Column E Explanation

This form is intended as an aid to complete the Column E explanation. It is not an official form and its use is voluntary. Annual Reports and explanations should NOT include PII information such as names (principle investigators and research staff), addresses, protocols, meeting notes (either in part of in full), the animals room numbers, grant information, veterinary care programs, and the like. A Column E explanation must be written so as to be understood by lay person as well as scientists.

1. Registration Number: 51-R-0018

2. Number of animals categorized as column E used in this study _____176_____.

3. Species (common name) of animals used in this study. Guinea pig

4. Explain the procedure producing pain and/or distress.

   Animals will be exposed (via oral administration) to lethal doses of chlorpyrifos, which could cause signs of acute toxicity including profuse secretions, respiratory distress, and convulsions. These experiments are necessary to study potential treatments for people who may suffer from the effects of organophosphate intoxicants used as chemical weapons.

5. Attach or include with the reason(s) for why anesthetics, analgesics and tranquillizers could not be used. (For federally mandated testing, see Item 6 below).

   Animals that receive supra-lethal doses will receive atropine (standard treatment for organophosphate toxicity) or experimental treatments, but may still experience acute signs of toxicity that may be life-threatening.

6. What, if any, federal regulation require this procedure? What, if any, federal regulation require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9 CFR 113.102): If the requirement is per a guidance document, such as an Agency notice or harmonization guideline, please provide specific sufficient information to identify the cited document.

Agency:___N/A_____ CFR: __N/A_____

10 DEC 2018

12 DEC 2018

Column E Explanation

This form is intended as an aid to complete the Column E explanation. It is not an official form and its use is voluntary. Annual Reports and explanations should NOT include PII information such as names (principle investigators and research staff), addresses, protocols, meeting notes (either in part of in full), the animals room numbers, grant information, veterinary care programs, and the like. A Column E explanation must be written so as to be understood by lay person as well as scientists.

1. Registration Number: 51-R-0018

2. Number of animals categorized as column E used in this study: ___13_____

3. Species (common name) of animals used in this study: Miniature Swine

4. Explain the procedure producing pain and/or distress.

   Animals may experience unrelieved paid and/or distress as a result of acute radiation sickness.

5. Attach or include with the reason(s) for why anesthetics, analgesics and tranquillizers could not be used. (For federally mandated testing, see Item 6 below).

   Buprenorphine will be administered from the immediate post-irradiation period and continuing throughout the duration of the study, 2 times per day.

6. What, if any, federal regulation require this procedure? What, if any, federal regulation require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9 CFR 113.102): If the requirement is per a guidance document, such as an Agency notice or harmonization guideline, please provide specific sufficient information to identify the cited document.

Agency:___FDA Animal Rule_____ CFR: __ Title 21, Parts 314.600 through 314.650 – drugs or 601.90 through 601.95 – biological products ____

Column E Explanation

This form is intended as an aid to complete the Column E explanation. It is not an official form and its use is voluntary. Annual Reports and explanations should NOT include PII information such as names (principle investigators and research staff), addresses, protocols, meeting notes (either in part of in full), the animals room numbers, grant information, veterinary care programs, and the like. A Column E explanation must be written so as to be understood by lay person as well as scientists.

1. Registration Number: 51-R-0018

2. Number of animals categorized as column E used in this study: _____8_____

3. Species (common name) of animals used in this study: Guinea Pig

4. Explain the procedure producing pain and/or distress.

   Guinea Pigs will be immunized intranasally or intradermally then challenged with Shigella intrarectally. Animals may experience discomfort in the form of diarrhea, blood in the stool, and inflammation in the peri-anal region.

5. Attach or include with the reason(s) for why anesthetics, analgesics and tranquillizers could not be used. (For federally mandated testing, see Item 6 below).

   Analgesics will not be given because they may alter the course of infection or influence observed clinical signs, which are readouts for protection for vaccine efficacy.

6. What, if any, federal regulation require this procedure? What, if any, federal regulation require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9 CFR 113.102): If the requirement is per a guidance document, such as an Agency notice or harmonization guideline, please provide specific sufficient information to identify the cited document.

Agency:___N/A_____ CFR: __N/A_____

Column E Explanation

This form is intended as an aid to complete the Column E explanation. It is not an official form and its use is voluntary. Annual Reports and explanations should NOT include PII information such as names (principle investigators and research staff), addresses, protocols, meeting notes (either in part of in full), the animals room numbers, grant information, veterinary care programs, and the like. A Column E explanation must be written so as to be understood by lay person as well as scientists.

1. Registration Number: 51-R-0018

2. Number of animals categorized as column E used in this study: _____4_____

3. Species (common name) of animals used in this study: Sheep

4. Explain the procedure producing pain and/or distress.

   An artificial lung will be implanted onto the animal. Animals will be restrained in a in a modified metabolic stanchion for 10 days after surgical procedure, during which time it may be difficult for the animal to perform species-specific behavior.

5. Attach or include with the reason(s) for why anesthetics, analgesics and tranquillizers could not be used. (For federally mandated testing, see Item 6 below).

   Analgesics, including flunixin meglumine and fentanyl, will be used. Prolonged restraint is necessary to minimize the possibility of dislodgement of cannulae, incisional dehiscence, pneumo-/hemothorax during the recovery period.

6. What, if any, federal regulation require this procedure? What, if any, federal regulation require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9 CFR 113.102): If the requirement is per a guidance document, such as an Agency notice or harmonization guideline, please provide specific sufficient information to identify the cited document.

Agency:___N/A_____ CFR: __N/A_____

Column E Explanation

This form is intended as an aid to complete the Column E explanation. It is not an official form and its use is voluntary. Annual Reports and explanations should NOT include PII information such as names (principle investigators and research staff), addresses, protocols, meeting notes (either in part of in full), the animals room numbers, grant information, veterinary care programs, and the like. A Column E explanation must be written so as to be understood by lay person as well as scientists.

1. Registration Number: 51-R-0018

2. Number of animals categorized as column E used in this study: _____4_____

3. Species (common name) of animals used in this study: Yucatan Swine

4. Explain the procedure producing pain and/or distress.

   Diabetic swine will be given a series of full-thickness skin wounds/ along the dorsum. Pain assessments of the area will be performed with a pressure algometer and with a laser.

   Animals may experience pain at the wound sites, as well as transient pain during procedures.

5. Attach or include with the reason(s) for why anesthetics, analgesics and tranquillizers could not be used. (For federally mandated testing, see Item 6 below).

   Buprenorphine will be given pre-operatively. Carprofen will be administered on the day of surgery, and 3 days after surgery (a total of 4 days).

   Further analgesic dosing would interfere with the pain assessments that are being used throughout the study,

6. What, if any, federal regulation require this procedure? What, if any, federal regulation require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9 CFR 113.102): If the requirement is per a guidance document, such as an Agency notice or harmonization guideline, please provide specific sufficient information to identify the cited document.

Agency:___N/A_____ CFR: __N/A_____

Column E Explanation

This form is intended as an aid to complete the Column E explanation. It is not an official form and its use is voluntary. Annual Reports and explanations should NOT include PII information such as names (principle investigators and research staff), addresses, protocols, meeting notes (either in part of in full), the animals room numbers, grant information, veterinary care programs, and the like. A Column E explanation must be written so as to be understood by lay person as well as scientists.

1. Registration Number: 51-R-0018

2. Number of animals categorized as column E used in this study: _____32_____

3. Species (common name) of animals used in this study: Non-Human Primates

4. Explain the procedure producing pain and/or distress.

   Animals may experience unrelieved pain and/or distress as a result of acute radiation sickness/syndrome.

5. Attach or include with the reason(s) for why anesthetics, analgesics and tranquillizers could not be used. (For federally mandated testing, see Item 6 below).

   Analgesics are administered as soon as potential pain and distress are detected.

6. What, if any, federal regulation require this procedure? What, if any, federal regulation require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9 CFR 113.102): If the requirement is per a guidance document, such as an Agency notice or harmonization guideline, please provide specific sufficient information to identify the cited document.

Agency:___N/A_____ CFR: __N/A_____

Column E Explanation

This form is intended as an aid to complete the Column E explanation. It is not an official form and its use is voluntary. Annual Reports and explanations should NOT include PII information such as names (principle investigators and research staff), addresses, protocols, meeting notes (either in part of in full), the animals room numbers, grant information, veterinary care programs, and the like. A Column E explanation must be written so as to be understood by lay person as well as scientists.

1. Registration Number: 51-R-0018

2. Number of animals categorized as column E used in this study: _____2_____

3. Species (common name) of animals used in this study: Rabbits

4. Explain the procedure producing pain and/or distress.

   Animals will receive localized lung irradiation, similar to that used to treat human locally-advanced non-small cell lung cancer or small cell cancer. Neither pain nor distress are expected as a sequela to this procedure.

5. Attach or include with the reason(s) for why anesthetics, analgesics and tranquillizers could not be used. (For federally mandated testing, see Item 6 below).

   Buprenorphine will be administered if pain is suspected at any time throughout the study.

6. What, if any, federal regulation require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9 CFR 113.102): If the requirement is per a guidance document, such as an Agency notice or harmonization guideline, please provide specific sufficient information to identify the cited document.

Agency:___FDA_____ CFR: __Title 21 Parts 314.600 – 314.650 (drugs) or 601.90 – 601.95 (biological products)_____

Column E Explanation

This form is intended as an aid to complete the Column E explanation. It is not an official form and its use is voluntary. Annual Reports and explanations should NOT include PII information such as names (principle investigators and research staff), addresses, protocols, meeting notes (either in part of in full), the animals room numbers, grant information, veterinary care programs, and the like. A Column E explanation must be written so as to be understood by lay person as well as scientists.

1. Registration Number: 51-R-0018

2. Number of animals categorized as column E used in this study: _____113_____

3. Species (common name) of animals used in this study: Hamsters

4. Explain the procedure producing pain and/or distress. Explanations should include a brief description of the procedure, but also explain what the animal's experience, examples of which may include, but are not limited to: Neurological signs, seizures, tremors, paralysis, lethargy, inappetance, respiratory signs, GI distress, vomiting, and diarrhea.

Subsequent to testing efficacy of vaccine candidates in mice, hamsters (the gold standard for Clostridium difficile infection (CDI)) will be used to evaluate vaccine candidates in an effort to develop human therapies for the leading cause of nosocomial antibiotic-associated diarrhea and the etiologic agent of pseudomembranous colitis.

5. Attach or include with the reason(s) for why anesthetics, analgesics and tranquillizers could not be used. (For federally mandated testing, see Item 6 below).

This protocol will evaluate the efficacy of immune based interventions (vaccine and antibody therapies) against CDI. CDI in hamsters is fulminant and almost always rapidly fatal unless treated. Only new therapeutics that show excellent results in mice will be tested in hamsters. Analgesics cannot be used in this work because they mask clinical signs of disease and alter behavior. Clinical signs such as lethargy, depression and hunched posture are critical for determining severity of disease and alternative endpoints and it will satisfy the need for pre-clinical safety and efficacy data prior to conducting clinical trials in humans.

6. What, if any, federal regulation require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9 CFR 113.102): If the requirement is per a guidance document, such as an Agency notice or harmonization guideline, please provide specific sufficient information to identify the cited document.

Agency:___FDA_____ CFR: __21, § 314 & 601____

12 DEC 2019