This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. REGISTRATION NO. 84-R-0051 CUSTOMER NO. 1273

FORM APPROVED OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include Zip Code)*

GENESIS LABORATORIES, INC.
10122 N.E. FRONTAGE ROAD
WELLINGTON, CO 80549
(970) 568-7059

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS*(sites)*

See Attached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use APHIS FORM 7023A)*

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic,analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs					
5. Cats					
6. Guinea Pigs					
7. Hamsters					
8. Rabbits					
9. Non-Human Primates					
10. Sheep					
11. Pigs					
12. Other Farm Animals					
13. Other Animals					
WILD NORWAY RAT	40	59	22	2	83
MEADOW VOLE	0	2	1	19	22
WILD HOUSE MOUSE	0	10	2	58	70

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all the exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional official)

I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

[redacted] ICIAL

(b)(6),(b)(7)(c)

(b)(6),(b)(7)(c)

DATE SIGNED 2-9-09

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(AUG 91)

8-23 (Oct 88), whic

ART 1 - HEADQUARTERS

FEB 0 9 2009

This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. REGISTRATION NO. 84-R-0051 CUSTOMER NO. 1273

FORM APPROVED OMB NO. 0579-0036

CONTINUATION SHEET FOR ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include Zip Code)*

GENESIS LABORATORIES, INC.
10122 N.E. FRONTAGE ROAD
WELLINGTON, CO 80549
(970) 568-7059

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use this form.)*

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic,analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
DOMESTIC FERRET	0	3	0	27	30
FAT SAND RAT	0	28	0	0	28
BLACK-TAILED PRAIRIE DOG	0	22	1	0	23

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all the exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional official)
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

SIGNATURE OF INSTITUTIONAL OFFICIAL	NAME & TITLE OF INSTITUTIONAL OFFICIAL (Type or Print)	DATE SIGNED
(b)(6),(b)(7)(c)	(b)(6),(b)(7)(c)	2-9-09

AP
(AUG 91)

PREVIOUS VS FORM 18-23 (Oct 88), WHICH IS OBSOLETE

PART 1 - HEADQUARTERS

FEB 0 9 2009

ANNUAL REPORT OF ANIMALS USED BY GENESIS LABORATORIES, INC.
DURING THE 12 MONTH PERIOD OCTOBER 1, 2007 TO SEPTEMBER 30, 2008
February 9, 2009 Corrections

HEADQUARTERS OF RESEARCH FACILITY	FACILITY LOCATIONS
GENESIS LABORATORIES, INC. 10122 N. E. FRONTAGE ROAD WELLINGTON, COLORADO 80549 Registration # 84-R-051	(b)(2)High, (b)(7)(F) Registration #: 84-R-051

ANIMALS REPORTED IN COLUMN E

Wild Norway Rat (*Rattus norvegicus*)

Two (2) wild Norway rats used are being reported in column E of the Annual Report. All animals used were used in studies testing rodenticides. These animals were used for testing a rodenticide via feed trials and death of the rodent of the end point.

USEPA, Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Pesticide Assessment Guideline Subdivision G, Section 96-10, Commensal Rodents, was followed during these procedures. FIFRA mandates that efficacy data for specific rodents be generated to support label claims for rodent control as defined in 40 CFR 158. No anesthetics, analgesics, or tranquilizing drugs were used to relieve the pain. Animals displaying toxicosis were not euthanized. The USEPA policy on rodenticide testing (Attachment 1) forbids the use of pain-relieving drugs and premature euthanasia. Use of such drugs or procedures would negate the study. There are no alternatives available to this painful procedure. The only alternative to administration of a toxic product (which is intended to kill animals, and cause unavoidable pain in that process) is not to administer the toxic product. Poisonous substances cause tissue damage, which results in pain perception. One potential alternative is to develop products, which create unconsciousness or analgesia prior to death. However, information is not yet available to design such products, which would be effective for rodent control.

Meadow Vole (*Microus pennsylvanicus*)

Nineteen (19) meadow voles used are being reported in column E of the Annual Report. All animals used were used in studies testing rodenticides. These animals were used for testing a rodenticide via feed trials and death of the rodent is the end point.

USEPA, Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Pesticide Assessment Guideline Subdivision G, Section 96-12, Rodenticide on Farm and Rangelands, was followed during these procedures. FIFRA mandates that efficacy data for specific rodent species be generated to support label claims for rodent control as defined in 40 CFR 158. No anesthetics, analgesics, or

tranquilizing drugs were used to relieve the pain. Animals displaying toxicosis were not euthanized. The USEPA policy on rodenticide testing (Attachment 1) forbids the use of pain-relieving drugs and premature euthanasia. Use of such drugs or procedures would negate the study. There are no alternatives available to this painful procedure. The only alternative to administration of a toxic product (which is intended to kill animals, and cause unavoidable pain in that process) is not to administer the toxic product. Poisonous substances cause tissue damage, which results in pain perception. One potential alternative is to develop products, which create unconsciousness or analgesia prior to death. However, information is not yet available to design such products, which would be effective for rodent control.

Wild House Mice (*Mus musculus*)

Fifty-eight (58) wild house mice used are being reported in column E of the Annual Report. All animals used were used in studies testing rodenticides. These animals were used for testing a rodenticide via feed trials and death of the rodent is the end point.

USEPA, Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Pesticide Assessment Guideline Subdivision G, Section 96-12, Rodenticide on Farm and Rangelands, was followed during these procedures. FIFRA mandates that efficacy data for specific rodent species be generated to support label claims for rodent control as defined in 40 CFR 158. No anesthetics, analgesics, or tranquilizing drugs were used to relieve the pain. Animals displaying toxicosis were not euthanized. The USEPA policy on rodenticide testing (Attachment 1) forbids the use of pain-relieving drugs and premature euthanasia. Use of such drugs or procedures would negate the study. There are no alternatives available to this painful procedure. The only alternative to administration of a toxic product (which is intended to kill animals, and cause unavoidable pain in that process) is not to administer the toxic product. Poisonous substances cause tissue damage, which results in pain perception. One potential alternative is to develop products, which create unconsciousness or analgesia prior to death. However, information is not yet available to design such products, which would be effective for rodent control.

Domestic Ferrets (*Mustela putorius furo)*

Ferrets were used in two studies. The first study was conducted under Classification C, and the 30 ferrets were subsequently placed in holding under a separate housing and care protocol instead of purchasing and using additional ferrets. The second study, which used 27 of the 30 ferrets in the first study, was conducted under Classification E, which places the ferrets into category E for the Annual Report; per Animal Welfare regulations, animals are reported once and at the highest pain category for which they were used.

The second study, a secondary hazard study was conducted to address concerns of potential secondary hazards posed by chlorophacinone and diphacinone. The active ingredients (chlorophacinone and diphacinone) are known to be toxic to mammals. A thorough literature search was conducted that identified a gap in information pertaining to secondary hazards to carnivores with chlorophacinone and diphacinone. The ferrets were used as a secondary model for the evaluation of potential hazards. The goal of this study is to quantify the secondary hazards and publish the results (manuscript in preparation), filling the lack of available data regarding the secondary toxicity of

chlorophacinone and diphacinone to carnivores. Secondary hazard evaluation is often mandated by the USEPA under FIFRA for the registration of rodenticides. The data gathered for this purpose is submitted to the EPA for registration and not published in public literature. This study was designed to produce the information often mandated by the EPA and publish the data to eliminate the need for further studies using domestic ferrets for secondary hazard studies.

Ferrets were used as a carnivorous predator model and were not from the wild. The use of domestic ferrets for secondary hazard evaluation eliminates the use of wild carnivores, uses an established domestic animal research model, and supplies the data needed to evaluate the potential secondary effects posed to carnivores by the field use of chlorophacinone and diphacinone. The primary animal used was the Norway rat (40) and the secondary animal used was the domestic ferret (27). The primary animal was euthanized, gavaged with the respective test substance, and the ground and fed to the secondary animal. Feed consumption was measured every day during the 28-day study. Fresh water was provided *ad libitum* at all times. Observations were recorded at least one-time per day for the entire study. Ferrets were presented with either 1, 2, or 3 rats gavaged with either chlorophacinone or diphacinone. From this process 9 ferrets died from secondary exposure to an anticoagulant. No ferrets from the control group (n=9) died. The control group was only presented with fresh commercially ground hamburger. Six ferrets died from the chlorophacinone treatment group (n=9), and three ferrets died from the diphacinone treatment group (n=9). Of the total 27 ferrets being reported in Classification E, 18 of them showed no ill effects from the study.

Analgesics, anesthetics, and tranquilizing drugs were not used in the secondary hazard study, in part due to U.S.E.P.A. guidelines (see attached/following email dated July 6, 2004 by Dr. William Jacobs, U.S.E.PA. Office of Pesticide Programs). The core of Dr. Jacobs concerns are that additional drugs are confounding factors that would render anticoagulant pesticide studies useless as efficacy research, and thereby result in his rejection of the study ("The effects of the candidate compound must be isolated from other factors which might distort the observations..."). Specific to the concerns of the secondary hazard study, options that were considered for analgesia included non-steriodal anti-inflammatory drugs (NSAIDs) and opioids. NSAID potentiation of the effects of the hemorrhagic effects of anticoagulant pesticides and opioid side-effects (ie. vomiting, alterations in blood pressure, respiratory depression, hypothermia) are confounders that would have altered the clinical course of exposure to the product, and are consistent with the concerns that Dr. Jacob's indicated would be the basis for rejecting the study's results if they were used. It is also questionable as to whether the few ferrets with clinical signs experienced discomfort, as Dr. Jacobs referred to evidence from humans, where internal bleeding is not associated with significant discomfort.

ATTACHMENT 1

The following is an e-mail response from (b)(6),(b)(7)(c) of the USEPA, explaining his agencies position on the use of pain-relieving drugs or premature euthanasia in pesticide efficacy studies involving rodents. The e-mail was in response to a request by (b)(6),(b)(7)(c) at Genesis Laboratories, to state in writing and clarify the agency policy. Genesis Laboratories had been asked by APHIS, in 2004, to provide more detailed information on why pain relievers were withheld and why death was used as an endpoint in pesticide efficacy studies.

July 6, 2004:

"The issue of euthanasia was not mentioned in the "current" version of the [Pesticide Assessment] *Guidelines because it had not come into play with respect to efficacy testing protocols at that time. The Animal Welfare Act had been passed in the early 1970's, but there was common understanding that it was not to intrude upon the integrity of research. In efficacy studies involving toxicants, there must be a yes-or-no answer as to whether the poison killed the animal.*

The first instance that I remember encountering an efficacy protocol in which euthanasia was proposed happened in 1988. In that particular case, it appeared that the researchers were so intent on addressing euthanasia that they completely forgot what the research was about. In the course of reviewing that protocol, I drafted a response the gist of which was that the nature of the research was such that it was absolutely necessary to determine whether the poison killed the animal, that animals that recovered from having been poisoned with the rodenticide in question were not only likely to be the founders of the rebounding population but also would be behaviorally resistant (i.e., bait shy) to any bait containing the compound used in the initial trial. (The compound in question was an acute rodenticide.) Those are extremely important things to know about a rodenticide. I may have added that evidence indicating that a rodenticide routinely causes suffering should be considered in determining its suitability for future research and use

I currently am revising the Guidelines and plan to address the issue of euthanasia much as I did in 1988, adding only that it would be permissible to euthanize seemingly moribund animals if not only the event of poison-caused death but also the time to death could be predicted with virtual certainty. This is a very tricky area, however. If we were to register a rodenticide based upon the results of laboratory and field trials in which eager-to-please personnel collected and dispatched every target rodent that they could get their hands on as soon as the animals appeared to be affected to any degree, we might wind up with a real turkey of a rodenticide on the market. A circumstance

not quite so extreme but certainly affecting some of the results that were reported occurred a while back and was only discovered when one researcher decided to collect symptomatic animals and cage them to see whether they would recover or die. Many of them recovered. Ultimately, it was determined that the active ingredient concentration needed in baits was double that which was used in the original field testing.

If I received a report of a laboratory efficacy trial in which it were stated that animals were "humanely dispatched", I would reject the study flat out. Percent mortality is the dependent variable in those trials. Adding additional causes of mortality would render the study useless as efficacy research.

In the case of the Genesis ground squirrel field trials to which you alluded, it seemed to me that field personnel may have been too eager to euthanatize animals. I recall a line in the report that said, in effect, that personnel dispatched every squirrel that they could catch but some "were able to slip down their burrows" (approximate quote) before they could be caught. Animals capable of slipping "down their burrows" would not seem to be moribund by anyone's definition, and I recall having responded to that.

If it is decided that a candidate rodenticide causes so much pain that it should not be considered for further use, then animals on test should be euthanatized and the results should be written up, not so much as an efficacy study, but as research aborted for humane reasons. Apart from that, I see no proper role for analgesics in rodenticide research. Rodenticide efficacy trials basically are behavioral studies. The effects of the candidate compound must be assessed isolated from other factors which might distort the observations and, of course, the animal's viability and ability to make adaptive responses -- such as slipping down a burrow. There is no way to sensibly use analgesics in field trials of rodenticide baits that would not be likely to interfere with behavior and viability. Even if the animals die after they "slip down their burrows", it is important that they are able to as where they die affects the determination of percent surface kill and the degree to which carcasses are available to nonfossorial scavengers and predators (such as avian raptors).

When we attempt to impose human values on animals' circumstances, we risk deluding ourselves. In general, wild animals are all about survival and will do whatever it takes (even chewing off their own feet) to last as long as they can. (Tranquilizer tabs associated with leg-hold traps turned out to be a good idea because some animals were spared further, self-inflicted, injuries on top of what the traps did to them. That, however, is a really exceptional case; and one which does

not involve a vertebrate pesticide.) There also has been some discussion of whether what appears to be distress is consciously perceived by the animal. Some of the older rodenticides produce symptoms which clearly look like distress, although humans exposed to the same compounds sometimes had little recollection of the experience. Some have suggested that anticoagulants, with their protracted times to death, "must" be inhumane. However, some humans who have bled severely internally (for one reason or another) have reported little or no discomfort and sought help only because of other symptoms (e.g., lethargy, evidence of occult blood, loss of function, etc.)."

(b)(6),(b)(7)(c)