

Column E Explanation

- 1. Registration Number: 93-R-0026
- 2. Number of animals used in these studies: 17
- 3. Species (common name) of animals used in this study: Dog
- 4. Explain the procedure producing pain and/or distress:

The vehicle on this study had some unanticipated effects that included diarrhea and vomiting. Initially the animals remained bright and active, but on Day 6 one dog was found to be hypoactive and depressed and showed evidence of marked abdominal discomfort. Subcutaneous fluids were administered by veterinary staff. This animal was found dead the next morning. On that same morning, several other animals began showing signs of hypoactivity, and at this point the dosing was terminated (3 weeks ahead of schedule). Several of the dogs remained hypoactive for up to 6 more days, but were back to normal behavior after that.

- 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. (For Federally mandated testing, see Item 6 below).

Medications that could have prevented discomfort associated with gastroenteritis could not be provided to the animals as this might have caused confounding effects on this study. However, the Study Director stopped the dose administration after one animal died and several others began showing signs of discomfort.

- 6. What, if federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific number (e.g. APHIS, 9 CFR 113.102):

This was a study conducted to support a client IND application to FDA. These studies followed the FDA Good Laboratory Practice regulations 21CFR part 58.

Column E Explanation

1. Registration Number: 93-R-0026
2. Number of animals used in these studies: 45
3. Species (common name) of animals used in this study: *Saimiri Sciureus*

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

The potential for distress involves the administration of a neurotoxin for the purpose of creating an animal model of a central nervous system movement disorder and the secondary dyskinesias which are adverse complications of long term medical therapy for the neurological disorder. The neurotoxic drug may also have short term effects (days) on liver metabolism with resulting malaise.

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. (For Federally mandated testing, see Item 6 below).

The goal of these studies is to identify treatments for the primary central nervous system disorder and the secondary dyskinesias caused by our current medical regimens. Such work is only possible in an animal model. Use of sedatives or tranquilizers is not possible because the effects of these agents on the movement/coordination of the animals would interfere with the movement assays we use to determine efficacy of our novel treatments and thus would interfere with the results of our investigations. Analgesics are not considered to be drugs of choice for treatment of malaise in these animals as they can increase clinical lethargy and further depress the sensorium, exacerbating and further compromising the animal's clinical condition. We actively review current scientific literature, attend relevant scientific conferences, and discuss our findings and studies with experts in the field to assure that we are using the most refined methods on the fewest number of animals of the most appropriate species.

6. What, if federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific number (e.g. APHIS, 9 CFR 113.102):

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December 4, 2012

Dr. Robert M. Gibbens
Regional Director
U.S. Department of Agriculture
Animal and Plant Health Inspection Service
Western Sector, Animal Care
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Registration No.: 93-R-0026

Dear Dr. Gibbens:

SRI International's Annual Report of Research Facility for the period of October 1, 2011 through September 30, 2012 was submitted last week. It has come to my attention that the Column E Explanation for the 17 dogs failed to describe one animal's experience which was significantly different from that of the others on the same study. This omission was unintentional, but was unfortunately not realized until after the report had already been finalized and submitted.

Enclosed please find the amended Column E Explanation for the 17 dog study which was previously described in this report.
I apologize for the inconvenience this has created.

Very truly yours,

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A large grey rectangular redaction box covers the signature area of the letter.

SRI International

333 Ravenswood Avenue • Menlo Park, California 94025-3493 • 650.859.2000

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1. Registration Number: 93-R-0026
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3. Species (common name) of animals used in this study: Dog
4. Explain the procedure producing pain and/or distress:

The vehicle on this study had some unanticipated effects that included diarrhea and vomiting. Initially the animals remained bright and active, but as soon as the animals were noted to be hypoactive the dosing was terminated. Several of the dogs remained hypoactive for up to 6 more days, but were back to normal behavior after that.

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. (For Federally mandated testing, see Item 6 below).

Medications that could have prevented discomfort associated with gastroenteritis could not be provided to the animals as this might have caused confounding effects on this study. However, the Study Director stopped the dose administration as soon as any animal began showing signs of discomfort.

6. What, if federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific number (e.g. APHIS, 9 CFR 113.102):

This was a study conducted to support a client IND application to FDA. These studies followed the FDA regulation 21CFR part 58.

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