

**The Reality of Primate Experimentation in the United States:  
Lies, Greed, and Insanity**

**By**

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## Contents

Summary	1
Introduction and methodology	3
Experimentation Performed on Non-human Primates: What Happens to them?	4
Why are Primate Protocols Duplicated?	7
Violations of Federal Law Relevant to Experiments involving non-human Primates	8
USDA Reporting of Primate Use in Laboratories	10
How Many Primates are in Laboratories?	10
Pain in Primate Experimentation	11
The Psychological State of Non-human Primates in U.S. Laboratories	12
Appendix A	USDA Primate Statistics
Appendix B	2007 Virginia Commonwealth University report
Appendix C	Johns Hopkins University Addiction Experiments

## Summary

It is clear from government documentation that the use of non-human primates in experimentation is an area that is not effectively regulated. The basic needs of primates are not met, even in terms of food and water. Labs including: Yale, the University of Chicago, University of Alabama, Pennsylvania State University, Harvard, Catholic Healthcare (AZ), Brown University, University of California (Berkeley), the Salk Institute, Stanford, the Smith Kettlewell Eye Research Institute, University of Connecticut, University of Miami, MIT, University of Minnesota, the University of Texas (Austin), University of California (Davis), Johns Hopkins, Massachusetts General Hospital, Wake Forest, Washington University, University of Houston, Emory University, Columbia University, Oregon Health Sciences University, the University of Washington, University of California (San Francisco), Duke University, Princeton University, Cornell University (NY) are all listed in government records as depriving non-human primates of food and/or water and this list is nowhere close to all inclusive.

Additionally, many laboratories have committed violations of federal law that have either taken the lives of primates or caused serious injuries including: University of Wisconsin, Madison; the Southwest Foundation for Biomedical Research (San Antonio, TX), Alpha Genesis (SC), University of Texas (San Antonio), Emory University, Franklin & Marshall University, the SNBL facility (Everett, WA), Charles River Laboratories (Reno, NV); the Smith-Kettlewell Institute (San Francisco, CA), and Vanderbilt University. Again, the information available from the USDA is often incomplete. To our knowledge only one of these facilities suffered any meaningful consequences.

The National Eye Institute currently funds 75 grants that investigate the processing of visual stimuli in the brains of macaque monkeys. The protocols for many of these experiments are virtually identical, elucidating an area of serious waste and redundancy. Similar areas exist in other fields of primate experimentation. Research facilities have a major vested interest in promoting the highest possible number of research projects to be funded as they receive substantial amounts of funding in indirect costs for each and every grant that their staff produces.

The psychological stability of many primates held in laboratories is open to serious question due to information both from federal inspection reports and from internal health records for primates at laboratories such as the University of Minnesota, the University of Michigan, and the Medical College of Virginia (part of Virginia Commonwealth University). The sterile and simplistic nature of laboratory housing of non-human primates is designed primarily for ease of cleaning, and does virtually nothing to accommodate their psychological sophistication, often resulting in stereotypical behavior, self-injurious behavior, and even madness.

Information made available to the general public by the USDA, the federal agency responsible for regulating the use of animals in laboratories promulgates deceptive information regarding the use of non-human primates in labs. An examination of the number of primates actually confined inside a set of laboratories utilizing a substantial portion (app 1/3) of the national total (62,315 – an all-time high) of primates used in experimentation illustrates that these facilities confined 135% more primates than the USDA reported, due to the fact that the USDA does not report primates that are kept for later use or housed for breeding purposes.

The reporting of unrelieved pain in primate experimentation is no more accurate. Projects that actually state that the primates will experience pain are not reported as such, and other highly invasive experiments utilizing procedures which have been deemed by veterinary and scientific experts to cause unrelieved pain and/or distress are not reported in this way. Lastly, while some labs do report specific procedures as causing unrelieved pain/distress (i.e. those involving precipitated drug withdrawal) other labs using similar procedures do not report them in this way. The bottom line is that, again, the total number of primates experiencing unrelieved pain/distress is much higher than the USDA reports. This situation exists because labs apparently attempt to avoid reporting projects in this way and the USDA does not act forcefully to ensure that this regulation is followed.

In the past correspondence/complaints to the USDA have primarily fallen on deaf ears. Reporting has not changed, and if anything enforcement of the Animal Welfare Act has declined because as is exemplified in this report, meaningful enforcement actions regarding significant violations typically do not take place. In fact, the best information available is that regarding all of the information contained in this report regarding Animal Welfare Act violations, only one incident received any monetary penalty.

The bottom line is that the system is broken. Duplication is rampant; violations go unpunished and largely unpublicized unless an NGO steps in. The public is kept in the dark about the overall situation, while laboratories continue to proclaim their innocence in the face of documented violations – talking about the need for humane care of animals in labs, while they die of negligence.

This report will be forwarded to Senator Barak Obama Mr. Ralph Nader, Ms. Cynthis McKinney, and Senator John McCain in hopes that as Senators, public figures, and potentially as the next president of the United States this system will be reformed so that the negligence, abuse and rampant duplication can be removed from this system.

## **Introduction and methodology**

The use of non-human primates in experimentation has reached an all-time high in the United States as of 2006 as, according to the United States Department of Agriculture, over 62,000 rhesus monkeys, squirrel monkeys, baboons, chimpanzees, marmosets, aotus monkeys, vervets, and other species of primates fell under the knife. What happens to these animals in U.S. laboratories? Are they receiving even the basic necessities of life such as food and water? Are they receiving adequate protection under the Animal Welfare Act (AWA)? When laboratories violate the AWA regarding the use of primates, do they receive substantial penalties?

This report will investigate all of these issues based on available documentation. This documentation will include inspection reports and animal use reports from the United States Department of Agriculture for the years 2006 & 2007. Other sources of information will include grant applications from various parts of the National Institutes of Health, and accounts of specific incidents from news media.

However, it must be noted that the sources of information available for use in this report are incomplete. Despite improvements in efforts by the USDA in making documentation available regarding the use of animals in laboratories, substantial areas of incomplete disclosure exist. For example, while some level of availability of the annual report forms for research facilities for 2006 & 2007 exists, virtually all laboratories which use animals in experimentation involving unrelieved pain and/or distress are still unavailable – this includes many of the largest primate facilities. Additionally, for many laboratories for which the forms are available, the attachments which disclose important documentation regarding exceptions to standard care (i.e. severe limitations on availability of food or water, use of multiple survival surgical procedures on animals, inadequately sized caging, isolation housing for primates, etc.) are not available even though it is possible to demonstrate from other sources that such non-standard care is in existence. Many crucial reports are unavailable, including forms for the facilities of the National Institutes of Health intramural facilities. Additionally, a Freedom of Information Act request was placed with the USDA/APHIS/AC in 2006 for copies of the most recent inspection reports for all registered research facilities in the United States. At the time of writing, this request has not yet been fully met – leaving some substantial holes in the data. However, a fairly complete picture of primate experimentation can be compiled using a combination of data sources.

## **Experimentation Performed on Non-human Primates: What Happens to them?**

The perception which is held by the American Public of animal experimentation in general and primate experimentation in particular is of an area of scientific inquiry that is well-regulated and thoroughly examined during lengthy approval processes. The underlying assumptions of this perception would be that due to substantial regulation the animals (primates) used in this area must be well cared for and thoroughly investigated. One of the results of this kind of structure for the management of animal experimentation should be that the basic needs of the animals that are regulated in this manner are met.

Most people would agree that the basic needs of most animals would include adequate access to food, water, freedom of movement, and an adequate environment to allow the expression of the behaviors which are basic to the nature of the animal in question. Non-human primates, like all other species of animals, need adequate access to food and water and an environment that allows them to behave in a way that is natural to them. The complicated psychological nature of non-human primates has even led to regulations requiring provisions for environmental enhancement to support their ability to behave in complicated ways which stimulate them in such a way as to prevent the level of boredom that can lead to psychological abnormality.

The first area to examine is whether primates routinely receive the basic necessities. In other words, do they receive sufficient food and/or water? The Animal Welfare Act requires that animals receive food and water: Section 3.82(a) Feeding: The diet must be appropriate for the species and meet its normal daily nutritional requirements; Section 3.83 Watering: Potable water must be provided in sufficient quantity to every non-human primates housed at the facility. If potable water is not continually available to the non-human primates, it must be offered to them as often as necessary to ensure their health and well-being, but no less than twice daily for at least one hour each time, unless otherwise required by the attending veterinarian, or as required by the research proposal approved by the Committee at research facilities. (The full text of the Animal Welfare Act is available at: [http://www.aphis.usda.gov/animal\\_welfare/publications\\_and\\_reports.shtml](http://www.aphis.usda.gov/animal_welfare/publications_and_reports.shtml)). Are the provisions of this act followed and are there exceptions which are allowed?

Like many general regulations, the regulations providing for adequate food and water have exceptions. For example, Section 2.38(f)(2)(ii) Handling: Deprivation of food or water shall not be used to train, work or otherwise handle animals; Provided, however: That the short-term withholding of food or water from animals, when specified in an IACUC-approved activity that includes a description of monitoring procedures, is allowed by these regulations. What does this mean? What is considered short-term?

First, it must be noted that legitimate reasons for withholding of food and/or water from animals do exist, and that in some instances this is standard practice in veterinary and even human medicine. The most obvious example is in the period just before the performance of surgery. In this situation food and/or water are withheld to avoid vomiting during surgery and the potential aspiration of regurgitated food and/or water – this kind of food/water deprivation is not what will be discussed in this report. Additionally, some illnesses require the withholding of food and/or water during treatment to avoid excessive vomiting, again this is not the kind of food/water deprivation that will be discussed in this report. Regarding the training of animals to perform behaviors, the use of food as reward is not uncommon. Many private individuals use treats to encourage specific behaviors when training dogs, cats, and other domestic animals. Special rewards can be effective means of re-enforcement when training animals to do simple behaviors which are not unpleasant for the animal. This use of food/water as reward is not what we are discussing. This type of reward focuses on additional special items, not limiting access to basic foodstuffs or liquids.

The handling regulation listed above, while sounding innocuous has had extreme implications for non-human primates used in certain areas of experimentation. Many times researchers want primates to perform complicated behaviors which are either unpleasant to them (climbing into restraint chairs) and/or unnatural to them (tracking visual stimuli across video screens). The result of this situation is that the

primates must have a very strong motivation to perform these behaviors, and perform them consistently. Simple motivations of food and water rewards are apparently not sufficient. Apparently only severe hunger or thirst are sufficient motivations to coerce the monkeys into performing the desired behaviors in these protocols. Clearly these are very unnatural behaviors (i.e. tracking visual stimuli across a video screen) which are totally foreign to these monkeys when in their natural environment. So, effective motivations for these behaviors must be extreme. The result is that, on days when they are to participate in these behavioral experiments, these animals are often totally denied access to water (or less commonly food) except when they are performing the experimental paradigms. In reality, the behavioral parts of these projects when the primates have access to water or food varies from 2 – 8 hours. This leaves the monkeys deprived of water for periods varying between 22 and 16 hours per day, often five days per week. They are given free access to water only on non-experimental days (mainly weekends) or at the end of the experimental session. Examples of these protocols are available at: <http://www.all-creatures.org/saen/grants-gov.html>

The nature of these experiments is highly invasive and requires extremely unnatural behaviors for primates like rhesus macaque monkeys, the most common experimental subjects of these procedures. It must be noted that according to the National Institutes of Health CRISP system, other species of primates including squirrel monkeys, marmosets, and aotus monkeys are used in this general type of protocol.

How wide spread is something like water deprivation? Research facilities are required to file form 7023, Annual Report of Research Facility forms with the USDA. The forms include a requirement for disclosure of exceptions to standard care. Examples of this information may include things like food or water deprivation (called “regulation”). Facilities which have disclosed limiting the access of primates to water during 2007 include: Yale, the University of Chicago, University of Alabama, Pennsylvania State University, Harvard, Catholic Healthcare (AZ), Brown University, University of California (Berkeley), and the Salk Institute. During 2006 Stanford, the Smith Kettlewell Eye Research Institute, University of Connecticut, University of Miami, MIT, University of Minnesota, and the University of Texas (Austin) disclosed depriving primates of water. Grant applications obtained from the National Eye Institute of the National Institutes of Health reveal that Stanford, University of California (Davis), Johns Hopkins, Harvard, MIT, Massachusetts General Hospital, Wake Forest, Washington University and the University of Houston “restrict” primates’ access to water (this is water deprivation). Emory, Columbia, Oregon Health Sciences University and the University of Washington limit primates’ access to food (this is food deprivation). USDA inspection reports discussed in a subsequent section of this report reveal that many more laboratories severely limit primates’ access to water and/or food.

In addition to experiencing water and/or food deprivation, these neurological protocols require the monitoring of the activity of individual neurons in the brain. The preferred methodology for monitoring these individual cells is to literally hard wire into them using microelectrodes. This procedure requires that the skull of the primate be opened (holes are drilled in the skull) and recording cylinders are attached over the holes through which the microelectrodes are fed. These microelectrodes are attached to the skulls with metal screws. One other consequence of this type of experimental paradigm is that the head of the primate must be held in place. This both forces the animal to look at the visual stimuli as it is presented on the video screen, and it also prevents the microelectrodes from being dislodged by movements of the head. The immobilization of the head is accomplished by attaching a restraining bar to the skull, again with metallic screws, and during the procedure when the primate is confined in a sitting position in the restraint chair, the restraining bar is literally bolted to the chair.

This type of protocol is very widespread. Utilization of the NIH CRISP system provides access to a listing of 75 grants funded during 2006 by the National Eye Institute related to vision which use macaque monkeys. When the search is broadened by eliminating the relationship to a specific branch of the funding agency and thereby removing the focus on a specific area of neurological research, a similar search reveals that macaque monkeys are used in 160 protocols of this nature and squirrel monkeys, marmosets, and aotus monkeys comprise another 20 projects – totaling 180 separate examples of this basic experimental paradigm.

Other common areas of experimentation involving non-human primates are drug addiction, infectious diseases, etc. Of these, possibly the most common is addiction research which is exemplified by projects underway at the University of Michigan (Ann Arbor), the University of Minnesota, Johns Hopkins University, and the Medical College of Virginia. These protocols expose non-human primates to addictive drugs like cocaine, heroin, amphetamine, ecstasy, etc.

These projects have two basic paradigms. One paradigm confines the animals, usually either rhesus monkeys or squirrel monkeys to restraint chairs. They are trained to self-administer addictive substances (again using either food reward or liquid reward) such as pcpr, Heroin, cocaine, amphetamines, alcohol, etc. In some instances the primates later undergo precipitated withdrawal which can lead to abdominal discomfort, ataxia, tremors, vomiting, etc. Not unlike symptoms in humans. Another paradigm keeps the primate confined to their cages while wearing Teflon "jackets" which are connected to a spring arm through which the addictive drugs are delivered. In these projects primates are used in testing that compares the addictive nature of one drug to another.

Many other uses of primates in experimentation exist including infectious disease research, genetic research, etc. However, these paradigms vary substantially and have different effects on primates based on the exact protocols involved.

## **Why are Primate Protocols Duplicated?**

It may have become clear by now that many types of experimentation performed on primates are highly duplicated. While it is difficult to look at this issue in it's' entirety it is possible to examine one small area of it. As was stated earlier in this report, utilization of the NIH CRISP system provides access to a listing of 75 grants funded during 2006 by the National Eye Institute related to vision which use macaque monkeys. These projects all examine the firing of individual cells within the visual centers of the brain of macaque monkeys. The methodology used in these projects is strikingly similar.

Why would duplication of this nature happen? What is the real motivation? While the public is told that a certain level of duplication is necessary in science, do we need 75 projects that are all examining the same area? How could this happen?

As part of the issuance of this report approximately 50 grant applications which have been obtained from the National Eye Institute through the Freedom of Information Act have been placed on the SAEN website at: <http://www.all-creatures.org/saen/grants-gov.html>

When the front page of most of these grants is examined, it is easy to find the financial information relevant to these grants. The grant application for EY000745-34A1, of Albert Fuchs at the University of Washington in Seattle will be used as an example. This project has a direct cost of \$378,994, and a total cost of \$589,970 per year. The difference of these two numbers is \$210,976. This number is the indirect cost of this grant, and it goes directly to the University of Washington. The \$378,994 in direct costs pays for the animals, the researcher's salary, etc. The indirect cost pays for things like utilities, staffing, etc. During 2007 the University of Washington, Seattle had 42 grants that used primates. Each one of these grants has an indirect cost portion. If each one received only \$200,000 per year in indirect costs, then the University of Washington would receive \$8.4 million per year in indirect costs for these grants alone. Now, multiply this by all of the grants that the University of Washington receives for primates, dogs, cats, rabbits, rats, mice, guinea pigs, etc. This indirect cost number would reach into the tens if not the hundreds of millions in indirect cost dollars, for this university alone. Now multiply this by all of the 903 grants for primate research (this number is almost certainly incomplete because many grants use specific species names instead of general terms like primate) by \$200,000 per grant in indirect costs (a conservative number) and the result is over \$180 million in indirect costs alone. This is a conservative amount for only one species, and does not include the actual original grant amounts.

This high level of "indirect" funding is a powerful motivation for performing as many experiments as can possibly be funded at each and every research facility. Clearly, the project approval committees of all universities and laboratories that receive federal funding have serious vested interests in insuring that the highest possible number of research projects are funded. These grants provide a tremendous income stream for laboratories. This is not about science or health. Primate research, like all animal research, is about attracting grant funding. This issue is important not only because of the waste of tens of millions of tax dollars, but also because the Animal Welfare Act contains regulations regarding the unnecessary duplication of research, and the simplest way to produce more grants is to simply have many grants that do and re-do the same project, or at best very slight variations of the same basic project.

## **Violations of Federal Law Relevant to Experiments involving non-human Primates**

Animal research is governed by only one law, the Animal Welfare Act (AWA). This law is enforced by the United States Department of Agriculture. In order that some idea of the effectiveness of the enforcement of this law regarding primates, and thereby through inference regarding other species of animals, a Freedom of Information Act request has been filed with the United States Department of Agriculture for inspection reports for research facilities in the U.S. This request was filed in 2006 but the totality of the documents have still not been provided. Additionally, our ability to assess the frequency with which non-human primates are subjected to illegal practices has been hampered by the fact that the USDA often redacts the species names from inspection reports as part of the FOIA process. In other instances, USDA inspectors often list the regulations violated at a laboratory, and information about the incident that led to the violation, without providing the relevant species of animal. The result of this situation is that the occurrence of AWA violations relevant to primates is certainly much higher than can be demonstrated due to the vague nature of the documentation, or due to document redaction.

One relevant example of this phenomenon is relevant to the Motac Cognition laboratory in Cherry Hill New Jersey amassed 9 violations of the AWA during a period of just over a year. The relevant inspection reports disclose illegal activities such as depriving animals of food. However, no species are listed. We can only be sure that these violations are relevant to primates because the 2007 animal use report filed by Motac Cognition lists only primates as being used at the facility. Therefore, the 9 violations are relevant to the 16 primates that the facility holds.

It is not uncommon for the negligence of laboratories to either take the lives of non-human primates, or to cause serious suffering and/or injuries to these animals. A Decemer 2007 USDA inspection report for the University of Wisconsin, Madison discloses that a monkey died due to lack of veterinary care, after suffering with health problems for over a year. An April 2007 inspection report for the Southwest Foundation for Biomedical Research (San Antonio, TX) discloses an incident where the dissection of a baboon began before the animal had been euthanized, the USDA issued only an official warning -- no fine was paid. A May, 2006 report for the University of Texas (San Antonio) disclosed that a baboon had died after receiving inadequate post-surgical monitoring and treatment. In July of 2006 Emory University was cited in the death of a primate whose demise was caused by improperly assembled anesthetic equipment. In May of 2007 Franklin & Marshall University is cited for injury to an infant capuchin monkey caused by improperly housing him and his mother with other monkeys. According to a 2008 story by the *Everett Herald*, a monkey was killed at the SNBL facility in Everett (WA) when the animal was sent through a cagewashing system, the USDA took no punitive action. According to a 2008 Associated Press story, 32 non-human primates died at Charles River Laboratories in Reno, NV when a heating malfunction subjected them to excessively high temperatures (no action was taken by the USDA).

Information from multiple sources reveal that non-human primates have suffered pain and major injuries as a result of negligence. In January of 2007 the Smith-Kettlewell Institute of San Francisco was cited for performing unapproved surgical procedures on a primate that left screws in the animal's face and head. In December of 2006 Vanderbilt University is cited for performing a durascope (scraping of the membrane surrounding the brain) on a primate without anesthesia. In March of 2007 Charles River laboratories (facility in NV) is cited for improperly handling and transporting primates resulting in so severely that finger injuries occurred which required amputations of the primates' fingers. Internal documents leaked from the Alpha Genesis Corporation reveal that many primates at this facility suffer from traumatic injuries and are missing digits.

In August of 2006 the University of California (San Francisco) is cited for depriving primates of water. In August of 2007 Duke University was also cited for depriving primates of water. In April of 2006, Princeton University is also cited for depriving an animal of water. In April of 2007 Cornell University (NY) is cited for depriving 6 primates of water. In July of 2007 Massachusetts General Hospital is cited for inadequately monitoring primates whose access to water is restricted.

As has been previously stated, regulations for environmental enhancement for primates to prevent abnormal behavior have been instituted. Yeshiva University (NY), Yale, University of South Florida (Tampa), University of Pittsburgh, State University of New York (Brooklyn), Motac Cognition, Charles River Laboratories, Bucknell College, Boehringer Ingelheim Pharmaceuticals were all cited for violations of environmental enhancement provisions leading to abnormal behavior in primates from hair pulling to circling and other stereotypical behaviors.

## **USDA Reporting of Primate Use in Laboratories**

Since the USDA is responsible for regulating the use of all animals in laboratories they are often the primary source for information regarding the use of primates in laboratories. Laboratories are required by law to file facility reports with the USDA, which are then compiled to develop national statistics. Is this process done correctly? Does it give us an accurate picture of how many primates are in laboratories?

Additionally, these reports categorize experimentation that is performed by different facilities regarding the pain level associated with the experimentation? Is this information accurate and consistent?

### **How Many Primates are in Laboratories?**

The most basic answer to this question is that we simply don't know. During 2006 the USDA, in the annual Animal Welfare Enforcement Report, stated that 62,315 non-human primates were used in experimentation. However, this is not the whole picture. The USDA reports only animals that are actually used in experimentation during a given year. It is often assumed that this number is the actual total population of animals in a specific laboratory. However, the numbers reported by the USDA do not include animals kept for breeding, conditioning, or later use. Regarding non-human primate use this discrepancy is significant. In fact, for many laboratories, more primates are kept for breeding or conditioning than are used in actual experimentation.

(For details of the statistics in the following discussion please see Appendix A.)

This incomplete reporting leads to substantial misunderstanding of the overall situation regarding non-human primate use. To illustrate this issue, USDA statistics for 10 of the largest states for use of non-human primates (Alabama, California, Georgia, Florida, Louisiana, Oklahoma, Oregon, South Carolina, Texas, Washington) are compared to the actual total population of the largest primate laboratories in these states. For these 10 states, the USDA reported 21,051 primates used in experimentation. The actual total primate population of major labs in these 10 states during 2006 was a whopping 49,458. This is a discrepancy of 28,407 primates or 135%. Clearly, a substantial number of primates that are confined in laboratories do not figure into the USDA's calculations thereby providing a very misleading picture of primate experimentation.

## **Pain in Primate Experimentation**

The Animal Welfare Act requires that laboratories file annual reports with the United States Department of Agriculture which list how many animals are used in experimentation and also the level of pain that these animals experience. One of the most controversial areas is the reporting of projects that involve unrelieved pain and/or distress in experimentation. The reporting of this kind of experimentation is inconsistent and clearly questionable.

Earlier in this report neurological experimentation was discussed in some depth, including listing the procedures which are generally part of this area of experimentation including the surgical attachment of devices including restraining bars and recording cylinders to the heads of primates, confinement in restraint chairs, and severely limiting access to water. One of the most puzzling aspects of this area of experimentation is that it is typically not considered to cause unrelieved pain and/or distress for the animals used in this experimentation. Despite the widespread nature of this experimentation, it is virtually never reported as causing unrelieved pain and/or distress. If any additional reporting is done, some of the procedures are listed in areas for exceptions to standard care. Statements regarding this variety of research and the potential for causing pain and or distress in primates, made by veterinarians, primatologists, etc. are posted at: <http://www.all-creatures.org/saen/grants-gov.html>.

Another example of the inconsistencies in this area of reporting are relevant to the use of primates in drug addiction experimentation. In some varieties of this experimentation primates are forced to experience spontaneous withdrawal from addiction to powerful drugs, such as morphine. One laboratory that performs this variety of experimentation is the Medical College of Virginia, and in 2007 (see attached appendix B) this lab reported 21 primates as experiencing unrelieved pain due to precipitated drug withdrawal. However, not all laboratories report drug withdrawal as causing pain/distress. Johns Hopkins University, according to information contained in research publications (excerpts of which are attached to this report in Appendix C) subject primates to virtually identical withdrawal syndromes, and yet do not report this as causing pain/distress.

These areas hint at what is likely a much larger problem. Many other areas of experimentation have the potential to cause serious pain and distress in primates, but this is not acknowledged. For example, many primates are used in projects involving infectious diseases, such as simian immunodeficiency virus. Since this disease parallels AIDS in humans, it has the potential to cause very serious consequences for the animals. However, labs which conduct this kind of research such as the University of Wisconsin, often do not report these projects as causing pain. The research protocol itself states:

“Infection with SIV or related viruses results in the development of immunodeficiency disease. Thus, over a period of time the animals are expected to have fever, weight loss, periods of diarrhea, rash, decreased physical activity and possibly pain.”

And yet, this is not reported as causing unrelieved pain/distress even though the primates receive no pain relievers.

Taken together, this information can only lead us to believe that pain in primate experimentation is drastically under-reported. The information promulgated by the USDA on this topic is extremely flawed.

## **The Psychological State of Non-human Primates in U.S. Laboratories**

Earlier in this report it was stated that legal requirements exist so that the environment of primates in laboratories is enhanced to promote their psychological well-being. This is a very serious issue and deserves significant discussion.

The natural environment of free-ranging primates is complicated and elicits many intricate behaviors. The environment includes trees, predators, changing weather conditions, etc. All of these things give non-human primates a wide variety of experiences on a daily basis. It is not uncommon for some species of primates to range over 1 square mile of territory on a daily basis. However, the laboratory cage, is very different, extremely sterile, designed primarily for ease of cleaning.

The enclosures in which many primates are housed are listed by medical journals as being 83.3-cm long by 76.2-cm wide by 91.4-cm deep which translates into 33 inches long by 30 inches wide by 36 inches deep. To put yourself in their place you must imagine that your life consists of confinement in a small enclosure which only allows you to take at most one or two short steps in any direction and with just enough height to stand upright. You never have the opportunity to see the sun or breathe fresh air. This is in very stark contrast to what takes place in their natural environment. It is no surprise that this situation alone can have serious psychological consequences. Hair pulling, stereotypical behavior and self-mutilation are not uncommon.

USDA inspection reports provide some glimpses of what happens to the psychological state of primates. In October of 2006 primates at Yale are described as circling in their cages. In April of 2007, primates at the University of South Florida are described with hair loss and as circling in cages. In August of 2006 a primate at the University of Pittsburgh shows signs of distress. In August of 2006 several primates at the State University of New York, Brooklyn, are showing signs of distress. In March of 2007 primates at the Charles River laboratories are showing stereotypical behaviors. In February of 2006 six monkeys at the Boehringer Ingelheim facility in Connecticut are showing signs of distress. In March of 2007 primates at this same facility have significant hair loss. Internal records from several other facilities give us a more detailed look.

Internal documents from the Medical College of Virginia reveal that primates experience such severe stress that they often become self-abusive. Rhesus monkey M1390 endured a lifetime of suffering at MCV:

“Arrived years ago and from the beginning had difficulty adjusting to the lab. Throughout the years several attempts were made to address his behavior problems using enrichment and various experimental protocols. He would show improvement for a period but would return to bouts of stereotypic behavior including aggression and self injurious behavior. Due to recent indications that his behavior had worsened, the PI opted to remove the animal from study and request euthanasia.”

Many of the primates within this facility are so severely disturbed that they tear out their own hair. Fur is plucked from arms, legs, tails, and heads. One monkey was so disturbed that he/she removed all of the hair from his/her head, resulting in baldness.

Additionally, these animals suffer with surgically implanted catheters, which they often rip out. Infections are not uncommon. Jackets are placed on these monkeys in a vain effort to protect the catheters. This serves only to cause more stress as the monkeys chew and tear at the jackets in frustration. Some of these rhesus monkeys become so agitated that they shake and bang on the cages and tear at the restrictive jackets. Others, seeming to give up, simply lie on the floor of the cage and clutch their tails.

Internal records from the University of Michigan provide another look inside the laboratory. Almost every health record for the primates at UM which were used in addiction experiments lists a time when the monkeys are ripping out their hair, or worse. Several actually mention multiple incidents of severe self-mutilation. Other primates are listed as requiring the amputation of their tails due to self-inflicted lacerations.

One of the UM primates named Scallywag is listed as losing weight from the constant activity associated with psychologically abnormal behavior. Another primate named Clash had a 12% weight loss of unknown origin. Yet, another rhesus monkey is described as declining from 6.8 kg to 5.8 kg (15 pounds to 12 ¾ pounds) a 15% weight loss in just 3 months. This animal also has constant muscle contractions and is hypothermic which could be related to drug withdrawal. Yet, another primate named Data had a weight loss of 10.5% in a short period.

Harpo's records discuss four incidents of self-mutilation in five days during 2006; this comes after a long history of self-destructive behavior. Eminem wears a "long sleeved jacket due to history of self-mutilation." Scallywag behaves abnormally around people. The list goes on and on and on.

Similarly, documents from the University of Minnesota serve to complete the picture of mental abnormality that is the reality of the incarceration of primates in labs. Documents from this facility reveal very clearly what these monkeys endure. On 8/9/05, primate 05GP20 is listed as "Temp was up due to primate jumping back and forth wildly." On 8/23/05, primate #312E shows evidence of self-mutilation: "did bite knee after observation." Primate #45C on 3/21/06 is listed as "extremely thin, body condition is poor, severe alopecia . . . bruising on top of left ankle." Monkey #45D on 11/15/05 is described: ". . . ripping hair from the armpit area and chewing on the fur, each time he would grab a tuft of fur he would vocalize." Primate #25b was overdosed on 9/14/04 and was observed 11/15/05 ". . . ripping hair from the armpit area and chewing on the fur, each time he would grab a tuft of hair he would vocalize." Two separate primates are described this way. How many more are behaving like this without being noticed?

These are only glimpses inside a few laboratories, but the picture painted by them is not pretty. It is clear that the laboratory environment has a lasting impact on the psychological nature of on-human primates.

## Appendix A

2006                      Primate      Lab Use      Reported      by the      USDA

Alabama	1427
California	3769
Georgia	2849
Florida	795
Louisiana	2637
Oklahoma	156
Oregon	2034
South Carolina	649
Texas	3322
Washington	3413
<b>Total</b>	<b>21,051</b>

Taken	From	2006
Animal	Welfare	Report

	Experimental	Breeding	Actual	Taken	From	Individual
		Conditioni	Total	Facility	Reports	
<b>Large Primate Labs</b>						
<b>Alabama</b>						
U of Alabama (Birmingham)	186	178	364			
U of South Alabama (Mobile)	857	77	934			
<b>California</b>						
University of California, Davis	822	3654	4476	Based on	Primate	Center
Primate Products	0	1141	1141	Report	(likely incomplete)	
<b>Georgia</b>						
Primate Center at Emory	1686	1576	3262	Based on	Primate	Center
				Report	(likely incomplete)	
<b>Florida</b>						
Uof Miami	92		92			
Manheimer Foundation	246	1239	1485			
Dumond conservance	202	5	207			
<b>Louisiana</b>						
Tulane	1157	5029	6186			
U of Louisiana, Lafayette	1456	5033	6489			
<b>Oklahoma</b>						
Oklahoma Med Res Found	39		39			
U of OK	117	423	540			
<b>Oregon</b>						
Oregon Health Sciences U	2002	2283	4285			
<b>South Carolina</b>						
Alpha Genesis	541	5905	6446			
<b>Texas</b>						
Southwest Foundation	2449	3306	5755			
Scott & White Hosp	15	31	46			
Baylor	22	9	31			
U of Houston	126	42	168			
UT Austin	19		19			
UT Houston	143	961	1104			
<b>Washington</b>						
U of Washington, Seattle	138	783	921			
SNBL	2626	2842	5468			

<b>USDA</b>	<b>Under</b>	<b>Reported</b>
<b>These</b>	<b>States</b>	<b>by</b>
<b>28,407 primates or</b>		
<b>135%</b>		

<b>Actual Primate Lab Population Totals</b>	<b>49,458</b>
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# Appendix B

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 211.

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE  <b>ANNUAL REPORT OF RESEARCH FACILITY</b> ( TYPE OR PRINT )	1. CERTIFICATE NUMBER: 52-R-0007 CUSTOMER NUMBER: 493	FORM APPROVED OMB NO. 0579-0036
Virginia Commonwealth University Div Of Ani Racs, P.O. Box 980630 Richmond, VA 23298  Telephone: (804) -828-9837		

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 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 animal 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 in 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 reas such drugs were not used must be attached to this report	F. TOTAL NUMBER OF ANIMALS ( COLUMNS C + D + E )
Dogs			22		22
Cats			9		9
Guinea Pigs	2		16		16
Hamsters			8		8
Rabbits	12		435		435
Non-human Primates	9	5	18	21	44
Sheep			29		29
Pigs	6		226		226
Other Farm Animals					
Chickens		16			16
Other Animals					
Frogs		32	18		50
Ferrets			93		93

**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 res 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 if has required that exceptions to the standards and regulations be specified and explained by the principal investigator and an 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, the summary in 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 OF C.E.O. OR INSTITUTIONAL OFFICIAL 	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL ( Type or Print ) Francis L. Macrina, Ph.D., V.P. Research	DATE SIGNED 11/28/07
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## Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 52-R-0007
2. Number of animals used in this study: 21
3. Species (common name) of animals used in the study: rhesus monkeys
4. Explain the procedure producing pain and/or distress.

Twenty one rhesus monkeys were used as part of our program to evaluate drug dependence liability of new compounds. These rhesus monkeys are physically dependent on morphine. Periodically, they are allowed to go into spontaneous withdrawal, or withdrawal is precipitated by opioid antagonists. During this time they experience moderate to severe stress. Once in withdrawal, the monkeys are injected with the investigational compound, or morphine, or saline and then observed to assess their withdrawal state. On completion of the observation period, all withdrawal signs and symptoms are relieved by an injection of morphine. It is important to note that while these experiments are repetitive in nature, a new investigational chemical is being tested on each occasion. Many of these chemicals are opioid in nature and relieve the withdrawal signs and symptoms.

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

The distress produced by this procedure is the end-point being measured. As indicated above, many of the compounds tested relieve these symptoms and the experiment is terminated immediately after the observation period by the administration of morphine which also relieves the withdrawal signs.

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

The results from our testing are used by both the FDA and the DEA in making decisions concerning the Controlled Substances Act.

## Appendix C

### Johns Hopkins University Experiments

1: [Psychopharmacology \(Berl\)](#). 2006 Nov;189(1):71-82. Epub 2006 Sep 20.

#### **Chronic intragastric administration of gamma-butyrolactone produces physical dependence in baboons.**

[Goodwin AK](#), [Griffiths RR](#), [Brown PR](#), [Froestl W](#), [Jakobs C](#), [Gibson KM](#), [Weerts EM](#).

Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, USA.

**RATIONALE:** Abuse of gamma-hydroxybutyrate (GHB) and its precursors is a public health concern. Gamma-butyrolactone (GBL) is found in commercially available products and, when ingested, is metabolized to GHB. **OBJECTIVE:** The goal was to evaluate the physical dependence potential and behavioral effects of GBL. **METHODS:** Vehicle and then GBL were administered continuously (24 h per day) in baboons (*Papio anubis*, n=5) via intragastric catheters. GBL dosing was initiated at 100 mg/kg/day and then progressively increased stepwise by increments of 100 mg/kg to a final dose of 600 mg/kg. The number of food pellets earned, fine-motor task performance, and observed behaviors were used as dependent measures. Precipitated withdrawal was evaluated after administration of GABA-B and benzodiazepine receptor antagonists during chronic GBL dosing (400-600 mg/kg). Spontaneous withdrawal was evaluated after discontinuation of chronic GBL 600 mg/kg. Blood GHB levels were determined during chronic dosing of each GBL dose by isotope dilution assay. **RESULTS:** Chronic GBL dose-dependently decreased food-maintained behavior, disrupted performance on the fine-motor task, and produced signs of sedation and muscle relaxation. The GABA-B antagonist SGS742 [56 mg/kg, intramuscular (IM)] precipitated a withdrawal syndrome, whereas the benzodiazepine antagonist flumazenil (5 mg/kg, IM) produced little or no effect. Signs of physical dependence were also demonstrated when chronic GBL dosing was discontinued. Analysis of plasma indicated GBL was metabolized to GHB; levels were 825 to 1,690 micromol l(-1) GHB and 2,430 to 3,785 micromol l(-1) GHB after week 1 of 400 and 600 mg/kg/day, respectively. **CONCLUSIONS:** These data indicate that, like GHB, chronic GBL dosing produced physical dependence that likely involved the GABA-B receptor.

PMID: 17047936 [PubMed - indexed for MEDLINE]

1: [Eur J Pharmacol](#). 2005 Sep 5;519(1-2):103-13.

#### **Comparison of the behavioral effects of bretazenil and flumazenil in triazolam-dependent and non-dependent baboons.**

[Weerts EM](#), [Ator NA](#), [Kaminski BJ](#), [Griffiths RR](#).

Johns Hopkins University School of Medicine, Department of Psychiatry and Behavioral Sciences, MD 21224, USA. eweerts@jhmi.edu

Behavioral effects of the benzodiazepine receptor partial agonist bretazenil were compared with those of the benzodiazepine receptor antagonist flumazenil under conditions in which three baboons received continuous intragastric (i.g.) infusion of vehicle and then continuous i.g. infusion of triazolam (1.0 mg/kg/day). In each condition, acute doses of flumazenil (0.01-3.2 mg/kg) and bretazenil (0.01-10.0 mg/kg) were administered every 2 weeks (beginning after 30 days of treatment in the triazolam-dependent condition). Food pellets were available during daily 20-h sessions. Following test injections, 60-min

behavioral observations were conducted followed by a fine motor assessment. During chronic vehicle administration, neither drug produced changes in observed behaviors. Bretazenil increased pellets earned and time to complete the fine-motor task (10.0 mg/kg dose). During chronic triazolam dosing, both bretazenil and flumazenil precipitated benzodiazepine withdrawal syndromes, characterized by vomiting, tremors/jerks, and a decrease in pellets earned. Thus, bretazenil can function as an antagonist under conditions of benzodiazepine physical dependence.

1: [Psychopharmacology \(Berl\)](#). 2005 Jul;180(2):342-51. Epub 2005 Mar 1.

### **Involvement of gamma-hydroxybutyrate (GHB) and GABA-B receptors in the acute behavioral effects of GHB in baboons.**

[Goodwin AK](#), [Froestl W](#), [Weerts EM](#).

Johns Hopkins Bayview, Behavioral Biology Research Center, 5510 Nathan Shock Dr., Suite 3000, Baltimore, MD 21224, USA.

**RATIONALE:** Gamma-hydroxybutyrate (GHB) is used for the treatment of narcolepsy, but it is also a drug of abuse. The behavioral pharmacology of GHB is not well defined. **OBJECTIVES:** The current study was conducted to characterize the behavioral effects of a range of GHB doses in baboons (N=4) and to evaluate whether a GABA-B receptor antagonist and a GHB receptor antagonist would block a behaviorally active dose of GHB. **METHODS:** In the first experiment, GHB (32-420 mg/kg) or vehicle was administered via an intragastric catheter. Sixty min after dosing, subjects were presented with a fine-motor task and observed. Food pellets were available under a fixed-ratio schedule of reinforcement 20-h/day. In the second experiment, the GABA-B antagonist CGP36742 (10-56 mg/kg), the putative GHB antagonist NCS-382 (0.1-10 mg/kg), or vehicle were administered alone and then in combination with GHB (320 mg/kg). **RESULTS:** GHB dose-dependently decreased the number of food pellets earned. Performance in the motor task was also impaired and accompanied by signs of sedation and gastrointestinal discomfort. Pretreatment with CGP36742 antagonized GHB-induced suppression of food-maintained behavior and performance on the fine-motor task. Signs of abdominal discomfort, ataxia, and muscle relaxation produced by GHB were also reduced by pretreatment with CGP36742. In contrast, pretreatment with NCS-382 sometimes restored performance in the fine-motor task and increased food-maintained behavior, but the effect was variable across doses and baboons. Some doses of NCS-382 appeared to exacerbate ataxia and gastrointestinal discomfort produced by GHB in some subjects. **CONCLUSIONS:** These data indicate that while GABA-B receptors play a significant role in mediating the behavioral effects of GHB in baboon, the role of GHB receptors is less clear.

[Psychopharmacology \(Berl\)](#). 2005 May;179(3):678-87. Epub 2005 Jan 12.

### **Spontaneous and precipitated withdrawal after chronic intragastric administration of gamma-hydroxybutyrate (GHB) in baboons.**

[Weerts EM](#), [Goodwin AK](#), [Griffiths RR](#), [Brown PR](#), [Froestl W](#), [Jakobs C](#), [Gibson KM](#).

Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, USA. eweerts@jhmi.edu

**RATIONALE:** gamma-Hydroxybutyrate (GHB) is a current drug of abuse that may produce physical dependence. **OBJECTIVES:** The present study characterized the behavioral effects of chronic GHB in baboons (n = 4), and evaluated whether signs of withdrawal occurred (1) after administration of the GABA-B antagonist CGP36742 during chronic GHB administration (precipitated withdrawal) and (2) following discontinuation of chronic GHB administration (spontaneous withdrawal). **METHODS:** Water (vehicle) and then GHB was continuously infused via intragastric (IG) catheters. GHB administration was initiated at 350 mg/kg per day, and the dose was increased by 100 mg/kg over 4 days to 750 mg/kg per day. Food

pellets were available 20 h/day under a fixed ratio (FR5 or 10) schedule of reinforcement. Observation sessions and a 2-min fine motor task were conducted during vehicle and GHB administration. CGP36742 (32 and 56 mg/kg, IM) was administered during vehicle and chronic GHB administration. After a total of 32-36 days GHB administration was abruptly discontinued. Blood samples were collected during all interventions and analyzed for GHB content. RESULTS: Chronic GHB decreased food-maintained behavior, disrupted performance of the fine motor task, and produced ataxia, muscle relaxation, tremors and jerks. At the end of GHB administration, plasma levels of GHB ranged from 486 to 2080 micromol/L. Administration of CGP36742 during chronic GHB administration produced increases in aggression, self-directed behaviors, vomit/retch, tremors and/or jerks, which is consistent with a precipitated withdrawal syndrome. Similar signs were observed when GHB administration was discontinued. Seizures were not observed. CONCLUSIONS: These data indicate that chronic GHB administration produced physical dependence and that activation of the GABA-B receptor may be important for GHB physical dependence.

[Behav Pharmacol](#). 2003 Jul;14(4):331-42.

### **Physical dependence in baboons chronically treated with low and high doses of diazepam.**

**[Kaminski BJ](#), [Sannerud CA](#), [Weerts EM](#), [Lamb RJ](#), [Griffiths RR](#).**

Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21224-6823, USA. bkamins1@jhmi.edu

Physical dependence on diazepam was evaluated in male baboons chronically treated with either low or high doses of diazepam. Baboons received either a single oral daily administration of a low dose (0.5 mg/kg per day) of diazepam (n=4) or continuous intragastric infusion of a high dose (20 mg/kg per day) of diazepam (n=7). Development of physical dependence during chronic dosing with 0.5 mg/kg per day diazepam was assessed at 2 and 4 weeks and then monthly, during 1-h behavioral observations, following injections of the benzodiazepine competitive antagonist flumazenil. After 3-24 months of diazepam treatment, dosing was discontinued and physical dependence assessed via observation and responding for food pellets. In baboons that received 0.5 mg/kg per day diazepam, flumazenil precipitated a mild- to intermediate-intensity benzodiazepine withdrawal syndrome, which included decreases in the number of food pellets earned per day and increases in withdrawal postures, self-directed behaviors, aggressive behaviors and retching/vomiting. Three of four baboons showed signs of precipitated withdrawal after only 2 weeks of chronic low-dose treatment. Flumazenil continued to precipitate withdrawal signs, but with no systematic increase in severity, throughout the 6-10 months of 0.5 mg/kg diazepam administration. When 0.5 mg/kg per day diazepam dosing was discontinued, the number of food pellets earned per day decreased in two of the four baboons, but no systematic changes in behavioral signs were observed. In contrast, within 7-10 days of termination of 20 mg/kg per day diazepam dosing, withdrawal signs of intermediate intensity and a decrease in the number of food pellets earned per day occurred in all baboons. In the present study, physical dependence developed after 2 weeks of a chronic low dose of diazepam administration but did not increase further over long-term exposure to diazepam.