

### Column E Explanation

**1. Registration number.**

47-R-0004

**2. Number of animals used in this study.**

7 Ewes

**3. Species of animals used in this study.**

Sheep (*Ovis aries*)

**4. Explain the procedure producing pain and/or distress. (Procedure & animal experience)**

Procedure: Pregnant ewes are administered bacterial lipopolysaccharide (LPS) endotoxin, (a cellular component extracted from *E. coli* cells) in late gestation to induce moderate systemic inflammation. LPS has been widely used in sheep and other research animals to study systemic inflammation because a.) it is generally safer for researchers and animals than live-bacteria injections, B.) it results in a typical and well-characterized animal experience in most cases, and c.) the effects of LPS on immune stimulation can generally be quickly reversed by administration of dexamethasone.

Animal Experience: The LPS treatment is intended to reflect a mild to moderate systemic infection or illness in the pregnant female (i.e. flu-like illness). Animal experiences are largely consistent and are characterized by mild to moderate clinical and physiological symptoms consistent with an immune response to systemic infection.

**5. Explain why anesthetics, analgesics, tranquilizers could not be used.**

Pregnant women are typically discouraged from using non-steroidal anti-inflammatory drugs (NSAIDs) to treat fever and inflammation, as the effects on the fetus are not well understood. However, the effects of fever/inflammation proper on placental function and fetal development are similarly unclear. Pregnant sheep are a commonly-used animal model for biomedical research due to key similarities between the human and ovine fetus. Thus, the objective of this study is to better understand how moderate inflammation during late gestation affects placental function and fetal development in the well-characterized pregnant ewe model, and whether concurrent NSAID treatment lessens or worsens the impact on the placenta and fetus. Untreated systemic inflammation in these animals reflects a common but under-studied human medical condition that appears to adversely impact perinatal and early-life health of the offspring. Moreover, treatment of the clinical symptoms of inflammation with NSAIDs (most common anti-inflammation/fever reducer used in non-pregnant humans and animals) will comprise a treatment group that will then be compared to the untreated group. Animals are closely monitored under the direction of the attending veterinarians, and our previous experience with this technique combined with literature reviews has allowed us to understand the ewe's normal physiological responses to LPS and to intervene when appropriate.

**6. Federal regulations that require this procedure.**

None