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Envelope-to: hammond@sunshine-project.org
Subject: Response to your request
Date: Fri, 27 Oct 2006 15:45:16 -0400
Thread-Topic: Response to your request
Thread-Index: Acb59ND5UWfoLvnsEcaqfRK7hINK7gACvx9g
From: "Vander-Linden, Caree L Ms USAMRIID"
<caree.vanderlinden@us.army.mil>
To: <hammond@sunshine-project.org>
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Dear Mr. Hammond,
Attached are the files of the meeting minutes of the USAMRIID Institutional Biosafety Committee for the period requested by the Sunshine Project. Unfortunately, the minutes for 2003 and late 2005 are lacking, due to a loss of the records during a computer crash in December 2005. We've looked high and low but have been unable to come up with a back-up copy.

At any rate, here are the minutes we do have. Please let me know if you need further assistance. My contact information is below.

Regards,
Caree

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<<22 July 2004.pdf>> <<25 Apr 2006.pdf>> <<5 Nov 2004.pdf>> <<8 Aug 2006.pdf>> <<8-JUL-2005.pdf .pdf>>

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August 2, 2004

Minutes
Institutional Biosafety Committee Meeting
July 22, 2004

Agenda

I-Reorganization and Expansion of RIID Institutional Biosafety Committee

Meeting commenced with a discussion of the chairmanship position. Member recommended that he be the chairman of the IBC with current chair serving as Scientific chairman. He felt that this arrangment may aid in enforcement of the RIID regulation requiring that all investigators notify the IBC before beginning projects in which recombinant DNA methodology, or organisms derived from the methodology is used.

It was agreed that a draft memo will be prepared for Commander to circulate to all investigators restating the RIID requirement for notification of the IBC of all expeirments as outlined in the NIH guidelines.

Chairman also notified the committee that members of the committee will be officially appointed through a memo from the Commander's office. Chairman received several suggestions from committee member regarding potential members from outside RIID.

Chairman has had discussions with the RIID website designers regarding a portal on the RIID-Vision website for the IBC. The site will have the forms necessary for submission of new projects to the IBC. Minutes of past meetings of the committee will also be posted after members have the opportunity to edit a draft copy. Links to the NIH guidelines and other materials relevant to the IBC will be posted.

II- Operation of the IBC Committee

The frequency of formal IBC meetings was discussed but not agreed upon. Chairman stated that a past attempt to carry out the review of submitted registration protocols by email was not very successful.

A brief discussion dealt with the use at RIID of recombinant organisms developed in other laboratories. It was agreed that review by the IBC of another institution did not preclude registration with the RIID IBC. Two members both felt that IBC reviews from the other institutions should also be included with the RIID registration.

One member felt that better integration of the IBC with the LACUC would be obtained by having a line on the LACUC forms indicating, when appropriate, the RIID IBC registration and review had taken place.

Minutes compiled by
Committee Chair

USAMRIID Institutional Biosafety Committee Meeting
Minutes of November 5, 2004 Meeting

Those in attendance:
Seven members in attendance

The meeting came to order at 1:00 in the Virology Conference Room

Member inquired about committee members from Diagnostic Services and Aerobiology divisions. Chair stated that a new member will have to be nominated by DSD Chief. Chairman stated that he would also attempt to recruit two additional committee members from outside the institute to fill out the roster of the IBC.

No new registrations were submitted for review.

A lengthy discussion focused on the containment requirements for cDNA clones of several viral agents which are restricted to BSL-4 containment. One member and several other groups at USAMRIID are interesting in using full length cDNA clones of filoviruses, henipaviruses and some bunyaviruses to study aspects of virulence and pathogenesis. He explained that, in contrast to viruses such as alphaviruses and flaviviruses, virus cannot be rescued from these clones by introducing genomic RNA into appropriate cell lines. Instead, several accessory plasmids encoding various viral gene products are also required in order to induce the cloned sequences to produce virus. NIH guidelines have put forth a "two thirds rule" that requires that clones containing the equivalent of a full viral genome are also to be kept under BSL-4 containment also.

It is policy in other laboratories, because the RNA derived from full length clones of the viruses mentioned above is not infectious, that the clones are manipulated at lower containment levels. In order to adhere to the spirit of the NIH guidelines, Chairman is hoping to get a consensus opinion from the committee that USAMRIID also follow these procedures. A failure to do so would put researchers here at a distinct disadvantage to other laboratories operating under much less stringent containment conditions.

It was suggested that additional input regarding this discussion be obtained from other laboratory facilities.

The meeting was adjourned at approximately 2:15.

USAMRIID Institutional Biosafety Committee

Minutes of Meeting of July 8, 2005.

Members in attendance:
Eight members were in attendance

The meeting was called to order at 11:00 in the Virology conference room.

Registration Document Review
Generation of a B. anthracis Ames-like vaccine strain by tranduction of pXO2 into a Sterne-like, toxin-deficient strain

A plasmid containing numerous point mutations in genes encoding the B. anthracis lethal and edema factors will be introduced into a non-toxigenic Sterne strain of B. anthracis. The aim is to generte a derivative of the Sterne strain producing immunologically important determinants of the B. anthracis toxins while avoiding the toxic properties of the wt toxin.

It was emphasized that this effort is intended to allow greater characterization of the immunological determinants of B. anthracis toxin. The derivative strain will be attenuated due to the lack of active toxin.

The committee felt that the document should be modified with a brief lay explanation of the goals and the appropriate NIH guidelines governing this effort should be cited.

It was moved by member and seconded by member that the document be provisionally accepted, pending the two changes indicated above..

Transposon mutagenesis system for studies with B. anthracis. Using transposon mutagenesis, the surface antigens of B. anthracis spores recognized by monoclonal antibodies will be disrupted. Kanamycin will be the antibiotic selection marker and is deemed suitable as it is a non-clinically relevant drug for treatment of B. anthracis.

Following discussion with Principal Investigator, it was recommended that the document be modified with a clearer statement of the end goal and a statement should be added emphasizing that this is not a direct effort to modify virulence of B. anthracis.

It was moved and seconded that the document be provisionally accepted, pending the two changes indicted above.

Reverse genetics system for Ebola virus.

A single cDNA clone representing the genome of Ebola virus will be produced for the purpose of manipulating the viral genome. All procedures under which virus might be produced will be carried out under BSL-4 conditions as outlined under the NIH guidelines.

Discussion focused on the requirements for containment of the plasmid and minimizing the possibility of accidental generation of live virus. It was agreed that the two-thirds rule applies to these efforts such that manipulation of less than two thirds of the viral genome in an active form may take place at BSL-3 conditions. Extensive dicussions of the replication cycle of negative stranded virus, such as Ebola, took place. The committee agreed that the possibility of generating Ebola virus from a cloned cDNA of the entire Ebola genome harbored in E. coli was negligible. Efforts involved in manipulating more than two-thirds of the viral genome will be carried out only under BSL-4 conditions.

The committee recommended a clearer emphasis that no attempts will be made to modify the virulence of the virus and that a clearer statement is needed outline the reasons for doing these experiments.

Because the committee chair is the lead investigator on this effort, it was deemed appropriate that one member other than registrant review the modified registration document prior to its final acceptance.

It was moved and seconded that the document be provisionally accepted, pending the two changes indicted above.

Other Business

Chair asked for suggestions for the identification of additional outside members to fill out the IBC quorum. Several suggestions were made and will be pursued by chairmanr. The members will be periodically consulted as the process continues.

During the course of a recent CDC inspection, a request was made for copies of the letters of appointment for each committee member. No such letters were readily available. Member was asked if he could approach the commander's office to see that such letters could be made available. Chair asked if they should be posted on the IBC intraweb site. No decision was made.

Chair reported that a letter was recently received from the Office of Biotechnology Activities regarding a request from information from the Sunshine Project for information of the activities of the USAMRIID IBC. A reply to the letter was prepared and submitted and subsequently forwarded to the OBA refuting the claims of the Sunshine Project.

USAMRIID IBC website is only available on the USAMRIID intranet. Chairman asked if there was any way it could be made available on an open website. This would require funding not currently available. A consensus opinion was that outside individuals could contact the committee if specific requests for information are made from non-USAMRIID individuals or agencies.

The bottom line to this correspondence is that the Chairman and committee need to rigorously adhere to the NIH IBC guidelines in order to ensure timely compliance with those guidelines. This will undoubtedly result in increased communication among the members of the committee as well as stepped up efforts to ensure that all members of the USAMRIID community meet the requirements of the OBA, NIH and IBC guidelines

Member has inquired about the appointment of alternates for each of the committee members to fill in when the primary member in unavailable for consultation or meeting attendance. Chair will pursue this and provide the members with additional information.

Chairman asked about an appropriate method for long term storage for IBC documents, registration forms, etc. Member mentioned that long term archives are maintained by the Med Division and that an accommodation might be made for storage of IBC documents. Chair will pursue this with Med Division.

During the discussion of the registration documents, it was pointed out that there is a requirement for a better definition of a "foreign protein". This was brought up in the context of whether or not folowing in vitro genetic modification of a gene for a protein from, for example, B. anthracis, is considered a foreign protein if the gene is then introduced back into B. anthracis. Member indicated that he felt that this should be defined as a foregin protein. No motion was made, but this will be followed up as an item for the agenda of the next IBC meeting.

It was also agreed that the registration documents should be modified for the inclusion of a section for a layman's explanation of the method and goals of each registered project.

The meeting was adjourned at 12:40

With revisions of Member

USAMRIID Institutional Biosafety Committee Meeting April 25, 2006
Virology conference Room, 2:00 p.m.

Attending members
Eight members in attendance

Chair asked for a consensus that meetings be recorded for ease in preparing minutes and all members consented. Chair stated that the minutes of the the meeting last Fall were lost due to a computer crash that occurred during January of this year.

A discussion commenced regarding the posting of meeting minutes on the IBC windown of the USAMRIID website. Member pointed out that IBC meeting minutes are FOIable and member pointed out that since the meetings are technically open to the public, the posted minutes should be sufficiently detailed to convey the activities of the meeting but abbreviated sufficiently to protect any potentially proprietary information. Memberpoiinted out that privacy and security concerns allow for appropriate redaction of documents made public under FOIA or otherwise. Member suggested that research plans and registration documents should be include a title designed specifically for release and a more technical title to impart information for scientific considerations.
(Chair has made suggested changes to the RIID registration document available on the website).

The next topic was regarding the IBC review of recombinant VSV vectors expressing surface glycoproteins of viral hemmorhagic fevers. Concern has been expressed by others that determining the virulence of such viruses in mice may not be relevant to their properties in humans. Member supported that viewpoint and suggested that such viruses should be tested in primates before downgrading to lower containment levels. Member indicated that the lack of IBC registration prior to their use should be sufficient grounds to prevent their use until IBC compliance is established. He also pointed out that such noncompliance might be sufficient grounds for termination at NCI-Frederick. In order to accommodate multiple experiments with a single vector system, the registration can be written to encompass the multiple uses in a single document. It was agreed that these experiments should be covered, even retrospectively, to ensure compliance with the NIH guidelines. All such recombinant viruses should be registered in the RIID agent registry. It was agreed that the requirements for IBC registry should be in the form of a check off box on all MTA's, CRDA, LACUC forms and research plans.

First registration document for consideration:
"Molecular and genetic determination of *Bacillus anthracis* factors required for virulence"
Transposon insertion mutagenesis to identify virulence factors of B. anthracis. Two members expressed concern regarding the use of CAM since it is used to treat B.

anthracis meningitis. Member moved that the document be provisionally approved provided the questions regarding CAM can be resolved. The motion was passed on a unanimous vote.
(Chairman's note: Subsequent email and in person conversations resolved this question in that Physician indicated that CAM is no longer the primary treatment for BA meningitis. Additional scrutiny followed in order to ensure compliance with 42 CFR 73.13. Member asked aboout the wisdom of sending this proposal to the CDC to ask guidance. Physician again stressed the fact that no clinically relevant antibiotics were to be used in these experiments. Although most members expressed concern regarding multiple-resistance in B. anthracis, a consensus was reached……..

Second registration document for consideration
LcrV Allelic Exchange in *Yersinia pestis*.
Member explained the basics of allelic exchange for the committee. She pointed out that ampicillin is not a clinically relevant antibiotic for *Y. pestis* and the experiments with the *Y. pestis* strains will be carried out under BSL-3 containment. The plasmid constructions are carried out at BSL-2 and do not involve Y. pestis. Member moved that the protocol be approved without modification. Approved unanimously.

Nominations for committee members will be sought from DSD and aerobiology. An additional member from Virology will be sought. Physician suggested that an infectious disease physician might be a good addition to the committee. Chair will seek the nominations from the appropriate division chief.

Physician suggested that in the future, members should be allowed to recuse themselves from participation in those matters for which a conflict of interest might be a matter. The committee members agreed.

Member also suggested setting up an IBC website and had a poster that outlines the requirements for IBC registration and the NIH guidelines. A place to mount it will looked for.
(Chairman's note:The safety office has been contacted regarding putting an article regarding the IBC into the monthly Safety Gram that is visible all over RIID. Member also suggested preparing something for the RIID newsletter. I'll be contacting you all for editorial input toward those materials).

A brief discussion followed regarding the requirement for an IBC review for clinical trials being conducted utilizing recombinant materials from USAMRIID.
(Chairman's note: I believe that such reviews are required to be undertaken at the clinical site as indicated in the NIH guidelines. Section III-C-1. Experiments Involving the Deliberate Transfer of Recombinant DNA, or DNA or RNA Derived from Recombinant DNA, into One or More Human Research Participants.

The meeting adjourned at 3:45

Institutional Biosafety Committee Minutes -Tuesday August 8, 2006

Meeting Attended by:
Nine members in attendance

Meeting began at 2:30 in Virology Conference Room

Since the April meeting, numerous documents were submitted for review and were assisgned designations by the chairman. The chairman had assumed that the reviews could be open to all interested parties. However, the meeting began with an agreement among the committee members that each review should be conducted confidentially among the reviewers and investigator only rather than in open forum.

(Chairman's Note: While the IBC is to be conducted as an open forum, this decision was made because the large number of investigators defending registration documents caused an overcrowding of the conference room.).

Registration Review

1. Gene knockout and infectivity studies of YscN mutants of Y. pestis
2. Design and purification from E. coli of a next generation soluble vaccine effective against Y. pestis
3. Cloning and recombinant expression of Y. pestis proteins in E. coli

The concern over selectable antiobiotic resistance markers introduced into Select agents was brought up and each of the documents was shown to avoid introduction of inappropriate selectable antiobiotic resistance markers into Y. pestis.

Several revisions for each document were submitted and the committee voted that the documents be accepted pending receipt of these changes.

4. Replacement of plasmid-encoded genes of Y. pestis with inactivated derivatives of the encoded antigens to characterize their virulence and potential as new vaccine candidates.

The PI emphasized that the experiments have been designed to avoid introduction of resistance to clinically relevant antibiotics into Y. pestis.

5. Genetic footprinting of alphaviruses and Filoviruses. A brief description of the goals and location of the procedures was made the co-investigator on the document.

A request for citation of the relevant NIH guidelines for use of the agents was made.

The committee voted that the submission be accepted pending receipt of the revisions.

6 . WHO and CDC registered USAMRIID collection of variola DNA genes at USAMRIID.

This document was a list of a collection of Variola genes obtained for use at USAMRIID and their existence here at USAMRIID has been registered with the appropriate authorities.

Member had requested prior to the meeting, that a list of the virus strains from which the genes were derived should be supplied to the committee and included in the document. The committee also asked that a description be provided of the planned uses for the genes. That request had been forwarded to the PI on July 4, but no reply had been received.

A lengthy discussion was led by Member suggesting that the genes should be placed into the AIMS system in order to ensure that records of their location, disposition and appropriate supervision over these genes is maintained..

Chair indicated he would follow up with the PI.

(Chairman's Note: The PI has informed me that the location of all of the variola genes is tracked by the Poxvirus Laboratory at the CDC. He has not entered them into the AIMS database).

7. Vesicular Stomatitis Virus as a Vector for Expression of Heterologous Genes.

This is an expression system that was brought in under an MTA from Yale University and has been described widely in the literature. No problems were anticipated with this system and any virus obtained will be handled in in the same containment as required for the agents from which the heterologous genes are derived although the vector is commonly used under BSL-2.

A lengthy discussion yielded agreement that the component plasmids could be handled at lower containment levels as long as efforts are made to prevent the accidental rescue of virus. Due to the complexity of the system it was agreed that such an occurrence is extremely remote.

The document was accepted without further modification.

8. Reverse genetics system for Filoviruses.

This is an expanded document submitted to cover the system obtained from the University of Wisconsin and a similar system being developed here at RIID in the Viral Biology branch. The committee agreed that manipulation of the plasmids could be carried out at BSL-2 containment as long as all attempts to rescue the virus were carried out under BSL-4 containment only.

There was a reminder that the use of Vaccinia to provide the T7 polymerase during virus rescue requires that V-3 and V-4 be registered for vaccinia virus.

[Chairman's Note—it was subsequently determined that V-3 and V-4 are not currently registered for use of vaccinia virus. A plasmid expression system for T7 polymerase will be substituted for the recombinant vaccinia virus in these experiments.-October 15, 2006}

The document was accepted by unanimous vote.

9. Francisella tularensis cis complementation experiments

The discussion emphasized the thrust to compare the variations in metabolism between the available strains of F. tularensis that modify virulence.

The committee specifically addressed the need to be cognizant of the suitability of antibiotic resistance markers used in the experiments such that the manipulations avoid compromising susceptibility to clinically useful antibiotics.

The document was accepted without further modification.

10. Deletion of Yersinia pestis quorum sensing regulator genes. The document was introduced by the PI. The primary goal is to determine if quorum sensing systems in Y. pestis are involved in control of virulence. In their discussion, the author pointed out that only ampicillin and sucrose resistance will be used as selective markers.

The document was accepted without further modification.

11. Genetic Manipulation of Burkholderia pseudomallei and Burkholderia mallei. The PI is continuing his studies of the virulence mechanisms of B. mallei and B. pseudomallei using transposon mutagenesis and complementation analysis.
The amnoglycosides to be used as selectable markers include Kanamycin, Gentamicin, Strepomycin and Zeocin which are not clinically useful in treatment of Burkholderia infections. PI again empphasized that Burkholderia are naturally resistant to Kanamycin and the use of Kanamycin cassettes do not compromise potential therapeutics for Burkholderia infections. In compliance with regulations from the BSAT office, emphasis was repeated to the committee and the PI that <u>tetracycline is not to be used in any of these experiments.</u>
The PI agreed to submit a revised document.

In dealing with use of antibiotic resistance in select agents, it was suggested that a signature block be added to the registration document in which an infectious disease physician can indicate that concerns were addressed in the committee deliberations. This will be incorporated into the agenda for the next meeting for further clarification.

The meeting adjourned at 5:15.