SUMMARY OF EXCEPTIONS – Revised 15May23

Exceptions to the standards and regulations under the AWA for the annual reporting period October 1, 2021 – September 30, 2022, are noted below. No animals experience detrimental health effects.

1. The IACUC approved one study protocol proposing food fasting of diabetic pigs for up to 36 hours for bioavailability/pharmacokinetic studies. Food fasting periods were extended to up to 36 hours to 1) eliminate meal-induced endogenous insulins from cross-reacting with the analytical assay and 2) prevent blood glucose elevation from masking the true activity of the test insulin.

   Although this food fasting interval is IACUC approved, no pigs have experienced the 36-hour food fasting in relation to trials during the 2021-2022 reporting period.

2. The IACUC approved one study protocol proposing food fasting of dogs for > 24 hours but not to exceed 48 hours (average of 33 hours) prior to diabetic induction procedures to ensure low levels of glycogen in the liver as it may interfere with the efficacy of the induction agent.

   Although this food fasting interval is IACUC approved, no dogs have experienced the 24–48-hour food fasting in relation to trials during the 2021-2022 reporting period.

3. The IACUC approved one study protocol proposing food fasting of swine for 36-48 hours to empty gut contents prior to cecal cannulation.

   Although this food fasting interval is IACUC approved, no pigs have experienced the 36–48-hour food fasting in relation to trials during the 2021-2022 reporting period.

4. The IACUC approved one study protocol proposing water fasting for 34-38 hours to investigate kidney maximal tolerability for fluid and electrolytes regulation in the transgenic animals and provide solid data to support clinical application during kidney transplantation.

   Although this water fasting interval is IACUC approved, no dogs have experienced the 34-48-hour water fasting in relation to trials during the 2021-2022 reporting period.

Multiple major survival surgery –

1. The IACUC approved one study protocol proposing the potential for multiple major survival surgeries involving separate anesthesia events on pigs for a safety pharmacology colony. One surgical procedure is an ovariectomy surgery to prevent variations in an animal's diabetic status due to hormonal cycles. One surgery involves a flank incision or a midline abdominal incision to allow for a transmitter to be placed lateral to the incision between the peritoneum and abdominal muscle layer to prevent device migration or exposure. Additionally, animals that have undergone a transmitter implant surgery, but not an ovariectomy surgery, may be used under another protocol involving another major survival surgery, as described below.

   Although a second major survival surgery is IACUC approved, no pigs have experienced a second major survival surgery in relation to this protocol during the 2021 – 2022 reporting period.

2. The IACUC approved one study protocol proposing a second major survival surgery for recovery animals. The surgery involves the administration of the test article or vehicle within an extended surgery incision exposing muscle and bone on the lateral thigh of pigs. These animals will have previously undergone a transmitter implant surgery under a safety pharmacology colony protocol, as described above. Telemetry monitoring is required as the FDA has indicated a full cardiopulmonary safety pharmacology study for the test article and the second surgery is intended to mimic the clinical route for dose administration. Due to the unique nature of the test article molecule and its intended clinical use as a local therapy on the exposed tissues of surgery, the only appropriate manner in which it can be dosed to study cardiopulmonary safety is intra-operatively, necessitating the second major surgical procedure.

   Although this second major survival surgery is IACUC approved, no pigs have experienced a second major survival surgery in relation to trials during the 2021-2022 reporting period.