Column E Explanation Form for Regulated Species

1. Registration Number: 93-F-0006

2. Number of animals used under Column E conditions in this study: 2

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

4. Explain the procedure producing pain and/ or distress, including reason(s) for species selected:

The procedure with the potential for distress involves rabbits used to evaluate the potential for local mucosa irritation of test articles in rabbits. Test article is infused intranasally and animals are monitored at least twice daily and assessed for clinical adverse effects. Rabbits were chosen as the model because their sensitivity to botulinum toxin as a non-rodent species is more similar to humans than other commonly used non-rodent species.

5. Provide scientific justification why pain and/ or distress could not be relieved. State methods or means used to determine that pain and/ or distress relief would interfere with test results:

There are no alternative assays for testing the potency/ toxicity of botulinum toxin. Humane endpoints for this study include dyspnea, cyanosis, or bleeding from nasal cavity, as well as any signs of systemic toxicity that do not allow normal physiologic functions to be carried out (e.g.: eating/ drinking, ambulating, etc.). Animals exhibiting any of these clinical signs will be euthanized immediately.

Since the purpose of our study is to evaluate the potency and toxicity of botulinum and the study endpoints are based on symptom frequency and severity, it is not possible to provide treatment relief that may impact the manifestation or severity of symptoms unless the animal is in undue distress, at which point it will be immediately euthanized.

Review of current scientific literature, attendance at relevant scientific conferences, and continuing discussions with other experts in the field are used to determine that we are using the most appropriate species and most appropriate methods to obtain relevant research data.