I. GENERAL INFORMATION

A. File Number

NADA 139-633

B. Sponsor

Wildlife Laboratories, Incorporated
Hwy. 71 North
P. O. Box 308
Lowell, Arkansas 72745

C. Proprietary Name

WILDNIL

D. Established Name

carfentanil citrate

E. Dosage Form(s), Route of Administration and Recommended Dosage

The product is supplied as a sterile solution for parenteral administration into a large muscle mass at a dosage ranging from 0.005 to 0.020 milligrams per kilogram of body weight.

F. Dispensing Status

Prescription (Rx)

G. Indication

For use as an immobilizing agent in free-ranging or confined members of the family Cervidae (deer, elk, moose).

II. EFFECTIVENESS

The efficacy of Carfentanil as an immobilizing agent for members of Cervidae family has been demonstrated in 19 well controlled pivotal and corroborative clinical field trials conducted with 158 moose, 295 elk, 18 Axis deer, 9 Sika deer and 29 exotic Cervidae.

Due to the readily observable effect (immobilization), each animal served as its own control as provided under 21 CFR 514.111(a)(5)(ii)(a)(2)(iii). A summary of the data follows.

A. Studies in Moose

1. Study One in Moose

   Type of Study: Field study.

Name and Address of Investigator:

Dr. Albert W. Franzmann
Alaska Department of Fish & Game
Soldotna, Alaska

Study Design:

Purpose: Evaluation of Carfentanil as an immobilization agent for moose with antagonism by diprenorphine.

Test Animals:

1) Number: 92
2) Age and Sex: Adults of both sexes
3) Free-ranging moose.

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: Not applicable

Dose Forms:

Injectable liquid. Active chemical and vehicle are identical to formulation for which approval is requested.

Route of Administration: Intramuscular

Dosage Used: 0.006 to 0.014 mg/kg body weight

Test Duration: 12 months, March 1983 to March 1984

Parameters Measured:

1) Dose Administered
2) Time to Immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

Total dosage per moose varied from 2.5 to 5 mg Carfentanil (0.006 to 0.014 mg/kg). Mean induction time for moose receiving at least 3 mg was 5.0 minutes. Diprenorphine was used as the antagonist. During 1983, the dosage used was 14 mg IV and 6 mg IM. In 1984, the antagonist dosage was increased and 20 mg were given IV and 10 to 20 mg IM. Mean recovery time was 4.2 minutes. Hyperthermia, acute capture myopathy and/or

narcotic recycling were attributed to 6 mortalities (6.5%) directly associated with immobilization.

Statistical Analysis: None conducted.

Conclusions:

The data gathered during this study show that Carfentanil citrate administered at dose ranges of 0.006 - 0.014 mg/kg body weight intramuscularly to moose produces rapid immobilization and that the immobilization may be reversed by diprenorphine at a total dose range of 20 to 40 mg per moose.

Adverse Reactions:

Six mortalities were observed (6.5%) some of which may have been treatment related. These were a result of hyperthermia, acute capture myopathy and narcotic recycling.

Special Issues: None

2. Study Two in Moose

Type of Study: Field Study

Names and Addresses of Investigators:

Mr. John Kimball
Utah Game & Fish Department
Ogden, Utah

Dr. Ted Stanley
Department of Anesthesiology
University of Utah Medical Center
Salt Lake City, Utah

Study Design:

Purpose: Evaluation of Carfentanil as an immobilization agent for moose.

Test Animals:

1) Species Used: Moose (*Alces alces*)
2) Number: 9
3) Age: 4 adults, 4 calves and 1 yearling

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Forms: Injectable liquid.

Route of Administration: Intramuscular

Dosages Used: 0.006 - 0.015 mg/kg body weight

Test Duration: N/A

Parameters Measured:

1) Dose administered
2) Time to immobilization
3) Amount of antagonist
4) Time to recovery
5) Adverse effects

Results: Mr. Kimball, Regional Biologist for Utah Game and Fish utilized Carfentanil under "real world" situations to rapidly immobilize and remove moose in situations were they had locked antlers or had wandered near towns. Seven of the 9 moose that were immobilized were reversed with Diprenorphine at a ratio of approximately 7 mg of Diprenorphine per 1 mg Carfentanil. One of the nine was euthanized due to a fractured limb.

Statistical Analysis: None conducted.

Conclusions: Carfentanil citrate administered at 0.006 to 0.015 mg/kg produces immobilization in moose.

Adverse Reactions: None

Special Issues: None

3. Study Three in Moose.

Type of Study: Field Study

Names and Addresses of Investigators:

T. Newman, J. D. Port, T.H. Stanley and K. F. Willard
Department of Anesthesiology
University of Utah Medical Center
Salt Lake City, Utah

J. Kimball
Utah Division of Wildlife Resources
Ogden, Utah

Study Design:

Purpose: The 3 moose reported in this study were immobilized by aerial dart from a capture gun in order to investigate injuries or to relocate the animals.

Test Animals:

1) Number: 3
2) Age and Sex: 1 cow, 1 calf and 1 adult bull

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Forms: Injectable liquid.

Route of Administration: Intramuscular

Dosages Used: 0.005 - 0.012 mg/kg body weight

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to Immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results and Conclusions:

The 3 moose (cow, calf and adult bull) which received 5.5 or 12 micrograms/kg were immobilized within 6 to 22 minutes. Except for a slightly elevated temperature (40.6°C) no other problems were observed. The animals were removed or released 1 hour following immobilization. One animal had to be destroyed due to physical injuries received prior to the immobilization.

Statistical Analysis: None conducted

Adverse Reactions: Elevated body temperature

Special Issues: None

4. Study Four in Moose.

Type of Study: Field Study

Name and Address of Investigator:

Dr. William Taylor
Alaska Department of Game & Fish
Anchorage, Alaska

Study Design:

Purpose: Determine efficacy of Carfentanil in moose under field conditions.

Test Animals:

1) Species: Moose (*Alces alces*)
2) Number: 38
3) Age and Sex: Adults and subadults of both sexes.

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable Liquid

Route of Administration: Intramuscular

Dosage Used: 0.008-0.020 mg/kg

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to Immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

In these 38 animals with an average weight of 467 kg Carfentanil administered at an average dose of 0.012 mg/kg body weight produced immobilization in an average of 4 minutes. The immobilization was effectively reversed with a narcotic antagonist.

Statistical analysis: None conducted

Conclusions:

The data gathered by Dr. Taylor in Alaska support the label dose range for Carfentanil in moose of 0.005 - 0.020 mg/kg body weight.

Adverse Reactions: None

Special Issues: None

5. Study Five in Moose.

Type of Study: Field Study

Name and Address of Investigator:

Mr. William Dalton
Department of Natural Resources
Fort Francis, Ontario, Canada

Study Design:

Purpose: Demonstrate efficacy of Carfentanil in moose.

Test Animals:

1) Moose (*Alces alces*)
2) Number: 16
3) Age and Sex: Adults and subadults of both sexes

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosage Used: 0.0067 mg/kg body weight

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to Immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

Thirteen (13) of the 16 animals had acceptable induction times. Three (3) animals showed excessive induction times. These were interpreted by the

investigator as being due to improper injection of Carfentanil because of the type of dart used. All immobilized animals were successfully reversed within an average time of 4.5 minutes with the use of a narcotic antagonist.

Statistical Analysis: None conducted

Conclusions:

The data gathered by Mr. Dalton in Canada, support the recommended label dose range of Carfentanil in moose of 0.005 - 0.020 mg/kg body weight.

Adverse Reactions: None

Special Issues: None

B. Studies Conducted in Elk

1. Trial One in Elk.

Type of Study: Dose Determination

Names and Addresses of Investigators:

Thomas Meuleman, J.D. Port, T.H. Stanley and K.F. Williard
Department of Anesthesiology
University of Utah Medical Center
Salt Lake City, Utah 84132

John Kimball
Utah Division of Wildlife Resources
Ogden, Utah 84403

Study Design:

Purpose: Determine appropriate effective dose of Carfentanil in elk with antagonism by diprenorphine.

Test Animals:

1) Species: *Cervus elaphus*
2) Number: 58
3) Age and Sex: Adults of both sexes
4) Semi-confined facilities

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosages Used:

1.25 to 12 micrograms per kilogram body weight (0.00125 - 0.012 mg/kg body weight). Six milligrams of diprenorphine were used as an antagonist in each animal.

Test Duration: 72 hours

Parameters Measured:

1) Dose Administration
2) Time to Immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results of Meuleman Trials:

Dose in Microgram/kg	**Induction Time**
1.25 (10)*(a)	4.3 minutes
2.00 (14) (a)	3.5 minutes
5.00 (7) (a)	3.8 minutes
10.00 (6) (a)	1.8 minutes
4.4 to 6.6 (6) (b)	3.9 minutes
7.4 to 12.0 (7) (b)	1.8 minutes
7.9 (8) (c)	7.8 minutes

*Numbers in ( ) indicate the number of elk administered each dose.
(a) These animals were dosed by means of a hand-held syringe.
(b) These animals were dosed by means of a jab stick.
(c) These animals were administered the drug by a dart syringe.

Statistical Analysis: None conducted.

Conclusion:

The data show a dose-related response and indicate that 0.010 mg/kg delivered by hand-held syringe produces immobilization rapidly in this species. Data in eight animals indicate the need for higher doses in animals injected by aerial dart syringes. Six milligrams of diprenorphine effectively antagonized the immobilization effects of this dose range of Carfentanil.

Adverse Reactions: None Observed

Special Issues: None

2. Trial Two in Elk.

Type of Study: Field

Names and Addresses of Investigators:

Dr. Peter L. Bailey, J.D. Post, J.L. Giese, P. Zwanikken, N.L. Pace, T. H. Stanley and John Kimball
University of Utah Medical Center
Salt Lake City, Utah 84132

Study Design:

Purpose: Evaluate appropriate safe and effective dose of Carfentanil in elk with antagonsim by diprenorphine.

Test Animals:

1) Number of Animals: 18
2) Age and Sex: Adult and subadults of both sexes.
3) Semi-confined conditions after capture.

Type of Control:

Each animals served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosage Used:

0.00025 - 0.020 mg/kg body weight. Effects were reversed with 5.2 to 10.0 mg diprenorphine.

Test Duration: 24 hours

Parameters Measured:

1) Dose Administered
2) Time to Immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results of Bailey, et al. Trials:

Dose in Micrograms/Kg	Induction Time	Reversal Agent and Recovery Time
0.25 (1)*	Ataxia-never immobilized	
0.30 (1)	Ataxia-never immobilized	
0.50 (4)	Ataxia-never immobilized	
0.60 (4)	(1) 22 minutes	Treatment with M50-50 gave recovery in 3-7 minutes.
0.75 (3) 1.00 (2)	Mean time to immobilization was 16.2 minutes	Treatment with M50-50 gave recovery in 3-7 minutes.
6.00 (1) 20.00 (1) 20.00 (1)	Mean time to immobilization was 1.6 minutes	Treatment with M50-50 was successful.

* Figures in ( ) indicate the number of elk administered each dose.

Statistical Analysis: None conducted

Conclusions:

Doses of 0.006 mg/kg or higher produced satisfactory immobilization in elk. Doses of 0.001 mg/kg or lower did not produce immobilization.

Adverse Reactions: One of the three elk dosed at 0.0075 mg/kg was found dead 2 days later.

Special Issues: None

3. Third Study in Elk.

Type of Study: Field Study

Name and Address of Investigator:

Dr. Albert W. Franzmann
Alaska Department of Fish & Game
Soldotna, Alaska

Study Design:

Purpose:

Determine the effectiveness of Carfentanil to immobilize free-ranging elk following helicopter pursuit.

Test Animals:

1) Number: 8
2) Age and Sex: Adults females
3) Free-ranging

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular following helicopter pursuit.

Dosage Used: 0.015 mg/kg to 0.030 mg/kg

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to Immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

Carfentanil administered at an average dose of 0.020 mg/kg body weight (0.015 to 0.029 mg/kg range) produced an average time to immobilization of 4 minutes. These immobilizations were effectively antagonized by a narcotic antagonist.

Statistical Analysis: None conducted

Conclusions:

Free-ranging elk, pursued by helicopter, were effectively immobilized with Carfentanil at an average dose rate of 0.020 mg/kg body weight.

Adverse Reactions: None

Special Issues: None

4. Fourth Study in Elk.

Type of Study: Field Study

Name and Address of investigator:

Dr. Ted Kistner
Oregon Department of Game & Fish
Corvallis, Oregon

Study Design:

Purpose: Demonstrate efficacy of Carfentanil in free-ranging Roosevelt Elk following helicopter pursuit.

Test Animals:

1) Number 13
2) Age and Sex: Adults of both sexes
3) Free-ranging

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable

Route of Administration: Intramuscular

Dosage Used: 0.010 - 0.026 mg/kg body weight

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to Immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

An average dose of 0.0159 mg/kg body weight produced immobilization in these elk in an average of 2.5 minutes. Reversal was effectively accomplished with a narcotic antagonist.

Statistical Analysis: None conducted.

Conclusions:

This study supports the recommended label dose range of 0.010 - 0.026 mg/kg body weight.

Adverse Reactions: None

Special Issues: None

5. Fifth Study in Elk.

Type of Study: Field Study

Name and Address of Investigator:

Dr. Ted Kistner
Oregon Department of Game & Fish
Corvallis, Oregon

Study Design:

Purpose: Demonstrate efficacy of Carfentanil to immobilize free-ranging elk.

Test Animals:

1) Number: 70
2) Age and Sex: Adults and subadults of both sexes.

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosage Used: 0.009 - 0.025 mg/kg body weight (0.015 mg/kg body weight, average)

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to Immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

This group of animals was effectively immobilized at an average of 0.015 mg/kg body weight with a dose range of 0.009 - 0.025 mg/kg. Average time to immobilization was 4.6 minutes in this group of 70 animals. The immobilization effectively antagonized with a narcotic antagonist. Two mortalities occurred due to non-drug related injuries.

Statistical Analysis: None conducted.

Conclusions: This study supports the recommended label dose range of Carfentanil in elk.

Adverse Reactions: None

Special Issues: None

6. Sixth Study in Elk.

Type of Study: Field Study

Name and address of Investigator:

Dr. Ted Kistner
Oregon Department of Game & Fish
Corvallis, Oregon

Study Design:

Purpose:

Demonstrate efficacy of Carfentanil in free-ranging elk following helicopter pursuit.

Test Animals:

1) Number: 60
2) Age and Sex: Adult and subadult females

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosage used: Average 0.011 mg/kg body weight

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

An average dose rate of 0.011 mg/kg body weight of Carfentanil produced an average time-to-immobilization of free-ranging elk of 5.13 minutes. All immobilized animals were effectively reversed with a narcotic antagonist. One mortality occurred that was not drug related.

Statistical Analysis: None conducted

Conclusions:

Free-ranging elk in this study were effectively immobilized at an average dose rate of 0.011 mg/kg body weight and reversed with a narcotic antagonist.

Adverse Reactions: None

Special Issues: None

7. Seventh Study in Elk.

Type of Study: Field Study

Name and Address of Investigator:

Dr. Ted Kistner
Oregon Department of Game & Fish
Corvallis, Oregon

Study Design:

Purpose: Determine the efficacy of Carfentanil to immobilize free-ranging elk

Test Animals:

1) Number: 12
2) Age and Sex: Adults and subadults of both sexes

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular following helicopter pursuit.

Dosage used: 0.013 - 0.029 mg/kg body weight (0.017 mg/kg body weight average).

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

Eight of the twelve elk dosed at an average of 0.017 mg/kg were immobilized within an average time of 4.6 minutes. The remaining elk were immobilized within an average time of 16 minutes.

Statistical Analysis: None conducted

Conclusions:

The data gathered during this study are consistent with the data from previous studies on immobilization of free-ranging elk with Carfentanil and supports the recommended dose range.

Adverse Reactions: None

Special Issues:

The initial results in some of the elk in this study underscore the need for adequate injection of Carfentanil for maximum efficacy of the drug. Inadequate injection results in prolonged induction times as occurred in four of these elk.

8. Eighth Study in Elk.

Type of Study: Field Study

Name and address of Investigator:

Mr. Jim Unsworth
Idaho Game & Fish Department
Boise, Idaho

Study Design:

Purpose: Determine efficacy of Carfentanil in free-ranging elk.

Test Animals:

1) Number: 35
2) Age and Sex: Adults and subadults of both sexes

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosage used: 0.012 - 0.021 mg/kg body weight (0.011 mg/kg body weight average).

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

Elk under the conditions of this study were immobilized with an average dose rate of 0.010 mg/kg body weight in an average time of 4.7 minutes. The immobilization was effectively reversed with a narcotic antagonist.

Statistical Analysis: None conducted

Conclusions: These data support the recommended dose range for Carfentanil in elk.

Adverse Reactions: None

9. Ninth Study in Elk.

Type of Study: Field Study

Name and address of Investigator:

Dr. Jim Peek
University of Idaho
Moscow, Idaho

Study Design:

Purpose: Determine efficacy of Carfentanil in free-ranging elk.

Test Animals:

1) Number: 10
2) Age and Sex: Adult males

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosage used: 0.008 - 0.013 mg/kg body weight (0.010 mg/kg body weight average).

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

An average dose of 0.010 mg/kg body weight produced immobilization in 4.4 minutes in 9 out of 10 animals. The time to initial effect was not available on the tenth animal. Average time to reversal of the immobilization effect with a narcotic antagonist was 6.15 minutes.

Statistical Analysis: None conducted

Conclusions: This data supports the 0.005 - 0.020 mg/kg body weight dose range in elk.

Adverse Reactions: Re-narcotization was observed in one animal.

Special Issues: None

10. Tenth Study in Elk.

Type of Study: Field Study

Name and address of Investigator:

Dr. Jim Oosterhuis
San Diego Zoo
San Diego, California

Study Design:

Purpose: Demonstrate efficacy of Carfentanil in Eurasian species of elk under confined conditions.

Test Animals:

1) Number: 8
2) Age and Sex: Adults of both sexes

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosage used: 0.004 - 0.009 mg/kg body weight (0.006 mg/kg body weight average).

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

All animals were immobilized with Carfentanil at the indicated dose range and effectively reversed with a narcotic antagonist.

Statistical Analysis: None conducted

Conclusions:

The data gathered during this study support the recommended dose range for Carfentanil in elk.

Adverse Reactions: None

Special Issues: None

11. Eleventh Study in Elk.

Type of Study: Field Study

Names and Addresses of Investigators:

Mr. Jim Peek/Francis Cassier
Montana Cooperative Research Unit
Montana

Study Design:

Purpose: Demonstrate efficacy of Carfentanil in elk.

Test Animals:

1) Number: 3
2) Age and Sex: Adult females

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosage used: 0.010 - 0.022 mg/kg body weight

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

All three elk were successfully immobilized within these dose ranges and effectively reversed with narcotic antagonists within 3 minutes.

Statistical Analysis: None conducted

Conclusions: The data supports the recommended dose range for Carfentanil.

Adverse Reactions: None

Special Issues: None

C. Study in Axis Deer.

Type of Study: Field Study

Name and Address of Investigator:

James Oosterhuis, DVM
San Diego Zoo
San Diego, California

Study Design:

Purpose: Demonstrate efficacy of Carfentanil in axis deer with antagonism by diprenorphine.

Test Animals:

1) Number: 16
2) Age and Sex: Adults and subadults of both sexes

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosage used: 0.005 - 0.018 mg/kg body weight

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

All deer were effectively immobilized with an average of 0.010 mg/kg Carfentanil within an average of 6.5 minutes. All animals were reversed with Diprenorphine within 1 to 8.5 minutes.

Statistical Analysis: None conducted

Conclusions:

Axis deer may be effectively immobilized with Carfentanil at dose ranges from 0.0054 to 0.018 mg/kg body weight. Immobilization can be antagonized by a ratio of 11 mg diprenorphine per mg of carfentanil.

Adverse Reactions: None

Special Issues: None

D. Study in Sika Deer.

Type of Study: Field Study

Name and Address of Investigator:

Dr. Jim Oosterhuis
San Diego Wild Animal Park
San Diego, California

Study Design:

Purpose: Determine efficacy of Carfentanil in Sika deer with antagonism by diprenorphine.

Test Animals:

1) Number: 9
2) Age and Sex: Adults and subadults of both sexes
3) Confined Sika deer in a large animal park.

Type of Control:

Each animal served as its own control. No treatment type of control was deemed appropriate.

Diagnosis: N/A

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Dosage used: 0.005 to 0.010 mg/kg body weight (0.008 average).

Test Duration: N/A

Parameters Measured:

1) Dose Administered
2) Time to immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

The Sika deer in this study weighed an average weight of 90 kilograms. These nine deer were immobilized with an average dose of 0.00825 mg/kg Carfentanil with an average of time to effect of 12.33 minutes. Three deer had extremely long induction times. Extremely long induction times were due to incomplete discharge of the aerial dart or subcutaneous injection of the drug. Carfentanil was reversed by diprenorphine at an average ratio of 10 mg diprenorphine per 1 mg of Carfentanil administered. Reversal times ranged from 2-6 minutes with a 3.79 minute average.

Statistical Analysis: None conducted

Conclusions: The data support the label dose range for deer.

Adverse Reactions: None

Special Issues:

This study demonstrates the need for special care in the administration of Carfentanil. Inadequate injection results in prolonged induction times as occurred in three of these deer.

E. Exotic Cervidae

These data were gathered from the use of Carfentanil in several exotic species of Cervidae immobilized primarily in captivity at average doses ranging from 0.005 mg/kg to 0.064 mg/kg.

Species	**Number**	**Investigator**	**Dose Used**	**Average Time to Immobilization**
Indian Hog Deer	16	Oosterhuis	0.018 mg/kg	3.67 minutes
Pampas Deer	1	Oosterhuis	0.043 mg/kg	2.0 minutes
Red Deer	2	Oosterhuis	0.005 mg/kg	2.5 minutes
Muntjac	1	Oosterhuis	0.064 mg/kg	3.0 minutes
Axis	2	Oosterhuis	0.008-0.016 mg/kg	2.2 minutes
Eld's	4	Oosterhuis	0.020 mg/kg	2.5 minutes

III. TARGET ANIMAL SAFETY

Conventional safety studies are not feasible given the type of animals for which the drug is intended. These animals are free ranging or confined members of the family Cervidae which are the property of individual states or private organizations. Animal safety was determined under actual conditions of use whereby some of the members of the family Cervidae received elevated levels of Carfentanil without the occurrence of adverse effects.

In one study conducted by Dr. Oosterhuis in Formosa deer, 16 animals received Carfentanil above the highest recommended dose of 10 mcg/kg. The highest dose of Carfentanil recorded in this study was 37.74 mcg/kg, representing almost a 4X elevation. No adverse reactions were recorded and successful reversal with the antagonist was accomplished.

Other studies where doses of Carfentanil exceeded the recommended label dose involved 8 elk (immobilized by different investigators) which received Carfentanil at 25 mcg/kg or higher; 5 axis deer (immobilized by Dr. Oosterhuis) which received doses of Carfentanil between 15 mcg/kg and 17 mcg/kg and several of the exotic Cervidae which received average doses of Carfentanil ranging from 18 mcg/kg to 64 mcg/kg.

Safety to target animals is further augmented by the use of the reversal agent M50-50 (diprenorphine). This drug has been demonstrated in field studies to antagonize the narcotic effects of Carfentanil, leading to a more rapid reversal of the immobilization than if the effects were allowed to wear off without the use of an antagonist.

In one study, conducted by Meuleman, 4 elk were not administered diprenorphine following immobilization with Carfentanil. Reversal of the effects of Carfentanil by natural means required from 75 to 139 minutes. For free-ranging animals a prolonged down time is dangerous in that it increases the risk of death associated with rumen stasis and bloating and makes the animal more susceptible to attacks from predators.

The labeling addresses several adverse reactions observed when the product was used alone or in combination with other drugs under field conditions.

Safety Trial One

Investigator:

Dr. James Oosterhuis
San Diego Zoo
San Diego, California

Animals:

22 Formosa sika deer
Various ages, both sexes

Control: Each animal served as its own control.

Dosage: 6.59 mcg/kg to 37.74 mcg/kg

Dose Form: Injectable liquid

Route of Administration: Intramuscular

Parameters measured:

1) Dose administered
2) Time to immobilization
3) Amount of Antagonist
4) Time to Recovery
5) Adverse Effects

Results:

The average dose of Carfentanil used in this study was 16 mcg/kg which produced immobilization in 3.2 minutes. Immobilization was reversed in an average time of 1.14 minutes after receiving a narcotic antagonist.

Conclusions:

These data support the safe use of Carfentanil at levels beyond the recommended label dose.

IV. HUMAN FOOD SAFETY

A. Data on human safety, pertaining to consumption of drug residues in food, were not required for approval of this NADA. The drug is to be labeled for use in wild or exotic Cervidae (deer, elk, moose). Labeling contains the following statement: Do not administer 30 days before or during the hunting season. Do not use in domestic animals intended for food.

B. Human Safety relative to Possession, Handling and Administration:

Labeling contains adequate directions and WARNING statements for safe use, i.e:

1. WARNING: CARFENTANIL IS AN EXTREMELY POTENT DRUG AND MUST BE HANDLED WITH EXTREME CARE TO AVOID RISK TO USERS. AVOID ACCIDENTAL ADMINISTRATION TO HUMANS. PLEASE READ HUMAN WARNING SECTION CAREFULLY.

   Wildnil (Carfentanil citrate) is a synthetic opiate with a (clinical) potency 10,000 times that of morphine, Mather, L.E., Clin. Pharm. 8, 1983, pp. 422-446. Wildnil (Carfentanil citrate) is a Schedule II Controlled Drug Substance.

2. HUMAN WARNINGS: TREATMENT OF ACCIDENTAL HUMAN EXPOSURE

   Wildnil (Carfentanil citrate) is an extremely potent drug and is to be used ONLY by individuals experienced in handling potent immobilizing agents in zoos, exotic animal and wildlife practices, wildlife management procedures and biological research.

As with all potent drugs capable of producing rapid immobilization in wild animals, Wildnil (Carfentanil citrate) must be treated with extreme respect and caution. Human safety is critical.

Since Wildnil (Carfentanil citrate) may be employed in locations distant from emergency medical facilities, users must ALWAYS observe the following precautions:

1. User should seek professional medical attention immediately if the drug is accidentally ingested or injected.
2. At least two people in the field team should be able to recognize signs of toxicity if accidental exposure should occur. They should be familiar with emergency, cardiopulmonary resuscitation procedures plus have FIRST AID KITS containing resuscitation aids available.
3. WORK IN PAIRS when loading syringes or darts with Wildnil (Carfentanil citrate). Wear rubber gloves when loading syringes to avoid accidental spills on hands.
4. DO NOT SPRAY; squirt or spill the drug when filling syringes.
5. WASH AT ONCE with large volumes of water if Wildnil (Carfentanil citrate) comes in contact with skin or mucous membranes.
6. PRACTICE GOOD MEDICAL TECHNIQUES. Do not become careless. Do not hold used needles in mouth. Always ensure that darts and syringes contain proper dose.
7. REASONABLE EFFORTS SHOULD BE MADE TO LOCATE AND RETRIEVE any loaded darts that missed the target animal.
8. RESPECT all dart guns, darts and power delivery syringes as though they were cocked and loaded.

3. INFORMATION FOR PHYSICIANS:

Wildnil (Carfentanil citrate) is a powerful synthetic opiate. Accidental human exposure may produce severe central nervous system depression resulting in respiratory depression or failure followed by coma. Depending on route of administration, effects may be noted in 2 to 30 minutes. Treatment should start immediately by administering appropriate opiate antagonist, providing airway support, plus cardiopulmonary resuscitation techniques.

V. AGENCY CONCLUSIONS

Data submitted in support of this new animal drug application satisfy the requirements of Section 512 of the Act and demonstrate that Wildnil (Carfentanil citrate), when used under its proposed conditions of use, is safe and effective. The drug is restricted to use by or on the order of a licensed veterinarian engaged in zoo and exotic animal practice, wildlife management programs or research because special professional expertise is required to properly administer the drug and to safely monitor the patients. Additionally, the product is a Schedule II Controlled Drug Substance.

VI. ATTACHMENTS

1. Package insert
2. 10 mL vial box label
3. -10mL vial box label

Copies of applicable labels may be obtained by writing to the:

Food and Drug Administration
Freedom of Information Staff (HFI-35)
5600 Fishers Lane
Rockville, MD 20857

Or requests may be sent via fax to: (301) 443-1726. If there are problems sending a fax, call (301) 443-2414.

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.