

- Centrifuges with safety caps or sealed rotors should be used, or alternative practices should be used (waiting 15 minutes after spin stops before opening lid, additional PPE)
- Use of Biosafety Cabinets (BSC) is recommended whenever possible.
- Use of alternatives to needles and sharp instruments (e.g. Blunt cannulas, self-sheathing or retractable needles).
- Use of alternatives to glass (e.g. Non-glass vacutainer tubes, unbreakable or plastic-coated capillary tubes).
- Needles are not bent, broken, re-capped, removed from syringes, hand-manipulated, or placed un-capped into a researcher's hand.

Biosafety Guidelines and References:

- MCG Biosafety Web page: <http://www.mcg.edu/services/ehs/biosafe/biosafe.htm>
- MCG IBC Web page: <http://www.mcg.edu/research/ibc/>
- Center for Disease Control (CDC) Biosafety in Microbiological and Biomedical Laboratories (BMBL), 5th edition:
<http://www.cdc.gov/od/ohs/biosfty/bmb15/bmb15toc.htm>
- OSHA Blood-borne Pathogen (29 CFR 1910.1030) and Needle-stick Prevention Standards (also see Official Code of GA §31-12-13):
<http://www.osha.gov/SLTC/bloodbornepathogens/standards.html>
- Saf-T-Pak: <http://www.saftpak.com/>
- Department of Transportation Regulations for Hazardous/Infectious Material Shipping and Transport:
<http://a257.g.akamaitech.net/7/257/2422/01jan20061800/edocket.access.gpo.gov/2006/pdf/06-4992.pdf>
- Fed Ex Dangerous Goods Shipping:
<http://fedex.com/us/services/express/addservopt/dangerousgoods/>
- UPS Dangerous Goods Shipping:
<http://www.ups.com/content/us/en/resources/prepare/hazardous/index.html>
- USPS: <http://www.usps.com/cpim/ftp/pubs/pub52.pdf>
- CDC Etiologic Agent Import Permit Program: <http://www.cdc.gov/od/eaipp/>
- USDA/APHIS National Center for Import and Export: <http://www.aphis.usda.gov/NCIE/>
- Georgia EPA Solid Waste Management Rules:
<http://rules.sos.state.ga.us/docs/391/3/4/15.pdf>
- ABSA Risk Group Classification Database <http://www.absa.org/XriskgroupsX/index.html>
- Public Health of Canada Biological MSDSs <http://www.phac-aspc.gc.ca/msds-ftss/>
- NIH Guidelines for Research Involving Recombinant DNA Molecules ("NIH Guidelines"):
<http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html>
- CDC Select Agent Program:
<http://www.cdc.gov/od/sap/>



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MEDICAL COLLEGE OF GEORGIA



INSTITUTIONAL BIOSAFETY COMMITTEE & BIOSAFETY OFFICE

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Your clinical study will require IBC pre-approval if it involves:

- Human blood, urine or other fluids, or tissues
- Shipping of dangerous goods (dry ice is considered a "dangerous good", and possibly clinical/diagnostic specimens, cell culture, tissues, microorganisms, etc.)
- Any recombinant DNA (this includes both NIH "exempt" and "non-exempt" rDNA protocols)
- Cell, tissue or organ culture of human or primate material
- Other potentially infectious agents (e.g. viruses)
- Microbial agents which can be pathogenic to humans
- Toxins of biological origin with LD50 < 100 µg/kg or toxic or venomous plants, animals or insects
- Whole animals
- CDC/USDA Select agents and toxins

What is the Institutional Biosafety Committee (IBC)?

The purpose of MCG IBC is to assist MCG researchers in safely conducting research with biological materials while ensuring institutional compliance with Federal, State and local legislations and guidelines governing the proper handling, research with, and disposal of biological materials. The IBC also establishes policies, procedures, and practices to ensure that research at MCG does not present unacceptable risks to the health or safety of faculty, staff, students, visitors, or the general public or environment. IBC membership can be viewed at: <http://www.mcg.edu/services/ehs/biosafe/IBCmembers.pdf>

The MCG IBC has been delegated the authority to ensure that **MCG researchers and activities occurring in MCG facilities** comply with all pertinent regulations and guidelines related to handling of biological materials. Violation of these regulations or guidelines may not only elevate MCG's and individual MCG researcher's liability risk, but may place current and future research funding to the university's research in jeopardy. As a condition of funding acceptance from federal agencies, MCG has agreed to abide by guidelines established by the NIH, **for all research conducted at MCG, independent of the status and/or source of funding.**

What is the purpose of a Biosafety Protocol (BSP)?

The IBC is responsible for doing risk assessments for all MCG research with biological material. Risk assessment involves a comprehensive review of many aspects of a research project including biological agents, experimental procedures, standard laboratory practices, locations, the personnel and their expertise and training. The purpose of the BSP application is to detail this information for the IBC to review. Once risk has been assessed, the IBC can then address whether appropriate mitigating safety procedures and containment have been implemented to sufficiently reduce these risks.

All research involving biological agents must be reviewed and approved by the IBC before a PI is authorized to bring the agents to campus or initiate a research project.

Do I have to submit a new BSP application for each of my clinical protocols?

Not necessarily. BSPs are experimentally-based, in other words, they describe the biological material (e.g. human blood, urine or other fluids, tissue specimens, microbial cultures) and what manipulations will be done with these (e.g. centrifugation for serum/plasma preparation, culture, tissue sectioning) the locations/facilities in which the biological material might be, and the personnel involved in handling this material and their training. As long as your IBC-approved BSP **comprehensively** describes all of the above completely, one BSP often can cover multiple clinical protocols. This is often the case for "typical" Industry-sponsored clinical protocols involving interventions/treatments which do not involve delivery of any biological agent (i.e. recombinant DNA, blood products, cells, biological toxins (e.g. BoTox), tissues) *into* non-infectious patients, and the protocol involves drawing blood, preparation of serum/plasma samples and shipment to the industry sponsor. In these cases, the biological material (blood), manipulations (centrifugation for serum preparation, and pipetting into aliquots, shipment) may be identical, and as long as it's performed by the same personnel in the same facilities, one comprehensive BSP can "cover" multiple Clinical Protocols. Alternatively, collaborative projects involving multiple lab directors may require more than one approved "BSP" to detail all of the experiments in a particular project.

PIs will be required to submit a **new** BSP or **amend** an existing BSP to reflect any changes in location, personnel, procedures, and/or biological material agents in each project, and these may need to be reviewed by the IBC before authorization is issued to the PI to perform the research.

- Ground transport of biological material from /to extramural sites and/or on public roadways, packaging, labeling must comply with IATA standards.

Shipping:

- All shipping of hazardous material must comply with IATA standards.
- Any pertinent permits for interstate transport, import or export must be obtained prior to shipping.
- Anyone responsible for shipping will require current certification for shipping of dangerous goods (e.g. Saf-T-Pak training).

Medical Surveillance:

- All personnel working with human or non-human primate derived material must be offered Employee Health Screening and Vaccination program through the Employee Health Office or a signed waiver must be obtained by the PI.
- An infection control plan, including post-exposure medical follow-up must be on-hand at any facility in which personnel may be exposed to blood-borne pathogens.
- Any personnel who have had a potential exposure must seek immediate medical assistance at Employee Health or the Emergency Room (after hours). Any potential exposures must be reported to the PI and the BSO.

Surface Decontamination & Spill clean-up protocols:

- Each laboratory's procedures for surface decontamination and spill clean-up must be documented in their SOPs. This should include disinfectant, exposure times.
 - A freshly diluted (<24 hours) 10% bleach solution with an exposure time of 30 minutes is typically sufficient to decontaminate most biological agents.
 - Because bleach may etch stainless surfaces and provide microenvironments for pathogen growth, if 10% bleach is utilized as a decontaminant on these surfaces, a rinse with water or 70% ethanol to remove bleach should be considered, or use of an alternate decontaminating agent (e.g. phenol- or ozone- based agents) for stainless surfaces.
 - For assistance with selecting appropriate disinfectants and procedures, see: <http://www.cdc.gov/od/ohs/biosfty/bmb15/Appendix%20B%20%20Decontamination%20and%20Disinfection.pdf>
- Any large or public spills or any overt exposure should be reported to the PI and the Biosafety Officer (BSO).
- All work surfaces should be decontaminated at the end of the work day or after any spill.

Biological waste:

- Liquid wastes should be appropriately decontaminated, as documented in the laboratory's SOPs, prior to disposal down the sewer or in rigid, leak-proof biohazard waste containers.
- Solid wastes should be decontaminated prior to disposal into MCG-authorized biohazardous waste containers.
- Sharps (needles, syringes, glass) should be disposed in close-able, rigid, upright, leak proof standard sharps container.
- Animal carcasses should be transported to/from LAS facilities using transport guidelines above and disposed according to IACUC procedures.

Safety Precautions:

- Personal Protective Equipment (PPE): Gloves, lab coat and eye protection are standard for laboratory work. Full face protection or respiratory protection may be required for some applications.

What are Select Agents?

As defined in 42 C.F.R. Part 73, 7 C.F.R. Part 331, and 9 C.F.R. Part 121, Select Agents are specific biological agents that the DHHS and USDA have identified as having the potential to pose a severe threat to human, animal and/or plant health or to animal or plant products.

- To view a list of Select Agents, please see: <http://www.cdc.gov/od/sap/>
- To possess, transfer or do with research with a Select Agent, there are very stringent requirements, including:
 - Federal registration (CDC or USDA)
 - FBI security risk assessments
 - Federally-approved Safety plans
 - Federally-approved Security plans
 - Special Training
 - Federal inspections of the facilities

What considerations is the IBC looking to see documented on Biosafety Protocols and SOPs?

Biosafety Level (BSL):

- Most clinical IBC protocols which involve low-risk patients, involve specimens which still may harbor blood-borne pathogens. Therefore, Biosafety Level 2 (BSL-2) containment and practices, as defined by the CDC BMBL, should be used, at a minimum.
- Because Universal Precautions dictate all human specimens be treated as infectious, human specimens are considered "infectious" by the IBC.
- Patient specimens from patients who may be infected with higher-risk pathogens (BSL-3 or above, as defined by the CDC BMBL) will require higher BSL containment and practices.

Locations:

- When documenting locations on your BSP, list any and all locations ("cradle to grave") in which your biological material may be at any moment in time. Consider:
 - Where will your biological agent be obtained?
 - Where will it transported?
 - Where will it manipulated (e.g. serum/plasma separations)?
 - Where will it be stored (freezers, refrigerators, cryotanks)?
 - Where will it be shipped?
 - Where will it be disposed?
- Laboratory spaces should be in separate rooms from clinic or public spaces
- Access to laboratories should be controlled by the PI.

Storage:

Biological material should be stored:

- In well-labeled boxes, fridges, freezers
- In areas in which access to agents is restricted
- In locations where all personnel who may have access have knowledge of hazards

Transport:

- For intramural transport, agents should be in a closed, leak proof, primary container inside a well-labeled closed, leak-proof, durable secondary container. (Note: the IBC does not consider a ziplock bag "durable")
Example: Vacutainer of blood inside an air-tight plastic storage container labeled with biohazard stickers, contents and contact information.

How do I submit a new BSP application for IBC Review?

New Applications should be submitted on the appropriate application forms, which are available online :

<http://www.mcg.edu/research/ibc/apps.htm>

Submit to the Biosafety Office
Div. EH&S, CI-1006
or kraemers@mcg.edu

- All BSP applications require submission of the **BSP Primary Application form**.
- Completion of the "Biohazardous Material and Compliance Worksheet on p. iii of the BSP Primary form will direct which additional schedules will be required to complete your BSP Application.
- "Typical" industry-sponsored clinical trials involving interventions/treatments which do not involve delivery of any biological agent (i.e. recombinant DNA, blood products, cells, biological toxins (e.g. BoTox), tissues) *into* non-infectious patients and only require drawing and/or manipulation of human blood or other fluids from the patients require submission of **Schedule B in addition to the BSP Primary form**.
- To facilitate verification of IBC approval of any HAC/CCRI file to OHRP and/or sponsored project to DSPA, **Schedule O** can be used to document that the PI verifies that all experiments are "covered" in a particular BSP. Alternatively, this may also be accomplished via email from the **PI to the Biosafety office**. Any verification email should include the following information:

I verify that all experiments described in this project are fully documented in my IBC-approved BSP as indicated below

- The PI Name on the HAC/CCRI file or sponsored project (if someone other than the PI on the BSP)**
- BSP #*
- BSP Title (if available)*
- BSP Approval Date*
- Project title*
- Project funding agency*
- Anticipated funding period (until next competitive renewal application)*
- HAC/CCRI file # (if available)*

** This is often the case for student or postdoc fellowships, or sometimes collaborative research projects. If this is the case, we will need to contact both PIs to make sure the PI on the BSP is willing to assume ultimate responsibility for the biosafety on the other PI's research project.*

- Random audits will be performed by the Biosafety Office to verify that BSPs and the projects associated with them are harmonized in order to ensure compliance to the Research Office.

What other forms, other than the IBC Application, do I have to submit with my IBC application?

You will be asked to submit the following forms:

- Laboratory-specific Standard Operating Procedures (SOPs) which address the specific additional hazards which may be presented in your protocol.
- Laboratory Self-Audit form
- Training Documentation (copy of Saf-T-Pak Training and any as requested).

How do I submit an amendment to an existing BSP?

- The Biosafety Office requires some form of documentation to submit to the IBC with sufficient detail describing any changes to the original BSP to allow for a re-assessment of the risk.
 - Simple amendments may be requested in a fully detailed email from the PI to the Biosafety Office.
 - Alternatively, the original application form or schedule may be amended and resubmitted to the Biosafety office.
- If additional risk may be associated with the amended protocol, additional mitigation measures may need to be adopted (and documented in the lab SOPs).

What Training is Required by the IBC?

- **Biosafety Training:**
 - Initial Didactic Lab/Chem/Biosafety Training (once upon initial hire) (contact Ken Erondu to register)
 - Annual Biosafety Refresher Training (contact Stacey Kraemer kraemers@mcg.edu for information)
- **GA Board of Reagent's Online Right-To-Know (RTK) training:**
<http://www.mcg.edu/services/ehs/chemsafe/RTKTraining.htm>
 - Initial Board of Reagent's Basic Right-To-Know (RTK)
 - Annual Blood-Borne Pathogen Training (if working with fresh human or non-human primate material)
- **Certification for Shipping of Dangerous Goods:**
 - Saf-T-Pak Training CDs are available for loan through the Biosafety Office (call 1-2663 to arrange). Required once every 2 years.

How does the Biosafety Office process BSPs (i.e. how long will it take to get my IBC approval)?

1. After initial submission, the Biosafety Office will review the BSP application to determine :
 - A. Whether any immediate concerns that may pose a problem during IBC edit
Edits or clarifications may be requested (to facilitate IBC approval process) before submission to the IBC.
 - B. Which review "track" to submit the BSP application for IBC review
2. There are 2 "tracks" for BSP application review by the IBC:
 - A. **"Expedited" Review**
BSPs which do not involve recombinant DNA, involve only "exempt" recombinant DNA (as defined in Section III-F of NIH Guidelines), or do not involve high hazards (i.e. which involve Select Agents and/or may require BSL3 containment).
 - a) After initial edits, the BSP is submitted to the appropriate IBC subcommittee (clinical or basic/applied research) via email.
 - b) The subcommittee members evaluate the protocol and may request further information, details or clarifications from the PI.
 - c) The subcommittee members will vote to conditionally approve or disapprove the BSP, or they may request that the application be held over for full committee review
 - d) Conditional approvals are received in **approximately 3 business days from BSP submission to sub-committee members** unless held over for full-committee review by request.
 - e) Research can initiate upon conditional approval.
 - f) IBC verifications may be provided to the OHRP and/or DSPA upon conditional approval as requested.
 - g) Final IBC approval issued at next IBC meeting unless new IBC member concerns are raised.
 - B. **Full Committee Review**
BSPs which involve non-exempt recombinant DNA (as defined in Section III-A through E of NIH Guidelines), or involve high hazards or any BSP recommended for full committee review by a subcommittee member during expedited review.
 - a) After initial edits, **any BSP which is received by the first day of the month** is submitted to full IBC committee for review.
 - b) The IBC members vote to approve or disapprove at the next convened meeting of the full IBC (**typically on the third Wednesday of the month**).
3. The Biosafety Office will assess the facilities to determine whether they are appropriate for the research activities proposed and will report back to the IBC subcommittee and IBC.
4. The Biosafety Office confirm training by all personnel has been completed and documented.
5. After the IBC meeting, any remaining stipulations requested by the IBC will be forwarded to the PI and must be submitted to the Biosafety Office before approval letters are issued.

What considerations need to be made for shipping or ground transport of biological specimens, dry ice and other hazardous materials?

Multiple International, Federal, State regulations, as well as airline trade associations, courier companies, airlines govern the shipping and/or ground transport of hazardous (or dangerous) materials. The most restrictive of these is the International Air Transport Association (IATA), so compliance with IATA standards is typically sought. Among these are very specific requirements to properly classify, identify, pack, label, mark and document these materials. In addition, the shipper must be trained to handle these material by Federal law. This is because the primary risk for shipping lies with the shipper—the person who packs the material, signs a waybill and/or offers the material for shipment or transport. Criminal and civil liability for shipping may involve high fines and/or civil suits with no upper limits.

In addition, consideration must be given to obtaining appropriate permits which may be required for interstate transport of materials which may be infectious, and/or importation or exportation of biological materials may require permits from the CDC or USDA. International shipments may require special courier arrangements due to some country restrictions. Hazardous material must not be hand-carried, transported in checked baggage or in carry-on luggage, and must be fully declared.

Hazardous materials may include:

- Dry ice
- Biological materials
- Clinical/diagnostic specimens
- Cultures of microorganisms or cells
- Tissues
- Infectious material
- Toxins of biological origin
- Genetically modified organisms
- Liquid nitrogen

What is Recombinant DNA?

NIH Guidelines defines recombinant DNA molecules as either:

- Molecules that are constructed outside living cells by *joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell.*
- Molecules that result from the replication of those described above.

NIH defines 6 categories of recombinant DNA research (NIH Guidelines, Section IIIA-F), depending on the perceived risk of the experiments and the required approvals which must be obtained prior to initiation of the experiment or enrollment of study subjects.

What are Gene Transfer & Gene Therapy and what regulations exist governing this research?

- As defined in Section III-C-1 of NIH Guidelines: Experiments Involving the Deliberate Transfer of Recombinant DNA, or DNA or RNA Derived from Recombinant DNA, into One or More Human Research Participants.
- Gene Therapy=Gene Transfer with a Therapeutic potential
- NIH requires any Gene Transfer protocol to receive review and approvals from the IBC, Institutional Review Board (IRB), and NIH Recombinant DNA Advisory Committee (RAC) before enrollment of the first subject into the study.

What key words might cue a coordinator to ask whether a study involves gene transfer?

- Gene Therapy
- Recombinant
- DNA
- RNA
- Express (expression)
- Vector
- Plasmid
- Transfect (transfection)
- Transduce (transduction)
- Adenovirus (adenoviral)
- Retrovirus (retroviral)
- Adeno-associated virus (AAV)
- Lentivirus (lentiviral)
- Promoter (e.g. CMV promoter)
- Fusion protein
- Selectable marker
- Transcription