

United States Department of Agriculture Animal and Plant Health Inspection Service**Form 7023 Attachment – Category E Explanation (Pigs)**

Registration Number 74-G-0004

USDA-ARS Children's Research Nutrition Center

Number of Animals used in this study: 111 (Category D) and 49 (Category E)

Species (common name) of animals used in this study: Pigs

Explanation of the procedure producing pain and/or distress:

Development of necrotizing enterocolitis (NEC): NEC is a serious inflammatory condition that requires medical intervention in 5% of all premature infants. During NEC, portions of the distal small intestine and colon undergo intestinal injury, hemorrhaging, mucosal tissue sloughing and necrosis. The condition can also lead to bowel perforation and septicemia, fever, respiratory distress, cyanosis, labored breathing, blood oxygen desaturation and death. In these studies, intravenous and intragastric feeding protocols are used to induce or mitigate NEC incidence 2-7 days after birth. This provides a platform for testing how various diets (infant formula and breast milk) and clinical interventions (nasal oxygen and parenteral nutrition) influence the risk of NEC. Most of these conditions and symptoms of NEC seen in human infants are closely reproduced in this model and thus represent a highly clinically relevant model to study the disease.

Scientific justification why pain and/or distress could not be relieved, including methods or means used to determine that pain and/or distress would interfere with test results:

The reason for this classification is that NEC is variable in severity and onset in a manner that has strong clinical correlates in human infants. Thus, animals in these studies might die due to NEC rapidly, which in some cases might prevent timely intervention with analgesic drugs or euthanasia prior to the development of advanced disease.

We monitor pigs for clinical symptoms of NEC such as abdominal distension, persistent recumbence, and fever. If these clinical symptoms persist and also pigs develop signs of respiratory distress, cyanosis, labored breathing and desaturation below 80% SpO₂, then pigs are euthanized with commercial euthanasia solution. Prior to this palliative care (Buprenorphine 0.01 mg/kg every 6-12 hours) will provide relief from pain as much as possible without compromising life span of the animals.

It is noteworthy that this form covers unrelieved pain, but assumes that all such pain occurs because analgesics are being withheld for scientific reasons. Appropriate analgesia and euthanasia are not withheld in these studies. We make every effort to intervene during the course of disease as symptoms progress to an advanced stage.

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