPE

These policies and procedures apply to all IRB Compliance Staff.

3. RESPONSIBILITY

Institutional Official is responsible for establishing personnel requirements and for hiring and evaluating the ongoing performance of the Director of the Office of Research Compliance (or Program Coordinator) and for guiding the Director of the Office of Research Compliance (or Program Coordinator) in establishing personnel requirements for other IRB Compliance Staff.

Director of the Office of Research Compliance (or designee) is responsible for establishing personnel requirements and for hiring and evaluating the ongoing performance of IRB Compliance Staff.

IRB Chairperson (or designee) is responsible for providing input on the ongoing performance of the Director of the Office of Research Compliance to the Institutional Official.

4. APPLICABLE REGULATIONS AND GUIDELINES

TAMU 33.99.03.M!, 33.99.03, 33.99.01.M1, 3.99.01, 33.99.01.M1.02

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Director of the Office of Research Compliance Functions
Director of the Office of Research Compliance (or Program Coordinator) Functions
IRB Administrative Assistant Functions
HR - Performance Evaluation Form

7. PROCESS OVERVIEW

IRB management will maintain policies and procedures to promote the long-term commitment of employees and ensure the efficient and effective administration and enforcement of IRB decisions.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Program Coordinator	With the input of the Director of the Office of Research Compliance, establish the requirements for IRB Compliance Staff. Complete personnel recruitment and hiring as per HR policy.	
IRB Program Coordinator	Compose job descriptions. Ensure that IRB Compliance Staff are adequately oriented and trained.	Functions of all IRB staff – Job descriptions
IRB Director	Evaluate the performance of the IRB Program Coordinator	Applicable Human Resources (HR) Guidelines Performance Evaluations
Institutional Official	Evaluate the performance of the Director of the Office of Research Compliance	Use appropriate HR forms
Director of the Office of Research Compliance (or IRB Program Coordinator	Evaluate the performance of the IRB Compliance Staffs and IRB Administrative Assistants.	Use appropriate HR forms

100 – GENERAL ADMINISTRATION	
104. Conflict Of Interest	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and can only strengthen the research process. Therefore, conflicts of interest should be eliminated when possible and effectively managed and disclosed when they cannot be eliminated.

An investigator may have a conflict of interest when his/her judgment regarding the welfare of study subjects or the integrity of the research is biased by other interests such as financial or other personal gain. Researchers must disclose any conflicts of interest to the IRB, study subjects, and in any publications resulting from such research. The IRB will review the potential conflict and determine if the investigator has minimized the risks involved and if such information is disclosed to the subjects. Conflicts of interest can be viewed as a research risk.

Specific Policies

1.1 Definition of COI

Texas A&M University defines a potential *conflict of interest* as occurring when an individual's private interests compete with his/her professional obligations to the System to a degree that an independent observer might reasonably question whether the individual's professional actions or decisions are determined by considerations of personal gain, financial or otherwise. Regulation 15.01.03 address such conflicts when a significant financial interest (significant financial interest in the sponsoring company defined as $10,000 or 5% ownership) reasonably appears to affect or bias the design, conduct or reporting of research or educational activities funded or proposed for funding to sponsoring agencies.

Texas A&M University System's Policy on Conflict of Interest may be found at http://sago.tamu.edu/policy/15-01-03.htm.

A conflict of interest may also exist when the investigator serves dual roles, such as investigators and health care provider. Other interests, such as publications, promotions or tenure, may also become a COI.

Questions regarding COI may be referred to the Sponsored Programs Office.

The Conflict of Interest Committee has the authority to determine when COI exists as defined by institutional policy and to impose and recommend disciplinary action in the event that a COI is not disclosed.

1.2 Investigator Disclosure and Documentation of Financial Interest and COI

The investigator is responsible for disclosing any potential or actual COI when submitting a research protocol to the IRB Committee for review. A Conflict of Interest statement must be submitted with all IRB applications. This disclosure must be updated as the IRB protocol is renewed. It is required that all investigators comply with the conditions and/or restrictions imposed by the University to manage, reduce, or eliminate actual or potential conflicts of interest or forfeit IRB approval and possible funding.

If the Investigator is an IRB member or consultant he/she cannot deliberate, vote or participate in the initial, continuing review of any project in which they have a COI, except to provide information as requested.

1.3 IRB Member Disclosure and Documentation of Financial Interest and COI

No regular or alternate IRB member may participate in the initial or continuing review of any research project in which the member has a conflict of interest, except to provide information as requested.

It is the responsibility of each voting member or alternate member of the IRB to disclose any financial or non-financial COI to the IRB.

The IRB member must recuse themselves from deliberations and voting for research protocols in which there may be a COI.

The recusal of IRB members, including the Chairperson, from deliberating/voting on all protocols for which there is a potential or actual, both financial/non-financial conflict of interest is documented in the IRB minutes.

1.4 Employees of the University Disclosure and Documentation of Financial Interest and COI

Institutional staff whose job status or compensation is affected by research that is reviewed by the IRB must recuse themselves from attending any meeting at which such a protocol is reviewed.

In addition to University practices, COI information will be captured on the IRB submission and renewal form and forwarded to the COI Committee.

Final IRB approval will not be granted until the COI Committee has reviewed and approved the COI status or management plan.

1.5 Education and Training in COI

The research community, IRB members and staff are required to participate in education and training activities related to financial conflict of interest issues. Training is currently achieved through CITI.

2. SCOPE

These policies and procedures apply to all IRB members, staff and members of the Texas A&M University system.

3. RESPONSIBILITY

The Conflict Of Interest Committee is responsible for articulating and enforcing the conflict of interest policy (COI) at Texas A&M University.

Director of the Office of Research Compliance (or designee) is responsible for monitoring the COI status and disclosures of IRB members.

IRB Chairperson (or designee) is responsible for identifying COI disclosures before beginning protocol deliberations during the IRB meeting.

IRB Compliance Staffs are responsible for documenting all COI disclosures in IRB meeting minutes.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 46.103, 107
21 CFR 56.107
TAMU 15.01.03M1, 15.01, 15.01.03
FDA Information Sheets, FAQs, Section II, question 12
OHRP Draft interim Guidance on Financial Relationships 1/8/00

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

IRB Member Conflict Of Interest Statement

7. PROCESS OVERVIEW

Financial conflict of interest by the IRB members or management will be identified and documented during new member orientation. Members are expected to notify the Director

of the Office of Research Compliance (or Program Coordinator) if conflicts arise. In addition, conflicts will be disclosed on all new submissions forms as well as continuation request forms for all researchers.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Members	Disclose all financial and professional COI to the Director of the Office of Research Compliance or Program Coordinator when joining the IRB, and periodically update that information. Recuse self from IRB deliberations and voting where a COI exists or may appear to exist.	
IRB Compliance Staff	Document COI disclosures in IRB meeting minutes.	
IRB Chairperson Director of the Office of Research Compliance (or Program Coordinator) IRB Members	Ensure that IRB members with a COI do not participate in the IRB deliberations subject to their COI disclosures.	Conflict of Interest Statement
IRB Compliance Staff	Submit applications with COI disclosures to the COI Committee	IRB Submission and Continuing Review Form
IRB Compliance Staff	Ensure COI training occurs as part of the Human subjects training	CITI Training module

100 – GENERAL ADMINISTRATION	
105. Signatory Authority	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

The IRB Chairs, or designee are authorized to sign any and all documents in connection with the review and approval of research projects involving the use of humans as subjects, which have been reviewed and approved pursuant to Texas A&M University policies and procedures. In all cases individuals must sign their own name and no other and indicate their title under their signature.

Specific Policies

1.1 Authorization for Signatory Authority

Authorization to sign documents not described in this policy may be made in writing to the Director of the Office of Research Compliance (or Program Coordinator).

1.2 Results of Reviews, Actions and Decisions

The results of reviews and actions taken by the IRB, either by the full IRB or by expedited review, that grant or may appear to grant Investigators with initial or continuing approval of research, training or educational projects involving human subjects, may be signed by the Chair or designee. Electronic correspondence does not require signature but a copy of the electronic notification will be maintained in the IRB study file folder.

1.3 Routine Internal Correspondence

Designated staff members may sign any action, letters, memos or emails between the IRB, and members of the faculty or staff of the Texas A&M University that provides information concerning the review of research protocols by the IRB or staff which do not imply or appear to imply approval of this activity.

1.4 Correspondence with External Agencies

Any letters, memos or emails sent to agencies of the federal government, funding agencies (whether private or public) or their agents will be signed by the Institutional Official, IRB Chair Or Director of the Office of Research Compliance (or IRB Program Coordinator).

1.5 Decisions Made by Chairperson

Any letters, memos or email sent representing the decision or opinions of the Chairperson of the IRB or his/her respective designees, as long as such correspondence does not imply review and approval of research projects, may be sent electronically by designated IRB Compliance Staff.

2. SCOPE

These policies and procedures apply to all IRB Compliance Staff.

3. RESPONSIBILITY

Institutional Official is responsible for establishing the overall procedure for delegating signatory authority.

Director of the Office of Research Compliance (or designee) is responsible for implementing and controlling signatory authority delegations.

IRB Chairperson, members and staff are responsible for adhering to institutional signatory authority policies.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103, 46.115
TAMU 15.01.01.M5 (3.4)

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Letter Relating to Signatory Authority

7. PROCESS OVERVIEW

The IRB Chair or Institutional Official may delegate signatory authority to an IRB (member) designee.

The IRB member responsible for presiding over IRB meetings shall have authorization to sign resulting letters.

Correspondence may be sent electronically without signatures as long as the IRB Chair or designee approves the information.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool

Institutional Official, IRB Chair or Director of the Office of Research Compliance	Establish signature authority delegation based on nature of documents being signed. Sign all documents related to the review and approval of research projects and correspondence with external agencies. Staff members are not authorized to sign any correspondence with external agencies. In the absence of the Director of the Office of Research Compliance (or Program Coordinator), Institutional Official must sign such documents.
IRB Compliance Staff	Send electronically routine internal correspondence or actions taken by an IRB Chairperson if authorized to do so by the Chairperson.

STRUCTURE OF

INSTITUTIONAL REVIEW BOARD

200

200 – STRUCTURE OF INSTITUTIONAL REVIEW BOARD	
201. Composition Of The IRB	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

The IRB will be sufficiently qualified through the experience and expertise of its members and the diversity of the members' backgrounds, including diverse racial and cultural backgrounds of members and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

Each committee shall consist of at least five members and include both male and female members. Each committee shall have at least one non-affiliated member and at least one member whose primary expertise is in a non-scientific area (e.g., theology or philosophy). A single individual may meet these categorical requirements.

The IRB may, at its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. Such ad hoc members may not vote with the IRB.

Alternate members may be used if they are formally appointed as alternate members. The alternate member's qualifications shall be comparable to those of the primary member to be replaced. When an alternate member replaces the primary member, the alternate member shall have received and reviewed the same material that the primary member would have received. The IRB roster shall identify the primary member(s) for whom each alternate member may substitute. In addition, the IRB minutes shall document when an alternate member replaces a primary member.

When research involving a category of vulnerable subjects (e.g., elderly, children, individuals institutionalized as mentally disabled, prisoners) is reviewed, the IRB will include in its reviewing body one or more individuals who have as primary concern the welfare of these subjects.

The Chairperson of the IRB will be appointed by the Vice President for Research with the concurrence of other Deans and Center Directors and the Health Sciences Center, for a term of three years. The Chairperson must hold either a Ph.D. or M.D. degree. Vice-chairpersons may be appointed by the Vice President for Research to assist the Chairperson with his/her duties.

IRB MEMBER LIST WITH DEGREES AND APPOINTMENTS

A record of the names, degrees, qualifications, terms, affiliation, and voting status of the members of the IRB will be maintained in the IRB administrative office. *Ex officio* members will also be included in this record. The record represents the roster of members and will

serve monthly as the list by which attendance is determined. However, for purposes of determining quorum, only voting members will be counted.

Curricula vitae will be kept for each member in the IRB office. New appointments, dismissals, termination of appointments, and withdrawals of members will be noted at the monthly meeting when they occur. The appropriate regulatory agencies will be apprised of changes in committee membership, if any, at least annually.

Each IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. Each IRB should also be able to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

Therefore, each IRB shall consist of at least five regular, voting members. Qualified persons from multiple professions and of both sexes shall be considered for membership. IRB membership shall not consist entirely of men or of women.

The institution will make every effort to have a diverse membership appointed to the IRB, within the scope of available expertise needed to conduct its functions.

Specific Policies

1.1 Membership Selection Criteria

The members of the IRB shall be sufficiently qualified through experience and expertise, for reviewing research protocols in terms of regulations, applicable law and standards of professional conduct and practice, and institutional commitments. Therefore, the IRB shall include persons knowledgeable in these areas.

The membership shall be diverse, so selection shall include consideration of race, gender, cultural backgrounds, clinical experience, healthcare experience and sensitivity to such issues as community attitudes to assess the research submitted for review.

There shall be at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. There shall be one member who has no affiliation with the institution, either self or family member. For FDA-regulated research, there shall be at least one member who is a licensed physician.

1.2 Composition of the Board

Regular members: The backgrounds of the regular members shall be varied in order to promote complete and adequate reviews of the types of research activities commonly reviewed by the IRB. Regular members must include:

A. **Nonaffiliated member(s):** The nonaffiliated member(s), who can be either scientific or nonscientific reviewers, should be knowledgeable about the local community and be willing to discuss issues and research from that perspective. Consideration should be given to recruiting individuals who speak for the communities from which Texas A&M University will draw its research subjects. The nonaffiliated member(s) should not be

vulnerable to intimidation by the professionals on the IRB, and their services should be fully utilized by the IRB.

B. **Scientific members:** Most IRBs include physicians and Ph.D.-level physical or biological scientists. Such members satisfy the requirement for at least one scientist. When an IRB encounters studies involving science beyond the expertise of the members, the IRB may use a consultant to assist in the review, as provided by 21 CFR 56.107(f). However, when FDA regulated products are reviewed, the convened meeting must include a licensed physician member, therefore, at least one (1) member of each IRB must be a physician licensed in the State of Texas.

C. **Nonscientific member:** The intent of the requirement for diversity of disciplines is to include members whose main concerns are not in scientific areas. Therefore, nonscientific members are individuals whose education, work, or interests are not solely in medical or scientific areas.

D. **Representatives of special groups of subjects:** When certain types of research are reviewed, members or consultants who are knowledgeable about the concerns of certain groups may be required. For example, if an IRB reviews research involving prisoners, a member who can represent this group, either an ex-prisoner or an individual with specialized knowledge about this group, must be included on the IRB.

E. **Chairpersons:** The individual IRB Chairpersons should be highly respected individuals, from within or outside Texas A&M University, fully capable of managing the IRB and the matters brought before it with fairness and impartiality.

2. SCOPE

These policies and procedures apply to the membership of the IRB.

3. RESPONSIBILITY

Institutional Official is responsible for ensuring the IRB has adequate resources to identify and recruit qualified potential members.

Director of the Office of Research Compliance (or designee) is responsible for recruiting and installing new IRB members.

IRB Chairperson (or designee) is responsible for recruiting and evaluating new IRB members.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.107
21 CFR 56.107
TAMU 15.01.01.M3
FDA Information Sheets, FAQ section II, questions 14, 15.

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

IRB Roster

7. PROCESS OVERVIEW

The Texas A&M IRB is made up of two social/humanist/behavioral committees to meet the research needs of the University. Each member has a strong commitment to upholding the basic ethical principles regarding all research involving humans as subjects. The composition of the committees will be based on regulatory guidelines and institutional needs.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Chairperson, Deans, Chair of Executive Committee	Ensure the overall diversity of the IRB membership (gender, race, ethnicity, community affiliation and professional experience) through non-discriminatory selection methods.	
	Following established criteria, select new members, and replace members who resign or otherwise leave IRB service.	
Director of the Office of Research Compliance (or Program Coordinator	Maintain a roster of all regular and alternate members	IRB Roster
Program Coordinator	Maintain a file on all members, to include their curriculum vita, letters of nomination and other evidence of professional ability.	
Program Coordinator	Maintain a roster of available consultants who are eligible and qualified to attend meetings as invited consultants.	

200 – STRUCTURE OF INSTITUTIONAL REVIEW BOARD	
202. Management And Oversight Of IRB Membership	
Policy: **Effective Date:** **Revised By**	**Revised Date:** **Approved By:**

1. POLICY

The management of the membership of the IRBs and oversight of member appointments, IRB related activities, communications, and other administrative details are the responsibility of the Director of the Office of Research Compliance (or Program Coordinator).

Specific Policies

1.1 Term

Members, including the Chair, will serve on the IRB for a term of no more than *three* years. Reappointment for additional terms may occur, by mutual agreement of the IRB Chairperson and Institutional Official.

1.2 Appointments

The Institutional Official, in consultation with the IRB Chair or Director of Research Compliance, has the authority to appoint members to the IRB. Members will be solicited from the Texas A&M University and local communities.

1.3 Resignations and Removals

A member may resign before the conclusion of his/her term. The vacancy will be filled as quickly as possible. A member may be removed by the IRB Chair, or Institutional Official.

1.4 Compensation

Participation by Texas A&M University faculty, staff, or students is considered a component of their job responsibilities as established by their supervisors. Regular members who are not affiliated with Texas A&M University shall receive reimbursement for parking and other miscellaneous expenses upon request.

1.4 Liability Insurance

Regular and alternate members have liability insurance coverage as part of their IRB membership in their capacity as agents of Texas A&M University.

2. SCOPE

These policies and procedures apply to the IRB membership.

3. RESPONSIBILITY

IRB Program Coordinator is responsible for day-to-day management of the activities of the IRB members.

IRB Chairperson (or designee) is responsible for management of the activities of the IRB members relevant to meeting conduct and review of research.

4. APPLICABLE REGULATIONS AND GUIDELINES

TAMU 15.01.01.M3, 15.01(3)

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

New Member Information Packet
IRB Recruitment Letter
IRB Appointment Letter
Acknowledgement of Acceptance of IRB Appointment
IRB Member Confidentiality Agreement
Member Documentation Checklist
IRB New Member Orientation Checklist

7. PROCESS OVERVIEW

The IRB Director (or IRB Program Coordinator) shall ensure the membership has the expertise and commitment to meet its regulatory and institutional mandates.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
Institutional Official	In consultation with the Chairperson and other appropriate parties, identify members of Texas A&M University's faculty and staff and members of the local community to serve on the IRB(s).	
IRB Chair *Director of the Office of Research Compliance (or Program Coordinator)*	Discuss the responsibilities and time commitment of IRB membership with the interested parties. If the individual states he/she is indeed interested in becoming a member, the dates of all IRB meetings are given to the individual for consideration. Request the Curriculum Vitae (CV) for review. If appropriate, forward the CV to the Institutional Official with a cover letter requesting appointment of the individual to a particular IRB.	

	If the Institutional Official concurs with the recommendation of the IRB Director (or IRB Program Coordinator), an Appointment Agreement Letter is sent out to the interested party, with copies to their direct supervisor.	IRB Appointment Agreement
Program Coordinator	Add the new member to the appropriate IRB committee and provide the new member a list of the current members on the IRB, listing their areas of expertise and telephone numbers. Send new member information to Director of the Office of Research Compliance. The new member is also given the New Member Information Packet.	New Member Information Packet Checklist
Program Coordinator)	Notify the new member of the next meeting, sending a packet of agenda materials to review. Inform the member that he or she will not be assigned specific protocols to comment on until their second full meeting.	
IRB Member	Read information in the New Member packet. Sign and return agreements, and review designated educational materials.	IRB Member Confidentiality Agreement
	Attend the next meeting of the IRB as an observer, in order to meet colleagues and observe the review process. Arrive at the first meeting about 1 hour early to meet with the Chairperson and attend a brief orientation/training program.	IRB Appointment Letter
	New members are to be sensitive to conflicts of interest and confidentiality issues dealing with their service on the IRB.	Acknowledgement of Acceptance of IRB Appointment
IRB Chairperson or Program Coordinator	Meet with the new member and review the role and responsibilities of being an IRB member, as well as the expectations of the position.	

Program Coordinator	Document that the new member has completed required training. If the new member has not completed required training within 90 days, remind the member to do so. If the member does not complete required training within the next 30 days, notify the Chairman and Director of the Office of Research Compliance.	Member Documentation Checklist

200 – STRUCTURE OF INSTITUTIONAL REVIEW BOARD

203. Duties Of IRB Members

Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Each IRB member's primary duty is the protection of the rights and welfare of the individual human beings who are serving as the subjects of that research. The IRB member must understand that he or she is not serving on the IRB to expedite the approval of research, but to be a gatekeeper between the Investigator and the research subjects.

In order to fulfill their duties, IRB members are expected to be versed in regulations governing human subjects protection, biomedical and behavioral research ethics, and the policies of Texas A&M University germane to human subjects protection.

1.1 Duty to Texas A&M University

The IRB(s) is/are appointed as Institutional Committees. As such, the IRB members serve Texas A&M University as a whole, rather than a particular department. Therefore, members must not allow their own interest or that of their department to supersede their duty to protect the rights and welfare of research subjects.

1.2 Term of Duty

Regular IRB members and Chairpersons are expected to commit to a 3-year term and, during that time, to fulfill certain duties. These duties will be described prior to appointment and each IRB member is expected to fully understand the duties of IRB membership prior to accepting appointment as an IRB member.

1.3 Specific Duties – Regular Members

A. Nonaffiliated member(s): Nonaffiliated members are expected to provide input regarding their knowledge about the local community and be willing to discuss issues and research from that perspective.
B. Non-scientific members: Nonscientific members are expected to provide input on areas germane to their knowledge, expertise and experience, professional and otherwise. For example, members who are lawyers should present the legal views of specific areas that may be discussed, such as exculpatory language or state requirements regarding consent. Non-scientific members should advise the IRB if additional expertise in a non-scientific area is required to assess if the protocol adequately protects the rights and welfare of subjects.
C. Scientific members: Scientific members are expected to contribute to the evaluation of a study on its scientific and statistical merits and standards of practice. These members should also be able to advise the IRB if additional

expertise in a non-scientific area is required to assess if the protocol adequately protects the rights and welfare of subjects.

D. Chairperson: In addition to the above responsibilities (germane to the member's capacity), the Chairpersons chair meetings of the IRB. Chairpersons perform or delegate to an appropriate voting IRB member expedited review when appropriate. They are empowered to suspend the conduct of a clinical trial deemed to place individuals at unacceptable risk, pending IRB review. The Chairperson is also empowered, pending IRB review, to suspend the conduct of a study if he/she determines that an Investigator is not following the IRB's requirements.

E. The Chairperson may appoint a Vice Chairperson to assist or act on behalf of the Chairperson in particular IRB matters and at IRB meetings, either as a general procedure, or on a case-by-case basis. The Chairperson also may delegate any of his/her responsibilities as appropriate to other qualified individual(s). Such documentation must be in writing and maintained by the IRB Director (or IRB Program Coordinator). The Chairperson is responsible for securing appropriate consulting expertise as needed for selected reviews.

F. The task of making the IRB a respected part of the institutional community will fall primarily on the shoulders of these individuals. The IRB must be perceived to be fair and impartial, immune from pressure either by the institution's administration, the Investigators whose protocols are brought before it, or other professional and nonprofessional sources.

1.4 **Primary and Secondary Reviewers:** In addition to the duties described in section 1.3, each regular member will be expected to act as a Reviewer for studies at convened meetings. Primary and Secondary Reviewers will be assigned. The Primary Reviewer presents his or her findings along with the finding of the Secondary Reviewers resulting from review of the application materials and provides an assessment of the soundness and safety of the protocol and recommends specific actions to the IRB. He or she leads the IRB discussion of the study. The Primary Reviewers may be required to review additional material requested by the IRB for the purpose of study approval. The Secondary Reviewer, if assigned, adds to the discussion, as necessary.

1.5 **Alternate Members**

The DHHS and FDA regulations on the Protection of Human Subjects (45 CFR 46 and 21 CFR 56) do not address the use of alternate members on Institutional Review Boards (IRBs). The FDA "Guidance for Institutional Review Boards and Clinical Investigators" (1998) does, however, provide the following information:
"The use of formally appointed alternate IRB members is acceptable to the FDA, provided that the IRB's written procedures describe the appointment and function of alternate members. The IRB roster should identify the primary member(s) for whom each alternate member may substitute. To ensure maintaining an appropriate quorum, the alternate's qualifications should be comparable to the primary member to be replaced. The IRB minutes should document when an alternate member replaces a primary member. When alternates substitute for a primary member, the alternate member should have received and reviewed the same material that the primary member received or would have received."

- Alternates are appointed by the Institutional Official (IO). Alternates will be listed on the IRB rosters submitted to OHRP with Assurances. The IO for Texas A&M University is the Vice President for Research (VPR).

- There is a specific one-to-one designation of IRB members and alternates. This is necessary to ensure that a committee is properly constituted, even when alternates are serving. The alternate should have expertise or experience as the regular member.

- The IRB minutes must document when the alternate member serves in place of the regular member

- Alternate members are encouraged to attend IRB meetings and participate in other IRB activities even when the regular member is present, at the discretion of the institution, although they do not have to contribute to the formation of a quorum or vote unless the member for whom they substitute is not available

- An alternate contributes to the quorum and functions as an IRB member if the regular member for whom they serve as alternate is unavailable.

- Alternates should receive IRB training or orientation similar or identical to what is provided regular IRB members. The alternate will be given the same materials as the regular member since they may have to step in for the regular member at any time.

- Alternate members are expected to "vote their conscience" as opposed to representing the position of the regular member for whom they serve.

1.6 New IRB Member Orientation

All members appointed to the IRB must attend an orientation briefing to receive TAMU specific policies and procedures manuals and other documents.
The following documents will be given to the new members as part of an orientation packet:

Schedule of meetings
IRB Roster for all Committees
45 CFR 46
Declaration of Helsinki
Belmont Report
IRB Submission Forms
Consent Form Templates
Protocol Review Sheets
Human Subjects Training Information
Member Profile to complete and return to Research Compliance Office
Copy of Policy and Procedures Manual
Research Compliance Website Information and additional links
Research Compliance Contact Information

The Chair(s), assisted by the Program Coordinator, will conduct the orientation briefing, explain the processes and procedures used by the IRB, and answer any questions from the new members.

2. SCOPE

These policies and procedures apply to all IRB Members.

3. RESPONSIBILITY

IRB Director (or IRB Program Coordinator) (or equivalent) is responsible for clearly articulating all IRB members' duties to potential and current IRB members.

IRB Members are responsible for fulfilling their duties as specified.

4. APPLICABLE REGULATIONS AND GUIDELINES

OHRP IRB Guidebook
FDA Information Sheets FAQ, section II, question 17.

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

New IRB Member Orientation Packet

7. PROCESS OVERVIEW

The Director (or IRB Program Coordinator) or IRB Chair will ensure that IRB members are aware of their responsibilities.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Program Coordinator	With the input of the Director of Research Compliance and the IRB Chair, document the expectations for members of the IRB.	Member Responsibilities – SOP 203
IRB Chairperson	Meet with prospective members to discuss expectations.	New Member Orientation

IRB Director and IRB Program Coordinator	Periodically review members' duties. Update SOP 203 as needed.
IRB Program Coordinator	Ensure that members are carrying out their expected functions and that there is adequate staff support to ensure that members are able to function as documented.
IRB Program Coordinator	As needed, make recommendations to the Chairperson and Director regarding changes to descriptions, staffing, meeting scheduling, and other factors that affect members' ability to perform their roles.

REVIEW OF RESEARCH

300

300 – REVIEW OF RESEARCH	
301. Criteria For IRB Approval (Full Committee Review)	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

All research protocols that intend to enroll human subjects must meet certain criteria before study related procedures can be initiated. The criteria are based on the principles of justice, beneficence and autonomy as discussed in the Belmont Report and are specified below. In addition, certain other criteria that are unique to Texas A&M University's system may apply and must be met as well.

Specific Policies

1.1 Minimal Criteria for Approval of Research

In order for a research project to be approved, the IRB must find that:

A. Risks to subjects are minimized:

By using procedures that are consistent with sound research design, which do not unnecessarily expose subjects to risk and, whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

B. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result.

In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

C. Selection of subjects is equitable.

In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.

D. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with and to the extent required by appropriate local, state and federal regulations.

E. Informed consent will be appropriately documented as required by local, state and federal regulations.

F. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

G. Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

H. When some or all of the subjects, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence, or for subjects found at international sites, additional safeguards have been included in the study and in the IRB review process, to protect the rights and welfare of these subjects.

I. Studies are reviewed at periods appropriate to the degree of risk research subjects are exposed to due to their participation in the study, but at least annually.

1.2 Other Criteria

The IRB may require verification of information submitted by an Investigator. The IRB will determine the need to verify any information at a convened meeting. The purpose of the verification will be to provide necessary protection to subjects when deemed appropriate by the IRB.

The criteria used to determine whether third-party verification is required may include:

- Investigators that conduct studies that involve a potential high risk to subjects,
- Studies that involve vulnerable populations,
- Investigators that conduct studies that involve large numbers of subjects, and
- Investigators selected at the discretion of the IRB.

Projects that need third party verification from sources other than the Investigator that no material changes have occurred since previous IRB review, will have such assessment performed as necessary.

1.3 Reliance on Other IRBs for Review and Approval of Research Conducted at Texas A&M University

The Texas A&M University, IRB(s) may enter into joint review arrangements, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort as allowed and upon modification of the institutional Federal-wide Assurance agreements (FWA).

2. SCOPE

These policies and procedures apply to all IRB Compliance Staff and members and to research submitted to the IRB.

3. RESPONSIBILITY

Director of the Office of Research Compliance (or designee) is responsible for ensuring that IRB reviewers have all the tools and resources they need to complete their research reviews.

IRB Chairperson (or designee) is responsible for providing IRB members adequate submission review training and ongoing guidance, and for selecting primary and secondary reviewers with the relevant expertise to perform reviews and make necessary recommendations on approval decisions by the IRB.

IRB Reviewer is responsible for conducting a thorough review and making all appropriate approval recommendations for consideration by the IRB.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.111
21 CFR 56.108, 56.111
TAMU 15.01.01.M2, 15.01.01, 15.01

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Protocol Review (Critique) Sheet
IRB Submission Form
Checklist – Requirements for Research Involving Prisoners
Checklist – Research Involving Pregnant Women & Fetuses
Checklist – Requirements for Research Involving Children

7. PROCESS OVERVIEW

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Compliance Staff	Provide primary and secondary reviewers with appropriate protocol review worksheets.	Critique Sheet
IRB Program Coordinator	Select reviewers with appropriate expertise for the research to be reviewed.	
IRB Member (Reviewer)	Review research protocol and summarize findings on appropriate protocol review worksheet.	
IRB Member (Reviewer)	Ascertain whether any special considerations exist that may influence the review of a protocol.	
IRB Member (Reviewer)	Ascertain whether the evidence exists that third party verification of submitted information is needed.	
IRB Member (Reviewer)	Prepare summary of findings and recommendations for presentation at the next convened IRB meeting.	

300 – REVIEW OF RESEARCH	
302. Research Submission Requirements	
Policy: **Effective Date:** **Revised By:**	**Revised Date: 10-10-2005** **Approved By:**

1. POLICY

IRB members often rely solely on the documentation submitted by Investigators for initial and continuing review. Therefore this material must provide IRB members with enough information about a study to assess if it adequately meets the IRB's criteria for approval.

A submitted protocol will be scheduled for IRB review when staff has determined that the information and materials submitted present an adequate description of the proposed research.

The US population is becoming increasingly culturally, linguistically, economically, and ethnically diverse. The research needs to make a concerted effort to ensure that research subjects reflect the population demographically, including those groups that have been traditionally underrepresented. However, it is recognizable that the available pool of subjects may preclude having a balanced population. If the researcher cannot use a diverse population in the research, then he/she must justify this action in the protocol application.

Governing Principles

The governing principles for the TAMU IRB is 45 CFR Part 46 and 21 CFR Parts 50, 56. The TAMU Federal Wide Assurance specifies that the institution will follow 45 CFR 46 for all research regardless of the source of funding. If the research falls under both OHRP and FDA, then both rules apply.

Specific Policies

1.1 Submission Requirements for Initial Review

1.1.1 Any TAMU faculty, staff, or student who proposes to engage in any research activity involving the use of human subjects must submit a complete protocol application to the IRB office. The application may be downloaded at http://researchcompliance.tamu.edu. In the completed application, the following information must be included:

a. Protocol application with signatures, including: co-investigators, and Department Head (Advisor) if applicable.
b. Full Protocol - describing the rationale for the study, research questions to be answered, methods, procedures, data analysis plan, and other pertinent information
c. A lay summary describing the purpose of the study
d. A complete copy of the Federal grant application and budget if applicable, without appendices (required for federal granting agencies)
e. Conflict of Interest Statement from all Principal Investigators and Co-Investigators.
f. A dated informed consent form in the IRB approved format; unless waived by the IRB

g. If the study involves the use of questionnaires, surveys or similar instruments, copies of the same must be submitted.
h. Any materials that will be used to recruit subjects for the protocol and any other advertising materials (e.g., press releases, interview forms, etc.)
i. Proposed subject instructions
j. Any other supporting material

1.1.2 New protocols for review may be received in the IRB office at any time, however, investigators should be aware that processing time depends on the type of review: Exempts – approximately 3 working days, Expedited approximately 10 working days, and full reviews approximately 30 working days. Processing times are estimates and delays due to incomplete applications, requests for additional information, or other unforeseen complications could extend the listed time periods.

1.1.3 The Program Coordinator or designated staff member will determine if studies require full board review or may be approved by the Exempt or Expedited Review process. Generally, all protocols qualifying for Expedited Review are minimal risk. The protocol is reviewed by the IRB Chair or designated reviewer and signed. If he/she has any stipulations/comments, they are noted accordingly and passed on to the principal investigator via a written or electronic memo.

1.1.4 If a protocol can be approved by the Expedited Review Procedure (see Policy 304), a determination of whether or not informed consent and/or written documentation of consent are required must be made by the IRB Program Coordinator, IRB Chair or designee.

1.1.5 Research may <u>not</u> be initiated until the IRB and any other committees (i.e. , whose approval may be required) have given final written approval. The principal investigator will be responsible for notifying, in writing, all committees and other pertinent institutional officials of the respective committee approvals for the research protocol, prior to initiation of the protocol.

1.2 Administrative Protocol Review

The Program Coordinator or designated staff member assigns primary reviewers to protocols. This will be done by expertise, and to minimize the workload of the members. Protocols meeting the exempt criteria will be reviewed by a member of the Office of Research Compliance with adequate training and expertise. Only exempt protocols are subject to administrative review.

A specific IRB number is assigned to each new protocol by referring to the protocol database and using the next available number. This is a sequentially assigned number with a four digit prefix representing the year of initial submission, (e.g., 1999-56, 2005-112). All protocol information is entered into the protocol tracking database to track its original date of receipt, title, name of investigator, level of risk, review information, reporting and sponsor information, amendments, adverse events, correspondence, and approval status.

For each protocol received, electronic or written correspondence is sent to the principal investigator providing the IRB number assigned.

The original submission documents are kept for use by the IRB Compliance Staff attending the IRB meeting and taking minutes. Ultimately, the original documents will start the official protocol file maintained in the IRB office.

A file labeled with the IRB number and the name of the principal investigator will be created for each submitted protocol, which will contain the protocol application and other study-related documents.

The principal investigator is notified by email that the protocol has been assigned to an agenda. He/she is provided the date of the IRB meeting and invited to the meeting to represent their protocol.

1.3 Confidentiality of the Review Process

During the process of initial or continuing review of an activity, material provided to the IRB shall be considered privileged information and the Board(s) shall assure the confidentiality of the data contained therein. However, the Board(s) are subject to the Texas Open Records Act and requests for IRB meeting information will be reviewed based on this requirement.

1.4 The Administrative Review Process

The IRB office will review all protocols to ensure the criteria set forth in the Federal Regulations and institutional policies have been adhered to. Protocols are reviewed on a first come, first serve basis, and will be reviewed for completeness. Background information, purpose of the study, recruitment procedures, inclusion and/or exclusion criteria, research plans, data analysis plans, risks, benefits, alternatives, the consent process, and monitoring for adverse events are taken into consideration by the Program Coordinator before the protocol can be placed in an exempt, expedited, or full review category. **Incomplete protocols will not be further evaluated.**

1.5 Action Taken If Documentation Is Not Adequate or Additional Information Is Required

If the IRB reviewer or IRB Compliance Staff determines that the submitted documents are not complete Investigators may be required to submit additional information or their presence may be required at the IRB meeting to answer questions or explain the details of the study.

1.6 Withdrawal Process

Investigators are notified of incomplete applications and pending requests. A notice is sent to the PI requesting missing information and/or documents. Investigators are given 45 days to respond to such requests. If no response is received the investigator will be notified that the protocol application will be administratively withdrawn.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

Program Coordinator is responsible for maintaining current research submission requirements for interested Investigators and for preliminary triage of non-routine submissions.

Program Coordinator or designated staff is responsible for preparing member review materials and reviewing submission elements.

IRB designated staff is responsible for submission receipt, tracking and acknowledgements.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.115
21 CFR 56.108 (a) (4)
TAMU 15.01.01.M5, 15.01.01

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

IRB Submission Checklist
IRB Submission Application
Acknowledgement of Protocol Receipt
Pending Email Notice

7. PROCESS OVERVIEW

Investigators are responsible for submitting complete application and supporting information for IRB assessment.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool

Compliance Program Coordinator or designee	Receive initial submission Assign IRB number Send acknowledgement email to PI Enter protocol information into database Review submission for review type and completeness of submission Assign reviewer(s) and prepare file	*IRB Submission Checklist* *Acknowledgement/ Pending Email Notice*

300 – REVIEW OF RESEARCH	
303. Research Exempt From IRB Review	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Some research projects involving human subjects are exempt from full review by the IRB. (45 CFR 46, Section 46.101(b)) Sensitive topics and subjects such as children or minors, pregnant women and prisoners are not considered for exempt research. International studies are also not exempt from IRB review.

Research activities in which the only involvement of human subjects will be in one or more specific categories, which are listed in section 1.1 of this policy, may be exempt from IRB review. Determination of exemption must be based on regulatory and institutional criteria and documented. The final determination as to whether or not research activities are exempt from IRB review shall be made by the IRB.

1.1 Exempt Research Activities

Research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from IRB review:

1.1.1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

1.1.1.1. Research on regular and special education instructional strategies,

1.1.1.2. Research on the effectiveness of, or the comparison among, instructional techniques, curricula, or classroom management methods.

1.1.2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

1.1.2.1. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

1.1.2.2. Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

1.1.3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt, if:

1.1.3.1. The human subjects are elected or appointed public officials or candidates for public office; or

1.1.3.2. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

1.1.4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the Investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

1.1.5. Research and demonstration projects which are conducted by or subject to the approval of Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:

- Public benefit or service programs;
- Procedures for obtaining benefits or services under those programs;
- Possible changes in or alternatives to those programs or procedures; or
- Possible changes in methods or levels of payment for benefits or services under those programs.

1.1.6. Taste and food quality evaluation and consumer acceptance studies:

- If wholesome foods without additives are consumed
- If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

1.2 Ethical concerns of research that is exempt from regulation

1.2.1 The person who makes determinations of exemption will also conduct the ethical evaluation of exempt research per the ethical principles listed in "Belmont Report".

1.2.2 When appropriate, participants involved in exempt research are provided additional protections to ensure their safety and privacy.

2. SCOPE

These policies and procedures apply to Investigator claims for exemption from IRB review.

3. RESPONSIBILITY

The IRB Compliance Staff is responsible for evaluating submissions that claim exemption from IRB review. The submissions are then given to the Program Coordinator.

Program Coordinator is responsible for the review of submission and determination that submission can be exempted. The approved exempted protocols are listed on the agenda and reported at the next convened IRB committee meeting.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.101
21 CFR 56. 104, 105

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Sample Exemption Letters with Category
Claim of Exemption Checklist for Staff
Signature Authority for Exempt Protocols

7. PROCESS OVERVIEW

Provide review of protocols submitted for exemption status.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
Office of Research Compliance	Maintain and make available submission information regarding research that is exempt from IRB review.	SOP 303
IRB Compliance Staff	Review protocols submitted for exempted status and route to designated reviewer for review.	IRB Submission Application
Compliance Program Coordinator (Designated Reviewer)	Review study for exemption	Exemption Checklist
Director of the Office of Research	Provide guidance to IRB Compliance Staff or Designated Reviewer on Claims of Exemption as needed and requested.	
Compliance Program Coordinator	Document all determinations of exemption from IRB review including a brief description of the basis for exemption.	Exemption Approval Letter

300 – REVIEW OF RESEARCH	
304. Expedited Review	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

An expedited review procedure consists of a review of research involving human subjects by the Chairperson of each IRB or by one or more experienced reviewers designated by the Chairperson from among members of the IRB.

The categories of research that may be reviewed by the IRB through an expedited review procedure include research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the specific categories listed in the regulations at Federal Register Volume 63, No 216 (expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110).

Research Categories:
Categories one (1) through seven (7) pertain to both initial and continuing IRB review.
(1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
(a) from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
(b) from other adults and children[2], considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
(3) Prospective collection of biological specimens for research purposes by noninvasive means.
Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;

(f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject=s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

(8) Continuing review of research previously approved by the convened IRB as follows:

(a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

(b) where no subjects have been enrolled and no additional risks have been identified; or

(c) where the remaining research activities are limited to data analysis.

(9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

1.1 Definition of Minimal Risk

Minimal risk is defined as "...the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests...."

1.2 **Cautions**

1.2.1 The activities listed should not be deemed to be of minimal risk simply because they are included on the list of eligible research. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

1.2.2 The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability; be damaging to the subjects' financial standing, employability, insurability, or reputation; or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

1.2.3 The expedited review procedure may not be used for classified research involving human subjects.

1.3 **Authority of the IRB Chairperson for Expedited Review Procedure**

With regard to the Expedited Review Procedure, the IRB Chair (or designated reviewer) may exercise all of the authorities of the IRB, except that he/she may not disapprove the research. A research protocol may be disapproved only after review by the full IRB.

1.4 **Notification of the IRB**

When the expedited review procedure is used, all regular members shall be informed of actions taken by the IRB at the next convened meeting.

1.5 **Documentation**

If the study qualifies for expedited review, the IRB Chair or designee will document his/her determination of risk.

The minutes will include documentation of the studies that were reviewed via expedited review and any issues resolved relating to questions that IRB members had concerning the research reviewed.

1.6 **Additional Items That May be Reviewed by Expedited Review**

1.6.1 **Pending approval subject to minor revisions, clarification:**

Revisions to consent documents and other documentation or clarifications submitted as a result of full IRB review, and as a condition to final approval, may be reviewed by the IRB Chair or his/her designee. Final approval will be issued providing the revisions, documentation or clarifications do not indicate or result in a change to the study or change the risk/benefit ratio.

1.6.2 **Continuing review:**

The IRB Chair or designee may use the expedited review procedure to review renewal requests for previously approved research during the period for which approval is authorized.

1.6.3 Amendments:

Minor changes that do not affect the rights and welfare of study subjects, or do not involve increased risk or significant changes in study procedures, or addition of new procedures, may be reviewed and approved by the Chair/designee using the expedited review process. These changes would apply to but are not limited to:

- **Revisions to informed consent documents**
- **Unanticipated problems reports**
- **Change to study personnel**
- **Change in study enrollment**
- **Advertisements**
- **Translations of consent documents** – the investigator will provide certification that the translated consent form is appropriate for the study population.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB(s) that qualifies for expedited review.

3. RESPONSIBILITY

IRB Compliance Staff is responsible for identifying submissions that qualify for expedited review.

IRB Chair (or designee) is responsible for conducting expedited review.

The approved expedited protocols are listed on the agenda and reported at the next convened IRB committee meeting.

4. APPLICABLE REGULATIONS AND GUIDELINES

Minimal Risk:	45 CFR 46.102
	21 CFR 56.102
Expedited Review:	45 CFR 46.110
	21 CFR 56.110
	TAMU 15.99.01.M1
	FDA Information Sheets, 1998
	OHRP IRB Guidebook

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

IRB Submission Application
Expedited Review - Reviewer Checklist
Critique Sheet
Sample Expedited Approval Letter

7. PROCESS OVERVIEW

The IRB Compliance Staff will review the submissions and determine whether they can be expedited. Once that determination is made, the protocol will be routed to the IRB Chair or his/her designated reviewer. The reviewer will make the final determination of whether the protocol qualifies for expedited review. Once approved, the expedited protocols must be reviewed for approval annually.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

A. Expedited Review - New Study

Who	Task	Tool
IRB Compliance Staff)	Make initial determination regarding qualification for expedited review. Refer to SOP 304 as needed.	IRB Submission Application
IRB Compliance Staff	Forward complete application packet for expedited review, assemble reviewer's material and distribute to the chair or designee.	
IRB Member	Perform primary review; using all the appropriate worksheets. Document result of review	Expedited Review Checklist/Critique Sheet/ Expedited Approval Letter
IRB Compliance Staff	Upon completion of the review, update the database so that the protocol appears on the agenda for the next convened IRB meeting.	

B. Expedited Review - Renewal

Who	Task	Tool
Same as above		

C. Expedited Review - Amendments

Who	Task	Tool
Same as above		

300 – REVIEW OF RESEARCH	
305. Continuing Review - Ongoing	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1.0 POLICY

Investigators are expected to conform to the highest ethical standards of research conduct and to maintain communication with the IRB when needed.

IRB approval may be withdrawn at any time warranted as determined by the IRB. The regulations authorize the IRB to establish procedures for the concurrent monitoring of research activities involving human subjects. Periodic review of research activities is necessary to determine whether approval should be continued or withdrawn. All research involving human subjects must be reviewed no less than once per year.

IRB approval for the conduct of a study may be withdrawn if the risks to the subjects are determined to be unreasonably high, for example, more than an expected number of adverse events, unexpected serious adverse events; or evidence that the Investigator is not conducting the investigation in compliance with IRB or Institutional guidelines. Such findings may result in more frequent review of the study to determine if approval should be withdrawn or enrollment stopped until corrective measures can be taken or the research study terminated. Continuing review includes, but may not be limited to the following activities:

- Site Visits and Third Party Verification
- Review of Serious Adverse Events and Unanticipated Problems
- Amendments
- Review of Significant New Findings
- Reports from Employees, Staff and Faculty
- Noncompliance

1.1 Site Visits and Third Party Verification

The IRB or Office of Research Compliance has the authority to observe, or have a third party observe, the informed consent process of research it has approved, and to verify that the study is being conducted as required by the IRB and within the Institutional policies and procedures and site-specific procedures, as appropriate. IRB Compliance Staff or members may perform site visits or use another party, either affiliated or not with the institution, to verify information in the study application, or in any interim or continuing review submissions.

The criteria for selecting Investigators to be visited may include:

- Investigators who conduct studies that involve a potential high risk to subjects,
- Studies that involve vulnerable populations,
- Investigators who conduct studies that involve large numbers of subjects, and
- Investigators selected at the discretion of the IRB.

Other means of verification include questionnaires sent to investigative staff to verify information submitted by the Investigator. Sponsors may be asked to submit copies of monitoring reports, or may be requested to complete a questionnaire regarding the protocol and/or the investigative site.

Investigators may be asked to submit copies of signed informed consent forms or other documents to ensure their compliance with IRB requirements. The IRB may conduct interviews with screened and/or enrolled subjects as deemed necessary.

1.2 Serious Adverse Events and Unanticipated Experiences

Subject safety is of the greatest importance for both the individual subject and the goals of the research study.

Principal investigators are required by regulation and TAMU policy to promptly report any adverse event, regardless of the severity. As appropriate, the event will be reported to the institutional official and to OHRP. Adverse events must also be reported to the federal sponsor, if applicable.

1.2.1 Receipt

An adverse event is defined as any potential for harm or any unanticipated problem(s) involving risks to subjects or others. Such reports should be submitted to the IRB **within 24 hours**. Other documents, such as those provided by study sponsors, should be attached, but the report should summarize the event(s) and be signed by the PI. If the event occurred at TAMU when the IRB office is normally not open, a summary of the event should be sent via electronic mail.

1.3 Amendments

Changes in approved research, during the period for which approval has already been given, may not be initiated without prior IRB review (full or expedited review, as appropriate) and approval; except where necessary to eliminate apparent immediate hazards to human subjects.

1.3.1 Requests

Requests to modify or amend an IRB approved protocol, consent form, or any other document related to an IRB approved protocol must be made in writing by the principal investigator (PI) using an IRB Amendment Form. Upon receipt of the protocol change, the Chairperson or his or her designee, with assistance of the Program Coordinator, will determine if the revision meets the criteria for minimal risk. If the change represents more than a minimal risk to subjects, it must be reviewed and approved by the IRB. Minor changes, involving no more than minimal risk to the subject, will be reviewed by the expedited review procedure.

1.3.2 Review

A designated IRB member will review the request and approve, request clarifications, or refer the request to the full board for review, if the requested changes are more than minor. A request that should be forwarded for full board review would be one in which there is a change in methods, activities or procedures that would increase risks to subjects or decrease the potential for benefit.

1.3.3 Reporting

All requests for modifications are reported in the minutes for review by the full board at the next convened meeting.

1.3.4 Filing and Retention

Modification requests and any correspondence generated by the IRB in response to the request must be filed with the original file and retained for three years beyond the life of the protocol.

1.4 Significant New Findings

During the course of a study, the IRB should review adverse event reports, current literature, and other sources as it may find useful in order to ascertain the status of the study and assess whether or not the risk/benefit balance is still acceptable. The IRB will determine whether or not new information needs to be conveyed to subjects, or if a segment of the population may be bearing an undue burden of research risk or being denied access to promising therapy.

1.5 Reports from Employees, Staff and Faculty

It is the responsibility of the IRB Compliance Staff and IRB members to act on information or reports received from any source that indicate a study being conducted at any facility under the jurisdiction of the IRB that could adversely affect the rights and welfare of research subjects.

1.6 Ensuring Prompt Reporting of Any Serious or Continuing Noncompliance with Applicable Regulations or the Requirements or Determinations of the IRB

All credible reports of inappropriate involvement of human subjects in research must be investigated by an IRB Ad-hoc subcommittee established for that purpose by the IRB. The results of the investigation will be reported to the appropriate Texas A&M University official(s). Regulatory authorities or Sponsors may also be notified. Such reports of noncompliance may come from any source including IRB members, Investigators, subjects, institutional personnel, the media, anonymous sources or the public.

The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB policies, is not in compliance with federal regulations, or has been associated with unexpected serious harm to subjects. All such suspension and or terminations will be reported to the OHRP and FDA as appropriate.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

Director of the Office of Research Compliance or designee is responsible for establishing the processes for conducting ongoing IRB reviews of research.

IRB Chairperson or designee is responsible for preliminary assessments of adverse events, significant new findings and the need for third party verification.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.108, 56.109, 56.113
45 CFR 46.103, 46.109, 46.115
TAMU 15.99.01.M1
FDA Information Sheets, 1998

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Site Visit Confirmation Letter
Site Visit Checklist
Site Visit Report
IRB Modification Form
IRB Adverse Event Form
File Folder Communication Log

7. PROCESS OVERVIEW

Upon receipt of request for modification all required pages are date stamped, the document information is entered into the database, an email is generated to the PI indicating receipt of the document, the document is scanned including any attachments, the protocol file for which the request is made is pulled and the document is attached to the outside of the file jacket for review by a designated member of the IRB. After review, and providing that it is not referred for full board review, a letter to the PI is prepared stating that the modification is approved, conditionally approved, or the request needs further clarification (pending letter). A copy of the letter is made along with the request and filed in the protocol file.

If revisions to the consent form are required, the PI must submit two copies of the revised consent form with one copy noting where the changes were made using bolding or strike-through. Modification requests must come from the PI.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

A. Site Visits and Third Party Verification

Who	Task	Tool

Director of the Office of Research Compliance or designee	Call Investigator or contact key site personnel to set up a day and time to conduct a site visit. Three days prior to the site visit, confirm the date and time. The IRB or Office of Research Compliance may conduct unannounced site visits if they deem it appropriate.	Site Visit Confirmation Letter
Site Visitor	Bring a completed copy of the site's most recent Study Summary Form, the current protocol, informed consent document, and any adverse event reports submitted. Confirm that the study is being conducted in compliance with the information provided on these documents by observation, if possible, especially: the method of subject recruitment and in particular that there are safeguards in place for the recruitment of subjects vulnerable to coercion or undue influence; the process of obtaining informed consent; the consent form being used; and the facilities available in an emergency. If appropriate, obtain information about any adverse events that may have been reported. If project is inactive, suspended, or terminated, obtain information regarding this status. Complete the Site Visit Report and submit it to the Director of the Office of Research Compliance	Site Visit Worksheet Site Visit Report
Director of the Office of Research Compliance (or Program Coordinator)	Provide Site Visit Report to the IRB Chairperson for review. Include discussion of site visit in agenda for next IRB meeting.	
IRB Chairperson	Review Report and determine any necessary follow-up action.	

B. Serious Adverse Events and Unanticipated Problems

Who	**Task**	**Tool**

IRB Compliance Staff	Receive a report of a Serious Adverse Event via fax, mail/delivery, phone, internet or during a site visit. Upon receipt, date-stamp the current date on the upper right corner of the report. If notified by phone, indicate receipt of the phone call on the Communication Log. Using the Serious Adverse Event Report form, record the information conveyed and ask for additional information as indicated on the form. Input the adverse event into the appropriate database. Attached all information related to the adverse event to the report and give to the coordinator for review.	Adverse Event Form Communication Log
Program Coordinator	Review all serious or unexpected adverse event reports received. Triage, if necessary and give to the IRB designated reviewer for review.	
IRB Chairperson or designee	Review adverse event reports. If the reviewer determines that action may be needed to protect the safety of research subjects due to the nature or frequency of reported adverse events, he/she may take such action and/or the full IRB or designated subcommittee will review the adverse events and study in question to determine action, if any, by the IRB.	Adverse Event Form
Program Coordinator	Provide summaries of all safety reports and serious adverse events for the next convened meeting.	

C. Modifications

Who	Task	Tool
IRB Compliance Staff	Receive a modification or change in the research via mail, hand delivery or during a site visit. Upon receipt, date-stamp the current date on the upper right corner of the report. Input the information concerning the modification into the database. Send an acknowledgement of the receipt of the amendment to the Investigator. Attach all information related to the modification to the study file and give to the coordinator for initial review.	Amendment Form
IRB Program Coordinator	Review all modifications/amendments to determine which can be reviewed via expedited	

	review, and which are to be placed on the agenda for the next IRB meeting, and give to the IRB designee for review.
IRB Compliance Staff	Complete processing as instructed by the Coordinator.
IRB Committee	Modification submissions requests are reported at the next scheduled convened meeting of the IRB.

D. Reports of Noncompliance

Who	Task	Tool
IRB Program Coordinator	Receive a report of non-compliance via fax, mail/delivery, phone, internet, or during a site visit. Upon receipt, date-stamp the current date on the upper right corner of the report. If notified by phone, indicate receipt of the phone call on the Communication Log. Record the information conveyed. Input the report onto the database. Attach all information to the appropriate protocol file and give to the Chair or designee for review.	Communication Log
Director of the Office of Research Compliance	Review all reports received, obtain additional information if needed or available. Notify the IRB Chairperson, and then appropriate units/personnel at the University.	

300 – REVIEW OF RESEARCH	
306. Criteria For Renewal	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Any research activity involving the use of human subjects that has received initial review and approval by the IRB is subject to continuing review and approval. Time intervals for such reviews shall be made at the discretion of the Institutional Review Board, based on the risk to the participants, but shall occur no less than annually. The initial continuing review period will normally be during the eleventh month and the subsequent approval period will begin during that month. Continuing review for subsequent years will normally occur every twelve months with the approval period beginning on the last day of the month in which the protocol is reviewed. This procedure will ensure compliance with federal requirements and will ensure that protocols are reviewed "at least annually".

1.1 Interval for Review for Purposes of Renewal

The IRB must conduct continuing review of protocols for purposes of renewal of the IRB approval period, at intervals appropriate to the degree of risk, which is determined at the initial review, but not less than once per year. "Not less than once per year" means that the research must be reviewed on or before the one-year anniversary of the previous IRB review date, even though the research activity may not have begun until some time after the IRB gave its approval.

Investigators or qualified designees are required to submit a periodic report prior to the expiration of the study or as specified by the IRB, but at least annually. The report should normally be filed about 45 days before the study approval period ends.

1.2 Extensions of Approval Period

There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. Extensions beyond the expiration date will not be granted. If Continuing Review Report forms are not received as scheduled, the Investigator must suspend the study and study enrollment until reports are reviewed and approved.

FDA Studies Only:

If the Investigator is in communication with the IRB, the Continuing Review request form is forthcoming, and in the opinion of the IRB, subjects participating in such a study would suffer a hardship if medical care were discontinued, appropriate medical care may continue beyond the expiration date for a reasonable amount of time. However, new subjects cannot be enrolled. Prospective research data cannot be collected, and no procedures that are only being performed for the purposes of the protocol may be performed until a Continuing Review Report or other progress report is reviewed and approved.

1.3 Criteria for Renewal

Continuing review must be substantive and meaningful. When considering whether to renew a study, the IRB revisits the same criteria used to grant initial approval. Therefore, the IRB (or the reviewers for protocols reviewed under an expedited procedure) must determine that:

- The risks to subjects continue to be minimized and reasonable in relation to the anticipated benefits;
- The selection of subjects continues to be reasonable in relation to anticipated benefits;
- Informed consent continues to be appropriately documented;

Additionally, there are:

- Provisions for safety monitoring of the data,
- Protections to ensure the privacy of subjects and confidentiality of data, and
- Appropriate safeguards for vulnerable populations.

In some situations, it may be that only after research has begun that the risks can be fully evaluated and the preliminary results used to compute the actual risk/benefit ratio. Accordingly, the IRB can then determine whether or not the study can be renewed at the same risk/benefit ratio, or if new information has changed that determination.

In order to determine the status of the study, the following will be re-reviewed:

1.3.1 Consent document: the IRB shall review the currently approved consent document and ensure that the information is still accurate and complete. Any significant new findings that may relate to the subject's willingness to continue participation should be provided to the subject in an updated consent document.

1.3.2 Current approved protocol including any amendments to protocol since initial review: A copy of the protocol will be sent to the primary reviewer of the continuing review. Amendments and addenda to a research protocol should be submitted as generated during the course of the study and they should be submitted at the time of continuing review. A separate cover letter describing the change and all appropriate documentation (approved consent form) must accompany the continuing review application.

1.3.3 Continuing IRB review is required as long as individually identifiable follow-up data are collected on subjects enrolled in protocols. This remains the case even after a protocol has been closed at all sites and protocol-related procedures has been completed for all subjects. These renewal requests may qualify for expedited review.

1.3.4 Expired Protocols

If a PI submits a continuing review form for an expired protocol, the PI will be advised that all research must be halted immediately and a new protocol must be submitted for review. ***The IRB allows 10 days from the date of expiration before requesting a new submission.*** While it is a courtesy of the IRB to send out renewal notices, it is ultimately the responsibility of the PI to renew protocols in a timely manner in accordance with the Federal guidelines. Failure to adhere to these guidelines will be considered an act of non-compliance and the IRB could have the research and/or funding suspended.

1.3.5 Continuing Review Form:

All IRB members shall receive a continuing review form prepared and submitted by the Investigator along with the number of subjects enrolled since the last review. The continuing review form shall summarize adverse event experiences, amendments, changes in training of personnel and new COI disclosure as applicable, and provide a reassessment of the risk-to-benefit ratio.

1.3.6 Grant Applications

Grant applications will be reviewed to verify that there have been no changes.

1.4 Possible Outcomes of Continuing Review

As an outcome of continuing review, the IRB may require that the research be modified or halted altogether. The IRB may need to impose special precautions or relax special requirements it had previously imposed on the research protocol.

1.5 Expedited Review for Renewal

A protocol that was originally reviewed using the expedited review procedure may receive its continuing review on an expedited basis. Additionally, a full committee review protocol that had no accrual or which remains open only to data analysis may be reviewed using an expedited review.

When conducting research under an expedited review procedure, the IRB Chairperson or designated IRB member conducts the review on behalf of the full IRB using the same criteria for renewal as stated in section 1.3 of this policy. If the reviewer feels that there has been a change to the risks or benefits, he or she may refer the study to the full IRB for review.

1.6 Report Preparation

Each protocol requiring full board review and approval is presented individually and discussed at a convened meeting. Those protocols qualifying for and receiving administrative approval are reported to the IRB in a separate section of the agenda. The continuing review process is not a de novo review, and that unless there is an issue of new law, or in cases where risk to the participants has increased or changes are substantial, that the previous board decisions are generally accepted, as much as possible.

1.7 Continuing Review More Often than Annually

There are times when the risks associated with a particular protocol are such that continuing review should take place more frequently than annually. These risks include the possibility of death, severe injury, major damage or loss, and/or result in negative publicity for the participant involved. In these cases, the IRB may specify that the PI report to the IRB either at a shorter time interval or after a specified number of subjects is enrolled. The IRB may request the PI to report the observed effects of the research activities and/or how the subject(s) responded to the research interventions. The IRB will determine if continued close monitoring of the protocol is warranted, if so will specify the time frame for monitoring.

1.8 PI Notification

After the full board meeting, the disposition of the protocol is relayed to the principal investigator by email and letter. Any stipulations are also relayed in the letter. The consent form that is currently being used will be stamped with the IRB stamp and the date of approval.

1.9 Filing/Record Retention

All related continuation documentation, including new IRB Forms, copies of the new consent form, memoranda, and any other correspondence associated with continuing review will be filed in the protocol file. All continuing review documentation will be retained for three years after the protocol has expired. PIs will also be instructed to maintain research records according to the records management system currently in use by the University.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

Director of the Office of Research Compliance (or designee) is responsible for establishing and implementing processes for making research renewal decisions.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.108,111
45 CFR 46.111
TAMU 15.99.01.M1(3.2)
OPRR Reports 95-01

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Continuing Review Form
Expiration Notification email
Termination Notice
Approval Letter

7. PROCESS OVERVIEW

The IRB Compliance staff will identify those protocols that will require continuing review approximately 60 days prior to the expiration date. An expiration notification will be sent to the PI requesting completion of the proper paperwork to update the status of the protocol.

A second notice will be sent 30 days prior to the expiration date, if there has been no response to the first notice. If no response is received after two notices, an expiration notice will be sent on the day of expiration giving final notification that the protocol has expired. If the PI does not submit a continuing review form indicating completion or the need for renewal, the PI will be notified that the IRB approval has expired and that no human subjects research may continue without re- submission. The PI will have 10 working days from the expiration date to submit a continuing review form. If there is no response, a termination notice will be sent to the investigator, faculty advisor (for graduate students) and/or department head (for faculty and staff) and funding sponsor (if funded) stating that the file has been terminated.

It is the responsibility of the PI to submit a continuing review form in sufficient time for the protocol to be re-reviewed by the IRB. No human subject- research may take place after the expiration date without re-approval.

In completing the IRB Continuing Review Form, the PI will report:

(a) Whether the study was initiated, and if not, indicate if the protocol should be terminated.

(b) If the research protocol was unchanged from the approved protocol and if it was completed in a satisfactory manner;

(c) If the research protocol was modified during the project including, for example, changes in the informed consent form or any other modifications to the study (any changes to the protocol must be reviewed and approved by the IRB before being initiated);

(d) If the research protocol was changed significantly in regard to human participants. The researcher will explain on an attached page, or if the research has been completed, will submit copies of the final report sections that describe these changes as initiated (any changes to the protocol must be reviewed and approved by the IRB before being initiated);

(e) If the research is in progress and no changes in protocol have been made regarding human participants;

(f) If there have been any adverse events regarding human participants in the investigation (adverse events should be reported as required);

(g) The total number of participants approved and those utilized to date; and

(h) A progress report of the study to date or a final report if the study has been completed.

(i) If applicable, a copy of the written subject consent form currently being used for the activity, and a clean copy must also be sent for date stamping. If revisions to the consent form are required, the PI must submit two copies of the revised consent form with one copy noting where the changes were made using bolding and/or strike-through.

9. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool

Compliance Staff (Auto-generated alert notices)	Expiration Notification - Alert notices are generated from database 60 days and 30 days prior to expiration date of protocol. If no response from PI another alert notice is sent on the day of expiration stating protocol has expired and PI has 10 working days to submit Continuing Review Form. I	Expiration Notification Alert
IRB Compliance Staff	If no response from PI 10 days after protocol expires: Not funded – terminate protocol-send Termination notification. Funded – contact PI, advisor or Dept. Head by telephone – if no response by the following day – terminate protocol – send Termination notification.	Termination Notice
IRB Compliance Staff	When the continuation request is received, review the information to ensure it is complete. If it is complete, determine whether it can be expedited or whether it requires review at a convened meeting For expedited reviews, follow the expedited review process. For full reviews, distribute to 1 primary and 1 secondary reviewer as well as the other committee members for review.	Continuing Review Form
IRB Member(s)	When the Continuing Review Form is received, the IRB and/or its designee will review the form and associated materials to determine the status of continuation of the study. If the IRB does not re-approve the research by the specified expiration date, subject accrual should be suspended pending re-approval of the research by the IRB. Enrollment of new subjects cannot ordinarily occur after the expiration of IRB approval. In addition, continuation of research interventions or interactions in already enrolled subjects generally should be halted and may only continue when the IRB finds that it is in the best interests of individual subjects to do so. OHRP and IRBs must address on a case-by-case basis those rare instances where failure to enroll would seriously jeopardize the safety or well-being of an individual prospective subject.	
IRB Compliance Staff	Notify the Investigator as to the outcome of the Continuing Review. If the IRB does not re-approve the research by the specified expiration date, a research suspension letter will be sent. It will also outline the terms of the suspension according to the three regulatory categories (screening, enrollment of new subjects, and continuation of interactions/interventions in already enrolled subjects) as decided by the IRB or reviewer.	

IRB Compliance Staff	If the Continuing Review is approved – Approval letter is mailed to the Investigator.	Approval Letter

300 – REVIEW OF RESEARCH	
307. Classroom Research Guidelines	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. Policy

Research at Texas A&M University must meet the highest professional and ethical standards. As the interpretations of research and normal classroom activities vary, questions arise on what falls within the federal guidelines of research, and activities designed to train students in research methods in the normal classroom setting. Educational activities usually do not fall within the federal definition of research as described in 45 CFR 46.102(d).

Undergraduate or graduate student research activities, which reach outside of the classroom, may fall under the federal definition of research depending upon the type of interaction with the research participant(s) and the risk involved. Graduate thesis and dissertations are clearly understood as research, and fall within the IRB purview when human participants are involved. Any research conducted with the intent to either contribute to generalizable knowledge or to construct knowledge related to a specific situation that will be published or presented within an academic discipline, even that originating from the classroom activity, falls within the requirement for human subjects review.

1.2 Criteria for IRB Review of Classroom Assignments

To provide guidance to faculty members the IRB Compliance Office has developed the following criteria to determine if classroom assignments require IRB approval:

- Are the participants from a special population such as minors (under 18 years old), prisoners, patients, physically or mentally challenged individuals, or pregnant women?
- Does the assignment require using a setting such as prisons, nursing homes, hospitals, or schools?
- Does the assignment focus on topics such as alcohol/drugs, depression/suicide, learning disabilities, abortion/AIDS/HIV/Sex, sexually transmitted diseases, eating disorders, or psychological inventories?
- Does the assignment include audiotaping or videotaping?
- Will participants be directly identified through the assignment?
- Will the data be formally presented to any audience outside of the class?
- Will the research extend beyond the realm of the classroom environment?

If any of the listed criteria are met, then the projects must be reviewed by the IRB.

If the answers to all of those questions is no, then the classroom assignment may not need IRB review. Faculty and students may contact the IRB office at (979)458-4067 or by email at irb@tamu.edu to discuss the assignment and obtain assistance in determining if review is needed.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

The faculty instructor has the responsibility of ensuring that the student is educated on the general principles of research ethics, human subject protection, and that the students receive human subjects training.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.102(d)
TAMU 15.99.M1(6)

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Classroom assignment form

7. PROCESS OVERVIEW

The faculty instructor will complete an IRB application for the course being taught, including the course syllabus as an attachment and submit for approval.

If the student's research activity meets the criteria for a classroom research assignment, the student will complete the classroom assignment form and submit to the faculty instructor with all pertinent information necessary to determine if the project needs IRB review and/or approval. For these activities, faculty shall provide ethical supervision, followed by faculty advisors, committee chairs, department heads, and deans.

If the activity does not meet the criteria for the classroom assignment and requires IRB review, the student must complete an IRB application, provide a consent document, survey instruments or other items, and submit for approval. Areas in question such as certain types of self-reported behavior (abuse, drug use, etc.), special populations, or sensitive topic areas will need further review and may be resolved on a case-by-case basis through consultation with the IRB. Students should be aware that applications are processed daily and to allow sufficient processing time for approval and completion of their assignment.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Program Coordinator	Provide guidance in determining if assignment needs IRB review.	Classroom assignment sheet

300 – REVIEW OF RESEARCH	
308. Cooperative Research	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. Policy

The Institutional Review Board shall have special responsibilities in the review and approval of protocols involving cooperative activities. Cooperative activities are those in which TAMU faculty, staff, employees or students, obtain access to human subjects involved through one or more cooperating institutions, or when investigators from cooperating institutions obtain access to human subjects at TAMU.

1. If, in the cooperative activity, a faculty member, staff, or other employee or student from TAMU obtains direct access to any subject at a cooperating institution that has on file with Department of Health and Human Services (DHHS) an approved general assurance, or has a DHHS approved special assurance for the activity, then the Institutional Review Board from each of the cooperating institutions shall conduct an independent review of the cooperative activity. The cooperative activity shall not be initiated if either the Institutional Review Board of a cooperating institution or the TAMU Institutional Review Board finds reason not to approve the cooperative activity. The TAMU Institutional Review Board, at its discretion, may concur with, reject or further restrict the recommendations from the cooperating institution.

1.1. If the cooperating institution does not have a DHHS approved Federal Wide Assurance, then the cooperating institution may be required to obtain from DHHS a Federal Wide Assurance, applicable to the cooperative effort, in order that the joint review process described above shall be completed before the cooperative activity can be initiated.

1.2. If, in the cooperative activity, an investigator from a cooperating institution having a DHHS approved Federal Wide Assurance, desires to obtain direct access to any subject at TAMU, the cooperative activity must be jointly reviewed, and a TAMU faculty member must be listed on the protocol request. Also, any restrictions imposed by the TAMU Institutional Review Board are binding on the outside investigator.

1.3. Activities involving investigators from one or more institutions who may exchange or pool similar data obtained from human subjects who participate in independently sponsored projects are not cooperative activities as defined above (e.g., multi-center drug studies).

The Institutional Review Board shall not normally approve any activity involving human subjects unless the principal investigator is a member of the faculty, staff, or student body of TAMU, TAES, TEES, TTI, and/or the Texas A&M University System Health Science Center.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

The Director of the Office of Research Compliance (or designee) will provide additional guidance regarding cooperative research as appropriate.

4. APPLICABLE REGULATIONS AND GUIDELINES

TAMU 15.99.99.M1, 15.01.99.M1

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

5. ATTACHMENTS

TAMU FWA Institution Assurance

7. PROCESS OVERVIEW

It is likely that questions concerning cooperative research will be addressed to the IRB office. When answering these questions, IRB staff should refer to the above provisions to ensure proper and complete submission of all required materials. In addition, IRB members may request further clarification of cooperative research requirements

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Program Coordinator	Provide guidance to investigators involving cooperative activities	

300 – REVIEW OF RESEARCH	
309. Categories Of Action	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

As a result of its review, the IRB may decide to approve or disapprove the proposed research activity, or to specify stipulations required to secure IRB approval of the research activity. Except when the expedited review procedure is used, these actions will be taken by a vote of a majority of the regular and alternate members present at a meeting in which a quorum is present, except for those members who are required to recuse themselves from the meeting in accordance with the IRB's conflict of interest policies. When reviewed via expedited review, the Chairperson or designee can make any of the following determinations in the following section except to disapprove a study.

1.1 Determinations

The IRB may make one of the following determinations as a result of its review of research submitted for initial or continuing review:

1.2 **Approval**: The protocol and accompanying documents are approved as submitted. Final approval will commence on the day the study is approved by an action of the convened IRB or Chairperson or designee in the case of expedited review and expire within one (1) year of the meeting/approval date, but not later than the day preceding the date of review.

The conditions for continued approval, and the timeframe (if any) within which they must be met will be clearly stated in the approval letter. If the conditions of the approval are not met, approval may be withdrawn.

1.3 **Pending Approval (Conditional Approval)**: Minor modification of, or addition to, a protocol or accompanying document(s) is required. Required changes will be voted upon during the IRB's meeting, as well as the terms of approval. The Investigator will be informed by email of the required changes and requested information and must provide the IRB with the changes or information.

The IRB Chairperson or his/her designee has the authority to review the notification/information requested via expedited review unless the IRB requires that the material or information be reviewed by the full IRB, the primary reviewer or another individual delegated by the IRB to review the response. Upon satisfactory review, approval will be issued as of the date the requested information or materials are approved. However, the expiration date of IRB approval will be based on the anniversary date of the initial IRB review. Subjects must not be recruited into the study until final approval has been issued.

1.4 **Deferred**: Significant questions are raised by the protocol requiring its reconsideration or substantive changes are required. The PI response is forwarded to the committee that provided the initial review.

1.5 **Disapproval:** The protocol fails to meet one or more criteria used by the IRB for approval of research. Disapproval cannot be given through the expedited review mechanism and may only be given by majority vote at a convened meeting of the IRB. When the IRB suggest substantial clarifications, protocol modifications, or informed consent document revisions the protocol may be disapproved.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

Director of the Office of Research Compliance (or designee) is responsible for ensuring that all IRB decisions and actions are based on institutional and regulatory requirements.

IRB Chairperson (or designee) is responsible for ensuring the appropriateness of all IRB decisions and actions.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.109, 56.111, 56.113
45 CFR 46.109
TAMU 15.99.01.M1(3)

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Notification of IRB Decision (Sample Letters)

7. PROCESS OVERVIEW

When a response to stipulations is received from the PI, the response and the letter sent from the IRB office should be copied and distributed to the IRB prior to the meeting. In the event that the response is received too late to mail to members, the copies may be distributed at the full board meeting. The response should be reviewed as "Old Business", discussed and a vote taken on whether or not the protocol should receive final approval. If the protocol revisions are approved by the IRB, a final approval letter is prepared and sent to the PI. If not approved, the additional clarifications, protocol modifications, or informed consent revisions should be relayed to the PI. The additional clarifications or modifications, depending on whether or not simple concurrence or substantive changes are required of the PI, may or may not require full board approval.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Compliance Staff	Document IRB decisions in the minutes.	
IRB Program Coordinator	Prepare IRB decision letters	
IRB Chairperson (or designee)	Review and sign all IRB decision letters.	

IRB Compliance Staff	Distribute IRB decisions in a timely manner.
IRB Program Coordinator	Process responses to IRB requests from Investigators

300 – REVIEW OF RESEARCH	
310. Study Completion/Termination	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

The completion or termination of the study is a change in activity and must be reported to the IRB. Although subjects will no longer be "at risk" under the study, a final report/notice to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

1.1 Determining When a Project Is Completed

1.1.1 Department of Health and Human Services (HHS)-supported protocols: When individually identifiable follow-up data are no longer being collected on subjects enrolled in an HHS-supported protocol and analysis that could indicate new information is complete, the study may be closed.

1.1.2 Multi-site industry studies may be closed when the Investigator submits his or her final report or information to the main coordinating site.

1.2 Completion Reports

The Investigator, or the Investigator's designee at the investigation site, should submit Completion reports within 30 days after completion. The IRB Compliance Staff will review all reports of study completion and, if needed, request further information from the Investigator to clarify any questions that may arise.

A listing of completed studies will be presented to the IRB at the next meeting, and copies of the Completion Report and supplementary information are made available to the IRB members upon request.

1.3 Other Methods of Completion Notification

Notification of research completion may be made on the Continuing Review Form or by a separate memo to the IRB.

1.4. Documentation and File Disposition

Once notified of a termination, the protocol tracking database will be updated. The file will be pulled and the termination noted. If the termination was not made by the PI (i.e. sponsor), he/she will be informed of the change.

1.6 Record Retention

Once each year (or more often if necessary), the files are logged and placed in boxes according to Record Retention requirements and sent to the Records Retention area. Records may be accessed at any time by following the Records Retention recall procedures and completing the appropriate request. The request may be faxed to the Records Retention Office and the file will be delivered to the IRB office. Files are maintained in record retention for a period of three years after the completion of the protocol.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

IRB Compliance Staff is responsible for ensuring all study completion/termination documentation is received, reviewed, presented to the IRB, and filed appropriately.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.108, 56.109
45 CFR 46.103, 46.109

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Study Termination Report
Records Retention Request Form
Completion/Termination Acknowledgement Letter

7. PROCESS OVERVIEW

The IRB Compliance Staff will receive the Study Completion Report and will in turn check it to ensure it is complete. The report will be filed and the IRB database will be updated. Investigators may also indicate that the study is complete when completing the renewal request form, by email or by other methods of communication. If a study is not renewed within the IRB guidelines, it may be terminated administratively.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Compliance Staff	Instruct Investigators to submit a Completion Report upon completion of the study.	Continuing Review /Completion Report
IRB Program Coordinator	Review termination report and obtain any outstanding information or documentation from the Investigator to close the study. If there are inconsistencies or if clarification is needed, request additional information.	Completion/Termination Acknowledgement Letter
	If the study may be closed and the contents of the IRB file are complete, update the IRB database with the closure of the study.	
	Make a list of completed studies for presentation to the IRB at its next convened meeting.	
IRB Compliance Staff	Follow-up if needed.	

REVIEWS REQUIRING

SPECIAL CONSIDERATION

400

400 – REVIEWS REQUIRING SPECIAL CONSIDERATION	
401. Vulnerable Populations	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Some persons are in need of extensive protection, even to the point of excluding them from activities that may harm them. Other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequence. Indeed, some types of research may, in and of themselves, create a vulnerable group – that is, the subjects lose their autonomy or are exposed to unknown risks. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

Potentially vulnerable groups may include:

- Prisoners
- Children
- Pregnant women and fetuses
- Other vulnerable groups

Specific Policies

1.1 Prisoners

1.1.1 If an Investigator indicates in the study submission that prisoners will participate in the research, or that subjects may reasonably be expected to be incarcerated at some time point during the study, the following additional requirements will apply to IRB review of the project:

A. Local regulations: In addition to meeting federal regulations, the project must comply with local and state requirements for inclusion of prisoners as subjects.

B. IRB composition: A majority of IRB members will have no association with the prison(s) involved; and at least one member shall be a prisoner or prisoner advocate with appropriate background and experience to serve in that capacity. For research involving prisoners as subjects, the IRB must meet the special composition requirements of 45 CFR 46.304 for all types of review of the protocol, including initial review, continuing review, review of protocol amendments, and review of reports of unanticipated problems involving risks to subjects.

C. Additional duties of the IRB where prisoners are involved:

When an IRB is reviewing a protocol in which a prisoner is a subject, the IRB must make, in addition to other requirements under 45 CFR 46, subpart A, seven additional findings under 45 CFR 46.305(a), as follows:
(1) the research under review represents one of the categories of research permissible under 45 CFR 46.306(a)(2);

(2) any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

(3) the risks involved in the research are commensurate with risks that would be accepted by non prisoner volunteers;

(4) procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

(5) the information is presented in language which is understandable to the subject population;

(6) adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

(7) where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

D. Permitted research involving prisoners

For research conducted or supported by HHS to involve prisoners, two actions must occur:
(1) the institution engaged in the research must certify to the Secretary (through OHRP) that the IRB designated under its assurance of compliance has reviewed and approved the research under 45 CFR 46.305; and

(2) the Secretary (through OHRP) must determine that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2). The categories of permissible research are the following:

(i) study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

(ii) study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;

(iii) research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research; or

(iv) research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research.

1.1.2 When Subjects Become Prisoners During a Research Protocol

This policy applies whenever any human subject in a research protocol becomes a prisoner at any time during the protocol, *e.g.,* after the research has commenced. This is necessary because it is unlikely that review of the research and the consent document contemplated the constraints imposed by the possible future incarceration of the subject.

- If a subject becomes a prisoner after enrollment in research, the Principal Investigator is responsible for reporting this situation in writing to the IRB immediately.
- At the earliest opportunity after receiving the Investigator's notice or otherwise becoming aware of the prisoner status of a subject, the IRB should review the protocol again with a prisoner representative as a member of the IRB. The IRB should take special consideration of the conditions of being a prisoner.
- Upon this review, the IRB can either (a) approve the involvement of the prisoner-subject in the research in accordance with this policy or (b) determine that this subject must be withdrawn from the research.
- Additionally, the IRB should confirm that, when appropriate, the informed consent process includes information regarding when subsequent incarceration may result in termination of the subject's participation by the Investigator without regard to the subject's consent.

1.1.3 Documenting IRB Determinations for Approval of Inclusion of Prisoners as Research Subjects

1.1.3.1 Specific for Prisoners

In addition to the responsibilities prescribed for the Institutional Review Board in 45 CFR Part 46, Subpart A, the Board must follow special procedures with respect to approving the involvement of prisoners as research subjects.

Investigators must complete an IRB Submission Form to request approval for inclusion of prisoners as research subjects. The PI must certify that they have read 45 CFR Part 46, Subpart C, if they request approval to use prisoners. If the IRB, using the required criteria, determines that approval for inclusion of prisoners in the research activity can be granted, the following statement must be added to the minutes at the end of the summary of the protocol and the list of stipulations for approval:

The research requests inclusion of prisoners as subjects and was, therefore, examined against provisions of Subpart C of 45 CFR 46, particularly 46.305 and 46.306, as well as the current guidelines for inclusion of prisoners in research. The IRB found that the research represents one of the permissible categories under 46.306(a)(2), advantages of participation accruing to the prisoner are not coercive in relation to the limited choice environment, the risks are commensurate with those of non-prisoners, subject selection procedures are equitable, the consent form is in language that is understandable to the subject population, there are provisions to ensure that parole boards will not take a prisoner's participation into account in their decisions, and adequate provisions are made for follow-up examinations and care.

1.1.3.2 Special Notification of PI

If the research is federally funded and if the IRB determines that the research activity falls under 46.306 (a)(2)(C), the PI must be notified that the research may include prisoners as subjects only after the Secretary of Health and Human Services has consulted with a panel of experts and published in the Federal Register his/her intent to approve the research. This may also be true for research that falls under 46.306 (a)(2)(D) in which there is assignment of prisoner subjects to groups that may not benefit from the research. In these cases, it should be clear to the PI that approval for inclusion of prisoners as research subjects is not granted. If the research is industry sponsored or funded by the Division of Acquired Immunodeficiency Syndrome (DAIDS) at the NIH (and DAIDS has pre-approved the inclusion of prisoners), the IRB approval need only be reported to OHRP as described below.

1.1.3.3 Reporting

The IRB must also send a certification letter to the Office for Human Research Protections (OHRP) stating that (1) the IRB has been constituted according to the regulations, (2) the IRB has considered and made the seven findings set forth in 45 CFR 46.305, and (3) the IRB finds that category A, B,

C, or D of 46.306 permits the research to go forward with prisoners as human subjects. The certification letter will include the following:

1. OHRP assurance number;
2. Designated IRB number;
3. Site(s) where research involving prisoners will be conducted;
4. DHHS grant award number;
5. DHHS funding agency;
6. Funding agency grants/program officer name and phone number;
7. Title of DHHS grant.

The letter must also include:

1. Title of protocol (note if same as grant);
2. Version date of IRB-reviewed consent document for research involving prisoners;
3. Date(s) of IRB meeting(s) in which protocol was considered – specify type of review; and
4. Principal investigator.

One of the 3 applicable reasons for IRB review must be listed:

1. Non-prison study in which subject has become incarcerated and PI wishes to continue the subject's participation in the study;
2. Non-prison study with at-risk population (i.e., probationers, HIV, substance abuse); and
3. Study designed to be conducted in a prison using prisoners and PI wishes to enroll already incarcerated subjects.

The IRB will certify that the IRB was constituted as per the requirements in 45 CFR Part 46.304. The name of the prisoner advocate will be included. The institution will also certify that the IRB approved the research based on the seven findings in 45 CFR Part 46.305(a). The IRB must indicate in the certification letter which, if any, of the four categories of permissible research involving prisoners in 45 CFR 46.306(a) is applicable to the proposed research.

1.1.3.4 Federally funded protocols

The certification letter should also provide a brief description of the purpose of the study; study objectives or aims; study procedures; customary treatment in prison research site for the condition being studied; specify how risks are minimized; whether a Certificate of Confidentiality was obtained by the PI; and a description of recruitment procedures in the specific prison setting. This will allow OHRP to determine whether or not to concur with the IRB's findings or whether to consult with appropriate experts and publish a Federal Register notice. This report will include all new protocols and those approved through the continuing review process and continuing to enroll subjects.

Certification letters should be addressed and mailed to:

Prisoner Research Coordinator
Office for Human Research Protections
Department of Health and Human Services
The Tower Building
1101 Wooton Parkway, Suite 200
Rockville, MD 20852

1.1.3.5 Non-Prison Study in Which Subject has become Incarcerated

If a participant currently enrolled in a study becomes a prisoner, and the PI wishes to continue his/her participation in the study, Subpart C of 45 CFR 46 must be followed and the protocol must be re-reviewed for compliance.

1.1.36 Record Retention

Copies of the certification letters should be kept in the protocol file labeled appropriately for at least three years beyond the life of the protocol.

1.2 Children

1.2.1 Research in children requires that the IRB carefully consider consent, beneficence, and justice.

The determination of risk (possible harms) and possible benefit to the child is at the core of the concept of beneficence when considering research in a pediatric population.

Therefore, the IRB must consider the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the child before it can determine whether the IRB has the authority to approve the study.

1.2.2 Determination of risk:
When reviewing research conducted on children, risk is defined in terms of minimal and greater than minimal, and may only be approved by the IRB as follows:

Risk determination	Benefit assessment	IRB action
Minimal	With or without direct benefit	Approvable
Greater than minimal risk*	Potential benefit to child	Approvable
Greater than minimal risk	No direct benefit to child; offers general knowledge about the child's condition or disorder	Approvable case-by-case*

Greater than minimal risk	No direct benefit to child; offers potential to "understand, prevent, or alleviate a serious problem affecting the health and welfare of subjects"	Not approvable**

* Risk may not be more than a minor increase over minimal risk, consent of both parents or legal guardian required under normal circumstances.

**Approval to proceed with this category of research must be made by the Secretary of the HHS with input from selected experts, and following opportunity for public review and comment.

1.2.3 Children may be subjects of research only if informed consent is obtained from the parents or legal guardian. Children over the age of 6 must agree to participate in the research and provide an assent. Separate assent forms should be provided based on reasonable age ranges for comprehension.

1.2.4 FDA has recently adopted 45 CFR 46 Subpart D (the "HHS" Regulations, as an Interim Rule until implementation of the Final Rule) and also addresses the subject of children in its Information Sheets that address assent of minors. The HHS regulations, therefore, serve as the standard for all research activities involving children, irrespective of funding source.

1.2.5 Documenting IRB Determinations For Approval of Inclusion of Children As Research Subjects

In addition to the responsibilities prescribed for the Institutional Review Board in 45 CFR Part 46, Subpart A, the Board must follow special procedures with respect to approving the involvement of children as research subjects.

Investigators must complete an IRB Submission Form to request inclusion of children as research subjects. If the IRB, using the required criteria, determines that approval for inclusion of children in the research activity can be granted, one of the following statements must be added to the minutes at the end of the summary of the protocol and the list of stipulations for approval:

1.2.5.1 Minimal Risk With or Without Direct Benefit

The research involves children and was, therefore, examined against provisions of Subpart D of 45 CFR 46, particularly 46.404 (Research not involving greater than minimal risk) and 46.408 (Requirements for permission by parents or guardians and for assent by children), as well as the current guidelines for inclusion of children in research. The IRB found the research to be of minimal risk to the child, and after considering the age, maturity and psychological state of the children to be enrolled in this study, determined that adequate

provisions are made for soliciting the assent of the child and permission of a parent or legally authorized guardian who has been granted authority to consent for medical care including research. The IRB further determined that all children age 7-11 must be asked to verbalize their assent/dissent to participate, and children age 12-18 must indicate their assent in writing.

1.2.5.2 More than Minimal Risk With Direct Benefit

The research involves children and was, therefore, examined against provisions of Subpart D of 45 CFR 46, particularly 46.405 and 46.408, as well as the current guidelines for inclusion of children in research. The IRB found the research involves more than minimal risk to the child but presents reasonable prospect for direct benefit to the child. The IRB also found the research risks to be justified by the anticipated benefits to the child, and the risk benefit analysis to be at least as favorable as that presented by available alternative approaches. Also, after considering the age, maturity and psychological state of the children to be enrolled in this study, the IRB determined that adequate provisions are made for soliciting the assent of the child and permission of a parent or legally authorized guardian who has been granted authority to consent for medical care including research. The IRB further determined that all children age 7-11 must be asked to verbalize their assent/dissent to participate, and children age 12-18 must indicate their assent in writing.

1.2.5.3 More Than Minimal Risk With No Direct Benefit

The research involves children and was, therefore, examined against provisions of Subpart D of 45 CFR 46, particularly 46.406 and 46.408, as well as the current guidelines for inclusion of children in research. The IRB found the research involves more than minimal risk to the child and presents no reasonable prospect for direct benefit to the child, but is likely to yield generalizable knowledge about the child's disorder or condition. The IRB also found the risks represented a minor increase over minimal risk, the research procedures reasonably commensurate with experiences inherent in their actual or expected medical, dental, psychological, social, or educational situations, the research is likely to yield generalizable knowledge of vital importance for the understanding or treatment of the child's disorder or condition. Also, after considering the age, maturity and psychological state of the children to be enrolled in this study, the IRB determined that adequate provisions are made for soliciting the assent of the child and permission of both parents, if available, or a legally authorized guardian who has been granted authority to consent for medical care including research. The IRB further determined that all children age 7-11 must be asked to verbalize their assent/dissent to participate, and children age 12-18 must indicate their assent in writing.

The research involves children and was, therefore, examined against provisions of Subpart D of 45 CFR 46, particularly 46.407 and 46.408, as well as the current guidelines for inclusion of children in research. The IRB found the research to otherwise not be approvable but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. The IRB advised the investigator that a request to consider approval of the research must be made to the Secretary of Health and Human Services, through the IRB. If requested, the Secretary will convene a panel of experts to review the research for inclusion of children.

1.2.5.4 Special Notification of PI

If the IRB determines that the research activity falls under 45 CFR 46.406 or 21 CFR 50.53, the IRB can only approve this category if the increase in risk represents a minor increase over minimal risk. If the research falls under 45 CFR 46.407 or 21 CFR 50-54, the PI must be notified that the research may include children as subjects only after the Secretary of Health and Human Services (or FDA Commissioner) has consulted with a panel of experts and published in the Federal Register his/her intent to approve the research. In this case, it should be clear to the PI that approval for inclusion of children as research subjects is not granted.

1.3 Pregnant Women and Fetuses

1.3.1 Pregnant women or fetuses prior to delivery may be involved in research if all of the following conditions are met:

- A. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- B. The risk to the fetus is caused soley by interventions or procedures that hold out the prospect of direct benefit for the woman or fetus; or if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.
- C. Any risk is the least possible for achieving the objectives of the research;
- D. The woman's consent or the consent of her legally authorized representative is obtained as follows:

Risk determination	Benefit assessment	Consent	IRB action

Minimal or greater than minimal	Direct benefit to pregnant woman	Consent of woman or legally authorized representative	Approvable

- E. The woman or her legally authorized representative, as appropriate, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or resultant child;
- F. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46 subpart D;
- G. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- H. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- I. Individuals engaged in the research will have no part in determining the viability of a fetus or neonate.

1.3.2 Research involving fetuses (neonates) after delivery:

A. After delivery, neonates of uncertain viability and non-viable neonates, may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
2. The individual(s) providing consent under the applicable regulations is/are fully informed regarding the reasonably foreseeable impact of the research on the neonate;
3. Individuals engaged in the research will have no part in determining the viability of a neonate; and
4. The additional requirements set forth in Paragraphs B and C below have been met.

B. Neonates of uncertain viability: After delivery, and until it has been ascertained whether or not a fetus is viable, a fetus may not be involved in research covered by federal regulations unless the following additional conditions are met:

1. The IRB determines that:

(i) The research holds out the prospect of enhancing the probability of survival of the particular fetus to the point of viability, and any risk is the least possible for achieving that objective; or

(ii) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other

means and there will be no added risk to the neonate resulting from the research; and

(iii) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative, is obtained in accord with 45 CFR 46 subpart A, unless altered or waived in accord with Sec. 46.101(i) or Sec. 46.116(c) or (d); provided, however that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

C. Nonviable neonates: After delivery, a nonviable neonate may not be involved in research covered by federal regulations unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained in accord with 45 CFR 46 subpart A, except that the waiver and alteration provisions of Sec. 46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements. The consent of a legally authorized representative of either or both of the parents of a nonviable fetus will not suffice to meet the requirements of the regulations, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest..

- D. Viable neonates. A neonate, after delivery, that has been determined to be viable is a child as defined by 45 CFR 46.402(a) and may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR 46 subparts A and D.

1.3.3 Research involving, after delivery, the placenta, the dead fetus, or fetal material.

- Research involving, after delivery, the placenta, the dead fetus, macerated fetal material, or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.
- If information associated with material described in paragraph (a) of this section is recorded for research purposes in a manner that living individuals

can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent regulations apply.

1.4 Specific for Pregnant Women

In addition to the responsibilities prescribed for the Institutional Review Board in 45 CFR Part 46, Subpart A, the Board must follow special procedures with respect to approving the involvement of pregnant women, fetuses or *in vitro* fertilization as research subjects.

Investigators must complete an IRB Form to request the inclusion of pregnant women as research subjects. The PI must certify that they have read 45 CFR Part 46, Subpart B, if they request approval to use fetuses. If the IRB, using the required criteria, determines that approval for inclusion of pregnant women in the research activity can be granted, the following statement must be added to the minutes at the end of the summary of the protocol and the list of stipulations for approval:

The research involves pregnant women and was, therefore, examined against provisions of Subpart B of 45 CFR 46, particularly 46.206 and 46.207, as well as the current guidelines for inclusion of pregnant women in research. The IRB found that appropriate studies on animals and non-pregnant individuals have been done, the risk to the fetus is minimal and the least possible for achieving the objectives of the study, investigators do not have any part in decisions regarding pregnancy termination or fetal viability, no procedural changes causing greater than minimal risk to the fetus or the pregnant woman will be introduced into the pregnancy termination solely for research purposes, and no monetary or other inducements are being offered for pregnancy termination. In addition, the purpose of the research is to meet the health needs of the mother, the fetal risk is minimal, and there are adequate provisions to obtain informed consent.

Specific for Fetuses

Investigators must complete an IRB Submission Form to request the inclusion of fetuses as research subjects. The PI must certify that they have read 45 CFR Part 46, Subpart B, if they request approval to use fetuses. If the IRB, using the required criteria, determines that approval for inclusion of fetuses in the research activity can be granted, the following statement must be added to the minutes at the end of the summary of the protocol and the list of stipulations for approval (depending on whether or not the research involves fetuses *in utero* or *ex utero*):

The research involves fetuses *in utero* and was, therefore, examined against provisions of Subpart B of 45 CFR 46, particularly 46.206 and 46.208, as well as the current guidelines for inclusion of fetuses in research. The IRB found that appropriate studies on animals and non-pregnant individuals have been done, the risk to the fetus is minimal and the least possible for achieving the objectives of the study, investigators do not have any part in decisions regarding pregnancy termination or fetal viability, no procedural changes causing greater than minimal risk to the fetus or the pregnant woman will be introduced into the pregnancy termination solely for research purposes, and no monetary or other inducements are being offered for pregnancy termination. In addition, the purpose of the research is to meet the health needs of the fetus, the fetal risk is minimal and only to the extent

necessary, and there are adequate provisions to obtain informed consent of the parents.

The research involves fetuses *ex utero* and was, therefore, examined against provisions of Subpart B of 45 CFR 46, particularly 46.206 and 46.209, as well as the current guidelines for inclusion of fetuses in research. The IRB found that appropriate studies on animals and non-pregnant individuals have been done, the risk to the fetus is minimal and the least possible for achieving the objectives of the study, investigators do not have any part in decisions regarding pregnancy termination or fetal viability, no procedural changes causing greater than minimal risk to the fetus or the pregnant woman will be introduced into the pregnancy termination solely for research purposes, and no monetary or other inducements are being offered for pregnancy termination. In addition, the purpose of the research is to enhance the possibility of survival of the fetus, there is no added risk to the fetus, the vital functions of the fetus will not be artificially maintained, the activities do not terminate heartbeat or respiration, important biomedical information, that cannot be otherwise obtained will be derived, and there are adequate provisions to obtain informed consent of the parents.

1.5 Other Vulnerable Groups

Although federal regulations list specific vulnerable groups, there are other vulnerable groups such as mentally impaired persons, employees of the Sponsor or Investigator, terminally ill patients, university students, dependents, laboratory personnel, foreign cultures and the very elderly. The IRB will determine special protections for these groups on a case-by-case basis, taking into account the risks and benefits of the research and other protections afforded by institutional policies, state and federal law.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

Director of the Office of Research Compliance (or designee) is responsible for maintaining up-to-date review tools for review of research pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines.

IRB Chairperson (or designee) is responsible for ensuring the IRB members are well versed in new and evolving regulations and guidelines pertaining to vulnerable populations, for selecting primary reviewers with appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.

IRB Reviewer is responsible for conducting appropriate review of research planned for vulnerable populations, including an assessment of potential for coercion, in consultation with any appropriate experts and resources.

4. APPLICABLE REGULATIONS AND GUIDELINES

The Belmont Report
45 CFR 46: Subparts B, C, D
45 CFR 46.122
21 CFR 56.111
TAMU 15.99.01.M1 (5.3)
OHRP IRB Guidebook

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Checklist – Requirements for Research Involving Prisoners
Checklist – Requirements for Research Involving Children
Checklist – Requirements for Research Involving Pregnant Women & Fetuses

7. PROCESS OVERVIEW

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

A. Research Involving Prisoners

Who	Task	Tool
IRB Program Coordinator	Maintain and update checklist to conform to applicable regulations and guidelines.	Checklist – Requirements for Research Involving Prisoners
	Secure prisoner representative for IRB meeting.	
IRB Program Coordinator	Select appropriate primary reviewer(s).	
IRB Member (Reviewer)	Complete checklist during review of research and present recommendations at convened meeting.	

B. Research Involving Children

Who	Task	Tool
IRB Program Coordinator	Maintain and update checklist to conform to applicable regulations and guidelines.	Checklist – Requirements for Research Involving Children
	Confirm that protocol has informed consent and assent documents as appropriate.	

IRB Program Coordinator	Select appropriate primary reviewer(s).
IRB Member (Reviewer)	Complete checklist during review of research and present recommendations at convened meeting.

C. Research Involving Pregnant Women, Fetuses and Neonates

Who	Task	Tool
IRB Program Coordinator	Maintain and update checklist to conform to applicable regulations and guidelines. Confirm that protocol has informed consent and assent documents as appropriate.	Checklist – Research Involving Pregnant Women & Fetuses
IRB Program Coordinator	Select appropriate primary reviewer(s).	
IRB Member (Reviewer)	Complete checklist during review of research and present recommendations at convened meeting.	

D. Research Involving Other Vulnerable Groups

Who	Task	Tool
IRB Program Coordinator and Chairperson	Confer to determine whether any other special considerations apply or other vulnerable populations are to be the subjects of submitted research.	
IRB Members	Determine additional necessary protective stipulations to be applied to the research at a convened meeting.	

400 – REVIEWS REQUIRING SPECIAL CONSIDERATION	
402. Categories Of Research	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

The categories of research defined in these policies involve methodologies that might require additional considerations or for which there are federally mandated determinations that IRBs are required to make and document. The IRB will maintain a listing of persons with expertise in these areas and will enlist their services for review of protocols when warranted. These categories of research include, but are not limited to:

- Genetic research
- Protocols lacking plans for human involvement
- Medical records and chart review
- Residual body fluids, tissues and recognizable body parts
- Use of Electronic Equipment
- Hazardous Materials/ Animals

Specific Policies

1.1 Genetic Research

Genetic research may require special considerations.

1.1.2 Subjects of Genetic Research:

At first consideration, most genetic research may appear to meet the criteria for expedited review. These include:

- Pedigree studies, which look for a pattern of inheritance of a gene;
- Positional cloning studies, which are conducted to identify particular genes;
- Diagnostic studies, which gather samples to develop techniques to determine the presence of specific DNA mutations.

However, these studies may create a vulnerable population in that subjects' autonomy may be compromised. The type of IRB review for these studies is dependent on answers to the following questions: Will the samples be made anonymous to maintain confidentiality? If not, to what extent will the results remain confidential; and who will have access to them? Will the samples be used for any additional studies not made explicit at the time of donation, or will the samples be destroyed after specified, one-time use? Will the donor be informed of any and all results obtained from his or her DNA? Will the donor be informed

of the results of the entire study? Will family members be implicated in the studies without consent?

Because there is still little regulatory guidance and relatively few ethical precedents, genetic research will require close scrutiny, and the input of experts in this area.

1.2 Protocols Lacking Definite Plans for Human Involvement

Certain types of activities are planned and written with the knowledge that human subjects may be involved, but without definite plans for such involvement. Examples of such proposed activities are:

- Training programs in which individual training projects remain to be selected or designed.
- Research, pilot or developmental studies in which the involvement of human subjects depends on such things as the completion of survey instruments or prior animal studies.
- Institutional Support Programs where the selection of the project is the responsibility of the institution or program administrator. When supporting agencies require review and certification for such programs, protocols are to be submitted to the IRB with as much information as is available. The protocols must include assurances that additional information will be submitted when developed and, in the case of training grants, that all trainees will submit individual protocols if human subjects are to be used.

The IRB can give "General Expedited Approval" to programs like those mentioned above with the understanding that the specific research protocol will be submitted to them once it has been developed. "General Expedited Approval" is not appropriate for individual projects or to meet grant deadlines.

1.3 Medical Records and Chart Review

Studies involving the use of existing public or privately held records may qualify for exempt status or expedited review. However, if the nature of the research could put subjects' confidentiality at risk, the full IRB will review the study. Studies that involve only chart and record review can sometimes pose significant risk to patients.

The most common breach of confidentiality is exposure of possible embarrassing information without the knowledge or consent of the patient. Such studies may also lead to recruitment of patients into future non-therapeutic studies in a manner that may provoke the patient to ask how his/her record was revealed to someone not part of his/her therapeutic team. The present policy is to require IRB review of studies involving chart review or data collection and analysis.

If identifiers were to be recorded, the research would require IRB review to ensure that, among other things, procedures for protecting privacy and confidentiality are adequate. Furthermore, the Investigator studying cancer risk factors may propose to go on to contact the subjects (if still living) or family members (if the subject is deceased) to gather additional information, which may or may not be subject to the federal regulations.

1.4 Residual Body Fluids, Tissues and Recognizable Body Parts

Body Fluids & Tissues: Research on existing specimens ("on the shelf" or frozen) without identifying information (e.g., no names, initials, hospital number, etc.) may

be submitted to the IRB for expedited review, to include a short description of the research and where the tissue is coming from.

1.5 Use of Electronic and Stimuli-Generating Equipment

All equipment used in human subjects research that may be attached for recording purposes or produces any type of stimulus must be calibrated and maintained by a certified medical electronics technician. Such equipment may include, but is not limited to, electrocardiophic monitors (EKG), heat producing, electrical stimulus, noise, light, and/or other electronic devices. This equipment must undergo re-calibration and maintenance each year to ensure participant safety. The Environmental Health and Safety Office will review the equipment and protocols, in addition to the IRB. Investigators must submit all information relating to the equipment and its use (i.e. SOPs), lab use and safety procedures, and certification of calibration and maintenance. First aid procedures for lab personnel and subjects must be included in the protocol application. Investigators and lab personnel must be adequately trained to utilize such equipment. Whenever possible, these types of equipment should be developed and/or purchased from manufacturers who specialize in research and related purposes.

When using these types of equipment in research, investigators should evaluate the level of risk involved. High risk endeavors should be discussed with the IRB office prior to submittal to determine if any alternatives are available. Upon review and approval, the IRB may require continuing review to occur more often than annually.

In case of injury, the IRB must be notified immediately, and the procedures outlined in SOP 603, Adverse Event Reporting, must be followed. Principal investigators are required by regulation and TAMU policy to promptly report any adverse event, regardless of the severity. As appropriate, the event will be reported to the institutional official and to OHRP. Adverse events must also be reported to the federal sponsor, if applicable.

Any questions relating to the use of equipment or electronic devices in research should be directed to the IRB office at (979) 458-4067or irb@tamu.edu. In addition the Environmental Health and Safety office's Website may be accessed at http://finance.tamu.edu/ehsd/resources.asp and by telephone at (979) 845-2132.

1.6 Hazardous Materials/ Animals

In addition to IRB review, protocols for which hazardous chemicals, biological agents, infusion of radioactive substances, or use of ionizing radiation in a research activity must, at a minimum, be reviewed and approved by the TAMU Institutional Bio-safety Committee as appropriate. PIs submitting protocols for these types of procedures must be referred to the Institutional Bio-safety Committee (IBC) at (979) 458-3624. IRB staff should inform PIs of this requirement at the time of submission or as soon as possible after IRB submission.

The care and use of animals at Texas A&M University and the Texas Agricultural Experiment Station are regulated by federal law and by the University's commitment to adherence to the Public Health Service's *Guide to the Care and Use of Laboratory Animals*. PIs submitting protocols involving the use of animals in teaching and research must be referred to the Institutional Animal Care and Use Committee

(IACUC)at (979) 845-1828. IRB staff should inform PIs of this requirement at the time of submission or as soon as possible after IRB submission.

Protocols utilizing these methods and procedures will be flagged (on the original copy) to remind the coordinator of this requirement. After review and approval by the IRB, the requirement to seek appropriate safety committee approval will be added to the list of stipulations for approval sent to the investigator. Final approval for the protocol cannot be granted until a letter of approval from the appropriate committee is received in the IRB office.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

Director of the Office of Research Compliance (or designee) is responsible for maintaining up-to-date review tools for review of research pertaining to these categories based on new and evolving applicable regulations and guidelines.

IRB Chair (or designee) is responsible for ensuring the IRB members are well versed in new and evolving regulations and guidelines pertaining to these categories, for selecting primary reviewers with appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.

It is the responsibility of the Program Coordinator to coordinate with other Research Compliance committees (ULACC, IBC, etc.) on research programs to ensure complete compliance with all Federal laws related to research.

IRB Reviewer is responsible for conducting appropriate review of research planned for these categories in consultation with any appropriate experts and resources.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.104
45 CFR 46.101, 46.103, 46.118, 46.119
TAMU 15.01.01.M3

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Consultant Agreement Letter
IRB Protocol Review Sheet
IRB Submission Application
Research Related Web Links

7. PROCESS OVERVIEW

Review procedure for areas of research that may require additional considerations and expertise.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

A. Genetic Research

Who	Task	Tool
Chairperson(or designee)	Identify and invite appropriate consultant(s) who may assist the IRB in its deliberations.	IRB Submission Application/ Consultant Agreement Letter
Program Coordinator	Ascertain deliberations of other relevant research review groups (e.g., NIH, Institutional Bio-safety Committee).	Research Related Web Links

B. Protocols Lacking Definite Plans for Human Involvement

Who	Task	Tool
IRB Program Coordinator	Determine whether the research is exempt from IRB review, eligible for expedited review, or subject to full IRB review.	IRB Submission Application
IRB Compliance Staff	If subject to full or expedited IRB review, include the review sheet in the primary reviewer's packet.	IRB Protocol Review Sheet

C. Medical Records and Chart Review

Who	Task	Tool
IRB Program Coordinator	Determine whether the research is exempt from IRB review, eligible for expedited review, or subject to full IRB review.	IRB Submission Application
IRB Compliance Staff	If subject to full or expedited IRB review, include the review sheet in the primary reviewer's packet.	IRB Protocol Review Sheet

D. Residual Body Fluids, Tissues and Recognizable Body Parts

Who	Task	Tool
IRB Program Coordinator	Determine whether the research is exempt from IRB review, eligible for expedited review, or subject to full IRB review.	IRB Submission Application
IRB Compliance Staff	If subject to full or expedited IRB review, include the Checklist in the primary reviewer's packet.	IRB Protocol Review Sheet

400 – REVIEWS REQUIRING SPECIAL CONSIDERATION	
403. Guidelines Regarding Risk Level	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Categorization of Protocols:
Once a protocol is received, the IRB categorizes it as "minimal (standard) risk" or "high risk" for purposes of monitoring the research.

1.1 Minimal Risk

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. Minimal risk protocols (expedited/full) are reviewed annually.

1.2 High Risk

High risk protocols include studies where the chance of benefit is almost always low; studies in which the risk/benefit is high; and studies with other circumstances that are judged by committee to warrant a high risk designation based upon the IRB's judgment and experience. High risk protocols are reviewed every six months, or in some cases after a certain number of participants are enrolled.

2. SCOPE

3. RESPONSIBILITY

The reviewer is responsible for determining the risk status of the protocol.

4. APPLICABLE REGULATIONS AND GUIDELINES

46.102 Definitions

5. REFERENCES TO OTHER APPLICABLE SOPs

6. ATTACHMENTS

IRB Submission Form
IRB Protocol Review Sheet

7. PROCESS OVERVIEW

The reviewer will determine the risk level of the research based on the protocol review.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool

Reviewer	Determine whether the research is minimal risk or high risk based on review of the protocol.	IRB Submission Application/IRB Protocol Review Sheet

400 – REVIEWS REQUIRING SPECIAL CONSIDERATION	
404. Policy On Serious Or Continuing Issues Of Non-Compliance	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

In order to protect the safety and welfare of the research subjects, the Texas A&M University Institutional Review Board (IRB) has responsibility to oversee the use of human subjects in research.

This responsibility includes authority under the federal regulations as follows:

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's actions and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head. 45 CFR ñ 46.113.

To exercise this statutory authority, the IRB Chair shall appoint an ad-hoc committee for review of all allegations of non–compliance with human subjects regulations and review any study that has been associated with unexpected serious harm to research subjects. The ad-hoc committee will report their findings and recommendations to the Full IRB committee and IRB Chair. The IRB will take appropriate action to insure the safety and welfare of human research subjects. These actions may range from corrective or educational measures for the researcher to terminating IRB approval for all active studies of a research. Further, the IRB may suspend approval of research projects at any time during an inquiry or investigation to assure the protection of human subjects.

Upon determining that the acts of non-compliance must result in suspension or termination of research activities, a report must be submitted to the TAMU Institutional Official (Vice President for Research), the Research Compliance Office, the Office for Human Research Protections (OHRP), the dean and department head, the FDA (if the incident(s) were associated with an FDA regulated drug or device study), and the agency providing funding for the research. The report will include the findings and how the issue of non-compliance was handled. The report will be sent to OHRP at the following address:

Office for Human Research Protections
Division of Compliance Oversight
Department of Health and Human Services
The Tower Building
1101 Wooton Parkway, Suite 200
Rockville, MD 20852

Under the authority of the IRB, suspension and/or termination of a research activity may occur if human subjects are at risk beyond the approval of the protocol; any unintended adverse event

occurs; and/or failure to adhere to University rules and Federal laws. This serious action is used in cases where it is determined that there have been serious acts of non-compliance that are likely to cause harm to subjects, place subjects at unacceptable levels of risk, or there has been intentional non-compliance with regulatory and/or institutional policies. Suspension or termination of a protocol can only take place by a majority vote of a quorum of the IRB at a convened meeting.

1.1Application

These policies and procedures apply to all research activities of faculty, staff, students and others who are involved in research that falls under the jurisdiction of the Texas A&M IRB.

1.2 Non–Compliance

Non-Compliance - Conducting research involving human subjects in a manner that disregards or violates federal regulations governing such research. This can include, but is not limited to, failure to obtain IRB approval for research involving human subjects, inadequate or non-existent procedures for informed consent, inadequate supervision in research involving experimental drugs, devices or procedures, failure to follow recommendations made by the IRB to insure the safety of subjects, failure to report adverse events or proposed protocol changes to the IRB, and failure to provide ongoing progress reports.

2 PROCESS FOR HANDLING ALLEGATIONS OF Non–Compliance

2.1 Notification of an Allegation

There are two ways allegations of Non–Compliance may be submitted:

- Any individual or organization may submit a complaint or allegation of Non–Compliance to the IRB.
- The IRB itself may initiate a complaint based on information available to the IRB (e.g., deficiencies noted in IRB files, media or scholarly reports of research activity subject to IRB jurisdiction).

2.2 Inquiry

The IRB Chair will review information to determine if an investigation of the complaint is warranted. An inquiry is not a formal investigation or an in-depth analysis of the allegations; it is designed to separate allegations deserving further investigation from those that are frivolous, unjustified or related to minor infractions.

2.3 Investigation Process

Whenever an allegation or complaint of Non–Compliance is made, the IRB Chair will initially review it. If the Chair finds sufficient information to warrant an investigation, an ad-hoc committee, made up of at least 2 IRB members will be appointed to investigate; provided, however, that if the allegation or complaint is being investigated by another University committee in conjunction with the inquiry into or investigation of allegations of misconduct under another University policy, then it shall be sufficient that 1 IRB member serves on such committee and the allegation shall be investigated in accordance with that committee's process.

The IRB Office will send written notice of the allegations to the researcher and request information from the researcher within 10 working days. If the complaint raises issues of safety and welfare for research subjects that are apparent upon initial review, the Chair may notify the researcher to suspend enrollment pending the investigation.

The ad-hoc committee will review the allegation of non–compliance, the information from the principal investigator and any other information necessary to determine whether further action is warranted. The ad-hoc committee may interview the researcher and others, but is not obligated to do so. It may be necessary to secure critical data or materials at the outset of an inquiry to protect the integrity of those data or materials or records. The IRB maintains the authority to secure such materials at any time during an inquiry or investigation.

At the conclusion of its investigation, the ad-hoc committee will prepare a report summarizing the information it considered and outlining its conclusions and recommended actions.

2.4 Recommendations

At the conclusion of the investigation, the ad-hoc committee will make a recommendation to the IRB Chair. Possible recommendations include: 1) dismissal of the allegation or complaint as unjustified; 2) referral of the matter to another more appropriate system within the University for resolution (e.g., Academic Misconduct, Institutional Official); 3) resolution through corrective or educational measures where the violation of human subjects regulations is minor or inadvertent; and 4) suspension or termination of the study where the problems appear to be seriously impacting the safety of human subjects. The Chair will notify the IRB full committee and the Institutional Official.

The Chair will promptly act upon the recommendations of the ad-hoc committee and notify the researcher in writing of the outcome. This notice will include a statement of the reasons for the decision.

3 SUSPENSION AND REPORTING

At any time during the inquiry or investigation process, the IRB may determine that it is necessary to suspend accrual of research subjects to assure the protection of human subjects. The authority to suspend the entire approval of research rests with the IRB; both the Chair and ad-hoc committee may recommend suspension to the IRB. If suspension is warranted, it typically will occur at the end of the investigation phase, but may occur earlier if deemed necessary by the IRB due to patient safety or other considerations.

When the IRB makes a decision to suspend approval of research, it will notify the Institutional Officials, and other appropriate University officials. Written notice will also be sent to the following, as required under federal regulations:

- The Federal Office for Human Research Protection (OHRP);
- The Federal Food and Drug Administration (FDA) if the suspension of research approval involves an investigation drug or device;
- OHRP and FDA as applicable, if the matter involves the non-submission of a project which should have been reviewed by the IRB, and the researcher's failure to do so has resulted in unanticipated risks to human subjects or serious or continuing non–compliance with IRB requirements; and
- External and internal sponsors funding a study under suspension.

4 TERMINATION AND REPORTING

After review by the IRB Chair and the ad-hoc committee, a study suspension may result in termination of IRB approval. Generally, in cases in which the prescribed corrective action is not taken by the investigator or in which violations are too extensive and pose imminent safety threats to the subjects, the IRB Chair may recommend to the full IRB committee, that a study be terminated. Upon majority vote by the full committee, IRB approval for a study may be terminated, resulting in the investigator's inability to enroll any subjects, or perform procedures or study related interventions with subjects except those agreed upon by the IRB as essential to the subject's safety and general welfare. Further, the investigator will not be able to utilize the data gathered for any purposes, including but not limited to, data analysis, presentations, and publications. The IRB may contact the subjects directly or may request that the investigator contact the subjects to inform them of a study termination.

When the IRB makes a decision to terminate approval of research, it will notify the Institutional Officials, Vice President for Research Administration and other appropriate University officials. Written notice will also be sent to the following, as required under federal regulations:

- The Federal Office for Human Research Protection (OHRP);
- The Federal Food and Drug Administration (FDA) if the suspension of research approval involves an investigation drug or device;
- OHRP and FDA as applicable, if the matter involves the non-submission of a project which should have been reviewed by the IRB, and the researcher's failure to do so has resulted in unanticipated risks to human subjects or serious or continuing Non–Compliance with IRB requirements; and
- External and internal sponsors funding a study under suspension.

Reports will be filed within five working days of termination.

5. SCOPE

This policy includes written procedures for reporting actions to appropriate University and federal government officials as required by federal regulations.

6 RESPONSIBILITY

The Office of Research compliance is responsible for reviewing all allegations of non-compliance regardless of the source that places the safety and welfare of research subjects at risk.

7. APPLICABLE REGULATIONS AND GUIDELINES

TAMU 46.113, 15.99.03.M1.02, 15.99.03, 15.99.03.M1

8. REFERENCES TO OTHER APPLICABLE SOPs

9. ATTACHMENTS

10. PROCESS OVERVIEW

11 PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Chair	Will review allegations of non-compliance and determine appropriate actions.	

IRB Program Coordinator	Will send notice of allegations of non-compliance to investigators and route response to IRB Chair.

INFORMED CONSENT

500

500 – INFORMED CONSENT	
501. General Requirements And Documentation	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Informed consent must be legally effective and prospectively obtained.

Except as described below, investigators may not enroll human subjects in research unless they have obtained the legally effective, written, informed consent of the subject or the subject's legally authorized representative, prior to enrollment of the subject in the research. Investigators are responsible for ensuring that subjects, or their representatives, are given sufficient opportunity to consider whether or not to participate and must seek to avoid coercion or undue influence. Information given to potential subjects or their representatives must be in language that is understandable to the subject or representative. No process of obtaining consent may include exculpatory language through which the subject waives any of their legal rights or releases or appears to release the investigator, sponsor, or institution or its agents from liability for negligence. The IRB consent form checklist must be used to ensure compliance with all regulations. The IRB, at its discretion to comply with changing requirements, has the authority to alter these requirements and/or waive the informed consent process.

The IRB requires documentation of informed consent by use of a written informed consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative.

Specific Policies

1.1 Types of Consent Forms

A. A written consent document that embodies the elements of informed consent described in 21 CFR 50.25 and 45 CFR 46.116(a). This form may be read to the subject or the subject's legally authorized representative, but, in any event, the investigator shall give either the subject or the representative adequate opportunity to read the consent form before it is signed. The subject must also be given a copy of the signed consent form.

B. A "short form" written consent document stating that the elements of informed consent as required above have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be an impartial witness to the oral presentation. The IRB must approve a written summary of what is to be said to the subject or representative. The subject or the representative signs only the short form itself. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining the consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.

1.2**Required Elements of Informed Consent**

A. A statement that the study involves research, an explanation of the purposes of the research, the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

B. A description of any reasonably foreseeable risks or discomforts to the subject.

C. A description of any benefits to the subject or to others that may reasonably be expected from the research.

D. A disclosure of appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the subject.

E. A statement describing the extent to which, if any, confidentiality of records identifying the subject will be maintained and that notes the possibility that the FDA or other authorized government agencies may inspect the records.

F. For research involving more than minimal risk, an explanation as to whether any compensation is provided and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

G. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

H. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

1.3Additional Elements

When appropriate, one or more of the following elements of information shall also be provided to each subject:

A. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus if the subject is or may become pregnant), which are currently unforeseeable.

B. Anticipated circumstances under which the subject's participation may be terminated by the Investigator without regard to the subject's consent.

C. Any additional costs to the subject that may result from participation in the research.

D. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

E. A statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject.

F. The approximate number of subjects involved in the study.

1.4Other Requirements

A. Second person: The language of the consent document should be in the second person style so the consent form conveys a dialogue with information being provided and that there is a choice to be made by the subject rather than presumption of the subject's consent with the use of the first person style.

B. Language should be simple: The information provided in the informed consent

documents must be in language understandable to the subject. The informed consent document should not include complex language that would not be understandable to all subjects. Technical and scientific terms should be adequately explained using common or lay terminology.

C. Exculpatory language: Informed consent documents may not contain any exculpatory language through which the subject is made to waive or appear to waive legal rights, or releases or appears to release the Investigator, the Sponsor, or the Texas A&M University from liability for negligence.

D. FDA-regulated test articles: For all research involving test articles regulated by the FDA, informed consent documents must include a statement that the purpose of the study includes evaluation of both the safety and the effectiveness of the test article. The consent form must also include a statement that the FDA has access to the subject's medical records.

E. The IRB statement: "This research has been reviewed and approved by the Institutional Review Board – Human Subjects in Research, Texas A&M University. For research-related problems or questions regarding subjects' rights, the Institutional Review Board may be contacted through: Director of Office of Research Compliance at (979) 458-1467(irb@tamu.edu)

1.5 Documentation of Informed Consent

Each subject or his/her legally authorized representative must sign and date a copy of the current IRB-approved consent form prior to enrollment or any participation in any phase of the study, unless the requirement is waived by the IRB. The subject must also be given a copy of the signed consent form.

The IRB may approve procedures for documentation of informed consent that involve (a) a written consent form signed by the subject; (b) a "short form" written consent document with oral presentation; or (c) in limited circumstances, waiver of signed written consent form. Each of these three options is described in detail below. It is the responsibility of the IRB to determine which of the procedures described below is appropriate for documenting informed consent in protocols that it reviews. In the majority of cases, option (a) will be appropriate.

1.5.1 Written consent form signed by subject or legally authorized representative. In most circumstances, the IRB should require that informed consent is documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. The investigator should allow the subject or the legally authorized representative adequate opportunity to read the consent form before it is signed. A copy of the consent form must be given to the person signing the form.

1.5.2 The written consent form should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent (see section 1.2 Require Elements of Informed Consent).

1.5.3 Subjects who do not understand English should be presented with a consent form written in a language understandable to them.

1.6 Oral Presentation Using Short Form

As an alternative to standard written consent forms, oral presentation of informed consent information may be used.

In such cases, the subject must be provided with both:

- A "short form" written informed consent document stating that the elements of informed consent have been presented orally to the subject or the subject's legally authorized representative; and
- A written summary of the information that is presented orally.

1.6.1 A witness to the oral presentation is required. The witness must sign both the "short form" written informed consent document and a copy of the written summary.

1.6.2 The subject or the legally authorized representative must sign the short form written consent document.

1.6.3 The person obtaining consent (*e.g.*, the investigator) must sign a copy of the written summary of the information that is presented orally. The person obtaining consent may not be the witness to the consent.

1.6.4 Subjects who do not speak English: Where informed consent is documented using this short form procedure for non-English speaking subjects, the written informed consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent. When this procedure is used with subjects who do not speak English, (i) the oral presentation and the "short form" written informed consent document should be in a language understandable to the subject; (ii) the IRB-approved English language informed consent document may serve as the summary; and (iii) the witness should be fluent in both English and the language of the subject.

1.6.5 The IRB must receive all foreign language versions of the short form document as a condition of approval.

Expedited review of these versions is acceptable if the convened full IRB has already approved the protocol, along with the full English language informed consent document, and the English version of the short form document.

1.7 Cognitively Impaired Subjects

For studies that take place over extended periods involving subjects with potentially diminished capacity (to make decisions) the IRB should consider whether periodic re-consenting of individuals should be required to ensure that a subject's continued involvement is voluntary. The IRB may require that investigators re-consent subjects after taking into account the study's anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). Additionally, the IRB should consider whether, and when, it should require a reassessment of decision-making capacity.

1.8 Waiver of Documentation

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if the IRB finds either:

1. That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality;

Note: When the IRB waives the requirement for documentation under this condition, each subject must be asked whether the subject wants documentation

linking the subject with the research, and the subject's wishes will govern.

Or

2. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

1.9 Use of Facsimile or Mail to Document Informed Consent

The IRB may approve a process that allows the informed consent document to be delivered by mail or facsimile to the potential subject or the potential subject's legally authorized representative and to conduct the consent interview by telephone when the subject or the legally authorized representative can read the consent document as it is discussed. All other applicable conditions for documentation of informed consent must also be met when using this procedure.

2.0 Record Retention Requirements for Subject Consent Forms

The principal investigator or project director shall maintain, in a designated location, all executed subject consents. These consent forms are to be available for inspection by authorized officials of TAMU administration, the Institutional Review Board, the FDA, DHHS, regulatory agencies and sponsors. Consent forms must be maintained for three years following the completion of the study.

Should a principal investigator or project director depart from TAMU prior to the completion of an activity or less than the time specified, the investigator is responsible for initiating mutually satisfactory arrangements with their department and the TAMU administration as to the disposition of executed subject consents.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

IRB Program Coordinator is responsible for reviewing all incoming informed consent documents and for communicating with investigators to bring documents into compliance.

The investigator is responsible for ensuring that research subjects understand the research procedures and risks. Failure of the subjects to ask questions should not be construed as understanding on the part of the subject.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.116, 46.117
FDA Information Sheets, 1998

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Informed Consent Checklist
Informed Consent Document Template

7. PROCESS OVERVIEW

Informed consent must be documented by the use of a written consent form reviewed and approved by the IRB and signed by the subject or subject's legally authorized representative and a witness. Once approved by the Board, consent forms will be stamped for approval with the indication of the protocol number, approval and expiration dates. By signing the form, the witness is attesting to the fact that the subject, or the subject's legally authorized representative, actually signed the form and volunteered to participate in the research. A copy must be given to the subject or person signing the form. It is assumed that the consent form is only part of the total consent process in which the investigator, perhaps using the written consent form as an outline, describes all facets of the study and answers the subject's questions.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	**Task**	**Tool**
IRB Program Coordinator	Review proposed informed consent forms upon receipt of study, and confirm that all required elements are present.	Informed Consent Checklist
IRB Program Coordinator	If elements are missing, return consent document to investigator with request for revision and suggested language (where appropriate).	Informed Consent Document Template

500 – INFORMED CONSENT	
502. Exemptions	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

The IRB may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent (such as written documentation).

Specific Policies

1.1 Exemptions – IRB Waives One or More Requirements of Informed Consent
The IRB may waive the requirement to obtain informed consent provided the IRB finds and documents that:

1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
    - Public benefit or service programs;
    - Procedures for obtaining benefits or services under those programs;
    - Possible changes in or alternatives to those programs or procedures; or possible changes in methods or levels of payment for benefits or services under those programs; and
2. The research could not practicably be carried out without the waiver or alteration.

Or that:

1. The research involves no more than minimal risk to the subjects;
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. Whenever appropriate, the subjects will be provided with additional pertinent information after participation;
4. The research could not practicably be carried out without the waiver or alteration.

1.2 If the informed consent is waived, the conditions of the waiver must appear in the minutes.

There are more stringent and specific requirements for IRB waiver of informed consent in emergency situations in which the research involves more than minimal risk to the subjects. Information on the requirements and procedures may be obtained from the IRB office at (979) 458-1467.

13. Record Retention Requirements for Subject Consent Forms

The principal investigator or project director shall maintain, in a designated location, all executed subject consents. These consent forms are to be available for inspection by authorized officials of TAMU administration, the Institutional Review Board, the FDA, DHHS, regulatory agencies and sponsors. Consent forms must be maintained for three years following the completion of the study.

Should a principal investigator or project director depart from TAMU prior to the completion of an activity or less than the time specified, the investigator is responsible for initiating mutually satisfactory arrangements with their department and the TAMU administration as to the disposition of executed subject consents.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

IRB Program Coordinator or designee is responsible for determining whether informed consent exemptions are applicable and appropriate and for follow-up with investigators as indicated from the exemption assessment.

4. APPLICABLE REGULATIONS AND GUIDELINES
21 CFR56.109(c), 56.109(d)
45 CFR 46.116

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Waiver Approval Form

7. PROCESS OVERVIEW

The requirements for waiver of certain requirements of informed consent procedures and waiver of requirements for obtaining informed consent will be clearly documented.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Program Coordinator	Review and process request for waiver of informed consent. Indicate on the IRB Agenda/Minutes any stipulations of the waiver	Waiver Approval Form

500 – INFORMED CONSENT	
503. Assent	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

The principle of respect for persons requires that the choice of an autonomous person be respected. Under the usual conditions of research, this is accomplished by soliciting the informed consent of the prospective research subject.

In the case of the cognitively impaired adult or non-autonomous child, applying the principle of respect for persons is problematic. Therefore, consent of either the parent or legally authorized representative is required. However, any individual capable of some degree of understanding (generally, a child of seven or older, or a cognitively impaired adult) should participate in research only if they assent. When assent is required by the IRB, however, the decision of the individual assenting should be binding.

Specific Policies

1.1 Use of Assent

In instances where the subject is not legally capable of giving informed consent (*e.g.*, minors) or where the subject is cognitively impaired, the IRB must find that adequate provisions are made for soliciting the assent of the subject when in the judgment of the IRB, the subject is capable of providing assent.

1.1.1 Assent means a subject's affirmative agreement to participate in research. Mere failure to object should not be construed as assent.

1.1.2 In determining whether subjects are capable of assenting, the investigator and the IRB shall take into account the age, maturity, and psychological state of the subject involved. This judgment may be made for all subjects to be involved in research under a particular protocol, or for each subject, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the subjects is so limited that they cannot reasonably be consulted, or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the subject and is available only in the context of the research, the assent of the subject is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived as stated in section 1.1 of SOP 502.

1.1.3. When the IRB determines that assent is required; it shall also determine whether and how assent must be documented.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

IRB Program Coordinator or designee is responsible for determining whether assent is indicated and for follow-up with investigators, as appropriate.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46 Subpart D

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Assent Guide

7. PROCESS OVERVIEW

Assent of cognitively impaired adults and of children and permission from a legally authorized representative should be clearly documented.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	**Task**	**Tool**
IRB Program Coordinator	When research involves minors, include the assent guide with the primary reviewer's material.	Assent Guide

IRB COMMUNICATION AND NOTIFICATION

600

600 – IRB COMMUNICATIONS AND NOTIFICATIONS	
601. Investigative Staff	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

It is important that staff, subjects, and other interested parties have a means of communicating information about the conduct of a research project directly to the appropriate institutional officials. It is vital that IRB members, department heads, and other officials with responsibility for oversight of research have open and ready access to the highest levels of authority within the institution. The researcher and his/her research staff interact with subjects; therefore it is vital that open and frequent communication with the investigative team be maintained. Investigators and research staff should be open to participants' complaints or requests for information. Investigators and research staff should respond appropriately to such complaints or questions. Researchers are encouraged to submit questions, suggestions and comments regarding the TAMU IRB to the Office of Research Compliance via (979) 458-4067 or send an e-mail to irb@tamu.edu.

Specific Policies

1.1 Investigator Notifications

1.1.1 Initial submission: The investigator will be notified by letter or email of the IRB's decision as soon as possible after the meeting. If the approval is pending upon receipt and review of requested materials or responses from the investigator or sponsor, the IRB must receive the response within 45 days of the date of notification; however, this period may be extended if the investigator/sponsor communicates a need for an extension.

1.1.2 Renewals and amendments: Investigators will be notified by letter or email as soon as possible as to action taken by the IRB for any continuing reviews or admendments.

1.1.3 **Notification of final approval:** Investigators will be notified by letter of the final approval. Final approval letters will indicate the approval period, risk determination, any requirements by the committee, and information regarding adverse events. The IRB-approved consent form will be stamped with the approval period and submitted to the investigator with the final approval letter. Standard conditions for continued approval include, but are not necessarily limited to:

- Informed consent is obtained and documented.
- The IRB is notified of serious adverse events within appropriate periods.
- Changes to the protocol, and deviations from the protocol are reported
- Continuing review supporting documentation are submitted to the IRB
- Documentation of FDA approval prior to study initiation (if needed).

1.1.4 Disapproval: The IRB will provide to the research investigator a written explanation of the IRB's decision not to approve a research protocol and an opportunity for the research investigator to respond. The investigator may respond to the IRB in writing within 45 days, and the reply will be considered at the next convened meeting as a re-

review of the initial submission. Correspondence will provide the reason(s) for disapproval and instructions to the investigator for appeal of this decision.

1.2 Investigator Appeal of IRB Action

An investigator may appeal the revisions required by the IRB in the protocol and/or informed consent form. This appeal must be in writing and submitted to the IRB Program Coordinator. Investigators may also appeal an IRB decision to disapprove a study. Any such appeal may be in writing or in person and must be reviewed by the full IRB at a convened meeting. If the appeal is denied and the study disapproved, the investigator's institution cannot override the IRB's decision.

1.3 Appeal Board Review

When the IRB maintains disapproval of a protocol, after initial review, second review including the investigator's comments and reply to the IRB's first disapproval, and third review with the principal investigator and co-investigators in attendance at the convened meeting, the investigator may then submit an appeal of the final IRB disapproval to the Executive Associate Dean, with appropriate explanations. The Executive Associate Dean will seek expert opinions on the protocol from individuals within or from outside the University. These opinions will be submitted to the full committee for review. The IRB will reconsider the protocol in view of the expert opinions, vote on the protocol, and report its conclusion to the investigator, the Executive Associate Dean and others as deemed appropriate.

1.3 Suspension or Termination of IRB Approval

For Cause

The IRB will notify the Institutional Official, FDA (when the study involves an FDA regulated product) and federal agency head (if the research is federally funded), of the suspension or termination of a study for cause.

1.4 Noncompliance

Investigator noncompliance often may be the result of communication difficulties, therefore the IRB will attempt to resolve apparent instances of noncompliance without interrupting the conduct of the study, especially if stopping or interrupting the study will adversely affect the rights and welfare of subjects.

However, if it appears that an investigator is recklessly, intentionally or repeatedly in noncompliance, the IRB will notify the investigator by letter, detailing the alleged noncompliance, specifying corrective action, and stating the consequences. Copies of such correspondence shall also be sent to the sponsor, the investigator's supervisor, and the institutional official.

Should noncompliance continue, appropriate action will be determined at a convened meeting. Action by the IRB can include but is not limited to:

- Halting the research until the investigator is in compliance. If the research is halted, OHRP will be notified if the research is funded by a government agency, and FDA will be notified if the research involves an FDA regulated product or agent.
- Requiring the investigator to complete a training program.
- Barring the investigator from conducting further research.

- Any other action deemed appropriate by the IRB, including referral to appropriate University administrators.

When unapproved research is discovered, the IRB and the institution will act promptly to halt the research, ensure remedial action regarding any breach of regulatory or institutional human subject protection requirements, and address the question of the investigator's fitness to conduct future human subject research.

Serious or continuing noncompliance with federal policies on the protection of human subjects or the policies, procedures or determinations of the IRB must be reported promptly to the institutional official as well as to other appropriate University administrative officials and the appropriate department or agency head for funded protocols, sponsors if appropriate, and to OHRP and/or FDA as appropriate.

The IRB's responsibility is to protect the rights and welfare of research subjects, which could be placed at risk if there is misconduct on the part of an investigator or any member of the investigative team. It is, therefore, the duty of the IRB to be receptive to and act on good faith allegations of misconduct in research. The IRB will work to ensure that there is no retaliation against those who bring good faith allegations. Allegations of misconduct in science should be referred to the institutional official or the Office of Research Compliance for handling under Texas A&M University policies.

1.5 Communications to Others

The IRB is required by federal regulation and institutional policy to communicate certain actions to entities (i.e. appropriate institutional officials, funding sources, agency heads, and regulatory agencies) of:

- Any unanticipated problems involving risks to human subjects or others
- Any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB
- Any suspension or termination of IRB approval

1.1.1 Unexpected or serious adverse events: The investigator must notify the IRB and other entities as stipulated in SOP 602.

1.1.2 Suspension of a study for cause: The IRB will notify the institutional official; FDA when the study involves an FDA regulated product and federal agency head if the research is federally funded, as appropriate.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

IRB Program Coordinator is responsible for overseeing all IRB communications.

IRB Program Coordinator is responsible for corresponding with other interested entities concerning the status of research under review by the IRB.

IRB Chairperson (or designee) is responsible for ensuring appropriate discussion and IRB decision-making regarding adverse event assessments and investigator non-compliance, where communication with outside entities is necessary.

IRB Compliance Staff is responsible for generating appropriate correspondence in response to IRB meetings and decisions.

IRB Compliance Staff is responsible for generating appropriate correspondence in response to inquiries from the research community.

IRB Compliance Staff is responsible for distributing IRB correspondence to appropriate parties.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.109, 56.113
45 CFR 46.109, 46.113
TAMU 15.01.01.M5, 15.99.03.M1

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS
Sample Letters – Notification of IRB Decisions
Expedited of Full Approval Letter
Exemption Letter
Waiver Letter
Pending Notification
Disapproval Letter
Continuing Review Approval Letter
Continuing Review Notification
Modification Approval Letter
Adverse Event Form Notification
Termination Notification
Expiration Alert Notices:
Expiration Notification – 60 Day
Expiration Notification – 30 Day
Expiring Today
Receipt of Documents Alert Notices:
New protocol
Continuing Review
Amendment

7. PROCESS OVERVIEW

IRB actions will be communicated to the investigator consistently and promptly. IRB actions that must be communicated to various parties with an interest in the research program will be done promptly and consistently.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Program Coordinator	Ensure that all communications follow established procedures and format. Ensure that the determinations and requirements of the IRB are communicated to the investigator as soon as possible.	Sample Letters – Notification of IRB Decisions
IRB Chairperson (or designee)	Review and sign IRB decision communications.	
IRB Program Coordinator	Ensure that all communications with investigators, regulatory bodies, and others as appropriate are accurate and timely. Ensure that documentation, either electronic or paper, of any communication of determinations, requirements, or actions of the IRB or representatives of the IRB, when acting in a regulated capacity, are maintained, according to procedures in SOP 703 Documentation and Document Management. Ensure that all verbal communications are documented (either electronically or on paper) and retained in the study file according to procedures in section 703: Documentation and Document Management. Ensure that the appropriate entities are copied on the documentation and notification of any IRB determinations and actions. Monitor reports of serious adverse events from sponsors to ensure all reportable events are being reported to the IRB by the investigators.	
IRB Compliance Staff	Distribute correspondence as directed. Record communications as required.	

600 – IRB COMMUNICATION AND NOTIFICATION	
602. Adverse Events/Experiences	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Principal investigators are required by regulation and TAMU policy to promptly report any adverse event, regardless of the severity. An adverse event is defined as any potential for harm or any unanticipated problem(s) involving risks to subjects or others. As appropriate, the event will be reported to the institutional official and to OHRP. Adverse events must also be reported to the federal sponsor, if applicable. Such reports should be submitted to the IRB within 24 hours. Other documents, such as those provided by study sponsors, should be attached, but the report should summarize the event(s) and be signed by the PI. Serious adverse events, those requiring hospitalization or those resulting in death, are reported to a subcommittee, appointed by the IRB, to investigate.

Specific Policies

1.1 All adverse events that are serious AND unanticipated AND which are possibly, probably, or definitely associated* with the study procedures must be reported using the appropriate IRB Adverse Event Form, within 24 hours of the investigator's receipt of the information.

1.2 All deaths occurring during a research study must be reported according to the following timeframes:

a. If the death is possibly, probably or definitely associated* with the study procedures, it should be reported immediately by the investigator upon receipt of the information.

b. If the death is NOT possibly, probably or definitely associated with the study procedures (e.g., due to underlying disease progression), the death must reported on the IRB Adverse Event Form and submitted to the IRB within 10 days of the event.

1.3 All adverse events that are both unanticipated and Not serious which are possibly, probably, or definitely associated with the study procedures must be reported on the IRB Adverse Event Form and submitted to the IRB within 10 days of the event.

1.4 All anticipated adverse events regardless of the severity which are possibly, probably or definitely associated with the study procedures need to be reported. They must be submitted in summary format with the IRB Continuing Review Form at the time of renewal, unless they are occurring with greater frequency or at a higher level of severity than expected.

Any adverse events that were ***initially*** determined to not be associated with the study procedures and are subsequently determined to possibly, probably or definitely associated must be reported according to the listed criteria above.

1.5 Unanticipated Problems and Adverse Event Guidance Chart

Summary of Reportable Matters and Timeframe for Reporting

Event	Possibly/Probably/Definitely Associated With Study	Not Associated With Study
Deaths	Immediately	Immediately
Unanticipated Event that is Serious	10 calendar days	10 calendar days
Anticipated Event that is Serious	10 calendar days	At renewal*
Unanticipated Event that is Not Serious	At renewal	At renewal
Anticipated Event that is Not Serious	At renewal*	At renewal

* unless occurring with greater frequency or at a higher level of severity than expected

Adverse Event Assessment Committee

1. This Adverse Event Assessment Committee will comprise the designated IRB Chair, the Director of Research Compliance, and a community representative currently serving on the IRB.
2. If there is a conflict of interest between the principal investigator (PI) and the IRB Chair (such as same college affiliation), the Director of Research Compliance will assume responsibility for the entire proceedings.
3. The PI and all administrators will communicate with the Chair and vice versa, i.e., there will be only one line of communication.
4. The PI will be verbally notified of any violation within 24 hours of the report and informed of the actions necessary to correct the problem immediately.
5. The Adverse Event Assessment Committee will investigate any alleged violation within 72 hours of the report. At the end of this time, the PI will be notified in writing of the issues of non-compliance and provided with the opportunity to respond to the Committee.
6. Once the Adverse Event Assessment Committee has determined the response and informed the IRB Compliance Office, further communications will be subject to the policies of that Office.
7. In reports involving significant harm to human welfare, the entire IRB Committee will meet within 7 days of the investigation to recommend the course of action. At that time PI will be given the opportunity to address the committee. In other cases, the Adverse Event Assessment Committee will present the report and its investigation at a regularly scheduled IRB meeting.

1.7 Reporting

All reports of adverse events are reported in the minutes for review by the full board at the next convened meeting. Serious events should be specifically presented to the IRB by the reviewer or IRB Chair at the next convened meeting.

1.8 Filing and Retention

Adverse event reports and any correspondence generated by the IRB in response to the event must be filed with and retained for three years beyond the life of the protocol.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

IRB Compliance Staff is responsible for entering the adverse event into the database and forwarding to Program Coordinator for review.

IRB Chairperson (or designee) is responsible for IRB review of the adverse event and initiating appropriate action.

4. APPLICABLE REGULATIONS AND GUIDELINES

TAMU 15.01.01.M3

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Adverse Event Form
Adverse Event Acknowledgement Memo

7. PROCESS OVERVIEW

The IRB Compliance staff responsible for adverse event processing will check the email each workday morning for any reported event. If any, the IRB Compliance staff will record all pertinent information, such as principal investigator name, protocol number, a description of the event, date of occurrence, and any other information provided by the PI. This email "starts the clock" as to when a written report is required to be submitted. The written report must be submitted to the IRB office within 10 days of the event. In the event that the PI may not be informed of the event by the subject within the 10 day period, documentation should be placed in the file as to why the report is late.

Upon receipt of a completed IRB Adverse Event Form, the IRB Compliance staff will enter the report into the database, pull the file, attach the report and submit to the Program Coordinator. The file is then sent for review by the designated IRB chair(s) and or member(s). The IRB member will review the report and sign the report signifying acknowledgement of the report. Acknowledgement to the PI should be accomplished either by returning a copy of the report signed by the IRB reviewer or by memo acknowledging receipt of the report. If the IRB reviewer has concerns or questions regarding the report, relay them to the PI as soon as possible for resolution.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Compliance Staff	Receive adverse event report and enter into database.	Adverse Event Form
IRB Program Coordinator	Review adverse event report for appropriate action	Adverse Event Form
IRB Program Coordinator	Place on agenda for committee review	IRB Agenda/Minutes Template
IRB Chair (or designee)	Acknowledge receipt of adverse event report	Adverse Event Acknowledgement Memo

700 – FUNCTIONS AND OPERATIONS	
701. IRB Meeting Administration	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Aside from the review of research protocols that can be reviewed pursuant to an expedited process, the IRB will review all proposed research at convened meetings at which a quorum is present. Each IRB will meet *monthly*, or at some other frequency determined by the IRB Chairperson and the Director of the Office of Research Compliance (or Program Coordinator). A member of the IRB staff, to be designated by the Program Coordinator, coordinates meeting rooms, food and any invitations to guests for the IRB meetings. Scheduling of meeting rooms is done well in advance and for an entire fiscal year (September 1st through August 31st) and generally meets on the first and third Wednesdays of each month. IRB meetings are generally held in Room 130 H Centeq Building 1500 Research Drive, and the room should be scheduled for use at the designated meeting date and time. The Program Coordinator or IRB staff member will ensure that all members are informed well in advance.

Specific Policies

1.1 Quorum

1.1.1 A quorum is defined as attendance of a majority (greater than 50%) of voting members. (Examples: a majority is 9 members of a 17 member committee or 10 members of an 18 member committee.)

1.1.2 A quorum consists of regular and/or alternate voting members and includes: at least one member whose primary concerns are in scientific areas, and one member whose primary concerns are in nonscientific areas.

1.1.3 When FDA-regulated research is reviewed; there shall be one member who is a physician.

1.1.4 An alternate member may attend in the absence of the regular member for whom she/he is the designated alternate. Presence of such a designated alternate voting member counts towards meeting the quorum requirements stated above provided the alternate has had sufficient time to review the meeting materials.

1.1.5 The quorum must be present for each vote taken. If the quorum is not maintained when a member is recused, then that vote must be deferred until the next meeting at which a quorum remains effective during the time the member is recused.

1.1.6 A special consultant(s) must not be used to establish a quorum.

1.1.7 Requisite training must be completed, and a member's name must appear on the official roster of members prior to the first meeting in which they are to be counted as a voting member. The roster will be reviewed by the Director of the

Office of Research Compliance (or designee) prior to each convened meeting to ensure accuracy.

1.1.8 IRB members who have a conflict of interest, will not participate in any discussion or deliberation of the conflicted protocol. The conflicted member will recuse herself/himself during all matters related to the study including the vote.

1.2 Primary Reviewers

Prior to the meeting, the IRB Compliance Staff will designate primary reviewers for each research protocol. The primary and secondary reviewer's duties are described in SOP 203.

1.2.1 Absent Primary Reviewer

Each new protocol should be reviewed in advance by the primary reviewer assigned, who will present the protocol to the convened IRB. The primary reviewer's comments are to be recorded on the "Critique Sheet" sent to the reviewer by the IRB office. In the event that a reviewer cannot attend the IRB meeting, the reviewer should notify the Program Coordinator or one of the IRB staff, who should request that the reviewer forward one copy of his/her review ("Critique Sheet") to the IRB office. The IRB chair will then use the reviewer's "Critique Sheet" to present the protocol to the IRB. After presentation, discussion and a vote on protocol disposition, the IRB staff member present must ensure that the "Critique Sheet" is received for transcription into the minutes and filing with the protocol.

1.3 Meeting Materials Sent Prior to IRB Meetings

All IRB members will be sent study documentation and previous meeting minutes sufficiently in advance of the meeting to allow time for adequate review. These include:

1.3.1 Agenda: a meeting agenda (which details new business items) will be prepared by the IRB Compliance Staff or designee and distributed to IRB members prior to each meeting.

If a member has a conflict of interest with any study, they should inform the Chair prior to meeting. The Chair will ask for a declaration of such conflict before a protocol is presented and this will be incorporated in the minutes of the meeting. The IRB minutes should also specifically reflect such recusals as they occur during meetings.

1.3.2 Reviewer materials:

- A completed IRB submission form
- Proposed informed consent document(s) and/or script as appropriate
- Lay Summary
- Full Investigator's or Sponsor's protocol
- Copies of surveys, questionnaires, or videotapes
- Copies of letters of assurance or cooperation with research sites
- Investigator Brochure (if one exists)
- Advertising intended to be seen or heard by potential subjects, including email solicitations and physician letters

- Protocol Review and Informed Consent Checklist will be given to each member during orientation and should be used each time they review a study and to submit comments.
- Grant Application: The primary and secondary reviewers will review the grant application, if any, to ensure that the research described in the IRB protocol is consistent with the grant application. The grant application does not need to be reviewed by every IRB member. A copy of the grant application or protocol should be retained by the IRB Office and made available to any IRB member who may wish to review it. The IRB may require the investigator(s) to: (i) summarize, and cross-reference specific information contained in the grant application; (ii) identify any IRB-approved protocols that describe the proposed research; and (iii) either certify that the application or protocol is consistent with any corresponding IRB protocol(s) or submit protocol amendments to reconcile any discrepancies.
- IRB Review of NIH-Approved Informed Consent Documents for NIH-Supported Multi-center Clinical Trials: If available, for NIH-supported multi-center clinical trials the IRB must receive and review a copy of the NIH-approved sample informed consent document and the full NIH-approved investigator's protocol as a condition for review and approval of the local informed consent document. Any deletion or substantive modification of information concerning risks or alternative procedures contained in the sample informed consent document must be justified in writing by the investigator, and approved by the IRB.

1.4 Minutes

The Federal regulations for the protection of human subjects [45 CFR 46.115(a)(2)] require that "Minutes of IRB meetings... shall be in sufficient detail to show attendance at the meeting; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution." These requirements are minimal, and more detail may be included in the minutes as necessary.

1.4.1 Recording: The IRB Compliance Staff or designee will take minutes of each meeting using the IRB Agenda/Minutes. Minutes will be written in sufficient detail to show the following:

- Meeting attendance; the minutes will show the certification of a quorum, including status of each attendee (regular member, consultant, etc.), and that the members present certified that they held no conflict of interest with any of the protocols under consideration. The minutes will record the attendance at the meetings; actions taken by the IRB; protocol number and title for each protocol reviewed; the name of the principal investigator and collaborators; the primary, secondary, and tertiary reviewers; and the results of the IRB's vote.
- Actions taken by the IRB on each agenda item requiring full IRB action, including, the basis for requiring changes in or disapproving the research

- Summary of the discussion of controverted issues and resolution
- The minutes will also reflect the approval of exempt and expedited protocols.
- The minutes will reflect protocols that have been terminated.
- Requests for significant protocol modifications, issues of non-compliance and other issues of significance must be brought to the attention of the entire IRB at a convened meeting. When this is the case, the issues will be noted in the minutes.
- Voting results, including number for, against and members who recused themselves and reason for recusal

1.4.2 Approval: Draft minutes will be distributed to The Director of the Office of Research Compliance (or Program Coordinator) for review. After review, the minutes will be sent to the entire committee for review at least five days prior to the next convened meeting for approval/changes at that meeting.

- Corrections requested by the IRB will be made by the IRB Compliance Staff or designee and the minutes will be printed in final form and made available to members at the following meeting. The Chairperson or designee of the IRB shall sign and date final, approved minutes.
- The Director of the Office of Research Compliance (or Program Coordinator) will maintain copies of the minutes, as well as the agenda and pertinent materials on file

1.5 Telephone Use

1.5.1 Convened meeting using speaker phone:

Should a member not be able to be physically present during a convened meeting, but is available by telephone, the meeting can be convened using a speakerphone. The member who is not physically present will be connected to the rest of the members via speakerphone. In this manner, all members will be able to discuss the protocol even though one member is not physically present. Members participating by such speakerphone may vote, provided they have had an opportunity to review all the material the other members have reviewed.

1.5.2 Meetings Conducted Via Telephone Conference Calls:

On occasion, meetings may be convened via a telephone conference call. A quorum (as defined above) must participate for the conference call meeting to be convened. To allow for appropriate discussion to take place, all members must be connected simultaneously for a conference call to take place -- "telephone polling" (where members are contacted individually) will not be accepted as a conference call.

Members not present at the convened meeting, nor participating in the conference call may not vote on an issue discussed during a convened meeting (no voting by proxy).

1.6 Voting

Members of the IRB vote upon the recommendations made by the primary reviewers according to the criteria for approval. Members also will determine level

of risk, the frequency of review for each protocol, monitoring of the investigative site, and whether third party assessment and follow-up will be needed.

A protocol may be recommended for the following actions:

"Approved" – Approved with Full Board Continuing Review.

"Conditionally Approved" – Approved with stipulations for minor changes or simple concurrence of the principal investigator (PI), that will be identified to the PI and must be completed and documented prior to beginning the research. For these stipulations, the IRB Chair or designated reviewer can, upon reviewing the PI's response(s) to stipulations, approve the research on behalf of the IRB.

"Deferred" – The IRB recommends substantive changes that must be reviewed by the IRB before the research can be approved.

"Disapproved" – The protocol describes a research activity that is deemed to have risks which outweigh potential benefits or the protocol is significantly deficient in several major areas.

"Approved with Expedited Continuing Review" – At the time of full board review, the IRB may decide that although the research did not qualify for expedited review initially, it is, nevertheless, no more than minimal risk. Therefore, it can be reviewed at the time of continuing review using the expedited method.

1.7 Risk level

The risk level assigned to studies reviewed at the convened meeting will be standard (review annually) or High (more than minimal risk and will require review at intervals less than one year). The risk level assigned to a protocol will be indicated in the minutes.

1.8 Submission of the Minutes

A draft of the meeting minutes should be submitted to the Program Coordinator for editing, and the final version copied and distributed to all IRB members with next agenda. At the meeting, the minutes are presented, discussed and a vote taken for acceptance.

1.9 Record Retention

Minutes of the IRB meetings are filed by month in the IRB office. The files for the current year and the preceding year are maintained in the IRB office, and all previous year's files are stored in record retention for retrieval, if necessary. These records will be maintained for three years.

3. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

Program Coordinator is responsible for IRB meeting procedures, providing policy guidance and documentation.

Legal Counsel and/or the Office of Research Compliance shall be consulted in the event of any questions concerning regulatory requirements for meetings, voting and minutes.

IRB Compliance Staff is responsible for preparing IRB minutes.

IRB Chairperson (or designee) is responsible for IRB meeting review conduct and leadership.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103, 46.108
21 CFR 56.108, 56.109
TAMU 15.99.01.M1, 15.99.01
FDA Information Sheets, 1998

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

7. ATTACHMENTS

IRB Agenda/Minutes Template

7. PROCESS OVERVIEW

IRB meetings will be conducted and documented in a consistent manner in order to meet federal and institutional requirements. Attendance at IRB meetings is taken by the Program Coordinator or designated staff member on a pre-prepared attendance sheet and recorded in the minutes of the meeting. The attendance sheet identifies members present and voting and members not present for voting. A quorum of members (>50 %) is required at all meetings, and lack of a quorum prohibits convening a meeting. The presence of at least one non-scientist member is required to make up a quorum at IRB meetings. It is the duty of the Program Coordinator to inform the Chair when there are problems with achieving or maintaining a quorum.

At the beginning of each meeting, members should certify for the record that they have no conflicts of interest in any protocol currently under consideration. If any member who is a co-investigator or otherwise has a conflict of interest with a protocol, he/she must be excused from deliberations. IRB staff should be cognizant of co-investigator related conflicts and remind the IRB Chairs of the conflict, if it appears to go unnoticed. Also, it should be reflected in the minutes that members were not present for

deliberations of voting on their own protocols or those for which there was a conflict of interest. Voting will be documented in the minutes as "For = #, Opposed = #, Abstained = names of individuals abstaining." Abstentions count against the quorum.

Special attention must be paid to ensure that a quorum is not lost during a meeting. If a member abstains from voting or is excused from the room during deliberations due to a conflict of interest, a quorum of total members must still remain. If not, the protocol in question cannot be considered. Also, if members are required to leave the meeting for emergencies or for other reasons and the number of members present falls to a level below that required for a quorum, the meeting must be adjourned. It is important to note that protocols must be approved by a majority of the members present. Therefore, the number of votes "For" must exceed the number of votes "Opposed" plus the number of abstentions.

Motions to approve should include a statement regarding the timing of the continuing review, not to exceed one year. In the motion, there should also be a statement on whether continuing review can be done in an expedited review. All of this should be included in the minutes.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Compliance Staff	Complete agenda section of the IRB Agenda/Minutes Template.	IRB Agenda/Minutes Template
IRB Compliance Staff	Assemble reviewers' packets	
IRB Compliance Staff	Attend meeting of the IRB. Using IRB Agenda/Minutes Template, record proceedings of the meeting.	IRB Agenda/Minutes Template
IRB Compliance Staff	Provide IRB members with summary of exempt/expedited reviews conducted, serious adverse event reports received and terminations since the last IRB meeting.	Report of IRB Exempt-Expedited Reviews, Terminations (since the last IRB Full Board Meeting)
IRB Chairperson	Using the IRB Agenda as a guide, chair meeting. Ensure that all business is addressed, that proceedings are recorded, and that any member who has a conflict of interest does not participate in the IRB's consideration of the study, except as requested by the IRB, nor in voting.	IRB Agenda

IRB Compliance Staff	Complete draft of minutes within 10 days of the IRB meeting to send to the Program Coordinator.
IRB Program Coordinator	Review minutes and forward to Chair and committee members.

700 – FUNCTIONS AND OPERATIONS	
702. Administrative Review And Distribution Of Materials	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

The efficiency and effectiveness of the IRB is supported by administrative procedures that ensure that IRB members not only have adequate time for thorough assessment of each proposed study, but that the documentation they receive is complete and clear enough to allow for an adequate assessment of study design, procedures, and conditions.

Specific Policies

1.1 Exemptions

The Chair or Program Coordinator will review submissions for Exemption submitted by investigators. Once exemption determination has been made, the protocol is updated in the database as "Exempt from IRB Review" and filed.

1.2 Incomplete Submissions

Incomplete applications will not be accepted for review until the investigator has provided all necessary materials as determined by the Program Coordinator or designee. The Program Coordinator (or designee) will contact the submitting investigator to obtain any outstanding documentation or additional information before the application is scheduled for review.

1.3 Scheduling for Review

Complete applications that are not exempt are referred to the Chair for Expedited or Full Board Review.

1.4 Distribution to Members Prior to IRB Meetings

Copies of application materials will be distributed to all IRB members at least ten (10) days prior to the meeting. Each regular member of the IRB, and any alternate members attending the meeting in place of a regular member, will receive a copy of the initial application material. Consultants will only receive copies of material that pertain to their requested input.

The originals of submission materials will be retained in the IRB Office and are available for the IRB meeting.

1.5 Confidentiality

All material received by the IRB will be considered confidential and will be distributed only to meeting participants (regular members, alternate members and special consultants) for the purpose of review. All application materials will be stored in an IRB study file with access limited to the IRB members and staff.

All IRB members, staff members, and consultants will be required to sign confidentiality/non-disclosure agreements.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

The IRB Compliance Staff is responsible for conducting appropriate assessment of submissions for triage purposes.
The IRB Compliance Staff is responsible for providing complete review material packets to IRB members and other relevant parties.
IRB Program Coordinator is responsible for supporting and assisting the IRB Compliance Staff in submission triage activities and in ensuring that appropriate confidentiality/non-disclosure agreements are signed..

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.109
45 CFR 46.109
TAMU 15.99.01.M1

6. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

IRB Exemption Checklist
IRB Notebook Instructions
IRB Review/Critique Sheet
Pending Notification

7. PROCESS OVERVIEW

The Office of Research Compliance will receive all research protocols from principal investigators submitted for review by the IRB.

To submit a protocol to the IRB for review, an investigator must complete the application form according to detailed instructions and enclose supporting material as necessary:

- protocol application, with required signatures;
- a lay summary;
- consent documents, if applicable;
- questionnaires or data collection forms, if applicable;
- materials that will be used to recruit subjects for the protocol; and other advertising materials (e.g., press releases, interview forms, etc.).
- copy of the full grant proposal, if applicable.

Research may <u>not</u> be initiated until the IRB and any other committees whose approval may be required have given final written approval. The committee will notify both the IRB and

the investigator of its decision. The principal investigator will be responsible for notifying, in writing, all committees, any other pertinent institutional officials, and pharmacies of the respective committee approvals for the research protocol, prior to initiation of the protocol.

Research protocols are reviewed at one of three levels, depending on the IRB's interpretation of the project's risk to the human subjects and on the federal guidelines that define the categories of review, which are:

- Exempt from IRB Review
- Expedited IRB Review
- Full IRB Review

The IRB Chair or designee will determine whether the research protocol meets the criteria necessary for expedited review, or full review. The IRB Chair or designee will refer all non-exempt research protocols either to full committee review or expedited review.

The IRB requires that investigators disclose on their protocol application form all potential conflicts of interest(financial/non-financial). When such a conflict exists, a copy of the protocol is forwarded to the Conflict of Interest (COI) Committee and the IRB will withhold final approval until the COI Committee renders a decision. The COI Committee will evaluate the conflict per institutional policy and may impose conditions to manage potential or actual conflicts of interest involving research. Research may NOT be initiated until both the IRB and the COI Committee and any other committees whose approval may be required, have given final written approval. The COI Committee will notify both the IRB and the investigator of its decision.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
IRB Compliance Staff	Conduct preliminary assessment of submissions for exemption from IRB review. Forward non-exempt protocols to Program Cordinator.	IRB Exemption Checklist
IRB Compliance Staff	Conduct assessment of submission adequacy and contact investigators for any required elements/documentation.	Pending Notification
IRB Program Coordinator	Review and forward non-exempt protocols to Chair for Expedited or Full Board Review.	IRB Review/Critique Sheet
IRB Chair	Review non-exempt protocols for decision.	
IRB Compliance Staff	Assemble reviewers' packets for Full Board Review protocols. Send to all regular members of the IRB. Send reviewers packets to alternates as indicated. Send pertinent protocols to consultants invited to the meeting.	IRB Notebook Instructions

700 – FUNCTIONS AND OPERATIONS	
703. Records Management	
Policy: **Effective Date:** **Revised By: TMA**	**Revised Date: April 20, 2006** **Approved By:**

1. POLICY

The records section of the 42 CFR sets forth specific requirements which apply fairly to all entities required to be registered. A "functional or performance based" approach "to documenting replicating agents, such as using a logbook/data entry system to record information typically gathered during a research protocol as part of standard practice or GLP (*i.e.*, quantity of material inoculated, quantity of media added during the work, quantity material used/destroyed, final cell count, etc)." Records are required to maintain "accurate, current inventory for each select agent (including viral genetic elements, recombinant nucleic acids, and recombinant organisms) held in long-term storage (placement in a system designed to ensure viability for future use, such as in a freezer or lyophilized materials)." In addition, the amended interim final rule stated "for access to the area where select agents are used or stored that a record of the date and time the individual entered and left the area must be maintained." It is required that entities maintain records of all entries into areas containing select agents or toxins, including the name of the individual, name of the escort (if applicable), the date and time of entry in an effort to maintain records of access into areas containing select agents and toxins.

Specific Policies

1.1 Records

42 CFR § 73.17 states:

"An individual or entity required to register under this part must maintain complete records relating to the activities covered by this part. Such records must include: (1) Accurate, current inventory for each select agent (including viral genetic elements, recombinant nucleic acids, and recombinant organisms) held in long-term storage (placement in a system designed to ensure viability for future use, such as in a freezer or lyophilized materials), including: (i) The name and characteristics (e.g., strain designation, GenBank Accession number, etc.), (ii) The quantity acquired from another individual or entity (e.g., containers, vials, tubes, etc.), date of acquisition, and the source, (iii) Where stored (e.g., building, room, and freezer), (iv) When moved from storage and by whom and when returned to storage and by whom, (v) The select agent used and purpose of use,"

1.1. (1) *"Accurate, current inventory for each select agent (including viral genetic elements, recombinant nucleic acids, and recombinant organisms) held in long-term storage (placement in a system designed to ensure viability for future use, such as in a freezer or lyophilized materials)"*

As a mechanism to maintain complicity, Texas A&M has positioned the use of an *Agent Access Log* as standard use select agent laboratories. Each select agent Principal Investigator is required to maintain correct inventory records by:

- Ensuring all authorized personnel for each laboratory completes sections of the *Agent Access Log* to reflect all movement of the select agent (see instructions in Table);
- All Principal Investigators are responsible for reconciling these records and ensuring the validity of the recorded information;
- Principal Investigators are responsible for ensuring that all personnel are trained on the use of the *Agent Access Log*;
- The Biosafety Officer (BSO) is responsible for completing annual reviews of these records at the time of the annual inspection;
- Principal Investigators are responsible for noting any discrepancies that may occur to the Office of Research Compliance (ORC);

1.2 ORC Administration of Documents

42 CFR § 73.17 (6) (b) states:

"(b) The individual or entity must implement a system to ensure that all records and data bases created under this art are accurate, have controlled access, and that their authenticity may be verified.

1.2.(1) The Texas A&M Office of Research Compliance (ORC) will retain a general copy of each select agent Principal Investigator records, to include Standard Operating Procedures, Biosafety Plans, various tables, etc.

42 CFR § 73.17 (6) (c) states:

"(c) All records created under his part must be maintained for three years and promptly produced upon request."

1.2.(2) The ORC must retain all records regarding protocols that are approved and the research initiated for at least three (3) years after completion of the research.

1.3 Destruction of Copies

All material received by the ORC, which are considered confidential and in excess of the required original documentation and appropriate controlled forms, will be collected at the end of the meeting and destroyed by a method deemed appropriate.

1.4 Archiving and Destruction

After 3 years from date of creation or submission, all documents and materials germane to IRB determinations will be archived according to institutional policy. Archiving policies of the Texas A&M University will determine when such archived records may be destroyed, provided however that in the case of protocols that are approved and research initiated, all records will be kept for at least three years after completion of the research.

2. SCOPE

The policies and procedures apply to all controlled documents used in the submission, initial review, and continuing review of research submitted to the ORC for the use of select agents.

3. RESPONSIBILITY

The Director of the ORC (or designee) is responsible for maintaining complete files on all research reviewed by or submitted for all applicable regulatory compliance requirements.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 73.17
21 CFR 56.115
TAMU 61.99.01

5. REFERENCES TO OTHER APPLICABLE SOPS

This SOP affects all other SOPs.

6. ATTACHMENTS

Agent Access Log

7. PROCESS OVERVIEW

Documents will be maintained in a secure file room with access by ORC Staff or members (who are not conflicted). Documents will be maintained until 3 years after the study has been completed and then they will be archived.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

A. Instructions for completing the *Agent Access Log*

Who	Task	Tool

Principal Investigator & Personnel

1. Before accessing the select agent, ensure the *Agent Access Log* is available. Unless this is a new page, the **Agent/Characteristics, Location**, and **Freezer/Cabinet I.D.** sections at the top of the page should be filled in. If not, please complete these sections before continuing with inputting data.

Agent Access Log in bound folder

2. Begin entry on a new line.

Date

- Enter the date (mm/dd/yy) of which the entry is being made.

Name

- The whole name of the person moving the agent from storage.

Container Label

- Place from where the sample is being derived (e.g. containers, vials, tubes, etc.).

Source

- Place the origin of receipt of agent, differentiating between *Clinical/Diagnostic*, *Environmental*, or *Other*. If the source is Clinical, please place a "C" in the box; if the source is Environmental, place an "E" in the box; if the source is Other, place "O" in the box along with stating the other source (e.g. "O"- Recombinant).

Purpose of Use

- This column is merely to record the disposition of the agent. One may denote entries such as: research, destruction, transport, etc.

Conc/Sample Size

- This column notates the concentration or the sample size of the agent. Please provide the initial and current quantity amount (e.g. milligrams, milliliters, grams, etc.).

Agent Removal

- Amount Removed (Qty) - Please provide the amount of the agent that will be removed. Specify the removal quantity amount (e.g. milligrams, milliliters, grams, etc.).
- Removed by whom- Please provide the name (first and last) of the individual removing the agent.

Method of Removal

- Please provide the method in which the agent will be removed.

Return to Storage

- Amount Returned (Qty) - Please notate the

Director of the Office of Research Compliance (ORC)	All copies of this form will be kept in the .
IBC Program Coordinator	Ensure that all records are accessible for inspection and copying by authorized representatives of the sponsor, funding department or agency, federal (FDA, OHRP) and institutional auditors at reasonable times and in a reasonable manner.

B. Using Electronic Systems

Who	Task	Tool
IRB Program Coordinator (or IRB Compliance Staff)	Ensure that the IRB's electronic systems and records are maintained in a manner that contains a complete history of all IRB actions related to review and approval of a protocol, including continuing reviews, amendments and adverse event reports.	
IRB Program Coordinator	Ensure that all IRB Compliance Staff members are trained on the proper use of all electronic systems used to document protocol review and compliance activities. Maintain specific operations and procedures manuals to train staff and assure consistency of operations.	
IRB Program Coordinator	Maintain appropriate security methods, such as issuance and revision of ID/passwords, to ensure limited access to secure areas.	

RESPONSIBILITIES OF INVESTIGATORS

800

800 – RESPONSIBILITIES OF INVESTIGATORS	
801. IRB-Required Investigator Actions	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

All investigators should have an understanding of the basic ethical principles, Federal rules and regulations, and University policies and procedures for conducting research involving human subjects. Investigators will ensure that:

1. The ethical principles in research are applied;

2. The rights, welfare, and safety of the subjects are protected from harm;

3. Research complies with Federal and institutional requirements; and

4. Manage those personnel involved in the research project.

   Investigators should not commence a research study without adequate resources to protect participants and should stop a research study if resources become unavailable. These resources might include personnel, space, equipment, and time.

Between IRB initial approval of a protocol and the time of continuing review of a study, it is the investigator's responsibility to keep the IRB informed of unanticipated non-serious and serious adverse events and other unanticipated findings that could affect the risk/benefit ratio of the research.

An investigator is responsible for the accurate documentation, investigation and follow-up of all possible study-related adverse events. Investigators are also responsible for informing government and other sponsors of any unanticipated or serious adverse events, as appropriate.

Specific Policies

1.1 IRB Review of Research

All human subjects research that is conducted by or under the direction of any employee, faculty, staff, student or agent of Texas A&M University in connection with his or her institutional responsibilities must be reviewed by the IRB.

1.2 Informed Consent

The investigator must obtain informed consent from subjects prior to their enrollment into the research. The investigator must use the informed consent document approved by the IRB. Approval and expiration dates are indicated on the first page of the consent document. Consent documents are valid only during the dates indicated on the form; and

the investigator may use the forms only during the period for which they are valid. Investigators must follow the IRB guidelines for obtaining informed consent.

1.3 Adverse Event Reporting

The IRB must be informed of any unanticipated problems and adverse events that occur during the approval period in accordance with SOP 602. An IRB Adverse Event form for reporting adverse outcomes is available to the investigator at the IRB website, but reports of serous adverse events will be accepted in any format. Investigators or sponsors must also submit sponsor-generated reports of adverse events occurring at other investigative sites.

1.4 Amendments/Revisions to an Approved Protocol

Changes in approved research, during the period for which approval has already been given, may not be initiated without IRB and approval; except where necessary to eliminate apparent immediate hazards to human subjects. Investigators or sponsors must submit requests for changes to the IRB using the IRB Amendment Form. Upon receipt of the amendment, the IRB Chair will determine if the revision meets the criteria for minimal risk. If the revision represents more than a minimal risk to subjects, it must be reviewed and approved by the IRB. Minor changes involving no more than minimal risk to the subject will be reviewed by the expedited review process. Revisions to the protocol that involve deleting procedures, adding new procedures, or changes to enrollment must be approved by the IRB.

1.5 Continuing Reviews

The length of time approval is given to a research protocol will be no more than one year, and is dependent on the risk involved with the research. Investigators are responsible for requesting renewal in anticipation of the expiration of the approval period. Investigators or their designees and/or sponsors are required to provide a periodic report regarding their investigation prior to the end of the approval period, or upon completion of the study. An IRB Continuing Review Form will be available to the investigator for this purpose.

1.6 Student-Conducted Research

As stipulated in Statement of Authority and Purpose all activities that meet the definition of research with human subjects and that are conducted by students for a class project or for work toward a degree must be reviewed by the IRB. For example, activities that must be reviewed and approved by the IRB include: (i) All master's theses and doctoral dissertations that involve human subjects; and (ii) All projects that involve human subjects and for which findings may be published or otherwise disseminated. All students/fellows applying for IRB review must obtain the signature of their faculty advisor on the IRB Submission Application.

1.7 Conflict of Interest

The protection of human subjects requires objectivity in communicating risks, selecting subjects, promoting informed consent, and gathering, analyzing and reporting data. Therefore, the IRB should consider conflict of interest issues in its deliberations of applications.

All investigators must reveal on their application to the IRB whether they or any other person responsible for the design, conduct, or reporting of the research has an economic interest in, or acts as an officer or a director of any outside entity whose interests (financial/non-financial) would reasonably appear to be affected by the research.

2. SCOPE

These policies and procedures apply to all researchers in the TEXAS A&M UNIVERSITY system.

3. RESPONSIBILITY

IRB Program Coordinator is responsible for tracking investigator compliance with IRB requirements stipulated during the IRB's review of the investigator's research, and for engaging appropriate investigator sanctions when investigators are not in compliance with IRB requirements.

IRB Chair (or designee) is responsible for facilitating investigator compliance with IRB requirements through his/her management of IRB deliberations, and providing investigators clear guidelines pertaining to that compliance through IRB communications to the investigator.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.109, 56.111
45 CFR 46.109, 46.111
TAMU 15.01.01.M2, 15.01
OHRP COI Policy Draft

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

5. ATTACHMENTS

IRB Submission Application

7. PROCESS OVERVIEW

In order to secure approval, investigators should submit complete applications with required documentation. When submitting a hard copy application, the IRB requires 1 original and 1 copy of the complete application packet.

Amendments/revisions to an approved protocol can not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool

IRB Compliance Staff	Provide investigators with complete information package on preparing IRB submissions, securing initial and ongoing approval of research, and providing all required reports.	IRB Website, IRB Manual, IRB Compliance Staff
IRB Program Coordinator/ IRB Compliance Staff	Contact investigators as often as needed to assist in the development of submission materials and to secure all necessary information for ongoing IRB review and approval.	
IRB Program Coordinator	Provide investigators with appropriate training in preparing IRB submissions and in conducting the informed consent process and other subject protection activities	
IRB Chair or designee	Identify investigator non-compliance as soon as possible and initiate IRB sanctions.	
Program Coordinator/IRB Compliance Staff	Distribute communications to and from investigators to appropriate IRB Compliance Staff and members in a timely manner.	

QUALITY ASSURANCE

900

900 – QUALITY ASSURANCE	
901. Quality Assurance/Quality Control Program	
Policy: **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Quality assurance and control of the daily operations of the IRB ensure effective support of the IRB's mandate. Therefore, the QA/QC program consists of three components:

- Training and continuing education of IRB Compliance Staff
- Interactions with the IRB community outside the Texas A&M Community
- Regular review and assessment of procedures

Specific Policy

The Director of the Office of Research Compliance, the Institutional Official or the IRB Chair has the authority to implement a QA/QC program and to act on identified deficiencies by implementing corrective action which may include implementing revisions to the Standard Operating Policies and Procedures.

2. Audits of IRB Records and Database

Arrangements will be coordinated by the Program Coordinator to schedule an internal audit of the IRB records and database on an annual basis. For audits of the database, the auditors will compare data contained in the IRB protocol files with the information contained in the IRB database. For audits of IRB protocol files (records), the presence of the following documents in a sampling of IRB files will be verified:

Original and approved IRB Protocol
Original and approved Consent Form (if applicable)
Final protocol approval letter to PI
Continuing Review Forms for every year past the initial approval period
Acknowledgement of adverse event reports by designated members
Approvals for amendment/modification requests

Verification of documentation of amendments/modifications, adverse events, and continuing review will be accomplished by checking the Report of Administrative Actions of the IRB.

An audit plan will be developed by the Program Coordinator and presented to and approved by the Chair(s) and Director of Research Compliance by March 1st of each year. The annual audit will by completed by August 31st of each year. A report of the findings shall be forwarded to the Director of Research Compliance. Discrepancies will be corrected immediately and, if required, reported to the Office for Human Research Protections.

3. SCOPE

These policies and procedures apply to all IRBs in the Texas A&M University system.

4. RESPONSIBILITY

Director of the Office of Research Compliance (or Program Coordinator) in conjunction with the Institutional Official or the IRB Chair is responsible for the establishment, implementation and oversight of the QA/QC program.

5. APPLICABLE REGULATIONS AND GUIDELINES

6. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

7. ATTACHMENTS

8. PROCESS OVERVIEW

IRB personnel and the research community are responsible for maintaining and ensuring continuing quality and standards for all IRB procedures.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
Director of the Office of Research Compliance (or Program Coordinator)	Review IRB operations at least annually. Develop and implement quality improvements as indicated by periodic assessments.	

900 – QUALITY ASSURANCE	
902. Audits By Regulatory Agencies	
Policy: QA 902 **Effective Date:** **Revised By:**	**Revised Date:** **Approved By:**

1. POLICY

Texas A&M University acknowledges that certain regulatory agencies have the authority to audit the operations of IRBs, and supports such audits as part of its continuing effort to maintain high standards for human research protections.

Entities that may audit IRBs include: FDA, OHRP, and appropriate certified auditors of foreign countries. Sponsors or funding entities of research may also be authorized to audit specific documents and procedures.

Specific Policies

1.1 Preparing for an Audit

1.1.1 For external audits involving OHRP or FDA, the following must be notified immediately:

- The Directory of the Office of Research Compliance, who in turn will notify
- The Institutional Official
- IRB Chair,
- other organizations as needed
- The IRB Compliance Staff designated to participate in the audit are required to follow the steps outlined by this institution for preparing the site for an audit.

1.2 Participating in an Audit

1.2.1 IRB Compliance Staff are expected to know and follow the procedures outlined by this Institution for the conduct of a regulatory audit.

1.2.2 Prior to being granted access to IRB documentation, inspectors or auditors must exhibit proof of their authority or authorization to conduct the audit and to access IRB documents, and no entity other than those listed on the consent forms may have access to any document that includes subject identifiers.

1.2.3 Auditors will be provided with adequate working area to conduct an audit and IRB Compliance Staff and members must make every reasonable effort to be available and to accommodate and expedite the requests of such auditors.

1.2.4 Documents may be copied and taken off-site only by individuals authorized in writing by the Director of the Office of Research Compliance or Program Coordinator.

1.3 Follow-up after an Audit

Reports of the audit, either verbal or written, should be addressed by the Institutional Official, (with the assistance and support of the Office of Research Compliance), as soon as possible after the audit.

2. SCOPE

These policies and procedures apply to all IRBs in the Texas A&M University system.

3. RESPONSIBILITY

Institutional Official is responsible for serving as the responsible institutional official in all regulatory agency matters regarding regulatory compliance, participating as needed in regulatory agency audits, and providing support in responding to and correcting audit findings.

Director of the Office of Research Compliance (or designee), with input from IRB Chair, Institutional Official and Office of Research Compliance, is responsible for all formal regulatory agency correspondence and interactions, establishing logistical support during regulatory agency audits, serving as key institution contact during such audits, and drafting responses to regulatory agency correspondence received following such audits.

IRB Chair, members and staff are responsible for participating in regulatory agency audits as determined by the Director of the Office of Research Compliance (or Program Coordinator), and in fully cooperating with government officials during their participation in such audits.

IRB Chair is responsible for assisting the Director of the Office of Research Compliance (or Program Coordinator) in formal responses to regulatory agency audits and in implementing policy and procedure changes indicated by such audits.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.115
45 CFR 46.115
TAMU 15.99.01
FDA Compliance Program Guidance Manual 7348.809, Institutional Review Boards

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

Internal Audit Plan
Audit Report Policy
FDA's A Self-Evaluation Checklist for IRBs

7. PROCESS OVERVIEW

Guidelines concerning preparation for regulatory audits of the IRB and appropriate behavior toward regulators will be adhered to continually.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
Director of the Office of Research Compliance (or Program Coordinator)	Upon being notified of an impending audit, notify all IRB Compliance Staff, and staff of any other institutional entity designated, including the IRB Chair, Institutional Official, and the Director of the Office of Research Compliance	Internal Audit Plan Audit Report Policy
	Using the Audit Preparation Checklist, assign responsibilities as indicated on the checklist.	FDA's A Self-Evaluation Checklist for IRBs.