MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2002-02

DATE: June 23, 2003

PRESENT: Lorraine Albritton, Rebecca Burger, John Coleman, Jim Gaut, John Kirkley, Linda Harris (Chair), Robert Ogg, Derek Persons, Allen Portner, Brian Robbins, Karen Slobod and Glen Ulett

ABSENT: Dr. Edwin Horwitz, Dr. Karen Slobod, Dr. Brian Robbins

GUESTS: Dr. Patricia Gordon

PRESENTER(S): Dr. Patricia Flynn, Dr. Richard Webby

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting started at 1:00 with Linda welcoming everyone.	
Minutes of last meeting	The minutes were e-mailed the Friday before this meeting. The approval of the minutes was deferred until everyone has had a chance to read them and then a voting memo will be sent within the next week.	Voting memo sent to the Committee within the next week.
Biological Safety Officer Report		
Biological projects approved April 16, 2003-June 23, 2003	Judy Edwards reported that since the last meeting of April 16, 2003, there were 15 projects approved, Nine projects were at Biosafety level 2, four at Biosafety level 1, and one exempt project that needed approval because of a grant. Nine projects were pending approval. Committee members were asked to send their voting memos or comments for Dr. Sorrentino's and Dr. Kidd's projects. She thanked the committee for getting other votes and comments back quickly.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Adverse events	Nothing to report	No follow up needed
Variance Report	Dr. Gaut reminded the committee that it was decided in the last meeting that the variances will come through Dr. Jim Knight's office and will only relate to the gene therapy protocols and stem cell processing. The new procedure has not begun but should start next month. There were a few variances received but they were not within the committee's purview.	No follow up needed
4 ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Cunningham	Mr. Coleman reported that the construction phase is done and they are now going through the commissioning validation of the facility. The goal is to have the facility in operation by September. Dr. Gaut has talked to Jim Knight about a facility tour in July.	
New Business		
AAALAC Inspection	The AAALAC inspection starts Wednesday, June 25, which has caused a rush review of several projects. The inspection will be heavily focused on BL2 facilities in the animal care center. There have been several walk throughs to make sure that they are ready for the inspection	
Presentations		
Presentation by Dr. Richard Webby for Project : O3A-110 – Influenza pandemic preparedness in Asia. O3A-136 – New Approaches to control influenza/Alternative Host Cell Systems in Influenza O3A-137- Pandemic influenza vaccines. Principal Investigator: Dr. Robert Webster.	Dr. Webster was out of the country and unable to present his project. Dr. Richard Webby filled in and presented these three projects. All three projects are similar in that they focus on producing influenza vaccines. The O3A-137 project focuses on the transition from the laboratory to GMP production. Project O3A-136 focuses on the laboratory testing of influenza vaccine. Project O3A-110 is a poultry infectious Bursal disease virus that will be brought in and tested. Dr. Webby gave a brief presentation. The influenza viruses that are mentioned in these studies are found in poultry species. The highly pathogenic influenzas come from the poultry species to humans. Dr. Webster's group has a considerable amount of experience with these viruses under biosafety level 3	

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	conditions. The pathogenicity of these viruses is determined in part, by the presence of basic amino acids at the cleavage site. For influenza to be effective, the hemagglutinin must be cleaved. A routine low pathogenic flu virus does not have these basic amino acids. Its replication is confined primarily to the respiratory and gastro-intestinal tracts. When these viruses pick up the basic amino acids, they can then start to replicate systemically. They can move into other organs in the body and cause mortality in poultry species. In early 2003, they are seeing human infection with these highly pathogenic viruses with two incidents having fatal outcomes. Projects O3A-136 and O3A-137 are to create vaccines to combat these highly pathogenic flu viruses. The normal human viruses do not have these basic amino acids and are not highly pathogenic. In the past, vaccines were made by growing the virus in eggs and isolating genetic reassortants. Antigenic proteins were used to make the vaccine. This virus was safety tested and grows to high titers in eggs. The goal was to prepare 6+2 reassortants utilizing six genes from the high growth A/PR/8/34 (H1N1) influenza virus plus the hemagglutinin (HA) and neuraminidase (NA) genes of the currently circulated strain. Such reassortant viruses have been made by conventional mixed infections and have supported the large-scale manufacture of vaccines prepared in the allantoic cavity of embryonated chicken eggs. Using conventional methods, both the high growth and circulating strains are injected into a single egg and reassortant progeny virus are produced that contain gene segments derived from both parental viruses. The resulting reassortants are screened and a specific 6+2 combination, which is the two major antigenic proteins from the circulating strain and the six from the high growth strain. However, this does not work with highly pathogenic influenzas. The major reason being is that these kill the embryonic chicken eggs. The standard procedures cannot be used for making these vaccines. It is also pathogenic for both human and poultry species. Vaccine strain development and vaccine production are difficult as they are only acceptable under appropriate biosafety conditions. There are few of these facilities available. The one facility that is available in Europe is not capable of	

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	producing enough vaccine. Reverse genetics technology can be used to eliminate the HA pathogenicity motif and produce a virus with properties that are suitable for large-scale manufacture. It is possible to develop non-pathogenic H5N1 viruses by reverse genetics, whereby the NA gene and modified HA gene of an H5N1 virus were reassorted with genes from the high growth strain. By cloning each of the individual gene sequence of flu and transfecting into various cell types, a specific reassorted virus can be custom made. This is achieved by combining the six genes from PR8 high growth strain with the two that encode these surface antigenic proteins. The DNA that encodes the basic amino acids in the HA that are responsible for high pathogeneticity can be first removed. The plasmids encoding these genes are transfected into vero cells. What is developed is a 6+2 virus that is attenuated and does not have basic amino acids regimen. It can now grow in eggs and be handled under biosafety level 2 conditions. There are several plasmid based reverse genetics systems available for influenza viruses. Any of which would be suitable for the generation of influenza virus vaccine strains. Both the 8- and 12-plasmid reverse genetics systems have previously been shown to be effective of rescuing H5N1 and HA and NA genes in a background of A/PR/8/34 using 293T and MDCK cells or 293T cells alone. Dr. Webby referred to the World Health Organization document that was distributed with the projects regarding safety testing. This document gives guidelines on what should be done before conditions are moved from biosafety level 3 to biosafety level 2. This covers the new process using reverse genetics and the animal testing of these vaccines before distribution of these vaccines. Due to safety concerns, these reassorted viruses are treated as BL3 agents as with all the highly pathogenic flu viruses. Standard biosafety level 3 procedures are used until they reach the criteria as defined by the World Health Organization guidelines. The World Health Organization will authorize release of candidate vaccine viruses (passaged in eggs) to qualified laboratories for preparation of reference reagents and vaccines after satisfactory pathogenicity	

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	test in chickens and ferrets; and validation through antigenic testing and analysis of sequencing data showing that amino acids have been removed. Production will be in GMP facilities instead of BL3 facilities. At this time Dr. Webby does not know how much will be produced. These viruses have been made by removing these basic amino acids and making the 6+2 reassortant attenuated. All influenza vaccines made under BL3 conditions in the GMP and transferred to BL3+ space in the IRC for testing. They will not be released from the GMP facility until they have undergone all the safety testing as outlined the WHO guidelines. There was a question asked as to if all product made in the GMP comes back to the IRC. Dr. Webby stated that it comes back to the animal facility. It was asked if the World Health Organization is asking that the reassortant be under BL3. Dr. Webby explained that outcomes have shown that it is attenuated after going through the procedure. Dr. Coleman clarified that the initial viral batch will be made under BL3 and if the vaccine were made later, it would be under BL2 after it is animal tested. Dr. Webby agreed with this and added that it is made under BL3 conditions because they do not know its pathogenicity until it is tested and then it is moved down to BL2. A member asked if these BL3 facilities were built into the design of the new GMP facility. Mr. Coleman replied yes and added that there are two BL3+ suites and that they can do bag in, bag out HEPA –filter changes on the exhaust air if needed. It was asked if the plasmids will be derived in the GMP facility. Dr. Webby said that the plasmid would be derived in the laboratory until they are mixed together in the cell and the attenuation will take place before they have infectious virus. When the virus is attenuated, will it then be used as a vaccine? Dr. Webby replied that what is being produced here is a seed not a vaccine. The product will be dispersed to vaccine manufacturers. A member asked if the viral seed lot is infectious. Dr. Webby said yes but it is	

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	not pathogenic. Dr. Webby stated that in the O3A-110 project it will ask how these pathogenic flu viruses are derived. What is known is generally low pathogenic precursors of these viruses circulate in duck populations and somehow these viruses transfer to poultry species (chickens and wild turkeys). In these hosts, they obtain these basic amino acids. The virus is not born pathogenic, it develops after passage through these domestic poultry species. The project involves finding out if immunosuppression by pathogens plays a role in allowing these influenza viruses to evolve into highly pathogenic viruses. One virus in poultry that is different in this project is the involvement of infectious bursal disease virus. IDBV infects and is confined to chickens and cannot replicate in humans. It is a viral infection of young chickens that involves immuno suppression of these birds by depleting B cells. This project looks at the effects of IBDV infection on subsequent infection with flu. It asks if this leads to increased accessibility to flu viruses. Does this lead to a selection of more pathogenic virus? The experimental design of O3A-110 will be to infect young birds with or without IBDV with low path flu infection. After a period of time, it will be determined if the bird carries the virus. Each of the agents in this project is Biosafety level 2 agents or less. Because of what is being done, all procedures will be carried out under BL3+ conditions. One hypothesis involves these viruses becoming pathogenic variants. It was asked if there was a plan to develop them and if it becomes non-pathogenic in the animal studies would they work with them under BL2 conditions? A member also asked that after the chickens are infected with IBDV, will any of the serum samples be taken out of the lab. Dr. Webby said that all tests will be done in the laboratory. However, there are procedures in place for carrying material out of the laboratory. A member asked if security in these areas is by card reader and if everyone is fully trained in BL3 procedures. Dr. Webby replied yes and there will be a limited number of people allowed in the laboratory.	

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	A member asked if those working on the project have contact with patients. Dr. Webby said that no one involved in the project will have patient contact or contact with other animals. Dr. Webby left the room. Dr. Harris asked if there any questions or comments regarding Dr. Webster's projects. It was asked that when the projects are ready to go to GMP for production that the IBC is notified. Dr. Harris explained that a Biological Project form will need to be completed and an IBC approval letter issued for the GIMP core laboratory that will be handling it before the production is allowed. A member needed clarification on discrepancies found in O3A-110 and O3A-137. They seem to be using the same influenza strains. One of the forms says that it is a BL3 select agent the other one does not. Are these different strains? It also says on one form that they are going to store serum samples, the other form does not ,yet they are working with the same BL3 agent. In part, 5 of O3A-110 project form it lists the BL3 agents. There seems to be a discrepancy of what is actually being used. Dr. Gaut will talk to Dr. Webster to clarify what influenza strains are being used. There was a motion to approve the projects pending clarifications. The projects were approved pending clarifications.	
Presentation by Dr. Patricia Flynn, Principal Investigator O2C-134 – Phase I study of Recombinant oral BAH-2 cholera Vaccines in Healthy Adults.	Dr. Flynn presented her project involving cholera. This is an extension of a project approved by the IBC in 1999 started by Dr. Claudia Hase who is not longer with this institution. This is before the new process was in place and Dr. Flynn was asked to re-present this information. The long-range goals of the project are to bring some of these cholera vaccine strains into clinical trials. They have now drafted a clinical trial that has been approved by the CPSRMC and they are in the process of submitting an IND to the FDA by the end of this year. Cholera is a infectious disease that causes significant serious world health	

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	problems that has pandemic and epidemic cycles. It mostly affects children and the elderly in developing countries. This disease causes severe diarrhea, which can rapidly dehydrate individuals. If they are not treated with fluid rehydration or with antibiotics, it can be fatal particularly with young children within 24 hours. This disease is transmitted via contaminated food and/or water by a fecal oral route. The virulence of the bacterium can be explained by two factors: pili, which mediate adherence of the bacterium to the mucosal cells; and extoxin, which acts on mucosal cells to produce severe diarrhea. Because this is such a devastating disease, there have been ongoing efforts for the past 30 years to develop a vaccine. The initial vaccines that were tried were largely abandoned because they induced only weak or short-term immunity. The limited successes of these vaccines have attributed to the inability to induce local intestinal or mucosal immune response, which appears to be a critical feature of natural convalescence from cholera leading to long lasting immunity. Two different types of oral vaccines are being actively pursued; inactivated vaccines and live attenuated vaccines. In the killed oral vaccines, they found that it has short-lasting immunity. It also tends to be less effective in children and patients who have blood type O. It also has a very complex manufacturing process. The attenuated live vaccines have all been facilitated by recombinant genetic technology. The first step done in all of these cholera vaccine trials is to delete the gene for producing the cholera enterotoxin. In these trials, they were able to demonstrate by oral administration of the attenuated strain a four-fold immune response. Recipients of the experimental vaccine had significant gastrointestinal and systemic side effects, termed "reactogenicity". The conclusion from this was that even though the toxin is the major virulence factor there may also be other factors other than enterotoxin. Adherence of the bacteria itself can induce secretions and diarrhea. In order to use the vaccine where it can most benefit to humans, which is in the developing countries, you cannot have the vaccine causing even these mild symptoms because the prevention could be almost worst than the disease.	

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	In the mid 1990s, David Taylor and a group of investigators, headed by Dr. John Mekalanos at Harvard studied these attenuated vaccines that were associated with reactogenicity. They discovered a variant Peru-14, which was a strain developed in Peru that was non-modal. When this strain was tested in humans, they found that it retained its immunogencity but was non-reactigenic. They tested it into clinical trials, where they came back and challenged the patient with live virulent cholera after the immunization. They found that there was some protection. This is a stable gene and has completed the phase II trial. What Dr. Hase has done was to look more specifically at motility and deleted genes associated with motility in these strains. A flagellum is present in one investigational strain and the parent; and absent in the other investigational strain. In an effort to reduce reactogenicity of the strains, they have also introduced the HAP mutation. The series of mutant strains she created are organisms that have a single mutation. The first is the lost of the flagella and since it does not have this it does not have motility. Since the motility is gone the organism cannot move but the flagella is there can serve as an antigen. BAH2, FliG, Hap, recA, ctxB is named Bah 18 SH. It shows a loss of flagella and motility and hemaggutinin/protease. Bah2, moX, hap, recA, ctxB is named Bah 19 SJ. It shows a lost of Hap and motility but intact flagella. Bah 2, recA, ctxB is named Bah 21 SJ or Bah 3. All have had the toxin removed. The CTX is taken out, and the three genes of interests are recA, moX and FliG. The gene responsible for the recombinant is also taken out along with the toxin gene to prevent recombination. Cytotoxin B is reinserted into recA, which also helps to prevent recombination. Dr. Flynn stated that what they hoped to do in this clinical trial is to learn about the immunogenicity and the reactigenicity and look at one that will be brought into a larger phase II trial. They propose to look at the two double mutants in the parent strain. The measure of immunogenicity will be examined by serologic assessment of the vibriocidal antibody titer. Reactogenicity will be examined by clinical symptoms observed or reported by the study subject. They plan to study cohorts of patients, four at a time. The patients will be blinded to the vaccine that they received. The reason for this is to standardize	

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	the product it has to be made fresh that it is live bacteria vaccine. Rather than have three or four different vaccines made for each of the patients, when they start the study group of patients all will get the same vaccine. The study requires that they are hospitalized four eight days. They will receive 10^6 or 10^8 organisms mixed in 200ml of CeraVax® buffer. They have serology measured on 0, 7, 14, 21, 28 days. The reason for the hospitalization is so they can be monitored daily for local gastrointestinal symptoms and can receive immediate therapy. All patients are treated with antibiotics after they leave the hospital. The protocol will be studied in-groups of four patients. Each of the vaccines will have a random order in one group of four studied. If the vaccine proves reactigenic after four patients they will stop. If the vaccine does not prove reactigenic, they will repeat the cohort. The parent strain has been evaluated in another clinical trial. They do expect there to be moderate side effects mainly abdominal cramps and nausea. They anticipate studying eight patients and they will meet their reactigeneticity criteria on the parent only study for patients. It was asked where this study would take place. Dr. Flynn said that the inpatient part of this study will take place at UT Bowld in the Clinical Research Center. The outpatient screening and follow up visits will be conducted at St. Jude. A Committee member asked if they have diarrhea are they secreting bacteria. She replied that they are secreting bacteria but it is attenuated. In the previous trials, they have looked at the genetic composition of cholera that they secrete and found it to be recombinant. The subjects will be in isolation at UT Bowld. They expect those patients receiving the parent strain to get diarrhea but they do not expect the other groups to get diarrhea. It was asked why she said that there was no treatment of sewage. Dr. Flynn stated that the sewage is already chemically treated and it should kill the bacteria. A Committee member asked if it was necessary to evaluate the parent strain. Dr. Flynn said that it is being done as a comparison.If the parent strain is not analyzed it will not be scientifically credible to say that the reason why the patients did not have symptoms was because of the deletions. The worst	

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	symptoms reported were 300mls of diarrhea in a day. It was asked that since she is going to collect bowel samples has she checked with the City of Memphis or Shelby County Department of Health that disposal in the regular sewage is appropriate. Dr. Flynn said that stool samples will be inspected by personnel from the CRC (Clinical Research Center) who will characterize the stool as normal, soft or watery. These samples (a swab) will be obtained from the patients daily and disposed of in the toilet. Dr. Kirkley was asked to check with the City and county officials regarding this issue. Dr. Flynn added that the final strains of the virus were sent to Walter Reed and they have cell banks here in the freezer. They plan to go back and characterize the organism from that stock. This will probably be done in the IRC and the vaccine production in the GMP. Is there a chance for genetic variation when the vaccine is done in batches? Dr. Flynn said that there is a chance of variance in the number of organisms. They have a procedure on how to get a certain amount of organisms in a buffer. Other clinical trials have given 10^4 or 10^8 organisms. They have not looked at the variance but plan to before they go farther with the clinical trial. Because of the symptoms, they have decided to give 10^6 of the parent strain and 10^8 of the mutants, which they think will be less toxic. The investigator and the patient will be blinded. The biostatiscian will provide a random order for the first three cohorts to the GMP. A member said that in the informed consent it states that they will be given antibiotics when they are discharged from the hospital. Is there a reason why they cannot be given antibiotics the day before they discharge? This thinking in terms of protecting the public, since you do not know the potential of these attenuated organisms in that they may replicate more slowly. Dr. Flynn explained that the timeframe was set so they would have seven days of exposure to allow the patients to have time to develop the immunogenic response and balance that with discharging them from the hospital. Another concern expressed by a member was even in the general population, when people are sick, they have poor compliance with antibiotics. If you send	

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	them home with the medication they may start but not take a full 48 hours of antibiotics. Dr. Flynn stated that when other studies were reviewed they looked at shedding and by seven days, most people had finishing shedding. She said that they could build in other safety features where the study staff calls the subjects to make sure they are taking their antibiotics. A member asked why a vaccine is currently not available in this country. Dr. Flynn explained that the one that is currently available has very short immunity. She did not know exactly why that vaccine is not available in this country, but it may be because no one has made an effort of sending through the paperwork to be licensed. A member asked that a statement be added to the protocol that states that officials of the City of Memphis and County officials have been consulted and accept the protocol is safe. Dr. Kirkley will talk to city and county officials requiring this request. There was a motion to approve the protocol pending changes to be made. The project was approved pending changes in the protocol.	
Change in IBC Members	Dr. Harris mentioned that the new committee should be in place by July and she is due to rotate off the committee. There will be a training meeting in July for new members.	
Adjournment	With no further topics of discussion, the Chair then closed the Committee meeting and thanked everyone for their attendance.	

The meeting was adjourned at 2:15 p.m.

Judy Edwards, Biological Safety Coordinator, recorded the minutes.

Linda Harris, Ph.D.
Institutional Biosafety Committee Chair

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2003-03

DATE: July 29, 2003

PRESENT: Elisabeth Adderson, Rebecca Burger, Martha Brackin, Cheryl Chanaud, John Coleman, Jim Gaut, Derek Persons, (Chair), Allen Portner, Brian Robbins, Glen Ulett, Edwin Horwitz, and Richard Webby

ABSENT: Lorraine Albritton, Brian Robbins, John Kirkley, John Gray

GUESTS: None

PRESENTER(S): Dr. Gene MacDonald

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	Meeting started at 11:35 with Dr. Persons welcoming everyone to the meeting. This was the first meeting with the new committee so Dr. Persons asked everyone introduce themselves.	None needed.
Orientation	Dr. Persons explained the charge of Committee. He said that the IBC is responsible for reviewing and approving research that involves pathogenic organisms and their use *in vitro* studies and laboratory animals. In addition, the Committee is also responsible for reviewing all human gene therapy trials and the use of investigational biologicals in humans. According to IBC policy and procedures, the Committee will meet at least once a quarter. The Committee physically meets to review biosafety level 3 and all projects involving human subjects. Review and voting are done electronically for other projects. The two references used in assisting members in reviewing protocols are the rDNA NIH guidelines and Biosafety in Microbiological and Biomedical Laboratories (BMBL)	None needed

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	handbook published by the U.S. Department of Health and Human Services. Dr. Gaut gave a presentation reviewing the history of the IBC and gave background information that can be used in reviewing projects. He referred to the compact disc that was sent to Committee members with information that will assist them in reviewing projects. He explained that institutional biosafety committees were established 20 to 25 years ago with the idea of reviewing hazardous research being conducted by institutions. The guidelines originated from the Asilomar Conference in 1972. Gene transfer studies were later added to the IBC's purview. He said that there have been recent changes made to role of our IBC as suggested by the OHRP. These changes focus on increased emphasis on the role of the IBC to commensurate more with the IRB. The IBC's institutional role is to evaluate containment levels and the facilities offered for different projects. In addition, the IBC should improve and expand on institutional policies and procedures. The IBC has responsibility to the principal investigators to review their projects, set the containment level and provide approval. Dr. Gaut explained that the IBCs provide local oversight to implement and act on NIH guidelines and Recombinant DNA Advisory Committee (RAC) at the national level. These groups communicate through conferences and e-mails. Guidelines are implemented through the local IBC. The biosafety level guidelines are obtained from the BMBL manual. Dr. Gaut explained the biosafety levels as described in the BMBL see if they have become exposed during the course of research and provide to immunizations. He explained that biosafety level three is the highest level at this institution. Dr. Gaut summarized how to use this information in evaluation projects.	

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	Risk assessment analysis involves minimizing the personnel and patient risk, and containment of any agent in use at this institution. He explained that a biosafety level is a set of circumstances and practices that we can use to minimize the risk that is assigned to a risk group. He emphasized the points to consider in the evaluation process such as does the risk change if it is manipulated genetically. In addition, what are the factors that could influence the risk of the experiment? Are the proper containment levels being used and what are the containment levels for the risk? What is the vector and gene involved in any DNA review? What is the vector composition and promoters, the viral vector envelope, and the protein used for packaging? Are the genes coding for toxins or for an agent that could cause problems in other organisms? The reviewer should show how well trained the personnel on the project. When evaluating potential hazards of DNA work the reviewer should consider such things as the vector backbone, whether it is a toxin or encodes an ocogene. He explained that if the evaluation involves a select agent, there is a new level of responsibility that has been placed on the committee. After the incident on September 11, 2001, select agents have to be registered with the CDC or USDA if they are listed as potential weapons of mass destruction. He referred to the information he obtained while attending a conference on IBCs in San Diego, California in which results of a survey given by the OBA was presented. Dr. Gaut mentioned the amendment up for review involving the use of VEE without vaccination. This goes against the recommendation of the BMBL but the vaccine for VEE is no longer available. He said that this project would be difficult to conduct without finding alternatives to using	

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	the vaccine. This is a departure from what the BMBL recommends so it is important that everyone understand their role in order to make a recommendation regarding to this project. Dr. Gaut concluded his presentation reiterating if anyone have any questions regarding IBC activities to contact him or Judy Edwards.	
Committee Reports – Due to time constraints only orientation and presentation of the amendments were conducted.		
Presentations		
Amendments: O2A-045 – Arbovirus Pathogenesis and Immunity O3A-031 – The Role of Immune Cells in Alphavirus Pathogenesis. Principal Investigator: Dr. Gene MacDonald	Dr. Gene MacDonald was present to explain amendments submitted on IBC approved projects O2A-045 and O3A-031. Project O3A-031 involves Venezuelan Equine Encephalitis and O2A-045 involves the use of Dengue Virus. A segment of the Dengue research involves work in the BL3 lab, which involves any animal work. There are two changes, outlined in the letter she submitted. The first amendment involves O3A-031. In the previous approval it was required that everyone entering the BL3 Lab be vaccinated against VEE and they demonstrate effective antibody titers. This project was approved prior to the attacks on September 11, 2001, and now there are restrictions to that vaccine because VEE is considered a bio-warfare agent. The vaccine is no longer accessible to the public and has been restricted to only military personnel. This is due to terrorist concerns and because it was in phase III clinical trials and there is a limited amount of vaccine available. Dr. MacDonald has not been able to get access to this vaccine. She has been vaccinated and has an effective antibody titer. None of her	

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	personnel have been vaccinated and cannot enter the BL3 laboratory. Dr. MacDonald proposed that the IBC requirement of all personnel being vaccinated be amended to use the PAPR (Belt-Mounted Powered Air Purifying Respirators) as a substitute. These respirators are designed to protect against aerosol pathogens with a HEPA filter. She said that they are currently approved for use in Dr. Webster's BL3 lab. They are also approved by the CDC and are recommended in the CDC's infection control guidelines for transmission-based precautions as an alternative to the N95 mask. This is also recommended for infection control in clinical settings for use in respiratory infection control. The PAPR would be used in lieu of vaccination. She said that under these conditions, the biosafety protocol for work with the virus in BL3 labs will not change and all the standards approved for biosafety protocols will stay in place. The greatest risk of contamination by VEE for staff is aerosol. A secondary risk is inoculation (breaking the skin barrier). She said that these devices would protect against aerosols and they would continue to work with the virus using standard protocols in the biosafety cabinets. However, because the PAPR does not protect against needle sticks, personnel using these devices, who are not vaccinated will not be able to work with any protocols that involve injection, handling of infected mice, or anything that could risk a skin barrier exposure. In response to a question, Dr. MacDonald clarified that she will be the only one conducting animal work. A Committee member asked that since those working with select agents would be inspected, how this affected this protocol. Dr. Gaut explained that the inspection involves security and safety and they would recognize that this change is necessary. He has spoken with Dr. Nesby O'Dell, then the Chief of External Activities Programs in the Office of Health and Safety at the CDC. She explained to Dr. Gaut that the BMBL guidelines should be used as a guideline but it is not mandatory that they be	

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	followed. He said that if the practices are reasonable, and there are no alternatives, then there should be no problems. In addition, with the conditions that Dr. MacDonald has offered, in terms of not involving work with sharps, and the PAPR represents the same level of protection from aerosols that a vaccination provides if it should work. He said that in terms of select agent inspections, as long as the personnel in the lab are registered and a background check has been conducted it should be acceptable. In response to questions, Dr. MacDonald said that the virus is spread by mosquitoes. It was also asked what is the incubation period for an individual infected by aerosol and what are the chances that the individual would go home infected, is bit by a mosquito and the mosquito picks up the virus. Dr. MacDonald said that the incubation period is approximately one week and she did not think that statistical data is available as to the other scenario. She added that if someone follows the guidelines, the PAPR should be enough. However, she did not know what level of protection they have against aerosols. The N5 is based on 95% protection; the PAPR is supposed to have a higher level of protection because they are HEPA filtered. She said that there is always a possibility that someone does not use it correctly. That is not the only level of protection offered through the established guidelines and that the major level of protection against aerosols is that the virus is worked on in a biosafety cabinet. No virus is ever worked with on the bench. Dr. MacDonald said that the highest risk of aerosols comes from centrifugation. Errors or breakdown of the centrifuge is historically where the largest number of infections had occurred before the vaccine was used. The current protocol requires that everything be centrifuged in a closed container. Before the chamber is opened, it is vented for 15 minutes through a HEPA-filtered vacuum to exchange room air with the chamber air. When the centrifuge is opened, the container that has been centrifuged is taken to the biosafety cabinet and opened. That level of	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	protection should protect a naïve individual against aerosols. If this was not sufficient in the past, they had the vaccine. However, since the vaccine is not available she suggests the use of the respirator. She explained that if someone sticks themselves, they report immediately to Occupational Health. The occupational health nurse will take over monitoring their condition. She said that natural infection is only one percent lethal. A Committee member asked what is the probability of aerosol exposure. Dr. MacDonald did not have statistics, but said that it depended on the load and how much is inhaled as well as host factors. She added that the BL3 is designed to have very rapid turnover of air, therefore, the aerosol does not stay in the space for long. If a spill occurs, there is a protocol for immediate evacuation of the space. A Committee member asked what is the size of the virus. Dr. MacDonald replied that the full-length virus is 11 kilobases, or 50 nanometers. Dr. Gaut explained the size of the virus that can be caught is within the HEPA filter limits. It was asked if the facemasks were recommended and if other labs were working on this virus. Dr. MacDonald explained that facemasks are not recommended but other labs are working with this virus using the PAPR in lieu of vaccine. Dr. Scott Weaver's lab, which is one of the larger VEE labs, have been using respirators. Alpha Vax is another lab that develops VEE based vaccine vectors. Dr. Gaut added that he had spoken to Dr. Weaver and he indicated that those who had the vaccine were having a difficult time with getting a titer. Therefore, even if the vaccine was available it may not be the titer needed. Dr. Gaut said that when the BMBL was written the vaccine was heavily emphasized because it worked well, but things have changed since it	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	was written in 1999. It was asked if an assay was available to determine if a person has a titer to take for a baseline serum of personnel to monitor. Dr. MacDonald said yes, and said that it has already been implemented in the event if they were vaccinated. Personnel have also been bled for Dengue. Dr. MacDonald said that the last part of this protocol explains how to store the PAPR. The units that are used by Dr. MacDonald's personnel during laboratory procedures would be dedicated to only her personnel. Because they would use these respirators in the presence of virus there is a small risk that the unit itself may be contaminated. These units would then be cleaned, disinfected with Lysol and stored in a dedicated cabinet in the entry room of the BL3. These respirators would never leave this space and service personnel would use them only after all virus has been put away. There is very little risk of exposure to virus. These units will have much lower probability of being contaminated and will be stored in a separate dedicated unit for those personnel only. She stressed that VEE is not passed by particle contact. Dr. MacDonald explained that the amendment to project O3A-031 addresses the facilitation of research with Dengue virus with animals in the BL3 and the status of the BL3 before there is any VEE in that space. She stressed that currently there is no partial or full length VEE anywhere at St. Jude. There are partial DNA constructs, approved for use but are not located in the BL3. She said that when she packaged the replication or propagation defective VEE replicon particles, the packaging must be done in the BL3, in the event there is recombination that generates a proprogation competent form of the virus. Ten percent of that prep is screened for the presence or absence of proprogation competent virus. If there is proprogation competent virus present, they destroy the preparation. If there is no indication in the 10% screen, it is approved to be removed from the BL3 and worked with in the BL2.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	She proposed that as long as there is no full-length virus or two-thirds or greater genome virus in the BL3 and all replicon-packaging runs have proven to be negative for prorogated virus, that personnel who have permission to access the BL3 may do so without the use of a PARP respirator. This is designating this BL3 space as clean and free of VEE as long as a replicon run is proven negative. In the event that she brings full-length virus in, or one replicon run proved positive for competent virus, at that point this amendment would stop. Personnel would at this point only enter the space vaccinated or with approved PAPR respirator. She asked that they consider that BL3 space safe to enter without protection against aerosols. A Committee member asked what is the length of time for a production. Dr. MacDonald replied that it was two weeks. She added that during that two-week period from the initiation to the final reading of the proprogation test, the BL3 space would be closed to anyone that is not vaccinated. This would require stringent record keeping for every replicon run, demonstrating the results of the screening protocol. Those results will be communicated to Dr. Gaut and at that point, the status would be reevaluated and approved for re-entry. She said that they are doing few packaging runs and it takes two weeks start to finish. Dr. MacDonald explained that the probability that a run is positive is very low. By doing this run it would allow her personnel to get in the lab to do work on the animals. With agreement that the space is clean, it would allow them to get in without vaccination or without using PAPR respirators. The PAPR are time sensitive because they have batteries. They are not required to wear masks for Dengue work or if they are vaccinated. By AAALAC standards foot protection, gloves and tie back gowns are the only requirements. In response to a question, Dr. MacDonald said that the assay used has the capability of detecting one infectious forming unit of virus. It is the	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	most sensitive assay detecting for viral proprogation positive. This screening protocol has worked out at the University of North Carolina. They put it through many stringent biosafety tests and presented it before the biosafety committee. It is now a standard screening protocol with 10% percent of the prep screened because you cannot screen the entire prep. A comment was made in regards to personnel being compliant with wearing the masks when needed. Dr. MacDonald said that she has not had a problem with compliance but she could see where this could be a problem. She said that there would be times when there would be only one or two additional people working in the space that she could monitor. It was asked that in regards to the animal work, do ARC personnel get special training and who handles the cages? She answered that no ARC personnel have assess to that space. Dr. MacDonald's lab personnel do all the work and maintain there own animals. Her lab and maintenance personnel are the only people allowed in this lab. Maintenance personnel are escorted when in the lab. The only contact ARC has is removing cages and bedding that have been disinfected, autoclaved and placed in trash bags. They only take the trash out to be incinerated. For maintenance personnel, the lab will be shut down, the virus secured, and surfaces decontaminated. In response to a question, Dr. MacDonald said that the proprogated positive virus detected during a previous replicon run was created using a single helper system. These particles were tested for virulence and were tested a number of times at the University of North Carolina. They are placed in immune incompetent mice and mouse pups by IC, which is the most lethal direct route of virulence. In no case did any of the replicon particles produce any symptoms or mortality. There is a chance that there is a recombinant particle in these preps after they have been screened negative. The approved protocol states this will cover the 2-3	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	day incubation period in a mouse, when you begin to see symptoms of ruffled fur and fever, the mice will be held in quarantine for seven days. She said that her personnel do the inoculations in a biosafety cabinet in the BL2 animal facility. The mice are restricted to be maintained by her personnel with the indication of "do not change" cards on the cages. They are monitored everyday for symptoms. There have been no cases of mice showing symptoms or infections with the use of these replicon particles. If they do have symptoms they are destroyed in a biosafety cabinet and reported to Dr. Gaut. After day seven, her personnel change the mice into clean cages. At that point, they take the "do not change" cards out then ARC takes over the handling. This is for ARC personnel protection. After Dr. MacDonald's presentation, the committee asked Dr. Gaut to contact someone from the CDC regarding current practices. He stated that he as had difficulty in contacting someone because of changes in their personnel. He also said that part of the problem to get the vaccine for VEE is that the current IND will expire soon and no one seems interested in renewing it. Dr. Gaut also that as part of the approval for this amendment, it is stated that this procedure should be used until a vaccine becomes available. There was discussion on whether personnel authorized to conduct work on this project sign an informed consent stating the risk involved. In addition, there was discussion as to whether there should be signed documents stating that they may be taking risks in not wearing a PAPR. This would provide the institution with documentation that personnel were advised of the risks. Dr. Gaut said that because this is a select agent the institution is required to show documentation of training. The plan for the training is to make the risk known for that specific agent, so by having participated in the class, the institution can show that personnel have been advised of risks. There is documentation in place in which	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	personnel sign indicating their understanding the standard operating procedures. As to amendment to O3A-031, it was asked for a baseline serum study to be done. As to amendment O2A-045, it was discussed as to being able to know when the assays come back and if they are negative but also know when the work was started. The personal protective equipment (PPE) notification posted on the door has to be with each change in VEE use and Dr. Gaut asked that he be involved in the changing of the PPE notice. There were comments to what standard should be set for the lab instead of changing the PPE. A comment was made that if the mask are not uncomfortable, maybe they should be required to wear them at all times. Since Dr. MacDonald has only a third of the genome, the chances of recombination is extremely slim and maybe they do not have to wear the masks. A member commented that there might be confusion about compliance when they the guidelines are not consistent. It was asked what are the guidelines of working with Dengue in animals. Dr. Gaut will research this and relay the information to the Committee via e-mail. Dr. Persons also asked the Committee to e-mail him other questions they may have regarding these amendments. He will then communicate these questions to Dr. MacDonald to answer.	
Adjournment	With no further topics of discussion, the Chair then closed the Committee meeting and thanked everyone for their attendance.	

The meeting was adjourned at 1:00p.m.

Judy Edwards, Biological Safety Coordinator, recorded the minutes.

Derek Persons, Ph.D.
Institutional Biosafety Committee Chair

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2003-04

DATE: November 5, 2003

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting started at 10:30 a.m. with the chair welcoming everyone.	
Minutes of last meeting	The chair asked everyone to review the IBC minutes. A voting memo to approve the minutes would be sent to the Committee.	Voting memo sent to the Committee within the next week.
Welcome – New Biological Safety Officer	The Director of EHS introduced the new Biological Safety Officer.	No follow up needed.
Biological Safety Officer Report		
Biological projects approved July 29, to November 4, 2003	The BSO updated the Committee on IBC activity. He reported that there have been nine projects approved since our last meeting of July 29, 2003. Five projects at biosafety level one, three projects at biosafety level two and one project amendment at biosafety level three.	No follow up needed
Regulatory reviews	The Committee was updated on the USDA inspection, which took place October 15. The compliance date of November 12, 2003 was set for the entire country to comply with the guidelines set forth by the PATRIOT Act but has been extended. Anyone that has submitted their information as our institution has will be allowed to continue with their research.	No follow up needed
Adverse events	None to report	No follow up needed
Variance Report	None to report	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
ICC report	Nothing to report	No follow up needed
GMP Report	It was reported that the laboratories are being set up.	No follow up needed
Old Business		
Update -Amendments to O3A-031 and O2A-046	A memo has been has been sent to a principal investigator regarding O2A-046. The other protocol amendment for O3A-031 was approved.	No follow up needed.
Update on Dr. Webster and Dr. Flynn projects	A memo was sent to two investigators to address issues brought forth by the Committee. One investigator has answered all questions and has agreed to the Committee's recommendations. The other investigator has not responded to the memo. A reminder will be send to the investigator this week.	No follow up needed.
New Business		
IBC Policy & Procedures Changes - Committee Criteria for Reviewing biologicals	The Chair explained that this issue came up because of the review of the protocol. When the protocol was first received for review, according the IBC policy and procedures, since our institution was not involved in the quality assurance of this product, the IBC is not required to review this protocol. However, it is a biological, and an investigational, new drug that is not approved by the FDA. The chair proposed that the definition of biologicals is changed to state "investigational biological material derived from a biological source that is not currently FDA approved for license in the United States or is licensed, but will be used investigationally for a non-label use or new indication." He also proposed that investigational devices involved in biological processes be defined as "those devices characterized as having biological components and which are used in the derivation of a product to be used clinically and that is not currently FDA approved for license in the United States or is licensed but will be used investigationally for a non-label use or new indication." This change was discussed with the previous IBC chair, the IRB chair, and the Vice President of Clinical Research. This will allow the Committee to independently review projects without relying on others to recommend what will be reviewed.	No follow up needed.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	A member explained to the Committee that this change in the definition of devices now covers all transplant protocols. The chair referred to the data distributed to the Committee that had current data listing St. Jude INDs. This data indicated that there are very few biologicals. A member recommended that the transplant protocols be reviewed as a group since they are using the same device. Another member questioned the need to review devices that are commercially available around the world but not licensed in the United States. Moreover, there were questions on whether it is necessary to review devices already used by Bone Marrow Transplant. A member explained the use of these devices and how the FDA licenses devices for specific indications. If the device approved by the FDA were used "off label" then the Committee, under the amended policy would need to review the device. There was discussion on "emergency use" protocols. Review of these single treatment plans have not been conducted by the IBC in the past with the exception of one investigator asking for review of his protocol. There was a motion that the amendment to the policy be approved as it is written. The motion carried with unanimous approval.	
IBC Policy & Procedure Changes – Review of Amendments	The Chair reviewed changes to the IBC policy and procedures regarding amendments. The policy has been changed to state that the "review of amendments to an approved project will be conducted in the context of the entire project." If the Committee has questions or concerns regarding biosafety issues of the amendment and the project in its entirety, the Committee will request that the principal investigator address such points." A motion was made for approval of the changes and it passed unanimously.	No follow up needed.
Presentations		
New Clinical Protocol: DETIDE	The principal investigator was present to explain the use of his protocol. He explained that this protocol was originally written as a compassionate use protocol and several emergency INDs using the product have been used for	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	patients with veno-occlusive disease In the patients that have been treated, (approximately nine) there has been no toxicity directly attributed to the use of this product. In all three studies, the efficacy rates were higher than expected based on the history of VOD. In response to a question, the investigator said that in the one study that enrolled 19 patients there were no toxicities attributed to the product. In another study by the same investigators involving 88 patients, there were no reports of toxicities. Another member recommended approval of the study because of the favorable risk/benefit ratio. Several of the members agreed that the risks are minimal compared to the patient dying of VOD. The Chair informed the Committee that a voting memo will be sent out and if they have additional questions or comments over the next few days, place them on this memo.	
New Clinical Protocol: SIVFRC	The investigators were present along to present this protocol. She said that the objectives of this study are to determine the origin of isolated influenza viruses and to detect potentially epidemic-causing influenza viruses in children. Standard precautions recommended by the CDC will be employed by all personnel. Each collaborating site will fax the completed "eligibility checklist" and a copy of the signed informed consent to the principal investigator at St. Jude. The principal investigator or designee will fax the completed checklist and consent to the CPDMO. The investigator will send a modified version of the protocol for Committee approval.	The investigator will send an amended version of the protocol for Committee review.
New Project - O2-155	The investigator was present to explain her study. The goal of this study is to identify risk factors associated with the development of Dengue Hemorrhagic Fever (DHF), which is severe outcome of infection of dengue virus. In most cases, dengue virus is asymptomatic but Dengue Fever (DF) results in a high	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	fever for 5 to 7 days with severe flu like symptoms. A small percent of DF cases go on to develop Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS). This is characterized by capillary leakage that occurs between days five to day seven. The virus appears to be subsiding with decrease in fever, but within 24 hours, the patient goes into severe shock. There is a high mortality rate and there is no support provided. The investigator proposed this protocol as a pilot study to ascertain if a retrospective case controlled study could determine if the nutritional status of children who have DHF is higher than that of control groups. A member commented that the analysis of data linking DHF to nutritional status could be complicated. The investigator agreed and added that the interpretation can be complicated and that this is the first step to determine whether a more in depth study is warranted. This study will not determine the causal affect, it will only determine the association whether there is a risk associated with malnutrition status. The investigator said that the IRB would be reviewing this protocol.	
	The discussion ended and the Chair asked the Committee if they have additional comments or questions to place them on the voting memo that will be send out.	

The meeting was adjourned at 12::00 p.m.

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2004-01

DATE: February 23, 2004

PRESENT: Lorraine Albritton, Martha Brackin, Rebecca Burger, Cheryl Chanuad, John Coleman, Jim Gaut, James Henry, Derek Persons (Chair), Allen Portner, Brian Robbins, and Richard Webby

ABSENT: Edwin Horwitz, Elizabeth Adderson, John Kirkley, Glen Ulett, and John Gray

GUESTS:

PRESENTER(S): Dr. Sima Jeha, Dr. Jon McCullers

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	Meeting started at 1:00.	
Minutes of last meeting	A motion was made and seconded that the minutes be approved with corrections of Mr. Coleman's name and Mr. Henry added to those that were present. The motion passed unanimously.	No follow-up needed.
Biological Safety Officer Report		
Biological projects approved November 5, 2003- February 23, 2004	Mr. Henry reported that thirteen projects were approved since the last IBC meeting. Four projects at BL1, and nine at BL2.	No follow up needed
Pending Projects	Mr. Henry informed the Committee that approximately 10 projects are pending approval. Most are in the process of answering questions from the Committee. He is asking investigators to respond in a timely manner with follow up e-mails.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed
Variance Report	Mr. Henry reported two variances that were received, but they were not within the Committee's purview.	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
ICC report	Dr. Gaut reported that there were exposures that were research related. One employee was sorting mouse carcasses in the bend and stuck him or herself with a surgical instrument that was used in the animals. Testing was done and there has been instruction and training by Occupational Health. The other incident was exposure by a needle stick from a monkey causing a risk from Herpes B. The person is being tested. Dr. Gaut has also asked Occupational Health for assistance in devising a formal line of communication when these incidences occur.	No follow up needed
GMP Report - Mr. John Coleman	Mr. Coleman reported that the facility is up and running. Three projects will be sent to the Committee for review. It was decided that they would be submitting projects as changes in location under the current principal investigator. One project is with the influenza virus in which they receive the plasmids in the BL3 laboratory in the GMP even though the project is at BL2. The second is the HIV project and the third is the Sendai project, which is currently going through the Committee.	No follow up needed
Old Business		
O2C-149 –DETIDE Protocol Information	Dr. Persons explained that last November the Committee approved the Defribrotide clinical protocol. Subsequently, the principal investigator (Dr. Hale) learned the material, which was thought to be of bovine origin, actually is from pigs. Dr. Hale temporarily closed his protocol to submit new information. The Committee received this information with a cover memo from Dr. Persons. There were questions forwarded to Dr. Hale in which he has not responded. The question that needs to be addressed is to obtain formal documentation of the content of this material. A member asked where the confusion came from. Dr. Persons said that it has been very difficult for Dr. Hale to obtain this information. It is not contained in the package insert and what information they have received has been from the company's website. He said that they found out the website was incorrect. Dr. Persons has asked Dr. Hale to obtain a letter from the manufacturer stating what the origin of the product. A member commented that because there is still ubiquity as to the responses from company that because of safety concerns those handling the material to	Continued follow up until issues are resolved.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	treat it with universal precautions. Dr. Persons asked Mr. Coleman for comments regarding the specifications information provided to him. He responded that they have received very little information from the manufacturer. He could only say that it was approved in Europe.	
O3C-155 – Association between Nutritional State and Dengue Hemorrhagic Fever in El Salvador. Principal Investigator – Gene MacDonald, Ph.D.	Mr. Henry stated that Dr. MacDonald submitted a response to the queries that were forwarded to her by the Committee. She indicated that she would not remove the material that she would be receiving from the BL3 laboratory. This is in response to a Committee member's question as to whether the agent would be removed from the BL3 after testing. Dr. Persons said one of the four questions forwarded to Dr. MacDonald has not been answered. This question involves the classification of arenaviruses. Mr. Henry will ask Dr. MacDonald to respond to this question.	Continued follow up until issues are resolved.
New Business		
Meeting with Institutional Review Committees' on protocols utilizing the GMP facility.	Dr. Persons asked Dr. Chanaud to comment on the meeting she attended involving the chairs for all institutional review committees for clinical research protocols with the exception of the Radiation Safety Committee. She explained that Mr. Coleman suggested that the chairs discuss the purview of each committee for reviewing St. Jude studies that will be utilizing product made in the GMP facility. There was discussion on what documentation is generated and how committees know of what projects are approved and the details of the approval. The IRB is the final step in the approval of a protocol before it is activated. They formulated a plan in which the IRB receives other committees' approval letters. If approval is taking time, the IRB will ask to obtain the memo that contains the issues pertaining to the protocol. In particular, if they involve subject safety issues. Currently, the CPSRMC forwards their meeting minutes to the Chair of the IRB. A checklist in the CPDMO will assure they have all approvals before a study is activated. In response to a question, Dr. Chanuad said that this only pertains to clinical research protocols.	No follow up needed.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	It was asked that since the IBC and CPSRMC usually review studies simultaneously, how the IBC chair could obtain a copy of the comments from the CPSRMC. Dr. Chanuad said he should contact Dr. Jim Boyett. A member asked if there was overlap of issues from the Committees in the review of subject matter. Dr. Chanuad said there is generally not a considerable amount of overlap. The CPSRMC focuses on scientific design and statistical analysis. The IRB focuses on safety and risk/benefit ratio. The Radiation Safety Committee focuses research use of radiation and subject risks.	
Presentations		
Guidelines for Reassortment of Influenza viruses – Jon McCullers, M.D.	Dr. McCullers was at the meeting to present the revised guidelines for reassortment of influenza viruses. He explained that in last five to six years, there have been advances in the ability to manipulate the genome of influenza viruses. When these systems came into widespread use in the laboratories at St. Jude, it became possible to manipulate influenza viruses to the extent that it was not possible or practical in the past. In 2000, Dr. Webster wanted to inform the IBC of what was being done with the genetic systems in the laboratory. Because of these advances, he and Dr. Webster together developed a set of guidelines to police themselves in the reassortment of viruses. Dr. McCullers explained that because they can now manipulate the genome of influenza, they could actually make viruses that would not occur in nature. He said that they theorized that certain viruses built could be more dangerous than the parent virus and would need a separate lab containment and approval. Because they work constantly with reassortment, many combinations are put together, and it was not practical to get IBC approval for everything that is developed. He said that instead, they wanted to put forth guidelines to dictate how this process would go forward, what is allowed and would not be allowed at this institution. These guidelines will be brought to the IBC periodically for review and approval. These guidelines were approved in 2000, revised and approved in 2001 and are back again for re-approval. Dr. McCullers explained that even though he is presenting this information, most of work is done in Dr. Webster's laboratory. Dr. Webby is also involved with this work. He presented a diagram of influenza, explaining that it is a negative standard virus with 8 different genome segments. Because this is a segmented	Voting Memo will be sent to Committee members.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	virus and genes are in different segments, if two viruses were to infect one cell, they could mix, match, and develop a completely different virus. With eight segments and two different viruses, there is a possibility of developing 64 different viruses. He said that they could take advantage of this artificially by reassorting them in tissue culture intentionally or by reverse genetics. He said that this system is by-directional, meaning that from one plasmid they can develop a viral RNA. This is packaged into a virus, and will produce messenger RNA. This can be used to make protein, and they can transpect cells with 8 plasmids, each one coded for a gene segment. From this procedure, they can develop a virus within two days. Dr. McCullers presented a demonstration of how the two different viruses are typically made by using reverse genetics. Dr. McCullers explained that the influenza virus because of its ability to reassort does so frequently and that all characterized influenza viruses circulating the world are reassortments. He added that all influenza virus vaccine strains are artificially made reassortments. In nature, reassortment between human viruses is a frequent event. All viruses that are circulating amongst humans are constantly reassorting, and every new virus that comes around is a reassortment. He explained that between different species, which is what they worry about the most, reassortment between swine, human and avian viruses takes place frequently in swine, and infrequently in other species. One of the worries is that there could be a virus crossed between a human virus and an avian sub-type in which humans would have no immunity. This could cause an epidemic around the world. Of the last three pandemics, two have been reassortments, and the other was an avian virus that came into humans. Dr. McCullers said that all work with influenza viruses requires generation of reassortment viruses. This has been traditionally done by putting two viruses together in sub-culture and then characterizing what is developed using some methods of selection. He added that this could be done safely and more directly by using reverse genetics. Dr. Webster has been doing reassortment at St. Jude for more than 30 years.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	He said that traditionally influenza viruses are divided into three classes. The PR8 strain has been considered a class I agent because it is highly attenuated for humans. Class III is highly pathogenic avian flu viruses, typically the H5 and H7. These are considered class III because they can cause disease and death in domestic poultry, which is a concern in the agriculture industry. More recently, since 1997, a number of these viruses have been crossing sporadically into humans. All other influenza viruses, human and animal are in class II. He explained that traditional reassortment has been done by bio-containment specific for the highest class of viruses. In 2000, after they had the ability to tailor make viruses, there was concern that if they made certain combinations of viruses, that they could develop a virus that was more pathogenic for humans or animals. This could generate a virus that could cause a pandemic. Guidelines were developed to prevent this research from occurring and to regulate research through the IBC. Dr. McCullers said that no other groups in the United States at have worked with these influenza viruses have a set of guidelines such as these. He talked with NIH, Mt. Sinai and Wisconsin and they do not have these guidelines. He said that one of the items they had forbidden in the previous guidelines was conducting reassortment with elements of the 1918 virus, which was the great pandemic. Several of the institutions mentioned have been working with this virus under BL3 conditions, which they thought of as inappropriate until the pathogenicity was known. Dr. McCullers said that reassortments between class II and II viruses have been developed at these institutions under BL3 conditions. He added that there has been work ongoing for years in Dr. Webster laboratory with class III avian viruses under BL3+ conditions. The last schemes in 2001 were based on species of origin. They worried about H5 and H7 hemogluttins that were highly cleavable and could cause death in birds and turkeys. These viruses are a threat and have crossed into humans. Dr. McCullers said that they made rules for crossing between the classes and	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	determining the biosafety level based on the cross. They now know that there pathogenicity determinants in other genes. He said that from this information they decided to develop a more complex set of guidelines evaluating this scheme, looking at individual pathogenicity determinants. Dr. McCullers stated that since 2001, there have been advances, which have lead to a new set of guidelines. Laboratories have crossed high pathogenic avian viruses with low pathogenic avian viruses. The concern was that this may result in a virus, which was more pathogenic, but this has not occurred. Gene swapping has been done in research trying to determine the pathogenicity determinants. They have only seen attenuation of the virus. He said they know if one of the high pathogenic avian viruses, (H5, or H7) is used, reverse genetics can be used to alter the human gluttin and clip out the cleavage site. This is highly cleavable, pathogenic and develops a virus that is low pathogenic. This is done routinely in the lab. In addition, there have been human gene crosses to look at individual genes. This has created low pathogenic viruses except for one study that looked at multiple gene reassortments. This was done under BL3 and only detected in mice. Suggested guidelines that Dr. McCullers, Dr. Webby and Dr. Webster developed: • Reassortment between human viruses classified as BL2 agents may be done under BL2 conditions. • Reassortments between common animal influenza viruses classified as BL2 agents may be done under BL2 conditions. • Reassortment between human viruses classified as BL2 agents and common animal influenza viruses is considered attenuated for human hosts must be done under BL3+ conditions. • Reassortment between animal influenza viruses classified as BL3 agents and other animal influenza viruses must be done under BL3+ conditions. • All reassortments with unaltered gene segments from avian viruses that demonstrate the ability to crossover into humans must be done under BL3+ conditions. Reassortments between gene segments from unattenuated human viruses and gene segments from avian viruses that	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	demonstrate the ability to crossover into human cannot be done at this facility. Initial reassortment between genes segments from attenuated human viruses and gene segments from avian viruses that demonstrate the ability to crossover into human must be done under BL3+ conditions. • Novel reassortments that include gene segments from the 1918 genome may not be made at this facility. Reassortments that include gene segments from the 1918 genome and that have been well characterized in relevant host at other institutions may be recreated under BL3+ conditions. Suggested guidelines for protection of research and animal facility staff have not changed: • All employees who could potentially be exposed to infected animals should receive annual vaccination with the standard inactivated influenza vaccine. Dr. McCullers said that they may consider voluntary participation from staff in vaccine trials. • Prophylaxis will not be routinely employed due to concerns over unknown efficacy and safety with prolonged use. • Anyone who has had recent contact with viruses that require BL3+ containment who develops symptoms/signs of influenza infection should report via telephone to their supervisor, the occupational health nurse and the infection control officer. Signs of persons who have contact with other flu viruses should be handled as routine employee illnesses. The potentially infectious employee should not enter the institution, should avoid contact with other persons along with domestic poultry until the diagnosis is known. They should be seen by a physician was warranted by the severity of illness. A member commented that this could potentially develop select agents within the BL3+. It could be a novel select agent in terms of its strain. The member said that they might want to address in the guidelines a derivation of new strains under BL3+ and the necessity to register it with the CDC. Dr. McCullers said that he would contact the CDC for clarification.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	A member asked what ARC workers would be involved in BL3+. Dr. McCullers said that ARC staff takes care of changing cages and cleaning the area. For Dr. Webster's BL3, there is usually one person who is assigned to the project and someone on the weekends. He said they track staff to make sure they understand these guidelines and what their responsibilities are if they were exposed or infected. Dr. Webby added that once the animals are infected, the ARC staff is no longer responsible for the animals. The investigators and their staff take over these responsibilities. In response to a question, he said that at the end of the experiment, para formaldehyde is used on the isolators. Dr. McCullers added that staff is not restricted from coming into the area, but the investigators take responsibility for anything that they can do for themselves	
New Clinical Protocol O1C-169 - Evaluation of single agent rasburicase in treatment/ prevention of hyperuricemia associated with tumor lysis syndrome in adult and pediatric patients with lymphoma/ leukemia, solid tumor malignancies at their first relapse or refractory disease. Principal Investigator: Sima Jeha, M.D.	Dr. Sima Jeha was present to answer any questions regarding her protocol. She explained her protocol used Rasburicase, which is commercially available in part from research done at St. Jude. The difference between this study and the other study conducted at St. Jude is to check for antibody levels of patients. This drug is given freely by the company (Sanofi-Synthelabo) and there is no production at St. Jude. She explained that in a previous study there were over 800 adult patients enrolled, so there is data that has been published on the use of this agent in adults. Dr. Persons explained to the Committee that the primary reason for this study's review by the IBC is because the protocol includes enrolling patients 18 years of age or older. In that respect, it is an investigational agent because the FDA label is only for patients under 18. By IBC guidelines, if an agent is used off label in a study at this institution, it must go through the IBC for review. A member asked what they should consider in reviewing these protocols. Dr. Persons asked for review of information submitted, including the protocol, drug, prior data of the use of the drug in animals and humans. A member asked if there is an IND associated with this study. Dr. Jeha said yes and Mr. Coleman added that the IND is held by Sanofi-Synthelabo. He added that the adult study is the IND and the product is approved for pediatrics not for adults. The study is considered phase III.	A voting memo will be sent to Committee members.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	A member asked that if there is any reason to believe that this product could cause unique problems in adults that are not seen in the pediatric population. Dr. Jeha responded that from experience with the compassionate use of this protocol, the incidences of hypersensitivity or reaction in other trials have been less than 1%. A member stated that there was a report with healthy volunteers in which 64% incidence of neutralizing antibody developed over time. How do you reconcile the two different percentages? Dr. Jeha explained that it was clinical adult reaction and it may have something to do with how routinely it was given. A member asked if it is routinely given to patients that have relapsed. Dr. Jeha said that 17 patients had relapsed on a national study in which the patients received more than one dose. Most of the patients were treated two to three times and the incidents of reaction with these patients increased to 7%. The reactions such as fever and mood change were minor. She added that even with the reactions their uric acid levels dropped. A member asked that if currently they use the drug off label for patients over 18. Dr. Jeha replied yes and this institution has not used it because there are very few patients over 18.	

The meeting was adjourned at 2:05 p.m.

Judy Edwards, Biological Safety Coordinator, recorded the minutes.

Derek Persons, M.D., Ph.D.
Institutional Biosafety Committee Chair

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2004-02

DATE: **March 17, 2004**

PRESENT: Elisabeth Adderson, Lorraine Albritton, Martha Brackin, Rebecca Burger, Cheryl Chanuad, John Coleman, Jim Gaut, James Henry, John Gray, John Kirkley, Derek Persons (chair), Allen Portner, Brian Robbins, Glen Ulett, and Richard Webby

ABSENT: Dr. Edwin Horwitz

GUESTS: None

PRESENTER(S): Dr. Wayne Furman

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting started at 10:05 with Dr. Persons welcoming everyone.	
Minutes of last meeting	A motion was made and seconded for the minutes to be approved with a correction from Mr. Henry. In his BSO report, he stated that the number of pending projects was 10 when it should be eight.	No follow up needed.
Biological Safety Officer Report		
Biological projects approved	Mr. Henry reported that since the last meeting of February 23, 2004, four new projects have been submitted for review. One project was approved and 11 projects are pending approval. There have been two continuing reviews submitted with one approved and the other still pending. A question was asked as to why there were so many projects pending approval. Mr. Henry stated that most of the projects are awaiting communication from the investigators. There was discussion as to whether the investigators should have a time limit imposed in which they have to respond to communication from the Committee. Moreover, what are the consequences if they do not meet the time limit. A	Discussion ongoing.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	member commented that it might not be clear to the investigator the purview of this Committee. Dr. Persons said that he and Dr. Gaut have been working on training and there was a presentation explaining the IBC's purview in the last faculty meeting. A comment was made that there seems to be a considerable amount of overlap in the different committees especially with the IRB. Dr. Persons explained that for the clinical studies submitted to this Committee, with guidance from the OBA, there was agreement in the past of what types of protocols should be reviewed. It has been explicitly defined what protocols would come under the IBC's purview and has been included in the IBC policy and procedures. These include gene transfer in humans, and investigational biological agents or devices. He added that the IRB leaves it up to the IBC to analyze the agent in terms of how it was made, physical properties, purity of material and who makes it. The previous two clinical protocols reviewed by the IBC were referrals from the IRB. A comment was made by a member that the Committee is there to help the investigator. The member proposed that if a comment is forwarded to an investigator, the question should be asked with an explanation as to why it could be a biosafety issue. It was also added that questions from the Committee should be relevant to biosafety issues. Dr. Persons said that the policy and procedures explicitly explains what the Committee should be reviewing. He added that the members submit the questions to be answered by the investigator. It is up to the Committee members to formulate questions that are relevant. A member asked if this might be the reason why the responses may be slow in coming because they do not understand the questions. It was also asked if the memo sent to the investigator stating the questions from the Committee invite them to contact Mr. Henry if they have questions. The member added that maybe this memo requires a response time of three weeks, and what is the result if they do not make the deadline.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	Mr. Henry explained that he continues to follow up with investigators and discusses with them any issues. Dr. Persons added that he has received e-mails stating that Mr. Henry had been very helpful in assisting them in answering their questions. He has assisted in researching for the investigator if they do not have the time to get the information the Committee needs for proper documentation. A member asked that a motion be made on the change in the policy and procedures that state "All comments going back to the investigator for each point, that the biosafety issue be clearly defined." A member commented that maybe administrative issues should be exempt because some discrepancies are not directly related to a specific biosafety issue, but it involves clarity and accuracy of the information that is presented in the document. Dr. Gaut explained that part of Mr. Henry's responsibility is to act as a liaison between the Committee and the investigator. Dr. Persons explained that an informed consent form does not necessarily involve a biosafety issue, but the Committee has the responsibility to review the consent form in its entirety. The Committee should try to frame the questions in a biosafety context and if there are still issues, Mr. Henry is responsible for obtaining clarification. As the Committee changes, he will still be there for continuity. He added that as investigators know of his role, he hopes they will use him as a resource person for there projects to speed up the process. A member asked that the recommended policy and procedure changes be placed in writing and given to the Committee for a vote. There was also discussion on the correspondence sent to investigators. A member asked what does the investigators say when Mr. Henry calls them for the status and their response. He indicates that they have two options, one is to continue with the current process and the other is to withdraw the application and resubmits at amore convenient time Consequently, after being made aware of the options they usually respond in days. A member commented that the system currently in place seems to work and if there is no action by an investigator on the project, it should be brought back to the Committee for appropriate resolution.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	A member asked that James add in his correspondence to the investigator a statement that if they had any questions pertaining to the biosafety issues to contact him. Another member said that it is the investigator's responsibility to ask the Committee if they do not understand a question. Mr. Henry reiterated that he stays in close contact with the investigators and details do not seem to be the real problem. A member said that he would not be in favor of placing limits on the types of questions the members may have. Another member added that maybe this should be addressed in the training material. The training material could address the importance of clarity in the questions that are posed to the investigator.	
Regulatory reviews	Nothing to report.	No follow up needed
Adverse events	Nothing to report.	No follow up needed
Variance Report	Nothing to report.	No follow up needed
ICC report	Nothing to report.	No follow up needed
GMP Report - Mr. John Coleman	Nothing to report.	No follow up needed
New Business		
Presentations		
O1C-194 – ADVL0314, A Phase I Study of Bevacizumab in Refractory. Principle Investigator – Dr. Wayne Furman	Dr. Persons explained that this is a COG sponsored protocol that is using a reagent, which is a humanized anti-vegf antibody. This was an investigational agent, but in late February, it was FDA approved for first line treatment of metastatic colon cancer in combination with 5FU in adults. Currently, this drug has not been approved for use in children. He indicated that the reason the Committee is reviewing this protocol is because it is an investigational biological for pediatric population. A member asked why there are two consent forms. It was explained that one is for 18 years and under and the other is for 18 to 21 years of age.	A voting memo will be sent to the members after the meeting.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	Dr. Furman was present to introduce his protocol. He explained that this is a phase I study of Bevacizumab in refractory solid tumors. Bevacizumab is a humanized monoclonal neutralizing antibody binding all five isoforms of human VEGF. The reason why it is being evaluated is that VEGF is critical for tumor growth and angiogenesis. In pre-clinical models, it has been shown to inhibit tumor growth in mouse models and rhabdomyosarcoma xenograft tumors. In early adult trials, numerous tumors have shown marked responses to treatment. At present, it is now approved for use in metastatic colon cancer in adults. He stated that with respect to side effects, physeal dysplasia was shown in monkeys that were treated for four weeks at high doses. Also, it has been shown that there is a decrease in weight of the reproductive organs and that frequency of menstrual cycles in female animals treated with high doses for as long as 13 weeks. Two animals had antibody formation and both responses were weak and directed only at the Fab portion of the VEGF. In addition, he indicated that there has been some concern about wound healing and that the condition of proteinuria has been shown to be reversible. Dr. Furman explained that side effects observed in adults indicate there seems to be no dose limiting toxicity. There were adverse events during infusion, such as headache, vomiting, nausea, rashes and fever that were minimal. There were a few serious bleeding episodes at tumor sites in the lung and in patients with brain tumors. Thrombosis, hypertension and proteinuria have been more frequently seen. He indicated this is a phase I study. The patients that have not responded to conventional treatment and who have failed all known effective therapy are evaluated at the standard three patients per dose level. The starting dose is about half that used in the adult trials. It is increased in increments to avoid toxicity. If no dose limiting toxicity is observed, they move to the higher dose level and continue.. In the laboratory, they are observing the kinetics of the antibody and its formation of surrogate markers of VEGF expression. The exclusion criterion includes patients with either metastatic or primary CNS tumors. Patients with	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	chronic wound or had a major surgical procedure within a month of going on therapy. In addition, patients with known bleeding are excluded as well as patients with thrombosis or proteinuria. A member referred to the consent form, page 6, in which it states the side effects of chemotherapy and asked if this is a mistake. Dr. Furman explained that the template for the consent form comes from the IRB. A member asked that if a person were exposed to the agent, what would be the expected outcome. Dr. Furman said that he is not aware of any problems and there is no infectious agent in the drug. The FDA has also reviewed it for safety and there are specific handling instructions in the body of the protocol. A member asked if the physeal dysplasia is a real concern. Dr. Furman said that they are monitoring bone age and bone growth but patients that enroll on this trial are not going to be on the trial for a long period. As the trial continues, they will monitor this as well as menstrual calendars. However, patients that have cancer are not normal for several reasons. In response to a question, Dr. Furman said that the agent is approximately 97% humanized and there have been no antibody problems observed in the adult trials. A voting memo will be sent to the members after the meeting.	
Adjournment	Meeting adjourned at 11:05.	

Judy Edwards, Biological Safety Coordinator, recorded the minutes.

Derek Persons, M.D., Ph.D.
Institutional Biosafety Committee Chair

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2004-03

DATE: April 5, 2004

PRESENT: Elisabeth Adderson, Lorraine Albritton, Martha Brackin, Rebecca Burger, Cheryl Chanuad, John Coleman, Jim Gaut, James Henry, John Gray, John Kirkley, Derek Persons (chair), Allen Portner, Brian Robbins, Glen Ulett, and Richard Webby

ABSENT: Dr. Edwin Horwitz, Dr. Glen Ulett

GUESTS:

PRESENTER(S): Dr. Karen Slobod

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting started at 1:05 with Dr. Persons welcoming everyone.	
Minutes of last meeting	Minutes of the last meeting of March 17, 2004 are still in the review process.	
Biological Safety Officer Report		
Biological projects approved March 17, 2004 – April 5, 2004	Mr. Henry reported two projects submitted since the last meeting of March 17, 2004. Six projects have been approved with nine pending approval. There is one continuing review report pending approval.	No follow up needed
Summary of approval activity	Since last meeting of March 17, 2004, the average turn around time by the Committee is 3-4 days. A member asked for explanation on the length of time it took for Dr. MacDonald's project approval. Dr. Gaut explained that the voting process by the Committee took only a few days but the investigator in responding to comments or questions from the Committee and getting those questions resolved took a considerable amount of time.	No follow up needed
Regulatory reviews	There has been no regulatory information received since the last meeting of March 17, 2004. However, five new employees were fingerprinted and filed with the Department of Justice.	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Adverse events	Nothing to report.	No follow up needed
Variance Report	Nothing to report.	No follow up needed
ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Nothing to report	No follow up needed
New Business		
Review of Continuing Review Reports	Dr. Gaut explained that there is a policy regarding the review of amendments but there is no policy for the review of continuing review reports. He added that when reviewing a continuing review report the members would need to review the original submission. He suggested that language be added to the IBC policy and procedures are similar to that in the review of amendments. A member asked if it is in the purview of the Committee to have access to the clinical protocols involved in these projects. There was discussion as to whether Committee members need access to the online protocol database. Dr. Chanuad explained the online database would give access to all institutional protocols. In the other Committees, the members can request a hard copy of the protocol as needed. She added that members could e-mail requesting a copy of the protocol. A member informed the Committee that on the Animal Care and Use Committee form, there is a check-off box that is marked when there has been no change in the project. If there is no change, the Committee will not meet. "Is that basically what happens here, if there is no change in the protocol?" Dr. Gaut replied there could be developments outside this institution in terms of research that would cause a re-evaluation of the project. The investigator may indicate that nothing has changed within their project, but there may be other research necessitating a need to review the project. This gives the Committee the opportunity to meet to discuss the project in case of non-institutional developments.	The committee will be sent a voting memo on the changes in the IBC Policy and Procedures.

Presentations		
Continuing Review Report: O2C-074 - Evaluation of the safety of a polyvalent vaccinia virus -HIV-1 envelope recombinant vaccine (PolyEnv1) in healthy adults. Principal Investigator: Karen Slobod, M.D.	Dr. Slobod was present to answer questions concerning the continuing review report for her project. Dr. Persons thanked Dr. Slobod for her response to the Committee questions dated April 2, 2004. A member asked about the designation that it be not for transduction of DNA with question as to whether it was an infectious agent or a viral vector. "Should this perception be avoided since in this case it seems to do both?" Dr. Slobod said that she thinks it is a viral vector, but that is not an option because of the way the question is worded on the form. It is not a gene therapy vector in the traditional sense in that they think it transduces a gene for long-term expression but it is a viral vector. She added that if a search is conducted for vaccinia virus and transduction in PubMed there would be no information. She said that it is described on the form how they handle the vector. A member added that it is commonly considered as a gene therapy vector and many of these vectors are used for generating an immune response in the case of anti-cancer therapy. Maybe the form should be made clearer in this respect. A member asked in reference to the response to questions two and four, (see attached memo), that there had been six patients enrolled at the 10^5 dose and five at the 10^6 dose, when she says that the intended enrollment is three to six, does that refer to the second new protocol. Dr. Slobod answered yes and explained that there were originally three doses suggested in the protocol. They have completed the first two and the question will come as to whether or not they want to go up to the 10^7 dose and how many subjects will be enrolled in total. The final dose, whatever they select as the maximum dose, will enroll six subjects. Otherwise, if there were just dose escalation they would enroll three and progress. That is why it is between three and six depending on where the maximum is set. In response to a question, 10^5 has been completed and they are now in 10^6 in which they have completed two subjects and will complete one more subject. If that becomes the maximum dose, they will enroll three more and complete six in that maximum dose. Therefore, there will be four to seven more volunteers. She added that there are institutional decisions with the GMP Oversight Committee to decide on the use of 10^7 that is independent of the protocol. Dr.	A voting memo will be sent to members after the meeting.

	Coleman added that the GMP Committee met last Friday (April 2, 2004) and approved the release specifications for the 10^6 and 10^7 with 10^7 pending FDA approval. He will forward this information to the Committee. A member asked when Dr. Slobod went back to look at the CD4 cell counts, according to the NIAID criteria, how did it look? She replied that from the majority of their studies most of the subjects score over 400. The accepted norm in healthy people is approximately 300-400. These are healthy young people, and the accepted norm for these people is from 300-400. This is a reflection of there scoring systems and there were no changes in the pre- and post CD4 count. In response to a question on "vectorology", Dr. Slobod said that the polyvalent vaccinia virus is attenuated in that it probably replicates less and has less tropism to distant organisms in a model. It still replicates in tissue culture, which allows them to harvest large quantities. In response to another question, she said that they inject it subcutaneously so clinically they can see that it replicates under the skin site. However, there is no surface cutaneous virus. Additionally, in vaccinia there is never detection in the blood. Because it is derived from a cow, it sets up a limited replication and there is no wide dissemination of this virus. A member asked whether new modified variant of the virus are screened in a similar way and whether or not inserted genes might affect its robustness. Dr. Slobod said that it would more than likely replicate less effectively and they do not have any pre-clinical data to suggest this would happen. Another Committee member added that he could not think of a case where they have taken virus they use as a vector and it is not always attenuated. He added that the question is usually whether it will grow at all when you insert the new gene. A member explained the need to get a basic understanding as to how replication attenuated the virus is and what tests are conducted to see how genetic modifications will affect it. Dr. Slobod said the parent virus is the vaccine with a gene added and it is highly unlikely that the gene would enhance its activity. In *in vitro* data, it actually grows more slowly than the parent or unmanipulated virus. A member summarized the basic points in that they would be expressing an envelope protein from HIV using this procedure and that it has been established that the envelope protein does not assemble into vaccinia particles, so it would not change its host range. There is a long record of this vaccinia virus as having	

	a much defined replication capacity within an individual and records have shown that in the vast majority of cases, this is actively replicating well and kept in a localized region by the immune system. Moreover, it is expected that the gene would be less robust. Dr. Slobod agreed with the member's summarization. The discussion continued with regard to the number (in the millions) worldwide who have been vaccinated with vaccine and the amount of data available. Dr. Slobod said there are references in the protocol as to the data published and what happens when they knock out TK. A member referred to a previous statement from Dr. Slobod that it replicates less rapidly in the parent strain. "Is this documented or has this been done?" Dr. Slobod did not have the data with her but the data has been published and is sited in the protocol references. A member asked if this would cause a problem for an immuno-compromised person. Dr. Slobod replied yes and they go to extremes to ensure there are no immuno-compromised subjects. She added that everyone administering the vaccine has been vaccinated with vaccinia. The majority of the eligibility criteria for this protocol seek to identify immuno-compromised subjects. Dr. Chanuad said she has communicated with Dr. Knight in Regulatory Affairs in regards to receiving FDA approval for the indicated dose level. He said a response should be received within the next week. Dr. Gaut indicated that Dr. Slobod would need to submit an amendment to the IBC project since the dose level of 10^7 was not included in the original submission.	
Adjournment	The meeting was adjourned at 1:50 p.m.	

Judy Edwards, Biological Safety Coordinator, recorded the minutes.

Derek Persons, M.D., Ph.D.
Institutional Biosafety Committee Chair

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2004-03

DATE: July 21, 2004

PRESENT: Elisabeth Adderson, Lorraine Albritton, Martha Brackin, Cheryl Chanuad, John Coleman, Jim Gaut, James Henry, John Gray, Derek Persons (chair), Allen Portner, Brian Robbins, and Glen Ulett

ABSENT: Edwin Horwitz, Rebecca Burger-Bush, Richard Webby

GUESTS: None

PRESENTER(S): None

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting started at 10:00 with the chair welcoming everyone	
Minutes of last meeting		
Biological Safety Officer Report		
Biological projects Activity April 6, 2004 – July 20, 2004	The BSO reported that the total number of projects submitted during this period was 24 with the total number approved of 22. There are currently two projects pending approval. There were two continuing review reports submitted and approved. At present, the average turn around time by the Committee is 7-5 days, with the average number of days for approval at 22 days.	No follow up needed
Adverse events	There was one adverse event reported on April 12, 2004 and presented to the committee.	No follow up needed
Variance Report	Positive sterility was reported. Corrective action taken and medical director was notified. This was possibly the result of a technical error.	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
4 ICC report	Nothing to report	No follow up needed
GMP Report	It was reported that the HIV, Sendai and influenza vaccine programs are ongoing.	No follow up needed
New Business		
Public Availability of Minutes	It was reported to the Committee that a request for copies of the IBC minutes have been received by non-institutional individuals. Based on the NIH mandate, the minutes are to be made available for the public's review. The OBA has developed recommendations on how to prepare and distribute IBC meeting minutes. In addition to these guidelines, it was pointed that recommendations following the OHRP visit to our institution requested the minutes show a detailed examination of projects similar to IRB review. Additional guidance, obtained at a recent meeting with institutional officials, was to structure the minutes in a more corporate format. The previous Committee minutes of April 5, 2004 will be revised to a corporate format while being as detailed as possible to show due diligence. There will be a more formal structure to committee meetings to better show how the projects were discussed. The above-mentioned OBA guidelines will be distributed to IBC members for their review.	The Committee will receive the questions and answer format from the OBA.
Surveillance Reporting	IBC policies and procedures require the Biological Safety Officer to conduct surveys of laboratories to ensure proper safety procedures are being used. In part to comply with this requirement, the Environmental Health and Safety department is developing a laboratory safety risk assessment procedure that will be implemented in the near future. The BSO will report his findings as a standard part of the IBC meetings.	
Change in IBC Membership	Currently in the process of recruiting the replacement of one of our community members. We are hoping to identify a candidate within the Memphis/Shelby County Health department.	
Adjournment		

The meeting was adjourned at 10:20 a.m.

Derek Persons, M.D., Ph.D.
Institutional Biosafety Committee Chair

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2004-04

DATE: August 5, 2004

PRESENT: Elisabeth Adderson, Martha Brackin, Rebecca Burger-Bush, Cheryl Chanuad, John Coleman, Jim Gaut, Derek Persons (chair), Allen Portner, Brian Robbins, Glen Ulett, and Richard Webby

ABSENT: Dr. Edwin Horwitz, James Henry, John gray,

GUESTS: Dr. Jon McCullers

PRESENTER(S): Dr. Patricia Flynn

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting started at 9:06.	
Minutes of last meeting	Deferred to next meeting.	
Biological Safety Officer Report		
Biological projects approved July 23, 2004 – August 5, 2004	Dr. Gaut reported that there were no projects submitted or approved since in the meeting. There are currently four projects pending approval.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	There was one adverse event reported involving the PANG protocol. The subject died due to disease progression unrelated to study event.	No follow up needed
Variance Report	Nothing to report	No follow up needed
4 ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John	Nothing to report.	No follow up needed.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Coleman		
New Business		
Presentations		
O1C-206 Phase I Trail of FluMist in Immuocompromised Children. Principal Investigatror: Dr. Patricia Flynn	Dr. Flynn was present to explain her protocol. The primary objective of this study is to describe the safety of FluMist compared with placebo in mild to moderately immunocompromised children with cancer. The other objectives are to describe the immune response following vaccination with FluMist and determine the incident and duration of viral replication following vaccination with FluMist. The nasal spray offer several potential advantages: • It avoids patient discomfort as well as the risk of bleeding from the injectable vaccine. • The immunity may be improved in the immunocompromised patient due to increased CD4+ T-cell help for the B-cell response or due to the induction of CD8+ T-cell responses directed against the virus. • It might be expected to induce specific IgA responses localized to the upper respiratory tract that may provide protection from infection even in the patient with decreased B- or T-cell number following chemotherapy since this vaccine is given by the mucosal route. • A live, attenuated influenza virus vaccine may offer additional potential benefit with increased cross-protection in years that the vaccine does not match the strains of the circulating virus. The study will target the vaccination of 20 children between the ages of 5 and 17. In response to a question Dr. Flynn explained that patients will be carefully selected to include only those who mildly or moderately immunosuppressed in relationship to their cancer therapy and are not a recipient of a stem cell transplant. In response to a question, Dr. Flynn said that the patients and parents/guardians	Voting memo will be sent to members.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	enrolled will be educated about the importance of avoiding contact with other patients off campus including in St. Jude housing. During the first 28 days following vaccination, patients will be kept in isolation when visiting the St. Jude Campus.	
Adjournment	Meeting adjourned at 10:50 a.m.	

The meeting was adjourned at.

Judy Edwards, Biological Safety Coordinator, recorded the minutes.

Derek Persons, M.D., PhD
Institutional Biosafety Committee Chair

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2004-04

DATE: **September 8, 2004**

PRESENT: Elisabeth Adderson, Lorraine Albritton, Rebecca Burger-Bush, Charlotte Davis, John Coleman, Jim Gaut, James Henry, John Gray, Jon McCullers, Helen Morrow, Derek Persons (chair), Allen Portner, Brian Robbins, and Richard Webby

ABSENT: Dr. Edwin Horwitz, Dr. Cheryl Chanaud

GUESTS: None

PRESENTER(S): Dr. Jerry, Shenep, Dr. Katherine Knapp

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting started at 3:00 with Dr. Persons welcoming everyone and introducing new committee members. He explained how committee meetings are conducted and the procedure for reviewing and voting on projects.	
Minutes of last meeting	Voting memo and minutes for August 5, 2004 and July 23, 2004 will be sent to members after the meeting.	Send minutes to members.
Biological Safety Officer Report		
Biological projects approved August 5, 2004 through September 8, 2004	The total number projects submitted were eight with four approved and four pending approval. No continuing reviews were received.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Variance Report	Nothing to report	No follow up needed.
4 ICC report	Nothing to report	No follow up needed.
GMP Report - Mr. John Cunningham	Mr. Coleman reported that he will be sending the release specifications for the sendai virus to the committee within the next month.	No follow up needed.
New Business		
Committee minutes	Committee minutes that will be sent out will use a more streamline format. The content is still representative of what happened in the meetings. Dr. Persons asked for feedback from the minutes after review. There was a recommendation that oral comments from the committee are documented on the voting memo to get a documented response from the principal investigator. The response will be made available to the full committee. Motion was made that all oral comments from the committee from clinical and BL3 projects presented in the meeting be documented on the voting memo and forwarded to the principal investigator for a formal response. Motion passed unanimously.	No follow up needed.
OBA Information	The OBA has released information on acceptable ways of convening IBC meetings and if the IBC can conduct meetings by e-mail. The committee reviews the projects thoroughly and the members are given the opportunity and often write detailed questions in regards to the protocols. Dr. Persons made a motion that the committee continue to review non-clinical BL2 protocols by e-mail. At the next committee meeting the information from the protocols including when they were approved are documented in the minutes with a formal motion for approval. The gives the public an opportunity to ask questions. Motion passed unanimously.	No follow up needed.
Non-Human Primate Projects	Currently the committee reviews all non-human primate protocols that involve rDNA or infectious disease material. Because of a concern regarding the B virus a motion was made that the committee review all non-human primate protocols.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	The motion passed unanimously.	
Presentations		
O2C-135 – A Phase I Study of Recombinant Oral BAH-2 Cholera Vaccines in Healthy Adults. Principal Investigator: Elisabeth Adderson, M.D.	Dr. Adderson was present to explain her protocol. She explained that this protocol has been reviewed by the Committee before with Patricia Flynn as principal investigator. Dr. Flynn requested that Dr. Adderson assume responsibility for the protocol. She explained that cholera is a worldwide problem. The toxicity of the virus causes dehydration resulting from the system's inability to reserve sodium. Severe dehydration and shock is the cause of death. Dr. Adderson said some of the strains did not use human subjects because there were no good models to assess reactigencity of the vaccine. She explained the strains that they would be using one of which has been used in previous vaccines with no or only mild side effects. It will be a double blinded study whereby cohorts of four patients receive one of the three vaccines. There is assessment for toxicity after the four subjects. The lots of the virus were produced at another facility and the study will be conducted at Methodist University Hospital. The subjects will be in the hospital during the shedding phase and will have follow ups after the leave the hospital at St. Jude.	Voting memo will be sent out to members after the meeting.
O1C-209 – A Phase I/II Randomized Trial of the Safety and Immunogencity of Cold Adapted Influenza Vaccine (FluMist) in HIV-Infected Children and Adolescents. Principal Investigator: Katherine Knapp, M.D.	Dr. Knapp was present to explain her protocol. There will be 300 subjects (approximately 45 at St. Jude) enrolled at PACTG sites under two arms. One arm will received the vaccine the other arm will receive the standard flu shot. The population will be HIV-infected children and adolescents on a stable regimen with no anticipated change that show no severe immune suppression. All subjects will receive influenza immunizations and will be randomly allocated to either arm. These subjects will avoid close contact with immunosuppressed individuals for at least 21 days after receiving the vaccine. In response to a question, Dr. Knapp said that the subjects will be seen in the isolation rooms for sick visits.	Voting memo will be sent out to committee members.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
O2C-162 – A Phase I Study of Unmodified Live Intranasal Sendai Virus Vaccine in Children and Toddlers: Assessment of Safety and Immunogenecity. Principal Investigator: Jerry Shenep, M.D.	Dr. Shenep was present to explain his protocol. He said that this is a sendai virus vaccine to prevent para-influenza type 1 (hPIV-1) infections. This is the most common cause of croup which causes approximately 50,000 hospitals and few deaths yearly. There is no vaccine or anti-viral drug available. The objective of this study is to assess the tolerance and safety of escalating doses of intranasal sendai virus in children and toddlers. Also to assess the magnitude and duration of the immune response elicited by intranasal sendai virus. There has been a clinical trial with 9 adults who tolerated the drug well. In all cases the virus was cleared immediately from the nasal cavity. Some of the adults with pre-existing antibodies were shown to have a boost in their immunity. There were no signs of disease in any of those adults. This trial will be done in three steps. The first step will be with healthy seropositive children age three to six. The IRB has approved the protocol for group one only and they asked that Dr. Shenep come back to the IRB to receive approval for the other groups. After further discussion it was agreed that the IBC's approval will be for all three groups. The study will take place in the TTU isolation rooms and there will be home visits involved. On weekends the subjects will be seen the in the clinic isolation rooms. The GMP application to make the product has already been approved by the committee. The GMP production is underway and the final release specifications will come back to the committee for review.	
Adjournment	Meeting was adjourned at 4:35.	

Judy Edwards, Biological Safety Coordinator, recorded the minutes.

Derek Persons, M.D. Ph.D,
Institutional Biosafety Committee Chair

JG: je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2004-04

DATE: **November 12, 2004**

PRESENT: Lorraine Albritton, Rebecca Bush, John Coleman, Jim Gaut, James Henry, John Gray, Derek Persons (chair), Allen Portner, Brian Robbins, Jon McCullers, Helen Morrow, and Richard Webby

ABSENT: Edwin Horwitz, Elisabeth Adderson, Cheryl Chanuad

GUESTS: None

PRESENTER(S): Dr. Elena Govokova, Dr. Richard Kriwacki

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting started at 10:05 with Dr. Persons welcoming everyone.	
Minutes of last meeting	Minutes of the previous meeting was voted on and approved by the IBC electronically.	
Biological Safety Officer Report		
Biological projects approved September 9 – November 12	The number of new projects submitted for this period was eleven. Seven projects have been approved with four pending. There were two continuing reviews submitted with one pending and one approved.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed
Variance Report	Nothing to report	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
4 ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Nothing to report.	
New Business		
IBC Meeting requirements.	Dr. Persons distributed the IBC meeting guidelines from the NIH. After discussion of the guidelines the committee decided to continue with the current procedures with the addition of a once a month meeting to discuss and approve the projects submitted since the last committee meeting. A motion was made and second to start monthly meetings of the IBC. The motion passed unanimously.	A monthly meeting schedule will be set up .
Presentations		
O3A-212 – New Approaches to control of influenza; neuraminidase inhibitors in H5N1 influenza mouse model; combination therapy for pandemic influenza. Principal Investigator: Dr. Robert Webster.	Dr. Elena Govorkova, a co-investigator on the project was present to explain the project and answer questions. She explained that the goals are to develop an optimal strategy for the use of anti-influenza drugs against emerging pandemic influenza viruses. Additionally, to test combinations of these antivirals against avian and human influenza viruses, including newly emerging H5N1 and H9N2 subtypes isolated in Asia. They will evaluate the mode of action of the new neuramidase inhibitors in combination with amantadine and/or rimantadine to determine if there is more than an additive antiviral effect and to evaluate immunization with naked DNA as a strategy to induce immunity. Dr. Govorkova explained that they will be working in the biosafety level 3+ facilities, as well as the security and the personal protection equipment that will be used. There will also be special training on equipment and facilities. Restrictions have been established for personnel working in BL3+ and their movement throughout the institution. The lab supervisor is working with Dr. Gaut in regards to biosecurity measures and shipping of materials.	A voting memo will be sent to members.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	The committee discussed the transmission of these viruses and the precautions in place. This is the same work that has been conducted for several years with no incidents.	
Biofermentor Installation: Dr. Richard Kriwacki	Dr. Kriwacki was present to discuss the installation of the 120 liter biofermentor. He explained that this facility housed at St. Jude and will be available to serve a broad community of scientists in Memphis. The purpose of this facility is to enable the large-scale production of proteins and other bio-molecules for structural, biochemical and drug discovery studies. The use of a large-scale biofermentor allows large-scale experiments to be performed efficiently. Dr. Kriwacki showed a picture of the fermentor explaining that it has a secure entry door and requires care key privileges granted by the director of the ARC. There have been several investigators expressing interest in performing biosafety level one experiments in the next 24 months. At this time he only wants to conduct biosafety level one experiments with biosafety level 2 experiments starting after experience has been gained with BL1. He explained that guidelines used in standard microbiological practices for BL1 experiments will be used. Additional guidelines will be used to report spills, maintenance of the system, removal of cultures and minimizing aerosols during transfers. Standard operating procedures and forms will be in place to gain access to the fermentor. There will be a person in charge conducting all experiments with one person from the lab. Training of personnel will be conducted with special considerations given to cleaning the fermentor which is done by autoclave. The committee asked questions in regards to transportation/disposal of materials and approval of projects. A member explained that each project will have to go through the IBC review and approval process before the experiment can be performed. Users from other institutions will need to submit a copy of the approval from their IBC. There would also have to be some process to confirm the content of material used in	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	the biofermentor by non-institutional clients. Other St. Jude officials will also need to be involved to address other issues.	
Adjournment	The meeting adjourned at 11:36.	

Judy Edwards, Biological Safety Coordinator, recorded the minutes.

Derek Persons, M.D., Ph.D.
Institutional Biosafety Committee Chair

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2004-05

DATE: **December 8, 2004**

PRESENT: Elisabeth Adderson, John Coleman, Helen Morrow, Jim Gaut, James Henry, John Gray, Derek Persons (chair), Allen Portner, Brian Robbins, and Richard Webby

ABSENT: Lorraine Albritton, Cheryl Chanaud, Charlotte Davis, Rebecca Burger, Edwin Horwitz

GUESTS: None

PRESENTER(S): Dr. Karen Slobod, Dr. Julia Horwitz

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting started at 1:00 p.m. with Dr. Persons welcoming everyone.	No follow up needed
Minutes of last meeting	Will be distributed with a voting memo at a later date.	Follow up provided in next committee meeting.
Biological Safety Officer Report		
Biological projects approved (November 12, 2004 – December 8, 2004)	Since last meeting there were eight new projects submitted and one continuing review. There are ten projects pending approval.	No follow up needed.
Regulatory reviews	The institution's select agent program is currently being inspected by the USDA. Institutions have received correspondence from the OBA to remind all institutions receiving NIH funding to be diligent in documenting IBC review of	Chair to send memo and OBA memo to faculty. Chair to report on this issue at

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	all research involving recombinant DNA and biohazardous agents. In addition, the OBA stated that site visits are planned to ensure NIH guidelines are being followed. Failing to comply with these guidelines could result in disciplinary action from the NIH.	the next Faculty meeting
Adverse events	Nothing to report	No follow up needed
Variance Report	Nothing to report	No follow up needed
ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Sendai virus production is complete. They are waiting on testing. An HIV project, which has been approved by the committee, is starting production. There is a new project currently going through the IBC approval process.	No follow up needed
New Business – No new business discussed.		
Presentations		
New Project – Evaluation of the tolerability and safety of recombinant HIV-1 multi-envelope DNA plasmid vaccine (EnvDNA) in healthy adults. Principal Investigator: Dr. Karen Slobod	Dr. Slobod and Dr. Julia Hurwitz were present to explain and answer questions for the protocol. This is a phase I tolerability and safety study of EnvDNA. This study will be a prerequisite to future clinical trials aimed at determining the immunogencity and effectiveness of EnvDNA as part of a prime-boost-boost, multi-envelope, multi-component vaccine strategy to prevent HIV-1. The second objective is to characterize the kinetics, duration and magnitude of any HIV-envelope specific immune response elicited by EnvDNA. She explained the vaccine product consists of a mixture of recombinant, purified DNA plasmid vaccines, each expressing HIV-1 envelope protein. It consists of a mixture of 51 recombinant, purified DNA plasmids, each capable of expressing a specific HIV-1 envelope protein. Dr. Slobod said the product has been approved by the FDA. She added that DNA vaccines are not new and have been studied in humans for approximately a decade with thousands of human subjects receiving these vaccines. This product	Voting memo will be sent members after the meeting.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	has never been previously administered to humans. However, plasmid vaccines targeting HIV, malaria and hepatitis B are currently undergoing clinical examination. These vaccines have been well tolerated without major adverse events and have not caused systemic autoimmune disease. There was discussion on how the 51 plasmids were selected and what criteria were used. Dr. Slobod explained the procedures and the guidelines most commonly used. She also explained their rationale for the dose administration. The outline for the clinical trial, subject enrollment (suggested by the NIH) and the inclusion criteria was explained. Adverse events will be assessed using the FDA approved AIDS toxicity tables. There was discussion on minor discrepancies in the protocol. Dr. Slobod said that she would correct discrepancies. There was further discussion on the procedure for identity testing done by Therapeutics, Production and Quality.	

The meeting was adjourned at 1:45 p.m.

Derek Persons, M.D. Ph.D.
Institutional Biosafety Committee Chair

JG: je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-01

DATE: **January 13, 2005**

PRESENT: Elisabeth Adderson, Rebecca Bush, John Coleman, Jim Gaut, James Henry, Derek Persons (chair), Brian Robbins, Vishwas Parekh, Helen Morrow, and Richard Webby

ABSENT: Lorraine Albritton, Cheryl Chanuad, John Gray, Allen Portner, Charlotte Davis,

GUESTS: None

PRESENTER(S): None

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting started at 1:05 p.m. with Dr. Persons welcoming a new member, Dr. Vishwas Parekh	
Minutes of last meeting	Minutes from the previous meeting have been approved by the Committee.	No follow up needed.
Biological Safety Officer Report		
Biological projects activity December 9, 2004 through January 13, 2005	Sixteen projects have been submitted since last meeting. The number of projects approved is ten with six pending approval. There have been five continuing reviews submitted and two approved with 3 pending approval. (See attached summary of project activity.) The chair asked if there were additional questions or comments regarding projects submitted to the committee during this period. There were no questions and a motion was made to give final approval to a these projects. (See attached list). Motion passed unanimously.	No follow up needed
Regulatory reviews	Inspectors from the USDA conducted an unannounced inspection and review of the institution's select agent program. The inspection began November 29, and concluded December 8. An exit conference was given and t he inspectors	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	explained that the inspections were conducted at randomly selected registered institutions in an effort to ascertain the current effectiveness of the select agent programs throughout the nation. The institution has received official notification and certificate of registration to possess, use, or transfer select biological agents and toxins.	
Adverse events	Nothing to report	No follow up needed
Variance Report	Nothing to report	No follow up needed
4 ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	There are currently three projects that need IBC approval. Two have been submitted to the committee.	No follow up needed.
New Business		
Risk Assessment – Environmental Health & Safety	To meet OBA guidelines, risk assessments conducted by the Environmental Health and Safety Department are ongoing. Mr. Henry explained the risk assessment procedurc. This assessment includes, Industrial Hygiene, Radiation Safety, General Safety, and Biological Safety. Review of IBC projects is also part of the process. There was discussion on how often the departments are assessed and how this should be reported to the IBC. It was decided that the IBC receive a brief report on risk assessment activity.	No follow up needed.
Research on human tissue/cell lines	There was discussion regarding the xenograft, tissue banking and handling procedures. Those using equipments have asked the IBC for feedback on transporting materials and equipment as well as the containment level. There was discussion on whether this falls within the IBC purview. The IBC recommended that the Environmental Health & Safety Department set up a policy to monitor these activities and training of staff.	No follow up needed.

The meeting was adjourned at 1:45.

Judy Edwards, Biological Safety Coordinator, recorded the minutes.

Derek Persons, M.D. Ph.D.
Institutional Biosafety Committee Chair

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-02

DATE: **February 10, 2005**

PRESENT: Elisabeth Adderson, Lorraine Albritton, Rebecca Bush, Cheryl Chanuad, John Coleman, James Henry, (chair), Allen Portner, Brian Robbins, Vishwas Parekh, Jon McCullers, and Helen Morrow

ABSENT: Jim Gaut, John Gray, Derek Persons

GUESTS: None

PRESENTER(S): Richard Webby

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting was called order by Dr. Elisabeth Adderson, IBC Vice Chairman. She explained that Dr. Persons has taken a medical leave of absence from the Committee and she will take over his duties until he returns	
Minutes of last meeting	Minutes have been approved by the committee.	
Biological Safety Officer Report		
Biological projects approved January 13, 2005 through February 10, 2005	Mr. Henry gave his report for January 13, 2005 through February 10, 2005. There were nine projects submitted, seven projects approved with two pending. Three continuing review reports were submitted and approved during this period. A motion was made that the projects are given final approval. The motion passed unanimously.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed
Lab Risk Assessment	The Department of Environmental Health and Safety has conducted four risk assessments to date. Some of the common deficiencies that have been identified are: 1. Inadequate documentation of training.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	2. Submission of amendments to projects and personnel to the IBC 3. Recapping of needles without using the one hand technique in accordance to St. Jude Bloodborne Pathogens Exposure and Control Plan.	
Variance Report	Nothing to report	No follow up needed
4 ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Nothing to report	
New Business		
Presentations		
Characterization of highly pathogenic influenza viruses. Principal Investigator: Dr. Richard Webby	Dr. Richard Webby was present to explain his project to the Committee. He explained how the influenza virus works and how they obtain the different strains from various sources. These viruses are separated based on the serology of proteins. He explained what distinguishes a highly pathogenic influenza virus from a low pathogenic virus and how it occurs. Dr. Webby explained that this project is looking at the high pathogenic strains. He said that it is important to monitor the genetic and biologic evolution of these viruses and not all H5 and H7 viruses are highly pathogenic. The transfer of these viruses is highly regulated by the federal government. These viruses are transported directly to BL3 facilities for characterization. All samples are treated as highly pathogenic until their pathogencity can be confirmed. Dr. Webby left the meeting so the committee could continue the discussion of his project.	A voting memo will be sent to members.
Adjournment	The meeting was adjourned at 1:30 p.m.	

Judy Edwards, Environmental Health & Safety Coordinator, recorded the minutes.

Elisabeth Adderson, M.D.
Vice-Chair, Institutional Biosafety Committee

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-02

DATE:

PRESENT: Elisabeth Adderson, Lorraine Albritton, Rebecca Bush, Cheryl Chanuad, James Henry, Allen Portner, Brian Robbins, John Gray, James Gaut and Richard Webby

ABSENT: Jon McCullers, Helen Morrow, Vishwas Parekh, John Coleman

GUESTS: None

PRESENTER(S): Dr. Sima Jeha

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting was called order by Dr. Elisabeth Adderson, IBC Vice Chairman	
Minutes of last meeting	Minutes for the last meeting will be distributed after the meeting.	
Biological Safety Officer Report		
Biological projects approved February 11, 2005 through March 10, 2005	Mr. Henry distributed the BSO report for the period January 13 through February 10, 2005. He reported that there were 16 projects submitted during this period. Seven projects were approved with nine pending. There were no continuing reviews submitted during this period. A motion was made that the projects submitted during this period be given final approval. The motion passed unanimously.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Lab Risk Assessment	The Department of Environmental Health and Safety has conducted nine risk assessments to date. Some of the common deficiencies that have been identified are: 1. Inadequate documentation of training. 2. Submission of amendments to projects and personnel to the IBC 3. Recapping of needles without using the one hand technique in accordance to St. Jude Bloodborne Pathogens Exposure and Control Plan.	No follow up needed.
Variance Report	Nothing to report	No follow up needed.
4 ICC report	Nothing to report	No follow up needed.
GMP Report - Mr. John Coleman	No report	No follow up needed.
New Business		
Handling of antiretroviral caging material in the ARC.	Dr. Gaut explained that he had received calls from the ARC asking for direction from the Committee on how to handle caging materials from antiretroviral work. There are issues on how to handle material, decontamination and space. The Committee discussed the risks associated in working with these materials and the biosafety level requirements. There were questions in regards handling materials in BSL2 space for two weeks. Dr. Gaut will take these questions back to Dr. Rahiji and get more information for the Committee. Dr. Albritton will talk with other institutions to see how they handle these materials.	Dr. Gaut and Dr. Albrittion will report back to the Committee any additional information they receive.
IBC Policy & Procedures Revision	The current policy and procedure states that "meetings will be held at least quarterly". This statement will be changed to "meetings will be held at least monthly."	No follow up needed.
Presentations		
New Project- A phase II study of Campath-1H in Children	Dr. Sima Jeha was present to explain her protocol. The objectives of this study	A voting memo will be sent to members.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
with Acute Lymphoblastic Leukemia in second relapse (ADVL0222) Principal Investigator: Dr. Sima Jeha.	are to: 1. Determine the response rate of Campath-1H as monotherapy and in combination with chemotherapy in the setting of Acute Lymphoblastic Leukemia of childhood in second or refractory relapse. 2. Determine the toxicity of Campath-1H when used alone and in combination with chemotherapy. 3. Assess the pharmacokinetics of Campath-1H in pediatric patients. 4. Measure the immune responses to Campath-1H. She stated that the drug is approved by the FDA for use in adults. The Committee explained to Dr. Jeha the reason why they wanted to review this study. In their review they look at were the drug is made and risks associated with its use.	
Adjournment	The meeting was adjourned at 1:45 p.m.	

Judy Edwards, Environmental Health & Safety Coordinator, recorded the minutes.

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Elisabeth Adderson, M.D.
Vice-Chair, Institutional Biosafety Committee

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-04

DATE: April 14, 2005

PRESENT: Elisabeth Adderson, Rebecca Bush, Cheryl Chanuad, John Coleman, James Henry, James Gaut, Brian Robbins, Vishwas Parekh and Helen Morrow and Richard Webby

ABSENT: Lorraine Albritton, Allen Portner, Jon McCullers, Derek Persons,

GUESTS: None

PRESENTER(S): Dr. Larry Kun, Dr. Aditya Gaur

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting was called to order by Dr. Adderson, IBC Vice Chairman.	
Minutes of last meeting	Minutes from the last meeting will be distributed after the meeting.	
Biological Safety Officer Report		
Biological projects report March 10, 2005 – April 14, 2005	Mr. Henry reported that there were 13 projects submitted, 8 projects approved and 5 projects pending for this period. There were three continuing reviews submitted, with two approved and one pending approval. A motion was made and second that all approved projects be given final approval. The motion passed unanimously.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	There was an update from the TGT Clinical Research Office on an occurrence of a third SAE and update on previously reported SAEs in X-SCID gene transfer trial conducted in France. Three subjects enrolled on this protocol had severe adverse events associated with the clinical trial. As recommended by the FDA, they have revised the informed	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	consent documents to include the third adverse event. The Committee discussed the FDA's actions regarding these kinds of clinical trials. These clinical trials are not being conducted at St. Jude or in the United States. The French investigators are reporting their findings to the FDA.	
Lab Risk Assessment	There have been 13 risk assessments conducted to date. Some of the common deficiencies that have been identified are: • Inadequate documentation of training. • Submission of amendments/revisions to projects and personnel to the IBC. • Recapping of needles without using the one hand technique in accordance to St. Jude Bloodborne Pathogens Exposure and Control Plan. • Inadequate signage.	Follow up will continue.
Variance Report	Nothing to report	No follow up needed
ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Mr. Coleman gave an update on the projects the GMP is involved in. • They are producing the HIV components for the phase II HIV study. • The Sendai for the para-influenza flu has been completed and released. • Work continues on seeds stocks. • They are working on monoclonal for a neuroblastoma study.	Follow up will continue.
New Business		
IBC Review of clinical protocols	The Committee discussed the policy and procedures in regards to reviewing clinical protocols. The investigators who have submitted clinical protocols have voiced confusion on what is expected of them from the Committee. There was discussion on the IBC policy in reviewing FDA approved drugs. It was recommended that these protocols be given expedited review by the Chair. The chair will then decide if the investigator will need to present the protocol in a Committee meeting. The members will also have the right to call for a meeting.	Dr. Gaut will amend the policy and procedures and bring it back to Committee for approval.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Employee Off-site participation in projects	There are projects being conducted at other centers that involve St. Jude employees. The questions were centered on the institution and the IBC's responsibilities for these employees. There were questions as to whether this is an institutional issue or an IBC issue and should information regarding these off-site projects be submitted to the Committee? Distinctions between collaborations and consultations as well as biosafety levels were discussed. Dr. Gaut will amend the current IBC policy and procedures to take into account the biosafety levels, collaborations and consultations. This will be brought back to the Committee for review.	The amended IBC policy and procedures will be brought back to the committee for review.
Recent events regarding the exposure and handling of materials	Dr. Adderson distributed two reports concerning two inadvertent exposures to infectious material in different laboratories. The reports summarized the investigation by the institutions involved and the CDC. These findings underscore the importance of using appropriate biosafety practices and testing when working with materials that are believed to be inactivated. She also spoke of the recent reports in the media concerning the mailing of a highly contagious influenza strain to laboratories across the country. St. Jude's lab followed procedures correctly after receiving this strain. Mr. Henry added that as part of the Risk Assessment, they are evaluating documentation of staff training for the materials they are working with and biosafety levels. They are actively reviewing projects and meeting with laboratory staff. Findings are documented in the Risk Assessment Report and are given to the principal investigator. There was discussion as to future goals of having training modules that may be required by the Committee when a project is approved. These CBLs will also help track training of employees. Currently, as part of the risk assessment process a spreadsheet with employee training is sent to the PI prior to the risk assessment to review and update.	
Presentations		
New Clinical Protocol – PBTC013 "A Phase I/II Study of Recombinant Chimeric Protein	Dr. Kun was present to explain his protocol. This is a Phase I/II study of a recombinant, chimeric protein, composed of transforming growth factor (TGF)-α, which is the epidermal growth factor receptor binding legand, and a genetically engineered form of	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Composed of Transforming Growth factor (TGF) –alpha & Mutated Pseudomonas Extoxin Termed PE38 (TP-38) in Pediatric Patients with Recurrent or Progressive Supratentorial High Grade Gliomas. Principal Investigator: Dr. Larry Kun	pseudomonas exotoxin, TP-38, in children between 3 and 21 years of age with recurrent or progressive high grade gliomas. The primary objective is to describe the toxicities and estimate the maximum safe flow volume and maximum tolerated infusion concentration of TP-38, in children with recurrent or progressive malignant supratentorial high grade gliomas. There were questions in concerning how the TGF receptors work and patient dose volumes. Dr. Kun said that all patient registration and dose volumes are automated and will come the PBTC office. The pharmaceutical company will also monitor the protocol. He explained that the waste from the product is handled as biological waste. Mr. Coleman said that these protocols come through the NIH, so it is difficult to get quality assurance information for the product. But because it is coming from the government and made by a reputable company this should be of little concern. There was further discussion between Committee members on the difficulty in obtaining product information. This is a phase I safety study which may mean there is limited information available.	
New Clinical Protocol: "A Phase I Trial of Recombinant Vaccines Given to HIV+ Young Adults" Principal Investigator: Dr. Aditya Gaur	Dr. Gaur was present to explain his protocol. The primary objective of this study is to determine the safety and tolerability of recombinant modified vaccinia Ankara (MVA) and Fowlpox (FPV) HIV-1 vaccines in HIV-1 infected young adults with good control of HIV replication and stable antiretroviral therapy. In response to questions regarding cardiac risk factors, Dr. Gaur said there is a cardiac assessment before the subject is enrolled on study. Guidelines from the CDC have excluded certain modified vaccinia from the requirement of those handling vaccine to have a vaccination. These are replication incompetent vectors, therefore no shedding is expected. The Committee discussed the previous use of these vectors which have been used in other HIV trials.	
Adjournment	The meeting was adjourned at 2:30 p.m.	

Judy Edwards, Environmental Health & Safety Coordinator, recorded the minutes.

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Elisabeth Adderson, M.D.
Vice-Chair, Institutional Biosafety Committee

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-05

DATE: May 12, 2005

PRESENT: Elisabeth Adderson, Lorraine Albritton, Rebecca Bush, John Coleman, James Henry, Allen Portner, Brian Robbins, Jon McCullers, and Helen Morrow

ABSENT: Cheryl Chanuad, Derek Persons, Richard Webby, Brian Robbins, Edwin Horwitz, Vishwas Parekh,

GUESTS: None

PRESENTER(S): None

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting was called order by Dr. Elisabeth Adderson, IBC Vice-Chairman.	
Biological Safety Officer Report		
Biological projects approved April 15, 2005 – May 12, 2005	Mr. Henry reported that the total number of projects submitted was 11. Eight projects have been approved with three pending approval. There were three continuing reviews submitted with two approved and one pending approval. Motion was made to give final approval to the approved projects. The motion passed unanimously.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	There was one adverse event reported. A subject on the ETNA protocol was killed in a car accident.	No follow up needed
Lab Risk Assessment	Risk assessments are ongoing. The EH&S has conducted 19 laboratory risk assessments to date. Some of the current common deficiencies that have been identified are as follows: • Inadequate documentation of training; • Submission of amendment/revision to project(s) and personnel with IBC; • Recapping of needles without using one hand technique in accordance with SJCRH Bloodborne Pathogens Exposure Control Plan (*Appendix C1(d),(e), (f)*) • Appropriate signage.	No follow up needed
Variance Report	Nothing to report	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Nothing to report	
New Business		
Non-Human Primate Program and Exposure.	Mr. Henry distributed a memo sent to Dr. Rahija giving recommendations from a risk assessment conducted as a follow-up to non-human primate exposure. There has been an NHP exposure. There is an NHP exposure training program in place, but the employee was unable to perform the procedures as described in the NHP Exposure Plan. There was discussion on what other procedures could be put in place to help employees remember the NHP Exposure Kit, proper procedures and personal protection equipment. These employees go through an annual NHP orientation. The NHP training program is also being reevaluated.	Follow up will continue.
Handling of retroviral vectors in the ARC	Dr. Gaut updated the Committee on this topic discussed in the March IBC meeting. Dr. Rahija wanted guidance from the Committee on how to handle material from animals that have been transduced with non-replicating retroviral vectors in the ARC. Because these are non-replicating vectors and the limited BL2 animal space, it was recommended that work be conducted in a BL1 space with BL2 practices. When the animals are transduced with the vectors, the PI will be required to place a sticker on the cage indicating that the animals have been transduced. For one week these cages will be handled in a different manner than the other cages. After this time the stickers are removed and the cages handled as the other cages. The BL2 cages will be handled in accordance to IBC recommendations. There was discussion regarding the risk associated with these viral vectors and literature found regarding shedding.	Follow up will continue.

Judy Edwards, Environmental Health & Safety Coordinator, recorded the minutes.

Elisabeth Adderson, M.D.
Vice-Chair, Institutional Biosafety Committee

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-06

DATE: **June 10, 2005**

PRESENT: Elisabeth Adderson, Lorraine Albritton, John Gray, James Gaut, Rebecca Bush, John Coleman, James Henry, Allen Portner, Brian Robbins, Vishwas Parekh, , and Helen Morrow

ABSENT: Cheryl Chanuad, Edwin Horwitz, Jon McCullers, Derek Persons

GUESTS: None

PRESENTER(S): None

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting was called order by Dr. Elisabeth Adderson, IBC Vice Chairman.	
Minutes of last meeting	Minutes form last meeting will be e-mailed to members for voting. Minutes from April 14 meeting have been approved by the Committee.	No follow up needed
Biological Safety Officer Report		
Biological projects approved May 13, 2005 – June 10, 2005	Mr. Henry reported activities for projects submitted, reviewed and approved for the period May 13 – June 10, 2005. The total number of projects submitted were eight with three approved and five pending approval. Continuing review activities for this period were two submitted, one approved and one pending approval. At present, the average turn around time by committee is 3 ± 1 days and the median number of days for approval is 23 ± 9 for the period of May 13, 2005 through June 10, 2005. A motion was made to give final approval to approved projects during this period. Motion passed unanimously.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Lab Risk Assessment	The EHS Department has conducted 26 laboratory risk assessments to date. Some of the current common deficiencies that have been identified are as follows: 1. Inadequate documentation of training; 2. Submission of amendment/revision to project(s) and personnel with IBC; 3. Recapping of needles without using one hand technique in accordance with SJCRH Bloodborne Pathogens Exposure Control Plan (*Appendix C1 (d), (e), (f)*) and 4) Appropriate signage.	
Variance Report	Nothing to report.	No follow up needed
4 ICC report	Nothing to report.	No follow up needed
GMP Report - Mr. John Coleman	Nothing to report.	
New Business		
Lentiviral Vectors Safety Issues	Copies of part of a presentation entitled "Lentiviral Vectors: Safety Issues" from Dr. Daniel Takefman, Division of cellular and Gene Therapies, CBER, FDA was distributed to members. Dr. Gaut explained to members the rationale for conducting serum testing for staff working with viral vectors in the past. There was some question as to whether this should continue. After discussion with other Committee members there was another reason found to continue this testing. There may be a possibility for the wild type HIV to mobilize genes contained in the lentiviral vector. Dr. Gray added that those infected with HIV and exposed to lentiviral vectors may have an enhanced risk. This additional risk should be communicated to those who have tested HIV positive, and are or plan to work with lentiviral vectors. He said that research at other institutions is underway. There was discussion of how this communication will happen within the constraints of HIPPA regulations. Occupational Health is responsible for testing staff. Additional training and communication with staff will be needed. The BSO will talk with Occupational Health on the procedures currently in place.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Adjournment	The meeting was adjourned at 1:45 p.m.	

Judy Edwards, Environmental Health & Safety Coordinator, recorded the minutes.

Elisabeth Adderson, M.D.
Vice-Chair, Institutional Biosafety Committee

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-07

DATE: July 14, 2005

PRESENT: Elisabeth Adderson, John Coleman, James Henry, Allen Portner, Brian Robbins, Jon McCullers, and Helen Morrow, Richard Webby, and James Gaut

ABSENT: Lorraine Albritton, Cheryl Chanuad, Rebecca Bush, Vishwas Parekh, Edwin Horwitz and Derek Persons

GUESTS: None

PRESENTER(S): Dr. Peter Houghton

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting was called order by Dr. Elisabeth Adderson, IBC Vice Chairman.	
Minutes of last meeting	Minutes will be distributed and voted on electronically.	
Biological Safety Officer Report		
Biological projects approved June 11, 2005 through July 14, 2005	Mr. Henry reported that the number of projects submitted between June 11, 2005 through July 14, 2005 were 11. Total number of projects approved was nine with two pending. Three continuing reviews were submitted during this period with two approved and one pending. Motion was made to give final approval to the approved projects. Motion passed unanimously.	No follow up needed
Regulatory reviews	The USDA conducted an inspection of the GMP facility today. The purpose of this inspection was for the GMP to obtain approval for working with select agents.	No follow up needed
Adverse events	Nothing to report.	No follow up needed
Lab Risk Assessment	EH&S has conducted 32 laboratory risk assessments. Some of the current common deficiencies that have been identified are as follows:	No follow up needed.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	1. Inadequate documentation of training; 2. Submission of amendment/revision to project(s) and personnel with IBC; 3. Recapping of needles without using one hand technique in accordance with SJCRH Bloodborne Pathogens Exposure Control Plan (*Appendix C1 (d), (e), (f)*) and 4) Appropriate signage.	
Variance Report	Two variances were reported since last meeting. Both test samples tested positive but the down stream samples were negative to date. Corrective action was taken and medical director notified.	No follow up needed
4 ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Nothing to report	
New Business		
Consent for HIV Blood Test and Serological surveillance required for IBC Projects.	In the previous IBC meeting of June 10, 2004, there was discussion of HIV Blood test and serological surveillance conducted for staff. Mr. Henry has worked with Occupational Health on a form to address consent for testing and a memo explaining to employees the requirements for working with lentiviral vectors and the potential risks. The documents will become a part of these employees' job descriptions. The Committee asked for changes in the document regarding the possible risk associated with exposure. A motion was made to approve these documents pending recommended changes. Motion passed unanimously.	No follow up needed.
Presentations		
O2A-237 - Evaluation of a novel oncolytic virus (Seneca Valley Virus, SVV) to treat pediatric cancers with similar neuroendocrine features (neuroblastoma, retinoblastoma, medulloblastoma. Dr. Peter Houghton	Dr. Peter Houghton was present to answer questions regarding his project. The objective of this project is to determine the efficacy of Seneca Valley Virus 001 (property of neotropix Inc.) in various forms of pediatric cancer. The Committee asked for more information regarding the Seneca Valley Virus including any taxonomic classifications, molecular structures, and articles describing the agent. After further discussion the Committee recommended biosafety level 2 containment with biosafety level 3 precautions. The Committee will also ask that Dr. Houghton obtain a USDA permit for the transport of this agent.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Adjournment	The meeting was adjourned at 1:45.	

Judy Edwards, Environmental Health & Safety Coordinator, recorded the minutes.

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Elisabeth Adderson, M.D.
Vice-Chair, Institutional Biosafety Committee

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-08

DATE: **August 11, 2005**

PRESENT: Elisabeth Adderson, Lorraine Albritton, Rebecca Bush, John Coleman, James Henry, Allen Portner, Brian Robbins, Vishwas Parekh, Jon McCullers, and Helen Morrow

ABSENT: John Gray, Derek Persons, Cheryl Chanaud, Edwin Horwitz, Richard Webby

GUESTS: None

PRESENTER(S): Dr. Gerard Zambetti

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting was called to order by Dr. Elisabeth Adderson, IBC Vice Chairman.	
Minutes of last meeting	Minutes have been approved by the committee through electronic vote.	
Biological Safety Officer Report		
Biological projects approved July 15, 2005 through August 11, 2005	The total number of projects submitted for this period is 19. Fifteen projects have been approved with four pending. There were 14 continuing reviews/amendments/revisions submitted. Twelve projects have been approved with two pending. Motion was made and seconded that the approved projects be given final approval. The motion passed unanimous.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed
Lab Risk Assessment	The Department of Environmental Health and Safety are continuing to conduct risk assessments. Some of the common deficiencies that have been identified are: 1. Inadequate documentation of training.	No follow up needed.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	2. Submission of amendments to projects and personnel to the IBC 3. Recapping of needles without using the one hand technique in accordance to St. Jude Bloodborne Pathogens Exposure and Control Plan. Mr. Henry is advising investigators and staff on the possibility of an inspection of their laboratories from the government's Office of Biotechnology (OBA) and processes they need to have in place. Dr. Zambetti's project was presented in this meeting because of a risk assessment recently conducted of his lab. There was discussion regarding the inadequate documentation of training of staff in the laboratory. Mr. Henry replied that a goal is to have some training available through CBLS in the future.	
Variance Report	Nothing to report	No follow up needed
4 ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Mr. Coleman updated the Committee on the transition of a portion of the GMP facility becoming a limited liability company, Memphis GMP, LLC, a wholly owned subsidiary of St. Jude.	
Old Business		
Follow up to Consent for HIV Blood Test	Mr. Henry spoke with Kathleen Speck to get Human Resources perspective regarding HIV testing of employees who will be working with specific materials. An employee will be given a form explaining the reason for testing. The employee can decline to be tested if the risk is to the employee only and not others due to a procedure such as certain surgeries. The employee will sign a release form if they chose not to take the test.	No follow up needed.
Presentations		
O2C-240 – International Pediatric Adrenocortical Tumor Registry. Principal Investigator: Dr. Gerard Zambetti	Dr. Zambetti was present to explain his protocol. The primary objective of this study is to collect demographic and medical information of children and adolescents with adrenocortical carcinoma to learn more about the clinical and epidemiological aspects, treatment modalities and outcomes of patients with this rare disease. The collection of these adrenocrtical tumors is part of the International Pediatric Adrenal Tumor Registry and Bank. Samples are received as frozen specimens that are then processed to total RNA, DNA and protein.	A voting memo will be e-mailed to members.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	He explained how this material is handled in the lab and the personal protective equipment used.	
Adjournment	The meeting was adjourned at 1:30 p.m.	

Judy Edwards, Biological Safety Coordinator, recorded the minutes.

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Elisabeth Adderson, M.D.
Vice-Chair, Institutional Biosafety Committee

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-02

DATE: **September 8, 2005**

PRESENT: John Coleman, James Henry, Brian Robbins, and James Gaut, Lorraine Albritton, John Gray, Richard Webby

ABSENT: Elisabeth Adderson, James Downing, Kip Guy, Mark Long, Jon McCullers, Helen Morrow, Robert Ruschman,

GUESTS: None

PRESENTER(S): None

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting was called order by Dr.Richard Webby, Vice Chairman.	
Biological Safety Officer Report		
Biological projects approved January 13, 2005 through February 10, 2005	Mr. Henry gave his report for August 12, 2005 through September 8, 2005. There were 17 projects submitted, nine projects approved with eight pending. Eight continuing review reports were submitted and approved during this period. A motion was deferred until the next meeting due to the lack of a quorum.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed
Lab Risk Assessment	The Department of Environmental Health and Safety has conducted four risk assessments to date. Some of the common deficiencies that have been identified are: 1. Inadequate documentation of training. 2. Submission of amendments to projects and personnel to the IBC 3. Recapping of needles without using the one hand technique in accordance to St. Jude Bloodborne Pathogens Exposure and Control Plan.	
Variance Report	Nothing to report	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
4 ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Nothing to report	
New Business		
Presentations		
Committee business	All committee business was deferred until the next meeting due to lack of a quorum.	
Adjournment		

Judy Edwards, Environmental Health & Safety Coordinator, recorded the minutes.

Richard Webby, Ph.D.
Vice-Chair, Institutional Biosafety Committee

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-010

DATE: **October 13, 2005**

PRESENT: Elisabeth Adderson, John Coleman, James Henry, John Gray Brian Robbins, Mark Long, Robert Rutschman, and Richard Webby

ABSENT: James Gaut, James Downing, Kip Guy, Lorraine Albritton, Jon McCullers, and Helen Morrow

GUESTS:

PRESENTER(S): Dr. Victor Santana

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	Dr. Adderson welcomed new members to the Committee. She gave a brief overview of the Committee and its responsibilities for the new members.	
Biological Safety Officer Report		
Biological projects approved August 12, 2005 through October 13, 2005	Mr. Henry reported for the period August 12, 2005 through October 13, 2005. The information given at last the IBC meeting on September 8, 2005 was again reviewed due to lack of a quorum to vote on an approval. The total number of projects submitted during this period was 30 with 19 approved and 11 pending. Continuing reviews, renewals and revision activities submitted was 16, with 13 approved and 3 pending. A motion was made to give final approval to the approved projects. The motion passed unanimously.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed
Lab Risk Assessment	The Department of Environmental Health and Safety has conducted 55 risk assessments to date. Some of the common deficiencies that have been identified are: 1. Inadequate documentation of training. 2. Submission of amendments to projects and personnel to the IBC	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	3. Recapping of needles without using the one hand technique in accordance to St. Jude Bloodborne Pathogens Exposure and Control Plan.	
Variance Report	Nothing to report	No follow up needed
4 ICC report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Nothing to report	
New Business		
IBC Review of clinical projects involving blood and tissue banking.	The Committee discussed the IBC policy and procedures in regards to reviewing samples of human origin (such as blood and tissue). After a lengthy discussion, the Committee concluded that protocols that include collection and routine blood and tissue samples are dealt with adequately by the Institutional Bloodborne Pathogens Exposure Control Plan and that these projects will not require IBC review. Laboratory workers involved in these studies should receive appropriate training in the use of universal precautions as directed by the Occupational Health Office. It was also decided that exceptions to this policy will include studies in which blood or other specimens of human origin are obtained from patients as part of a project that clearly involves increased risk to laboratory workers, such as subjects infected with select agent infectious agents. A memo will be sent to John Cunningham, IRB Chair, Cheryl Chanaud, Vice-President of Clinical Research and Bassem Razzouk, CPSRMC Chair.	A voting memo will be sent to members after the meeting.
Presentations		
New Clinical Protocol – O2C-249 NBL322 "A Phase II Study of Hu.18-IL2 in Children with Recurrent or Refractory Neuroblastoma (ANBL0322)" Principal Investigator: Dr. Victor Santana.	Dr. Santana was present to give a presentation on his protocol. He explained that the objectives for this study are to: 1) Determine the response rate to hu14.18-IL2 in 3 separate strata of patients with recurrent or refractory neuroblastoma. 2) Evaluate adverse events associated with hu14.18-IL2 infusion for 3 consecutive days administered on an every 4-week basis. 3) Evaluate the immunologic activation induced in vivo by hu14.18-IL2. 4) determine the induction of anti-hu14.18-IL2 antibody induced by treatment with hu14.18-IL2. 4) Test for associations between antitum or response and measurements of toxicity,	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	immune activation and anti-hu14.18-IL2 antibody activity. This clinical trial involves the use of a purified fusion protein (an antibody linked to IL2). In response to questions, Dr. Santana explained that this protein has been made under GMP conditions at the NIH, and has met all FDA requirements showing that the final purified clinical product is free of potential contaminants (including free of virus). There was additional discussion in regards to adverse events in previous pediatric studies.	
O2A-093 "Proliferation Control in the Retina, The RB Family, Principal Investigator: Dr. Michael Dyer.	Dr. Dyer was present to discuss the amendment to his protocol O2A-093. Dr. Dyer has requested an amendment to make a lentiviral vector that expresses a SiRNA to Human RB1 as well as a GFP reporter gene and the human MDM4 cDNA. Dr. Dyer answered questions from the Committee. After Dr. Dyer felt the room, there was further discussion. The Committee will ask Dr. Dyer to clarify the source of the primary tissue for possible safety issues (i.e. local hospital, international, etc.).	Additional question will be sent to Dr. Dyer regarding his amendment.
Adjournment	The meeting was adjourned at 11:50 a.m.	

Judy Edwards, Environmental Health & Safety Coordinator, recorded the minutes.

Elisabeth Adderson, M.D.
Vice-Chair, Institutional Biosafety Committee

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-010

DATE: **November 10, 2005**

PRESENT: Elisabeth Adderson, Lorraine Albritton, James Henry, John Gray, Brian Robbins, James Gaut, Jon McCullers, Mark Long, Robert Rutschman, and Richard Webby

ABSENT: John Coleman, Kip Guy, James Downing, Helen Morrow

GUESTS: None

PRESENTER(S): None

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	Dr. Adderson welcomed Committee members.	
Biological Safety Officer Report		
Biological projects approved October 14, 2005 through November 10, 2005 (See attached report)	Mr. Henry reported project activities from October 14, 2005 through November 10, 2005. There were 18 projects submitted for review. These projects are all pending approval. There were two continuing reviews submitted, both still pending approval. Mr. Henry reviewed the status of each project submitted and pending during this period. There was further discussion on Dr. Beere's project. A motion was made that a clarifying memo be sent to Dr. Beere specifically stating what vectors she has been approved to use. The motion passed unanimously.	A clarifying memo will be sent to Dr. Beere.
Dr. Green's projects O2-245, O2-246, O2-247, O2-248	Dr. Green's has submitted four projects for approval. After talking with Dr. Green's lab manager, the chair is requesting that the BSO meet with Dr. Green's lab manager to educate him on the Committee's recommendations. The three changes that have been requested by the Committee are: 1. Remove the statement that these "vectors are harmless". 2. Anything with tropism for human cells that contains an oncogene must be done at BL2+. 3. Please describe your procedures.	The BSO will meet with Dr. Green's Lab manager.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	There was further discussion on developing a document/template that describes procedures when working with specific vectors. There was also discussion on changing the current biosafety project registration form to get more specific information on what vectors and genes will be expressed. Dr. Gray volunteered to work on a document that investigators can reference before submitting their projects to help them give more specific information on the vectors and genes. Mr. Henry asked the Committee to send him any additional comments they may have on these projects.	
Regulatory reviews	EPA rules for operating the biofermentors in place at the GMP and the plaza level of the IRC required filing an Industrial Wastewater Discharge Agreement with the Memphis/Shelby County Division of Public Works. This division is responsible for assuring compliance of companies and organizations with EPA regulations. We were contacted by a representative from this division who requested a tour of these areas. Only the IRC location was toured and as a result of this tour, it was recommended that a barrier around the drain be installed to contain a large spill.	No follow up needed
Adverse events	Nothing to report	No follow up needed
Lab Risk Assessment	The Department of Environmental Health and Safety has conducted 61 risk assessments to date. Some of the common deficiencies that have been identified are: 1. Inadequate documentation of training. 2. Submission of amendments to projects and personnel to the IBC 3. Recapping of needles without using the one hand technique in accordance to St. Jude Bloodborne Pathogens Exposure and Control Plan.	No follow up needed
Variance Report	Nothing to report	No follow up needed
GMP Report - Mr. John Coleman	Mr. Coleman was not present.	No follow up needed
New Business		
OBA Guidelines for Project Approval	Mr. Henry reported information he obtained from Allan Shipp of the OBA in regards to Committee approval of projects. The Committee's current procedure of approving projects may not be adequate. After a lengthy discussion, the Committee decided to review all new projects prior to	IBC Policy and Procedures revisions. Submission deadline table for distribution to

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	Committee meetings. A comment/questions memo will be sent to members prior to the next IBC meeting for each project submitted. These questions will be compiled in memo form and sent to the investigator to address. If all questions have been addressed and there are no further questions in the meeting; the members will vote for approval of the project.	faculty. Revisions to policy and table brought back to the Committee for next month's meeting.
	Biosafety level 3 project procedures and clinical projects procedures will still require investigator attendance.	
	A deadline for submission table will be generated for all IBC meetings. This will be distributed to faculty. A standard memo will be sent to the investigator indicating receipt of project and review procedure.	
	A motion was made to amend IBC policy and procedures to reflect the new procedures in voting on BL1 and BL2 projects. The motion was approved unanimously.	
Amendment to O3A-137 and O3A-136 Dr. Webster.	Dr. Webby explained to the Committee the addition of Dr. MacDonald's old BL3 space for Dr. Webster's influenza projects. This space will be used as a diagnostic area to evaluate samples received from other facilities. After the strain is confirmed to be that listed on the label, it will be moved into the appropriate space. There is no other work being conducted in this area and there is an additional autoclave.	
	Dr. Webby left the room. After more discussion, a motion was made to approve this amendment. The motion passed unanimously.	
Guidelines for working with vaccina.	Currently the institution has several active projects working with vaccina. Mr. Henry said that they are currently evaluating the vaccination and training process to assure that it is being conducted in accordance with guidelines in the *BMBL*. He asked for direction from the Committee as to any changes in institutional guidelines.	Additional material with will sent to members for review. Discussion will continue at next month's IBC meeting.
	It was decided that Mr. Henry will send additional information for the Committee members to review for further discussion in the next IBC meeting.	
New Clinical Protocol: O1C-252 Phase I/II Trial of Intracerebral IL13-PE38QQR Infusion in Pediatric Patients with Recurrent Malignant Glioma. Principal Investigator: Dr. Larry Kun	Dr. Kun was not able to attend the meeting. The presentation and discussion of this protocol will be placed on the December 8, 2005 meeting agenda.	Dr. Kun will be asked to attend next month's meeting.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Adjournment	Meeting adjourned at 12:10.	

Judy Edwards, Environmental Heath & Safety Coordinator, recorded the minutes.

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Elisabeth Adderson, M.D. Chair, Institutional Biosafety Committee

JG:je

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2005-12

DATE: **December 8, 2005**

PRESENT: Elisabeth Adderson, Lorraine Albritton, John Coleman, Jim Gaut, James Henry, Brian Robbins, John Gray, Helen Morrow, Rutschman, and Kip Guy

ABSENT: Jon McCullers, James Downing, Mark Long, Richard Webby

GUESTS: None

PRESENTER(S): Dr. Larry Kun

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Welcome	The meeting was called order by Dr. Elisabeth Adderson.	
Minutes of last meeting	A motion was made and second to approve the November 10, 2005 minutes. The motion passed unanimously.	
Biological Safety Officer Report		
Biological projects approved November 11, 2005 through December 8, 2005	Mr. Henry gave his report for November 11, 2005 through December 8, 2005. There were nine projects submitted, seven projects approved with two pending. Three continuing review reports were submitted and approved during this period. He has excluded the summary information due to the change in the policy requiring all projects to be approved in the monthly IBC meeting.	No follow up needed
Continuing reviews		
O2C-135 – Phase I Study of recombinant oral BAH-2 cholera vaccines in healthy adults. A motion was made to approve the continuing review.	There were no questions. Motion was made to approve this project. The motion passed unanimously.	
O2C-162 - A phase I study of unmodified live intranasal sendai virus vaccine in children and toddlers: Assessment of safety and immunogenecity.	There is currently a clinical hold on this project issued by the FDA. One patient has been enrolled on this protocol but was not given the vaccine. A member asked that the PI submit communication from the FDA in regards to the clinical hold for record keeping purposes. A motion was made to approve the project pending FDA documentation on the clinical hold. The motion passed unanimously.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Amendments: **O2C-154** – Function of cyclin C/CDK8 – Amendment to utilities lentiviral vectors.	There were questions regarding the change in the Biosafety Level to BL2+ precautions and if this should be considered a new project.A motion was made to approve the project pending the resubmission of the amendment form with the addition of screening pre-project HIV serum levels. Also an explanation of the cell line that will be used in this project. The motion passed unanimously.	
O3A-212 – New approaches to control of influenza; neuroaminidase inhibitors in H5N1 influenza mouse model; combination therapy for pandemic influenza.	There were no comments. A motion was made to approve this continuing review. The motion passed unanimously.	
New Projects: **O2-245** – Heat shock-induced apopotosis **O2-246** – Activation-induced cell death T Lymphocytes. **O2-247** – Stress-induced apoptosis in T cells. **O2-248** – Central mechanisms of apoptosis in the immune system.	Dr. Green's projects were combined into one discussion and vote. These projects are resubmissions based on the Committee's recommendations. There was additional discussion in regards to additional precautions to be used for these projects. A motion was made to approve these projects. The motion passed unanimously.	
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed
Lab Risk Assessment	The Department of Environmental Health and Safety has conducted 64 risk assessments to date. Some of the current common deficiencies are: 1. Inadequate documentation of training. 2. Submission of amendments/revisions regarding personnel changes. 3. Recapping of needles without using the one hand technique in according with	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	the SJCRH Bloodborne Pathogens Exposure Control Plan. 4. Appropriate signage.	
Variance Report	Nothing to report	No follow up needed
4 ICC report	No report.	No follow up needed
GMP Report - Mr. John Coleman	Mr. Coleman reported that they are currently making new H5N1 strains and he will be presenting a new project in this IBC meeting. The Board has approved the formation of the LLC which should become official in January. This means that the LLC is a wholly owned company of St. Jude. This Committee will continue to review projects from the LLC. The LLC will be leasing space from St. Jude and there are other agreements between St. Jude and the LLC that will allow employees to conduct work between the two entities. They are also in the process of getting select agent approval.	
New Business		
IBC Review of projects and reports to the Committee.	**BSO Report** - Mr. Henry asked the Committee for recommendations regarding changes in the BSO report. He has reported over the last year the turnaround time of projects. The Committee now knows the average time it takes for a project to receive approval. The process has also changed in that all projects are approved during Committee meetings. Now it takes 30 days for approval of a project. **Deadline for review** - Mr. Henry also asked the Committee if they would like to have a deadline for review of projects. Currently projects are submitted and distributed to the Committee for review and comments as they come in. This usually gives time to submit questions and/or comments to the investigator to hopefully address before the next IBC meeting. The proposed deadline would only affect those projects that are received less than a week before the monthly meeting. The members recommended that projects continue to be submitted but they reserve the option to table the project if more time is needed for review. **Submission of amendments** - A suggestion was made to have the PI submit the originally approved projects with the changes instead of a separate amendment form. This discussion will continue in future Committee meetings.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Vaccina Policy	The IBC is charged with have oversight of vaccination for projects involving vaccina. This project was tabled until the next meeting to give members more time to review the policy.	
Discussion regarding BL2+ and using more specific precautions in projects.	There was discussion regarding BL2 enhancements and how to communicate specific precautions to investigators. The Committee also discussed developing more specific guidelines for investigators to refer to when completing there project applications. The guidelines could be placed on the intranet for investigators to refer to. This discussion will continue in future Committee meetings.	
Presentations		
New Clinical Protocol: O1C-231 PBTC-013 Phase I/II Trial of Intracerebral IL13-PE38QQR Infusion in Pediatric Patients with Recurrent Malignant Glioma. Principal Investigator: Dr. Larry Kun	Dr. Kun was present to explain his protocol. This is a phase I/II study of IL13-PE38QQR, a tumor targeted cytotoxin, which is a potent recombinant protein consisting of human IL-13 and an enzymatically-active portion of pseudomonas Exotoxin. The study involves children between the ages of 3 and 21 who have recurrent or progressive high grade gliomas. Initially, in the dose-finding (phase I) study, an escalation of flow rate and concentration will be undertaken. In the safety 78 efficacy (phase II) study, the efficacy of IL13-PE38QQR will estimated by survival post-infusion. There were questions regarding previous toxicity. Dr. Kun said that there has been no toxicity in the adult studies. This study will be conducted at LeBonheur in cooperation with UT. There were questions regarding the IRB and IBC approval process for LeBonheur and UT. Dr. Albritton is the chairman of the IBC at UT confirmed the receipt of Dr. Kun's project. The Committee will ask the PI to submit IBC approvals from the other institutions involved in this protocol. Motion was made to approve this protocol. The motion passed unanimously with two members obtaining.	
O2-253 - Production of Transduced NK cells for immunotherapy of leukemia.	Mr. Coleman was present to explain his project. Developmental work is starting to prepare for a proposed protocol in which patients with B-cell ALL will be treated with an infusion of gene modified Natural Killer cells (NK cells) obtained from a	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Principal Investigator: Mr. John Coleman	haploidentical donor. The gene modification adds a cell surface ligand to the NK cells that will aid in targeting the NK cells to the B-cell-ALL tumor cells that are the desired target in vivo. This project is being transferred to TPQ for scale-up and demonstration that it can be translated to a clinical scale. Mr. Coleman left the room. Motion was made to approve this project. Motion passed unanimously.	
Adjournment	The meeting was adjourned at 1:30 p.m.	

Judy Edwards, Environmental Health & Safety Coordinator, recorded the minutes.

Elisabeth Adderson, M.D.
Vice-Chair, Institutional Biosafety Committee

MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2006-01

DATE: **January 12, 2006**

PRESENT: Elisabeth Adderson, John Coleman, James Gaut, Helen Morrow, James Henry, John Gray, Jon McCullers, Brian Robbins, Robert Rutschman, and Richard Webby

ABSENT: Mark Long, James Downing

GUESTS: None

PRESENTER(S): Richard Webby

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Minutes of last meeting	December minutes were not available for the meeting.	
Biological Safety Officer Report		
IBC activity Report	Mr. Henry reported that there were 10 projects in from last month's meeting with nine approved. Project O2A-152 required re-submission. Three projects were continuing reviews.	No follow up needed
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed
Lab Risk Assessment	The Department of Environmental Health and Safety has conducted 68 risk assessments to date.	
Variance Report	Nothing to report	No follow up needed
ICC report	Dr. McCullers informed the Committee that the Pandemic Preparedness Plan will go the ICC for approval next week.	No follow up needed
GMP Report - Mr. John Coleman	Mr. Coleman reported that the LLC is now operational and they have received select agent approval.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
New Business		
Continuing Reviews		
O2A-137 - Pandemic influenza vaccines. Principal Investigator: Dr. Robert Webster	There were no questions. A motion was made to approve the continuing review. The motion passed unanimously. Dr. Webby abstained.	No follow up needed.
O2C-149: Compassionate use of Defibrotide for Patients with Veno-Occlusive Disease. Principal Investigator: Dr. Greg Hale.	There were questions about the rapid dose escalation. The project was tabled until next month's meeting to give the PI time to respond to questions from the Committee.	No follow up needed.
Amendments:		
O2A-152 - Function of cyclin C/CDK8. Principal Investigator: Dr. Jill Lahti.	This was a resubmission of Dr. Lahti's amendment clarifying questions from the Committee. A motion was made to approve this amendment. The motion passed unanimously.	No follow up needed.
O2-165 - cGMP production of the flu vaccine seed stocks using reverse genetics. PI: Mr. John Coleman.	Dr. Coleman explained that this is an amendment adding the LLC to the project. A motion was made to approve this amendment. The motion passed unanimously.	No follow up needed.
O2A-181 - Treatment of EAE Using Genetically modified CTL. Principal Investigator: Dr. Terrence Geiger	There were no questions. A motion was made to approve this amendment. The motion passed unanimously.	No follow up needed.
New Projects:		
O2A-264 – Arf Tumor Suppressor -2. Principal Investigator: Dr. Charles Sherr.	Dr. Gray informed the Committee that he has worked with Dr. Sherr on additional precautions that they need to use for the tumorigenic vectors. A motion was made to approve this project. The motion passed unanimously.	No follow up needed.
O2A-259 - CKIs CNS Development and Tumorigenesis Principal Investigator: Dr. Martine Roussel	Dr. Gray informed the Committee that he has worked with Dr. Roussel on additional precautions for this project. A motion was made to approve this project. The motion passed unanimously.	No follow up needed.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
O2-255 - Retroviral transduction of siRNA to modulate expression of ABC transporters in neuroblastoma cell lines. Principal Investigator: Dr. Clinton Stewart	There were no questions/comments. A motion was made to approve this project. The motion passed unanimously	No follow up needed.
Presentations		
New Project: O3A-254 - DNA vaccines against influenza viruses. Principal Investigator: Dr. Richard Webby.	Dr. Webby was present to explain his project. This project seeks to address issues relating to influenza immunity and vaccination by using DNA vaccine technology. He explained that the expression vectors to be used in the protocol have been developed by collaborators from outside the institution. Using these expression vectors, DNA vaccines expressing proteins of influenza viruses (either individually or in combination) will be administered to mice and ferrets via intramuscular routes. After set periods of times and doses (almost exclusively 2 doses 3 weeks apart) the animals will be challenged with influenza viruses of high and low pathogenicity. There were questions regarding reassortment and BL3 containment. The vaccination will be done at BL2 then transferred to BL3. The employees handling the animals will be vaccinated. Dr. Webby left the room. There was further discussion in regards this project. Dr. Downing has not officially approved this project due to issues regarding space. A motion was made that the project be approved. The motion passed unanimously.	No follow up needed.
Adjournment		
Old Business		
IBC Policy and Procedures and Vaccina Policy	The Committee was asked to review its policies and procedures. Mr. Henry explained that it is important that the policy and procedures encompasses every step in the approval process and what projects should be approved by the Committee. The Vaccina Policy was also distributed for Committee review. Dr. McCullers explained to the Committee information regarding administering vaccina to anyone with cardiac problems because the unknown factor of vaccina and myocardidis syndrome. The CDC has stated that there is not enough evidence at this time to link the syndrome with vaccina. As principal investigator over the vaccina study, Dr. McCullers has taken	Amended minutes will be brought back to the Committee for vote.

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	the step of limiting people with known heart conditions from receiving vaccina. A motion to approve these changes in the policy and procedures was tabled until all revisions are made.	

James Henry, Biological Safety Officer, recorded the minutes.

Elisabeth Adderson, M.D.
Chair, Institutional Biosafety Committee

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MINUTES
Institutional Biosafety Committee
St. Jude Children's Research Hospital

MEETING: 2006-02

DATE: **February 9, 2006**

PRESENT: Elisabeth Adderson, Lorraine Albritton, James Henry, James Gaut, John Gray Brian Robbins, Kip Guy, Helen Morrow, Jon McCullers, Mark Long, Robert Rutschman, and Richard Webby

ABSENT: John Coleman, James Downing

GUESTS: None

PRESENTER(S): Dr. Patricia Flynn

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
Minutes of last meeting	Minutes from the December 8, meeting and January 12 meeting were unavailable.	
Biological Safety Officer Report		
Biological projects submitted for Committee review: **New Projects:**		No follow up needed
O2-262 - Normal and oncogenic function of the BubR1 Gene. Principal Investigator: Dr. Rakeesh Goorah	There were no questions or comments. A motion was made to approve this project. The motion passed unanimously.	
O1A-261 – Bub1 knockout-mice project. Principal Investigator: Dr. Katsumi Kitagawa	There were no questions or comments. A motion was made to approve this project. The motion passed unanimously.	
Amendments:		
O2A-202 The Bcl-2/Bcl-x Pathway in Myc-Induced Lymphomagenesis. Principal Investigator: Dr. John Cleveland	There were no questions or comments. A motion was made to approve this amendment. The motion passed unanimously.	

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
R2/3-040 – Development of a novel multi-envelope AIDS vaccine. Principal Investigator: Dr. Julia Hurwitz	There was discussion on the response to Committee questions by the investigator. A motion was made to approve this amendment. The motion passed unanimously.	
Continuing Reviews:		
O3-222 Characterization of highly pathogenic influenza viruses. Principal Investigator: Dr. Richard Webby	Dr. Webby left the room. There were no questions or comments. A motion was made to approve this continuing review. The motion passed unanimously.	
O2C-149 Detide: Compassionate use of Defibrotide for Patients with Veno-Occlusive Disease. Principal Investigator: Dr. Greg Hale	This project was tabled from the previous Committee meeting. The investigator has answered questions from the Committee. There were no additional questions or comments. A motion was made to approve the continuing review. The motion passed unanimously. Dr. Albritton abstained.	
Regulatory reviews	Nothing to report	No follow up needed
Adverse events	Nothing to report	No follow up needed
Lab Risk Assessment	The Department of Environmental Health and Safety has conducted 75 risk assessments to date. One common deficiency that was identified is the use of substandard procedures. Dr. McCullers informed the Committee on risk assessment. He said that the risk assessment was very helpful. One of his action items was recapping of needles. He has reinforced the policy of no recapping of needles to his lab staff. But there are incidents where the capped needle is put in the container because only the syringe is used. There are also provisions in the Bloodborne Pathogens Policy for recapping needles under certain conditions.	Mr. Henry will develop strategies to promote a "no needle recapping" policy and report back to the committee.
Variance Report	Nothing to report	No follow up needed
4 ICC report	Dr. McCullers reported that the Pandemic Preparedness Plan has been approved by the Infection Control Committee. It is now on the intranet. The Committee also approved a policy for service animals (example: seeing eye dogs, seizure dogs) in the hospital. The policy details where the animals can go and what they can do.	No follow up needed

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
GMP Report - Mr. John Coleman	Mr. Coleman was not present.	
New Business		
Presentations		
O1C-263 -Inactivated influenza A/H5N1 vaccine for high risk employees. Principal Investigator: Dr. Patricia Flynn	Dr Flynn was present to explain her protocol. The primary objective of this protocol is to determine the safety of a subvirion inactivated A/H5N1 vaccine in healthy adults. Also to determine the immunogenicity of a subvirion inactivated H5N1 vaccine in healthy adults approximately 1 month following receipt of two 90-ug doses of inactivated influenza A/H5N1 vaccine. Dr. Flynn explained that this protocol will target employees who work with H5N1. There are several other studies only using this vaccine. These ongoing studies indicate that approximately 70% of patients vaccinated developing protective levels of antibodies. There were questions regarding side affects and how employees will be chosen for this study. Dr. Flynn said that they have contacted departments to help identify potential subjects. An information meeting will be provided to those employees working with this virus. Employees who decide to participate will be kept confidential. It will be stressed to those employees in the study to continue using precautions. Dr. Flynn left the meeting. The discussion continued with questions and comments regarding protection and inactivation of virus. A motion was made to approval this protocol. The motion passed unanimously. Dr. McCullers, Dr. Guy, Dr. Webby and Dr. Robbins abstained from voting.	No follow up needed.
Principal Investigator Project reporting requirements	Mr. Henry informed the Committee that through risk assessment they have identified projects that have not been reported to the IBC. The investigators were not aware of the policies for the work they were conducting. These situations have been corrected. There was discussion on IBC Policy and Procedures with regards to the necessity for review of projects using certain bacterial strains. The policy will be amended to clarify guidelines for what microorganisms require IBC approval prior to use.	Policy will be brought back to the Committee for review.
Replication Competent virus Screening Requirements	Dr. Gray informed the Committee that more investigators would like to use retroviral vectors containing oncogenes and related genes with tropism for human cells. It is a	Discussion is will continue in next

TOPIC	DISCUSSION/ACTION	FOLLOW-UP
	requirement that investigators screen those vector preparations for replication competent virus due to their enhanced risk. The current procedure is very slow. Dr. Gray would like to work with investigators to submit amendments to their projects not to screen for replication competent virus, but to implement controls which would be more consistent with the greatest concern regarding these agents, that they may be potent carcinogens. Dr. Gray will research this matter further and report to the Committee his findings.	month's meeting.
Wearing Gloves in Research Areas	Mr. Henry has received a request that the IBC review the policy in regards to personnel wearing gloves outside of the laboratories. There are concerns with staff opening doors with gloves on and personnel being allergic to latex. The current policy states that gloves are not to be worn in "public" space. Mr. Henry will distribute a memo in regards to this matter and get feedback from the Committee next month.	Discussion will continue in next month's meeting.
Adjournment	Meeting adjourned at 12:15	

Judy Edwards, Biological Safcty Coordinator, recorded the minutes.

Elisabeth Adderson, M.D.
Chair, Institutional Biosafety Committee

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