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 21!

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 14-R-0162
CUSTOMER NUMBER: 17008

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

FY 08 FINAL

1 OCT 2007 - 21 APR 2008

Nucryst Pharmaceuticals
50 Audubon Rd
Suite B
Wakefield, MA 01880

Telephone: (781) -224-1444

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

FACILITY LOCATIONS (Sites) - See Atached 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 animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o 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 an 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 wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this report	F. TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs					
5. Cats					
6. Guinea Pigs					
7. Hamsters		57	7	16	80
8. Rabbits					
9. Non-human Primates					
10. Sheep					
11. Pigs					
12. Other Farm Animals					
13. Other Animals					

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese 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 ap Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary inc 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)

SIGNATURE

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APHIS FORM
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NUCRYST PHARMACEUTICALS

(b)(6), (b)(7)c
Director, Microbiology and Immunology

30 April 2008

Elizabeth Goldentyer, DVM
Regional Director, Animal Care
USDA-APHIS Eastern Regional Office
920 Main Campus Drive, Suite 200, Unit 3040
Raleigh, NC 27606

Subject: Annual Report of Research Facility 1 Oct 2007 through End of AWA Registration on 21 April 2008
USDA Registration # 14-R-0162

Dear Dr. Goldentyer:

Attached please find our Annual Report (form 7023) pertaining to research activities at Nucryst Pharmaceuticals, Inc. for the period from the beginning of FY2008 through 21 April 2008, when our AWA Registration was terminated on Nucryst's request. The use of covered animal species reported in USDA Category E (animal pain and/or distress without alleviation) is explained below.

Syrian Hamsters were used to test the antibacterial activity of nanocrystalline silver in a model of *Clostridium difficile* post-antibiotic colitis [also called C difficile associated disease (CDAD), antibiotic associated diarrhea (AAD), or C difficile cecitis]. Disease is induced when the hamster is given a single oral dose of the antibiotic clindamycin, which is presumed to decimate the normal healthy bacterial flora in the GI tract, creating an environmental niche for *C difficile* to expand and overproduce cytotoxins. Animals were assigned to treatment groups and given prophylactic treatments prior to induction of disease. The treatments consisted of nanocrystalline silver. Negative controls included untreated animals and animals receiving only the vehicle used to deliver the nanocrystalline silver. Animals were monitored for signs of disease including: stool cultures that were positive for C difficile, diarrhea, weight loss, tachypnea, piloerection, and changes in grooming behavior. All of these characteristics except stool culture were monitored at least twice per day. Animals that appeared moribund were immediately euthanized by CO_2 asphyxiation; such animals were considered to have had lethal disease for the purposes of endpoint data.

In the experiments performed in FY2008, experimental conditions were optimized for determining prophylactic (as opposed to therapeutic) efficacy. Therefore, mild disease induction was used, resulting a less fulminant disease and a larger percentage of animals which did not acquire disease. For the purposes of Categorization, control animals that were not induced with clindamycin were placed in Category C, as were animals which showed no disease symptoms even on extended follow-up. Note that this categorization scheme is different than the scheme used for experiments performed in FY2007 (in which animals showing no outward signs of disease were conservatively placed in Category D rather than Category C). The reason for this change in categorization scheme is based on the difference in disease induction method. Experiments in FY2007 were intended to measure therapeutic effects, and were therefore optimized to produce disease in 100% of animals using fairly aggressive disease induction conditions. Under these conditions experience showed that virtually all animals were infected, and therefore, we felt it prudent to assume that all animals

experienced at least some disease symptoms (hence the conservative use of Category D). In contrast, experiments performed in FY2008 were designed to assess prophylaxis, so the conditions were optimized to mimic the onset of human disease as closely as possible and to maximize our ability to observe subtle effects on disease onset. Under these conditions, a large percentage (about 30%) of animals do not acquire infection at all, and we thus feel justified in categorizing these uninfected animals as Category C. Category D was assigned to animals that were euthanized. Category E was assigned to animals that were discovered dead, and were usually those that died in the middle of the night.

The Syrian hamster is one of four established small animal models of C difficile associated disease, the three others being mouse, rat, and guinea pig. The mouse and rat models demonstrate low-to-no lethality, which has been experimentally linked to an insensitivity of these rodent species to the protein toxins produced by C difficile (Lyerly, et al 1985 Infect Immun 47:349-52). This feature, unfortunately, makes the mouse and rat models poor correlates of human disease, since the latter is strongly dependent on the action of these C difficile toxins. Hamsters and guinea pigs are susceptible to the C difficile toxins. This makes these two animal models excellent correlates of human disease, but has the drawback that these models are ultimately lethal and euthanasia frequently must be provided. The hamster model was chosen over the guinea pig model since the hamster is the lower species. In addition to the susceptibility of hamsters to C difficile toxins, the hamster model also responds to antibiotic treatments in a manner that is highly predictive of human patient responses. Therefore, despite the inherent lethality, the Syrian hamster model is the preferred model for CDAD therapeutics research.

The use of analgesics during this procedure was given careful consideration, but was decided against due to concern of the undesired, unintended effects such analgesics may have on the development and the treatment of the disease state being studied. Specifically, since CDAD is a gastrointestinal infectious disease inextricably linked to the host animal's immune status and nutritional status, the investigators are concerned over the reported loss of appetite among human volunteers after opioid use (Yeomans and Gray 1997 Physiol Behav 62:15-21), and nausea associated with the use of buprenorphine (Fullerton, et al 1991 Pharmacotherapy 11:90-93). Other related areas of concern are published studies demonstrating immunosuppressive (Volker, et al 2000 Lab Anim 34:423-429) or unpredictable immunomodulatory effects (Van Loveren, et al 1994 Lab Anim 28:355-363) of buprenorphine. Because of these factors, the I as the Principal Investigator reluctantly decided to avoid the use of analgesics.

Please contact me a(b)(2)High, (b)(7)f if you require any additional explanation regarding our USDA Annual Report.

Sincerely

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NUCRYST Pharmaceuticals, Inc.