2006

Reduce, Refine, Replace: The Failure of the Three R’s and the Future of Animal Experimentation

Darian M. Ibrahim
William & Mary Law School, dmibrahim@wm.edu

Repository Citation
https://scholarship.law.wm.edu/facpubs/1691

Copyright c 2006 by the authors. This article is brought to you by the William & Mary Law School Scholarship Repository.
https://scholarship.law.wm.edu/facpubs
Reduce, Refine, Replace: The Failure of the Three R’s and the Future of Animal Experimentation

Darian M. Ibrahim†

The debate in animal ethics is defined by those who advocate the regulation of animal use and those who advocate its abolition.1 The animal welfare approach, which focuses on regulating animal use, maintains that humans have an obligation to treat animals "humanely" but may use them for human purposes.2 The animal rights approach, which focuses on abolishing animal use, argues that animals have inherent moral value that is inconsistent with us treating them as property.3

The animal welfare approach is the dominant model of animal advocacy in the United States.4 Animal experimentation provides a fertile ground for testing this model because a unique confluence of factors make experimentation appear susceptible to meaningful regulation. First, there is more opposition to using animals in experiments than to any other type of animal use.5

† Associate Professor, University of Arizona James E. Rogers College of Law. My thanks to David Adelman, Taimie Bryant, Dave Fagundes, Jamie Heisler Ibrahim, Tom Lindell, Marc Miller, Andrew Rowan, Roy Spece, and participants at the University of Chicago Legal Forum Symposium, held Oct 28-29, 2005. Special thanks are owed to Gary Francione. I also thank Nikia Fico and Maureen Garmon for their excellent research assistance.

1 Consider Gary L. Francione, Rain Without Thunder: The Ideology of the Animal Rights Movement 1-6 (Temple 1996) (discussing these two basic approaches to animal advocacy).

2 Id at 1.

3 Id. As Gary Francione discusses, some animal welfare advocates maintain that regulation is a means to abolition. Francione argues, however, that continuing to regulate animal exploitation will simply further entrench its acceptability and will not lead to abolition. Id at 110-41.

4 Francione, Rain Without Thunder at 32 (cited in note 1) ("Although virtually all modern animal advocates describe their various positions as embodying 'rights' views in their fund-raising literature and in the media, many leaders of the movement now explicitly dismiss the importance of rights notions."); Darian M. Ibrahim, The Anticruelty Statute: A Study in Animal Welfare, 1 J Animal L & Ethics 175, 178-79 (2006).

5 See, for example, Andrew N. Rowan, Of Mice, Models, & Men: A Critical Evaluation of Animal Research 31 (SUNY 1984) ("What is it about animal research that produces such strong reactions? Intensive farming methods, whereby animals are essentially protein factories, is of concern to animal welfare groups, but the issues does not evoke nearly as much passion."). Consider Deborah Rudacille, The Scalpel and the Butterfly:
Second, animal advocates and commercial researchers have agreed on a common approach for tackling that problem—the Three R’s—which require researchers to reduce the number of animals used in experiments, refine experimental procedures to minimize animal pain and suffering, and replace animal subjects with non-animal alternatives when scientifically feasible. Third, Congress has responded to public concern over animal experimentation by incorporating the Three R’s into the federal Animal Welfare Act (“AWA”), the most significant animal protection law in the United States. The Three R’s have also been adopted as federal policy for biomedical research and toxicity testing. Finally, the Three R’s provide specific guidance to researchers on how to implement the widely accepted principle that humans not inflict “unnecessary” suffering on animals. The principle against unnecessary suffering is contained in all animal protection laws, including state anticruelty statutes, but only the Three R’s make it context-specific.

Given this favorable confluence of factors, it stands to reason that if the animal welfare approach is to work anywhere, it will be in the context of animal experimentation. However, this Article will show that the Three R’s fail to meaningfully regulate animal experiments. There are three main reasons for this failure. First, the Three R’s do not provide a mechanism for challenging a researcher’s purpose in conducting an experiment that will use animals, even if that experiment is unnecessary. Second, animal advocates and commercial researchers have agreed on a common approach for tackling that problem—the Three R’s—which require researchers to reduce the number of animals used in experiments, refine experimental procedures to minimize animal pain and suffering, and replace animal subjects with non-animal alternatives when scientifically feasible. Third, Congress has responded to public concern over animal experimentation by incorporating the Three R’s into the federal Animal Welfare Act (“AWA”), the most significant animal protection law in the United States. The Three R’s have also been adopted as federal policy for biomedical research and toxicity testing. Finally, the Three R’s provide specific guidance to researchers on how to implement the widely accepted principle that humans not inflict “unnecessary” suffering on animals. The principle against unnecessary suffering is contained in all animal protection laws, including state anticruelty statutes, but only the Three R’s make it context-specific.

Given this favorable confluence of factors, it stands to reason that if the animal welfare approach is to work anywhere, it will be in the context of animal experimentation. However, this Article will show that the Three R’s fail to meaningfully regulate animal experiments. There are three main reasons for this failure. First, the Three R’s do not provide a mechanism for challenging a researcher’s purpose in conducting an experiment that will use animals, even if that experiment is unnecessary. Second, animal advocates and commercial researchers have agreed on a common approach for tackling that problem—the Three R’s—which require researchers to reduce the number of animals used in experiments, refine experimental procedures to minimize animal pain and suffering, and replace animal subjects with non-animal alternatives when scientifically feasible. Third, Congress has responded to public concern over animal experimentation by incorporating the Three R’s into the federal Animal Welfare Act (“AWA”), the most significant animal protection law in the United States. The Three R’s have also been adopted as federal policy for biomedical research and toxicity testing. Finally, the Three R’s provide specific guidance to researchers on how to implement the widely accepted principle that humans not inflict “unnecessary” suffering on animals. The principle against unnecessary suffering is contained in all animal protection laws, including state anticruelty statutes, but only the Three R’s make it context-specific.
ond, loopholes in the AWA have allowed researchers to avoid application of the Three R's in practice. Third, the Three R's were not designed to apply to new and emerging areas of biomedical research that have the potential to greatly escalate the use of animals in experiments. These areas include stem cell research, cloning, xenotransplantation, genetic modification, and bioterrorism defense, each of which will be discussed in this Article.

This Article proceeds as follows. Part I gives the basics of the Three R's and examples of reductions, refinements, and replacements. Part II discusses the general acceptance of the Three R's by both researchers and animal advocates and the incorporation of the Three R's into federal law and research policy. Part III explores the three main deficiencies in the Three R's.

I. BASICS OF THE THREE R'S

The Three R's were first proposed by scientists William Russell and Rex Burch in their 1959 book *The Principles of Humane Experimental Technique*. Russell and Burch assumed that scientific uses of animals were generally compatible with animal welfare. At the outset of their book, they stated:

It has sometimes seemed that there is an irreconcilable conflict between the claims of science and medicine and those of humanity in our treatment of lower animals. . . . The conflict disappears altogether on closer inspection, and by now it is widely recognized that the humanist possible treatment of experimental animals, far from being an obstacle, is actually a prerequisite for successful animal experiment.

Russell and Burch did not seek the abolition of animal experimentation, but only the “removal of [its] inhumanity” through implementation of the Three R's—a goal consistent with the animal welfare approach.

Reduce refers to improvements that minimize the total number of laboratory animals used to obtain a given set of data.

---

12 See Part III.B.
13 See Part III.C.
15 Id at 3.
16 Id at 3-4.
17 Id at 64.
18 Russell and Burch, *The Principles of Humane Experimental Technique* at 64 (cited in note 14) ("Reduction means reduction in the numbers of animals used to obtain infor-
Russell and Burch urged the reduction of animal use through controlling variance and better design and analysis of experiments.\(^1\)

In terms of variance, they observed that “[i]f every single individual (of a species, say) were absolutely identical in all respects, very few animals would be needed,” but that “[i]n the real world, individual animals do vary.”\(^2\) To reduce variance, Russell and Burch suggested using inbred strains of the same species of animal.\(^3\) In terms of experimental design and analysis, Russell and Burch suggested that researchers consult with statisticians either before or after experimentation.\(^4\) Consultation before experimentation can lead to better design, including use of the minimum number of animals necessary for statistical analysis and extrapolation purposes, while consultation after experimentation can salvage results of a bad design through the statistical isolation of variance, thereby avoiding repetition of the experiment.\(^5\)

Refine refers to improvements that minimize the suffering of animals that are used in experiments.\(^6\) Refinements can be general or specific. Russell and Burch described the general refinement of anesthesia as “the supreme refinement procedure.”\(^7\) Other general refinements include analgesia (local anesthesia), administering substances through inhalation rather than injection (to avoid the distress from needles), and restraining animals after experimentation (to prevent wound licking that could necessitate repetition of the experiment).\(^8\) Specific refinements

...
include the use of minor paralysis instead of death as an endpoint in some toxicity tests and restricting or eliminating the use of Complete Freund's Adjuvant, which causes a highly painful inflammatory reaction, in immunization studies. Improved living conditions can also reduce distress in laboratory animals, although Russell and Burch conceded that this was not possible in large laboratories where "imperfect handling, injection, housing, and general husbandry become virtually inevitable."

Replace refers to the use of a non-animal alternative in place of an animal during an experiment. Replacement techniques include in vitro studies on human cells and tissues, physico-

---

27 See Rowan, Of Mice, Models, & Men at 264-65 (cited in note 5).
28 See HSUS, Overview of the Issues, available at <http://www.hsus.org/web-files/PDF/ARI/Overview_of_the_Issues.pdf> (last visited Jan 12, 2006) (explaining Complete Freund's Adjuvant). Andrew Rowan suggests, however, that often the painful inflammation may be caused by non-sterile conditions rather than by the test itself. E-mail from Andrew Rowan to Darian Ibrahim (Dec 8, 2005) ("Rowan E-mail") (on file with author).
29 See, for example, Sarah Wolfensohn, Social Housing of Large Primates, Methodology for Refinement of Husbandry and Management 32 (Supp 1) Alternatives to Lab Animals 149, 149-51 (2004), available at <http://www.worldcongress.net/2002/proceedings/B2%20Wolfensohn.pdf> (last visited Jan 12, 2006) (proposing to reduce stress in rhesus monkeys by housing them loose in rooms without cages to promote the development of normal social relationships).
31 Id at 64 ("Replacement means the substitution for conscious living higher animals of insentient material."). However, Russell and Burch also deemed replacements to include "relative replacements," which did not completely eliminate the use of animals. Id at 70-71 ("[N]on-recovery experiments on living and intact but completely anesthetized animals" are "beyond reproach" if coupled with euthanasia and reduction.). The different meanings attached to terms by researchers and animal advocates can result in misperceptions over the amount of animal experimentation that is still occurring. See, for example, Rowan, Of Mice, Models, & Men at 261 (cited in note 5) ("[D]ifferent groups use the term 'alternatives' to refer to different sets of techniques. For example, one group may be referring to only those techniques that lead to total replacement of laboratory animal use, while another will include a broader range, such as techniques that reduce animal pain and suffering."); Rudacille, The Scalpel and the Butterfly at 169 (cited in note 5) (noting that the use of the word "alternatives" led to a delay in the National Institutes of Health ("NIH") 1994 Plan for the Use of Animals in Research, as NIH committee members feared that this word meant only replacements to animal rights groups, while the committee also wanted it to incorporate the ideas of reduction and refinement). For a discussion of how definitions can be used to further animal exploitation, see Taimie L. Bryant, Animals Unmodified: Defining Animals/Defining Human Obligations Toward Animals, 2006 U Chi Legal F 137, 148-62.
32 Russell and Burch counted as replacements in vitro studies made possible by the killing of animals for their cells and tissues. Michael Balls, Replacement of Animal Procedures: Alternatives in Research, Education and Testing, 28 Lab Animals 193, 194 (1994). These only constitute true replacements if the cells and tissues come from consenting humans, which is increasingly common. See C. Ray Greek and Jean Swingle Greek, Sacred Cows and Golden Geese: The Human Cost of Experiments on Animals 102 (Continuum 2000) ("[H]uman cells and tissues, removed during surgery, biopsies, or post-mortem, can be grown outside the body in a 'test tube' . . . and any types of cells can be
chemical studies, computer modeling, microbiological studies, clinical and epidemiological studies, and autopsy. Russell and Burch discussed the importance of fidelity and discrimination when analyzing replacements. Fidelity refers to how well a

kept alive almost indefinitely."

One example of in vitro usage comes from the search for the polio vaccine in the 1950s. Despite the death of over one million monkeys for this purpose, see Rowan, Of Mice, Models, & Men at 117-20 (cited in note 5), in vitro studies ultimately led to the development of the polio vaccine. See Francione, Introduction to Animal Rights at 38 (cited in note 9) ("Polio experiments involving monkeys falsely indicated that the virus affected only the nervous system, and this mistake—directly related to the reliance on 'animal models'—delayed discovery of the polio vaccine."); A. Sabin, Remarks, Statements before the Subcommittee on Hospitals and Health Care, Committee on Veterans Affairs, and House of Representatives (Apr 26, 1984) (serial no 98-48) (Testifying under oath, Dr. Albert Sabin, the inventor of the polio vaccine, stated that the vaccine "was long delayed by the erroneous conception of the nature of the human disease based on misleading experimental models of [it] in monkeys"). For further discussion of the development of the polio vaccine, see Rudacille, The Scalpel and the Butterfly at 98-119 (cited in note 5). For other examples of in vitro alternatives, see discussion at notes 120-34 and accompanying text.

Physiochemical studies have replaced the use of animals in some areas such as in fat-soluble vitamin assays, but they are more often used as screening tests for detecting the potential of a substance to be irritating. Animal tests are subsequently performed on potentially irritating substances. See Rowan, Of Mice, Models, & Men at 262 (cited in note 5); European Commission Health & Consumer Protection Directorate-General, Opinion of the Scientific Committee on Toxicity, Ecotoxicity and the Environment on The BUAV-ECEAE Report on "The Way Forward—Action to End Animal Toxicity Testing," available at <http://europa.eu.int/comm/health/ph.risk/committees/sct/documents/out217_en.pdf> (last visited Jan 10, 2005).

Computer modeling has been used in many ways, including for "actively designing drugs and chemicals for specific purposes." Balls, Replacement of Animal Procedures at 196 (cited in note 32). Computer modeling can predict how a human may respond to contact with certain chemicals by using mathematical algorithms and data from both human exposure and previous animal studies. See, for example, National Institutes of Environmental Health Sciences, Factsheet: NIEHS and the Use of Alternative Methods in Toxicological Research and Testing, available at <http://www.niehs.nih.gov/oc/factsheets/analt.htm> (last visited Feb 27, 2006).

Microbiological systems can serve as models of more complex systems and have completely replaced the need for animals in some cases by using bacteria to detect the presence of particular vitamins, mutagens, and even carcinogens. See, for example, Rowan, Of Mice, Models, & Men at 263 (cited in note 5). See also Russell and Burch, The Principles of Humane Experimental Technique at 98-104 (cited in note 14).

Epidemiological studies focus on the distribution and determination of disease in human populations to control health problems. By concentrating research on human patients, volunteers, or populations, the results obtained from these studies are often far more relevant than those obtained from animal studies. Rowan, Of Mice, Models, & Men at 264 (cited in note 5).

Autopsies are often neglected as an alternative to animal experimentation despite being an important means of studying the effects of an illness on the whole body. See David Dobbs, Buried Answers, NY Times 6-40 (Apr 24, 2005) (critiquing the underuse of autopsies as a means of studying human diseases); Americans, Europeans, Japanese for Medical Advancement, Replacing Animals, available at <http://www.curedisease.com/replacing_animals.pdf> (last visited Jan 10, 2006) ("Virtually every disease has either been discovered or clarified as a result of autopsy.").

Russell and Burch, The Principles of Humane Experimental Technique at 77-84 (cited in note 14). See also Rowan, Of Mice, Models, & Men at 265 (cited in note 5) (stat-
replacement replicates the original in an overall sense; discrimi-
nation refers to how well a replacement represents the original
in terms of a particular property of interest to researchers. For
example, a chimpanzee is a high fidelity model of a human, while
a "protozoan is a very low-fidelity model, but it may be a better
model in some studies—for example, vitamin assays—because of
its . . . discrimination."\footnote{Russell and Burch, The Principles ofHumane Experimental Technique at 79 (cited in note 14).} Russell and Burch argued that "in many
fields, discrimination is recognized in \textit{practice} to be the more de-
sirable quality,"\footnote{Id at 80-84.} and thus referred to the tendency of research-
ners to insist upon a high-fidelity model in all cases as the "high-
fidelity fallacy."\footnote{See HSUS, Current Projects of the Animal Research Issues Section, available at <http://www.hsus.org/animals_in_research/general_information_on_animal_research/current_projects_of_the_animal_research_issues_section.html> (last visited Jan 12, 2006). The primary aim of The HSUS's Animal Research Issues section is to promote alternatives to the use of animals in harmful research, testing, and education. Alternatives are scientific methods that accomplish one or more of the Three R's: replace or reduce the use of animals in a scientific procedure, and/or refine a procedure so the animals experience less pain, suffering or discomfort. HSUS is the world's largest animal welfare organization, with approximately three and a half million members. Rudacille, \textit{The Scalpel and the Butterfly} at 294 (cited in note 5).\textsuperscript{41} Russell and Burch argued that "in many
fields, discrimination is recognized in practice to be the more de-
sirable quality,"\footnote{See Stephan L. Zawistowski, \textit{Operation: Three Rs} (ASCPA 1996), available at <http://www.aspca.org/site/PageServer?pagename=al_resources_operation> (last visited Jan 12, 2006) ("Our recent efforts have followed the 3Rs theme that guides the movement today—to reduce, refine, and replace the use of animals in research.").\textsuperscript{42} See AAVS, \textit{The Three R's}, available at <http://aavs.org/alternatives01.html> (last visited Jan 12, 2006) (promoting the Three R's). AAVS describes itself as "the oldest or-
ganization in the United States dedicated to eliminating experiments on animals." Id.\textsuperscript{43} Id at 80-84.} Russell and Burch argued that "in many
fields, discrimination is recognized in \textit{practice} to be the more de-
sirable quality,"\footnote{Id at 80-84.} and thus referred to the tendency of research-
ners to insist upon a high-fidelity model in all cases as the "high-
fidelity fallacy."\footnote{Id at 80-84.}

II. ACCEPTANCE OF THE THREE R'S AS FEDERAL LAW AND
RESEARCH POLICY

A. Acceptance of the Three R's by Animal Welfare Advocates
   and Commercial Researchers

Many large animal welfare organizations and prominent
animal advocates support the Three R's. Organizational support-
ers include the Humane Society of the United States ("HSUS"),\footnote{See HSUS, Current Projects of the Animal Research Issues Section, available at <http://www.hsus.org/animals_in_research/general_information_on_animal_research/current_projects_of_the_animal_research_issues_section.html> (last visited Jan 12, 2006). The primary aim of The HSUS's Animal Research Issues section is to promote alternatives to the use of animals in harmful research, testing, and education. Alternatives are scientific methods that accomplish one or more of the Three R's: replace or reduce the use of animals in a scientific procedure, and/or refine a procedure so the animals experience less pain, suffering or discomfort. HSUS is the world's largest animal welfare organization, with approximately three and a half million members. Rudacille, \textit{The Scalpel and the Butterfly} at 294 (cited in note 5).\textsuperscript{41} See Stephan L. Zawistowski, \textit{Operation: Three Rs} (ASCPA 1996), available at <http://www.aspca.org/site/PageServer?pagename=al_resources_operation> (last visited Jan 12, 2006) ("Our recent efforts have followed the 3Rs theme that guides the movement today—to reduce, refine, and replace the use of animals in research.").\textsuperscript{42} See AAVS, \textit{The Three R's}, available at <http://aavs.org/alternatives01.html> (last visited Jan 12, 2006) (promoting the Three R's). AAVS describes itself as "the oldest or-
ganization in the United States dedicated to eliminating experiments on animals." Id.\textsuperscript{43} Id at 80-84.} the American Society for the Prevention of Cruelty to Animals
("ASPCA"),\footnote{See HSUS, Current Projects of the Animal Research Issues Section, available at <http://www.hsus.org/animals_in_research/general_information_on_animal_research/current_projects_of_the_animal_research_issues_section.html> (last visited Jan 12, 2006). The primary aim of The HSUS's Animal Research Issues section is to promote alternatives to the use of animals in harmful research, testing, and education. Alternatives are scientific methods that accomplish one or more of the Three R's: replace or reduce the use of animals in a scientific procedure, and/or refine a procedure so the animals experience less pain, suffering or discomfort. HSUS is the world's largest animal welfare organization, with approximately three and a half million members. Rudacille, \textit{The Scalpel and the Butterfly} at 294 (cited in note 5).\textsuperscript{41} See Stephan L. Zawistowski, \textit{Operation: Three Rs} (ASCPA 1996), available at <http://www.aspca.org/site/PageServer?pagename=al_resources_operation> (last visited Jan 12, 2006) ("Our recent efforts have followed the 3Rs theme that guides the movement today—to reduce, refine, and replace the use of animals in research.").\textsuperscript{42} See AAVS, \textit{The Three R's}, available at <http://aavs.org/alternatives01.html> (last visited Jan 12, 2006) (promoting the Three R's). AAVS describes itself as "the oldest or-
ganization in the United States dedicated to eliminating experiments on animals." Id.\textsuperscript{43} Id at 80-84.} and the American Anti-Vivisection Society
("AAVS").\footnote{See HSUS, Current Projects of the Animal Research Issues Section, available at <http://www.hsus.org/animals_in_research/general_information_on_animal_research/current_projects_of_the_animal_research_issues_section.html> (last visited Jan 12, 2006). The primary aim of The HSUS's Animal Research Issues section is to promote alternatives to the use of animals in harmful research, testing, and education. Alternatives are scientific methods that accomplish one or more of the Three R's: replace or reduce the use of animals in a scientific procedure, and/or refine a procedure so the animals experience less pain, suffering or discomfort. HSUS is the world's largest animal welfare organization, with approximately three and a half million members. Rudacille, \textit{The Scalpel and the Butterfly} at 294 (cited in note 5).\textsuperscript{41} See Stephan L. Zawistowski, \textit{Operation: Three Rs} (ASCPA 1996), available at <http://www.aspca.org/site/PageServer?pagename=al_resources_operation> (last visited Jan 12, 2006) ("Our recent efforts have followed the 3Rs theme that guides the movement today—to reduce, refine, and replace the use of animals in research.").\textsuperscript{42} See AAVS, \textit{The Three R's}, available at <http://aavs.org/alternatives01.html> (last visited Jan 12, 2006) (promoting the Three R's). AAVS describes itself as "the oldest or-
ganization in the United States dedicated to eliminating experiments on animals." Id.\textsuperscript{43} Id at 80-84.} HSUS, for instance, gives a "Russell and Burch Award" to "a scientist who has made an outstanding contribution

towards advancing the Three R’s.” Deborah Rudacille notes that even “PETA, the perceived arch nemesis of the research community . . . attended an FDA meeting on alternative testing, sitting around the table with FDA officials and representatives of Colgate-Palmolive Company to discuss possible areas for cooperation.” Individual supporters include Andrew Rowan, an Executive Vice President of HSUS, who argues in favor of collaboration with researchers to improve animal welfare through implementation of the Three R’s. Another individual supporter of the Three R’s was Henry Spira, one of the most influential animal advocates of the past century, who stated that “what’s practical and doable is the concept of the Three R’s. I don’t believe that there’s anyone who can rationally or reasonably make a dent in the Three R’s. That’s something that is unassailable, I believe.”

While the Three R’s are now seen by many animal advocates as an important means of reducing animal suffering, they were largely ignored at first. According to Rudacille, “[a]lthough certain people . . . had continued to promote the ideas advocated by Russell and Burch . . . throughout the sixties and seventies, for the most part the book remained obscure until a new generation

---

45 See HSUS, Van Zutphen Wins 2005 Russell and Burch Award, available at <http://www.hsus.org/animals_in_research/general_information_on_animal_research/the_russell_and_burch_award> (last visited Feb 27, 2006) (“The Russell and Burch award is bestowed every few years by The Humane Society of the United States to a scientist who has made an outstanding contribution toward advancing the Three Rs of replacement, reduction and refinement of animal use in research.”); Rudacille, The Scalpel and the Butterfly at 294 (cited in note 5) (“The Humane Society of the United States . . . awards certificates each year to scientists who have made outstanding contributions toward the advancement of alternative methods in research, education, and testing.”).

46 Rudacille, The Scalpel and the Butterfly at 184 (cited in note 5).

47 See Rowan, Of Mice, Models, & Men at 261-73 (cited in note 5); Andrew Rowan, The Alternatives Concept, available at <http://www.nal.usda.gov/awic/alternatives/rowan.htm> (last visited Jan 12, 2006). Some abolitionists believe that all animal research should stop today while others are willing to be more pragmatic. Most animal welfare supporters would like to see the end of animal use in research but do not perceive this to be a realistic or practical goal at the moment. Instead, they believe that the research establishment should devote more time and money to finding ways to eliminating animal pain and distress in research techniques (in other words, the three R’s—Reduction, Refinement, and Replacement).

48 See Francione, Rain Without Thunder at 85 (cited in note 1) (stating that Spira “is thought to be one of the most influential [animal advocates] of this century”).

49 Id at 86, quoting interview with Henry Spira, Foundation for Biomedical Research Newsletter (Jan/Feb 1993). Spira sought to abolish animal exploitation, but viewed regulation as a means to that end. Francione, Rain Without Thunder at 62 (cited in note 1) (“Spira concluded that his abolitionist efforts up until 1979, although highly successful, were ‘largely symbolic, involving a few thousand animals.’ He became willing to reform institutionalized cruelty. Spira adopted a more welfarist approach in undertaking a more ambitious project—the use of animals in cosmetics and product testing.”) (citation omitted).
grasped its relevancy to the testing controversy. Since then, "the three R's approach has spread throughout the industry, regulatory agencies, and the research community, giving scientists and animal protectionists a common language and a vehicle for identifying common goals." According to Rowan, the "key is that the idea of 'alternatives' offers a pro-science notion of gradual reform and is therefore not inimical to biomedical research."

Among the research community, the Foundation for Biomedical Research ("FBR"), "the nation's oldest and largest organization" advocating for the use of animals in experiments, purports to accept the Three R's. FBR claims that:

Here in the United States, our scientific and medical research communities are committed to supporting the development of research techniques that reduce the number of animals used in each and every study, replace lab animals with non-animal models whenever possible, [and] refine the tests to ensure the most comfortable and humane conditions possible.

Many large corporations that use animals for biomedical research and product testing proffer similar support for the Three R's. Even Charles River Laboratories, the world's largest com-

---

50 Francione, *Rain Without Thunder* at 167 (cited in note 1). See also Balls, *Replacement of Animal Procedures* at 194-96 (cited in note 32) (discussing events that led to the widespread acceptance of the Three R's).

51 Rudacille, *The Scalpel and the Butterfly* at 184 (cited in note 5).

52 Rowan, *Of Mice, Models, & Men* at 59 (cited in note 5).


54 See id (discussing FBR's concern for the conditions under which animals are studied and need for humane experimentation). See also Rudacille, *The Scalpel and the Butterfly* at 170 (cited in note 5) (noting that FBR represents "more than three hundred research institutions and companies"). See also Francione, *Rain Without Thunder* at 29-30 (cited in note 1) ("[T]he Foundation for Biomedical Research (FBR) and its lobbying arm, the National Association for Biomedical Research (NABR) . . . are heavily supported by commercial animal users and suppliers . . . as well as universities and individuals who use animals.").


56 See, for example, GlaxoSmithKline, *Animal Research*, available at <http://www.gsk.com/corporate_responsibility/cr_report_2004/ri_animal_research.htm> (last visited Jan 12, 2006) ("GSK is committed to the 3Rs—reduction, refinement and replacement—and to achieving the highest standards of animal welfare."); Abbott, *Global Citizenship: Managing Our Key Issues*, available at <http://abbott.com/citizenship/citizen_abbott/position.cfm> (last visited Jan 12, 2006) ("Abbott's approach is to employ the '3Rs' whenever possible, which include refining experimental procedures to avoid or minimize unnecessary pain or suffering; reducing the number of animals used in any tests we conduct to the minimum to get valid results; and replacing the need for animal testing through alternative research methods."); Johnson & Johnson, *Social Re-
commercial breeder of animals for sale to laboratories, claims to "fund[] organizations and projects that . . . advance the three R's of animal welfare." An exception to this unity of support for the Three R's among researchers comes from the academic research community, which is still resistant to the concept and instead favors unfettered research on animals.


In 1985, the growing power of the animal rights movement, the documentation of egregious abuses of animals at several research institutions, and the general acceptance of the Three R's by advocates and researchers prompted Congress to incorporate the Three R's into the AWA. Congress originally passed the AWA (first called the Laboratory Animal Welfare Act) in 1966 due to growing concern over the theft of family pets for sale to laboratories, which was detailed by a *Life* magazine story that included shocking pictures of how these animals were being kept by dealers. Since its enactment, Congress has amended the

---


*See* Rudacille, *The Scalpel and the Butterfly* at 169 (cited in note 5) ("The academic research community was more resistant and to this day is unhappy about the term 'alternatives' and only marginally more satisfied with the idea of the 3R's."). According to Rowan, "t]oxicologists and the corporate world have embraced the 3Rs but academic researchers . . . have not." Rowan E-mail (cited in note 28).

*See* Francione, *Rain Without Thunder* at 89-90 (cited in note 1) (discussing competing positions on the composition of the AWA amendments); Francione, *Animals, Property, and the Law* at 195-96 (cited in note 9) (stating that the 1985 amendments were the "result of various cases in which federally funded research facilities were shown to be involved in the egregious abuse of animals" and represent "the only really substantial revision of the AWA since its enactment"). The amendments to the AWA that incorporated the Three R's are discussed in notes 63-74.

*This prompted Senator Robert Dole to refer to this legislation as the "dognapping bill of 1966." 116 Cong Rec 40, 461 (1970) (statement of Senator Dole). According to Fran-
THE FUTURE OF ANIMAL EXPERIMENTATION

AWA five times for reasons including expanding its scope. The most significant amendments came in 1985, when Congress incorporated the Three R's into the AWA in several ways. First, although the original purpose of the AWA was to prevent pet theft, the 1985 amendments added the following policy language:

Congress finds that . . . methods of testing that do not use animals are being and continue to be developed which are faster, less expensive, and more accurate than traditional animal experiments for some purposes and further opportunities exist for the development of these methods of testing, [and] measures which eliminate or minimize the unnecessary duplication of experiments on animals can result in more productive use of Federal funds.

This language emphasized the newfound importance of the Three R's in animal ethics.

Second, the body of the AWA was revised to include the Three R's in several specific provisions. One such provision requires the Secretary of Agriculture to promulgate “minimum requirements . . . for the use of tranquilizers, analgesics, and anesthetics” in “any practice which could cause pain to animals” (in other words, procedures classified as category “D” and “E” studies by USDA), although it also allows researchers to withhold pain relief when “scientifically necessary.” A similar provision mandates “that animal pain and distress are minimized, including adequate veterinary care with the appropriate use of anesthetic, analgesic, tranquilizing drugs, or euthanasia.” These are clear examples of refinements. The ideas of replacement and reduction were also apparent after the 1985 amendments. For instance, one provision requires the Secretary to promulgate

cione, “[c]oncerned persons sent more letters to Life than the magazine had received on any other article, and sent more letters to Congress than were sent on issues such as civil rights and the war in Vietnam.” Francione, Animals, Property, and the Law at 192 (cited in note 9) (Feb 4, 1966 Life magazine on file with author).


7 USC § 2143(a)(3)(C)(v) (2000) (emphasis added). A requirement to use anesthetics was first added in the 1970 amendments to the AWA. See Pub. L No 91-579 (Dec 24, 1970) (amending § 13 of 7 USC § 2143 to read: “Such standards [governing research facilities] shall include . . . adequate veterinary care, including the appropriate use of anesthetic, analgesic or tranquilizing drugs, when such use would be proper in the opinion of the attending veterinarian of such research facilities . . . .”).


"minimum requirements . . . that the principal investigator considers alternatives to any procedure likely to produce pain or distress in an experimental animal,"66 while another provision mandates that the Secretary to establish an information service at the National Agricultural Library67 to provide information on methods that can "reduce or replace animal use; and minimize pain and distress to animals."68

Third, the AWA and its implementing regulations were amended to require that research facilities establish Institutional Animal Care and Use Committees ("IACUCs") to implement the Three R's.69 The AWA requires that IACUCs have at least three members, one of whom cannot be affiliated with the research facility.70 IACUC members must review the research

66 7 USC § 2143(e)(3) (2000) (emphasis added). See also Paul A. Locke, Presentation, The Animal Welfare Act and the 3Rs—Where Are We and Where Should We Go? (Sep 10, 2001), available at <http://cast.jhsph.edu/programs/workshops/20th/locke.htm> (noting that the 1985 amendments to the AWA added a provision mandating that alternatives be considered "if a procedure involves pain and distress" in an effort to strike a balance between the necessity of biomedical research and animal welfare).

67 For information on the National Agricultural Library, see <http://www.nal.usda.gov/> (last visited Jan 12, 2006).

68 7 USC § 2143(b) (2000).

69 7 USC § 2143(b)(1)(B) (2000). Specifically, the AWA's implementing regulations require IACUCs to ensure that:

[P]roposed activities or significant changes in ongoing activities meet the following requirements:

(i) Procedures involving animals will avoid or minimize discomfort, distress, and pain to the animals;

(ii) The principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to animals, and has provided a written narrative description of the methods and sources, e.g., the Animal Welfare Information Center, used to determine that alternatives were not available;

(iii) The principal investigator has provided written assurance that the activities do not unnecessarily duplicate previous experiments.

9 CFR § 2.31(d) (2005). IACUCs are somewhat similar to the Institutional Review Boards ("IRBs") that oversee experiments on humans. See 45 CFR §§ 46.101 (2005). However, there is a fundamental difference between animal experimentation and human experimentation, and therefore between the functions of IACUCs and IRBs. In the former, animals are used in experiments against their will; in the latter, we require humans used in experiments to have given informed consent. Informed consent is the primary safeguard for ensuring that humans are not used in unnecessary experiments, and this safeguard is absent in animal experiments. There are certain deviations from or exceptions to the informed consent paradigm for humans—for example, surrogate consent and rare contexts in which consent is deemed unnecessary. See 45 CFR § 46.116(c-d); Carl H. Coleman, et al, The Ethics and Regulation of Research with Human Subjects 527-650 (Lexis 2005). Nevertheless, informed consent is the central governing concept in legal and moral analyses of human experimentation.

70 9 CFR § 2.31(b)(3) (2005).
facility's program on animal welfare and inspect its facilities every six months. They must prepare reports on their findings which "shall be reviewed and signed by a majority of the IACUC members and must include any minority views." The main function of IACUCs is to reduce pain and distress, although IACUC approval is not required for experiments that are classified as unlikely to cause more than minor pain and distress. Rowan estimates that these category "C" experiments comprise approximately 60% of all experiments.

Finally, the AWA also requires that research facilities themselves submit an annual report that "[a]ssure[s] that each principal investigator has considered alternatives to painful procedures" and reports on painful experiments, both those that involved the use of pain-relieving drugs and those that did not.

C. The Three R's as Federal Research Policy

The Three R's are also prevalent in federal research policy. Many research facilities receive funding from the Public Health Service ("PHS") or its agency the National Institutes of Health ("NIH"). These facilities must comply with the PHS Policy on Humane Care and Use of Laboratory Animals and the NIH Guide for the Care and Use of Laboratory Animals, both of which incorporate the Three R's. The policies require IACUCs

---

71 9 CFR § 2.31(c)(1)-(2) (2005).
72 9 CFR § 2.31(c)(3) (2005).
73 Rowan E-mail (cited in note 28). Category C studies can include those that involve overnight food or water deprivation, as well as surgery under anesthesia that may include minimal post-surgical pain and distress.
75 Office of Laboratory and Animal Welfare/National Institutes of Health, Public Health Service Policy on Humane Care and Use of Laboratory Animals 7 (NIH 2002) ("PHS Policy") ("This Policy is applicable to all PHS-conducted or supported activities involving animals, whether the activities are performed at a PHS agency, an awardee institution, or any other institution and conducted in the United States.").
77 See PHS Policy at 15-16 (cited in note 75) (noting that institutions applying for funds from PHS must specify a "rationale for involving animals, and for the appropriateness of the species and numbers used" and "a description of procedures designed to assure that discomfort and injury to animals will be limited to that which is unavoidable in the conduct of scientifically valuable research, and that analgesic, anesthetic, and tranquilizing drugs will be used where indicated and appropriate to minimize discomfort and pain to animals"); NAS Guide at 10 (cited in note 76) (stating that protocols include consideration of "[a]vailability or appropriateness of the use of less-invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation," employing "[a]ppropriate sedation, analgesia, and anesthesia," and avoiding "[u]nnecessary
to have at least five members, one of whom cannot be affiliated with the research facility and one of whom has "primary concerns . . . in a nonscientific area (for example, ethicist, lawyer, member of the clergy)." They also require IACUCs to review research facility programs on animal welfare, inspect research facilities, and submit reports on both.

Federal agencies that oversee toxicity testing on consumer products have also begun to adopt the Three R's, albeit more slowly. Agencies including the Environmental Protection Agency ("EPA"), the Food and Drug Administration ("FDA"), the Consumer Product Safety Commission ("CPSC"), and the Occupational Safety and Health Administration ("OSHA") have traditionally relied on animals to test the toxicity of various substances. For example, the EPA requires animal testing for substances classified as "pesticides" under the Toxic Substances Control Act, and the CPSC requires animal testing to determine whether substances must be labeled as "highly toxic" under the Federal Hazardous Substances Act.

Some signs show that these agencies are becoming more receptive to the Three R's. Certain EPA regulations now explicitly allow for alternative tests that can reduce the number of animals used to determine toxicity, and the FDA does not require the

duplication of experiments"). The Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Education, which are a part of the PHS Policy and NIH Guide, also require adherence to the Three R's.

78 PHS Policy at 11 (cited in note 75).
79 Id at 12.
80 For an overview of federal toxicity testing laws, consider Megan Erin Gallagher, Toxicity Testing Requirements, Methods and Proposed Alternatives, 26 Environ Envir L & Pol J 253 (2003).
81 15 USC § 2603(b)(2)(A) (1996). See also 40 CFR § 799.9110 (2005) (oral toxicity test requiring the use of animals); 40 CFR § 799.9120 (dermal toxicity test requiring the use of animals); 40 CFR § 799.9130 (inhalation toxicity test requiring the use of animals).
83 See, for example, 40 CFR § 799.9110(d)(1) (2005) ("EPA will accept the following procedures to reduce the number of animals used to evaluate acute effects of chemical exposure while preserving its ability to make reasoned judgments about safety."). A relevant proposal is EPA's recent High Production Volume ("HPV") Challenge Program. This program was a response to an EPA study finding that very little toxicity information was available on most chemicals manufactured in the U.S. in amounts in excess of one million pounds a year ("HPV chemicals"). The program encouraged manufacturers to perform testing on all HPV chemicals they produced, with a goal of having all HPV chemicals tested by 2005. Those HPV chemicals that were not tested under the program would be subject to the testing requirements promulgated under § 4 of the Toxic Substances Control Act. EPA, Report on the Chemical Right-to-Know Workshop (Dec 16-17, 1998), available at <http://www.epa.gov/chemrtk/worksumf.htm> (last visited Feb 24, 2006). Initially, the EPA developed the program without concerns for animal welfare issues, but when the program was publicly announced in 1998, animal activists and scientists voiced concerns to the EPA, Congress, and other decisionmakers. In response, the Center for Alternatives
use of animals for cosmetics testing. Aiding this transition to
the Three R's, in 1997 the NIH Director established the Inter-
agency Coordinating Committee on the Validation of Alternative
Methods ("ICCVAM"), which Congress made permanent by the
ICCVAM Authorization Act of 2000. ICCVAM is comprised of
the heads of 15 federal regulatory and research agencies, includ-
ing the heads of the EPA, FDA, CPSC, and OSHA. Among
ICCVAM's purposes are to "reduce, refine, or replace the use of
animals in testing, where feasible." ICCVAM reviews and
evaluates alternative test methods by convening peer-review
panels composed of scientific experts, who then deliberate over
an alternative in public sessions. Public comments are also al-
lowed, after which ICCVAM makes recommendations to federal
agencies regarding the suitability of the alternative. Import-
tantly, however, the agencies retain complete discretion over
whether to accept the alternative recommended by ICCVAM,
although they must provide written justification for a decision to
reject an ICCVAM-approved alternative.

III. MAJOR DEFICIENCIES OF THE THREE R'S

Despite their mutual acceptance by adversaries in the fight
over animal experimentation, and despite their status as federal
law and research policy, the Three R's suffer from at least three

---

84 FDA Release, Animal Testing (June 9, 2005), available at
http://www.cfsan.fda.gov/~dms/cos-205.html (last visited Jan 12, 2006) (stating that
the Food, Drug, and Cosmetic Act does not require the use of animals to test cosmetics for
safety, although the FDA encourages "appropriate and effective" testing of products).
86 Operational support for ICCVAM is provided by the National Toxicology Program
Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM).
For more information about ICCVAM and NICEATM, see -http://iccvam.niehs.nih.gov/>
(last visited Jan 12, 2006).
87 42 USC § 2851-3(b)(5) (2000). As Rudacille notes, "ICCVAM addresses testing and
not basic research." Rudacille, The Scalpel and the Butterfly at 303 (cited in note 5) (em-
phasis added).
about/overview.htm> (last visited Jan 12, 2006).
89 See id.
90 42 USC § 2851-5(b) (2000) ("Nothing in this Act shall prevent a Federal agency
from retaining final authority for incorporating the test methods recommended by
ICCVAM in the manner determined to be appropriate by such Federal agency or regula-
tory body.").
main deficiencies that render them largely ineffective in regulating laboratory animal use.

A. The Three R’s Do Not Allow for Challenges to the Purpose of Experiments

The first main deficiency of the Three R’s is that, despite their goal of preventing the unnecessary suffering of laboratory animals, they were not designed to allow for challenges to the purpose of experiments that will use animals. Instead of challenging experimental purpose, the Three R’s are designed to accept that purpose, whatever it may be, and simply ask whether the use of animals can be rendered less frequent through a reduction, less painful through a refinement, or replaceable by a non-animal alternative. But suppose that for a given experiment many animals are needed, pain relief cannot be provided, and a non-animal alternative cannot be used. Further suppose that the necessity or usefulness of the experiment is questionable.91 If the Three R’s are meant to prevent unnecessary animal suffering, should they not allow an IACUC to prevent this experiment from taking place? The Three R’s stop short of making such an allowance.

A concrete example will help to illustrate this point. Assume that researchers wish to determine the effect of pain on a given human behavior—for example, whether human burn victims lose their appetites. To test this, they design an experiment using pigs as models for humans. They tie down and blowtorch the pigs, who are not given pain relief, over a large portion of their bodies. They then leave the wounds untreated for several days to observe the pigs’ eating habits. These facts are based on actual experiments said to have been performed and paid for with federal research funds.92

For this and other experiments, the Three R’s can be thought of in three ways: in their original form as a non-legal, guiding concept for researchers; as a legal mandate of the AWA; and as a regulatory measure implemented by federal agencies in

91 For more discussion on the idea of “necessity” in this context, see Office of Technology Assessment Publication, Alternatives to Animal Use in Research, Testing, and Education 80-81 (GPO 1986).
92 See Francione, Animals, Property, and the Law at 172 (cited in note 9) (discussing these experiments). Even if these experiments occurred before the 1985 amendments to the AWA, the amendments did nothing to change the status quo regarding purpose challenges, and therefore the same experiments could be performed today. See notes 96-99 and accompanying text.
conjunction with ICCVAM. As a nonlegal mechanism as developed by Russell and Burch, the Three R's provide no guiding principles for the burn experiment or other pain experiments. The researchers have decided to test the effect of pain, so refinements in the form of pain relief are not possible without hindering the success of the experiment. A non-animal alternative cannot replace the complex physiological and sensory workings of a sentient animal, so replacements are not possible either. And while some reductions may be possible if the experiment would use an excess number of pigs, researchers must necessarily burn some pigs. The Three R's would need an additional mechanism—one that allowed for challenges to experimental purpose to prevent experiments such as these on the grounds that they are trivial, unnecessary, or of insufficient utility to justify animal suffering. The literature contains numerous examples of bizarre and shocking experiments that the Three R's were not designed to reach.93

Implemented as a legal mechanism through the AWA, the Three R's are also unable to prevent the burn experiment or other pain experiments—an observation previously made by Gary Francione.94 On the one hand, the AWA requires researchers who seek to perform painful experiments on animals to confirm to IACUCs that they will provide pain relief and have considered non-animal alternatives.95 On the other hand, the AWA explicitly deprives IACUCs of the ability to challenge experimental purpose.96 Specifically, the AWA states that IACUCs cannot challenge the “design, performance, or conduct of actual research

---

93 See, for example, Animal Welfare Institute, Beyond the Laboratory Door 121-250 (1985) (reviewing the experiments detailed in scientific literature from 1978-1984 that “by design inflict great suffering of many kinds on a variety of animal species”); Peter Singer, Animal Liberation 80-81 (NY Rev 3d ed 2002) (describing the experiments that Thomas Gennarelli conducted at the University of Pennsylvania on monkeys, who were seen during these experiments “writhing, apparently coming out of anesthesia, as surgeons were operating on their exposed brains”). While Singer describes experiments that predominantly occurred before the 1985 amendments to the AWA, the point remains that without allowing purpose challenges, the Three R’s could not prevent such experiments if a researcher chose to perform them today. See notes 96-99 and accompanying text.

94 Francione, Animals, Property, and the Law at 172 (cited in note 9) (“[W]hether to use animals at all, and what limits should be placed on the types of experiments that may be done . . . are, for all intents and purposes, not addressed by the law.”); id at 200 (“[T]he AWA plainly states that it is legitimate—and perhaps morally obligatory—to use animals in experiments. The AWA also states that there are no limits placed on the permissible use of animals on the basis of experiment content or conduct.”).

95 See notes 63-74 and accompanying text.

96 Many animal advocates view IACUCs as important bodies despite this omission. See Francione, Animals, Property, and the Law at 203 (cited in note 9) (“[I]t is clear that most legal reformers have placed a great deal of emphasis on the IACUC.”).
or experimentation," and the Secretary of Agriculture is prohibited from "promulgat[ing] rules, regulations, or orders with regard to the performance of actual research or experimentation by a research facility as determined by such research facility." Consequently, IACUCs cannot ask whether an experiment is trivial, unnecessary, or likely to cause animal suffering that outweighs human benefits. Asking these questions might prevent many biomedical experiments, especially in the category of basic research.

Implemented as a regulatory mechanism, the Three R's are even less effective in preventing unnecessary animal suffering.

---

97 9 CFR § 2.31(a) (2005) (The Chief Executive Officer of the research facility shall appoint an Institutional Animal Care and Use Committee (IACUC), qualified through the experience or expertise of its members to assess the research facility's animal program, facilities, and procedures. Except as specifically authorized by law or these regulations, nothing in this part shall be deemed to permit the Committee or IACUC to prescribe methods or set standards for the design, performance, or conduct of actual research or experimentation by a research facility.) (emphasis added).


99 See Singer, Animal Liberation at 79 (cited in note 93) (Amendments to the [AWA] in 1985...failed to deal with the real issue of control over what happens during an experiment. The amendments set up institutional animal committees, but in keeping with the unchanged exemption from interference given to the experiments themselves, these committees have no authority over what goes on in the experiments.).

Rowan claims that some IACUC members do believe they have the power to challenge experimental purpose, although this seems to be in clear contradiction with the language of the AWA. Rowan E-mail (cited in note 28).

100 Basic research (also called fundamental or pure research) refers to research for purposes of advancing knowledge for its own sake, which has no ready aim or application. Applied research, on the other hand, refers to research undertaken to solve a specific, practical problem. See Lawrence Berkeley National Laboratory, Basic v. Applied Research, available at <http://www.lbl.gov/Education/ELSI/research-main.html> (last visited Jan 5, 2006). Most scientific organizations consider basic research to be at least as important, if not more important, than applied research. See, for example, America's Basic Research: Prosperity Through Discovery, available at <http://www.saaas.org/spp/yearbook/chap18.htm> (last visited Jan 5, 2005) (attributing the remarkable scientific progress which defined the 20th century to basic research); Jim Morris, Basic Scientific Research is Our Future, available at <http://www.scitechantiques.com/basic1> (last visited Apr 13, 2006) ("[Basic research is] one of the most reliable tools for building civilized civilizations. It gives us the why and how of things."); National Institute of General Medical Sciences, Curiosity Creates Cures: The Value and Impact of Basic Research, available at <http://publications.nigms.nih.gov/curiosity> (last visited Apr 13, 2006) (stating that basic research studies "may not have an immediate impact on our health, yet that such 'untargeted' research often leads to new medicines, technologies, and research tools").

It could be argued that pre-determining necessity in basic research is impossible, yet because even one experiment may turn out to be beneficial for humans, any amount of animal suffering for the sake of basic research should be allowed. C. R. Gallistel, The Case for Unrestricted Research Using Animals, Am Psychologist 36(4), 357-62 (1981). If this argument is accepted, however, it is clear that despite our near-universal proclamations, we do not in fact accept the principle against unnecessary suffering in the context of experimentation, as any amount of animal suffering could be justified for little or no human benefit.
This is due to the even weaker claims of "necessity" present in most toxicity testing. While popular opinion is generally more accepting of using animals in biomedical experiments aimed at curing serious human diseases, it is far less accepting of using animals to test the toxicity of consumer goods such as cosmetics and laundry detergents. Yet the ICCVAM and agency regulations, which together comprise the regulatory implementation of the Three R's, provide no mechanism for challenging purpose in toxicity testing. No regulatory body is allowed to ask whether consumer product tests are trivial, unnecessary, or likely to cause animal suffering that outweighs human benefits. If purpose could be challenged in this context, many toxicity tests might be prevented, as they cause significant animal suffering yet result in trivial human benefits—for example, a "new and improved" household cleaner. These tests are unnecessary both because the products being tested are unnecessary for humans to have, and because many such products are "new and improved" versions of existing products whose toxic properties have already been studied and are understood by researchers.

B. Loopholes in the AWA Allow Researchers to Avoid Application of the Three R's in Practice

The second deficiency in the Three R's is that their incorporation in the AWA created significant loopholes that allow researchers to avoid making changes in practice. Most significantly, the AWA only applies to six species of animals used in experiments: dogs, cats, nonhuman primates, rabbits, hamsters,

---

101 See Harold Herzog, et al, Social Attitudes and Animals, in Deborah J. Salem and Andrew N. Rowan, eds, The State of Animals 61 (Humane Society 2001) (52% of those surveyed approved of using monkeys in painful experiments to ensure that a new drug to cure leukemia in children is safe; only 6% approved of using monkeys in painful experiments to test whether an ingredient in cosmetics would be harmful to people). See also Market & Opinion Research International, Use of Animals in Medical Research: Research Study Conducted for Coalition for Medical Progress 26 (2005), available at <http://www.medicalprogress.org/uploads/docs/CMP_MORI_2005_Report.pdf> (last visited Feb 24, 2006) (76% of survey responders support animal experimentation "so long as there is no unnecessary suffering.").

102 According to Tom Regan, some of the consumer products that researchers test on animals include:

- Insecticides, pesticides, antifreeze chemicals, brake fluids, bleaches, Christmas tree sprays, church candles, silver cleaners, over cleaners, deodorants [sic], skin fresheners, baby preparations, bubble baths, freckle creams, depilatories, eye makeup, crayons, fire extinguishers, inks, suntan oils, nail polish, mascara, hair sprays and rinses, zipper lubricants, paints, thermometers and children's novelties.

and guinea pigs.\textsuperscript{103} It does not, however, apply to rats, mice, birds, fish, or farm animals. Rats and mice are believed to account for up to 90% of the animals used in experiments\textsuperscript{104}, with birds and fish added in, the figure may be as high as 97%\textsuperscript{105}.

The exemption for these animals has long been implicit in the AWA, but Congress did not codify it until 2002—suspiciously soon after the U.S. Department of Agriculture, which administers the AWA, finally agreed to include these animals within the AWA’s scope.\textsuperscript{106} Federal research policies do cover rats, mice, birds, fish, and farm animals, in addition to the animals covered by the AWA,\textsuperscript{107} but they do not cover all research facilities or have the status of federal law.\textsuperscript{108}

Even for those animals covered by the AWA, evidence suggests that researchers are taking advantage of other loopholes to avoid applying the Three R’s. First, the AWA urges reductions,\textsuperscript{109} and Russell and Burch advocated better design and statistical analysis of experiments as early as 1959.\textsuperscript{110} Yet one commentator observed in 1994 that “[r]elatively few attempts have been made to assess the quality of design of animal experiments,” and that poor statistical methods are common and are “not confined to toxicology.”\textsuperscript{111} Possible reasons for the lack of reductions include confidentiality concerns among competing researchers\textsuperscript{112} and lack of ready access to information about prior experiments.\textsuperscript{113}

\textsuperscript{103} 7 USC § 2132(g) (2000).
\textsuperscript{104} Orlans FB, \textit{Data on Animal Experimentation in the United States: What They Do and Do Not Show}, 37(2) Perspective Biology and Med 217, 218 (1994) (noting that the AWA does not apply to mice, rats, and birds, which make up between 80–90% of all animals used in experiments); Francione, \textit{Introduction to Animal Rights} at 34 (cited in note 9) (“The Animal Welfare Act does not cover rats and mice . . . which, according to the federal government, account for approximately 90% of the animals used.”).
\textsuperscript{105} Rowan E-mail (cited in note 28).
\textsuperscript{106} See David Favre, \textit{Animals: Welfare, Interests, and Rights} 361 (L & Hist 2003). See also Francione, \textit{Animals, Property, and the Law} at 211-33 (cited in note 9) (critiquing USDA’s enforcement of the AWA).
\textsuperscript{107} See PHS Policy at 8 (cited in note 75) (defining an “animal” as “[a]ny live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes”).
\textsuperscript{108} The PHS Policy is only applicable to research being conducted at a PHS facility or otherwise funded by PHS, and violations of the PHS Policy at most result in the suspension or revocation of NIH funding. Id at 7. In contrast, the AWA applies to all research, testing, or teaching involving animals covered by it regardless of the source of funding, and violations can result in criminal and civil penalties for both the lead researcher and the research facility. 7 USC § 2149 (2000).
\textsuperscript{109} See notes 67-68 and accompanying text.
\textsuperscript{110} See notes 22-23 and accompanying text.
\textsuperscript{111} Festing, \textit{Reduction of Animal Use} at 213 (cited in note 23).
\textsuperscript{112} See Paul Rincon, \textit{Animal Efforts 'Need Bigger Push'} (May 25, 2005), available at <http://news.bbc.co.uk/1/hi/sci/tech/4575371.stm> (last visited Jan 12, 2006) (discussing rivalry between scientific teams and commercial confidentiality as slowing information
Second, the AWA purports to require refinements in the form of pain relief, but it creates an exception for cases of "scientific necessity." Research facility reports submitted pursuant to the AWA suggest that researchers are frequently invoking this exception. For example, in the most recent figures from 2004, pain relief was withheld from 86,748 dogs, cats, nonhuman primates, rabbits, hamsters, and guinea pigs used in painful experiments. Animal advocates have argued that the limited AWA figures are actually low because researchers underestimate the number of experiments that cause pain or distress, choosing to categorize only the most painful experiments as such. Critics have also claimed that scientists lack a good understanding of what causes pain and distress in animals, and instead simply apply their knowledge of what causes pain and distress in humans, which may be underinclusive. Even if the AWA reports are accurate, 86,748 cases of "scientific necessity" in 2004 alone, for what constitutes less than 10% of laboratory animals, make this appear to be a significant exception that is allowing many researchers to avoid making refinements in practice.

Finally, with regard to replacements, recall that the AWA requires researchers to confirm to IACUCs that they have considered non-animal alternatives. Beyond this, however, IA-
CUCs cannot interfere with the design or performance of an experiment, so they appear to be bound to accept the researcher’s assertions that suitable non-animal alternatives do not exist. Evidence of what occurs inside research laboratories is notoriously difficult to get. However, what evidence there is suggests that replacements of animals with non-animal alternatives are still uncommon. Consider toxicity testing, a field of research for which non-animal alternatives have been developed. Some of these alternatives have been validated by ICCVAM, while others are now in the validation process. For instance, Corrositex and other in vitro testing methods have been developed to assess the potential of chemicals to cause skin corrosion, and four of these methods have been at least partially validated by ICCVAM. Corrositex was validated in 1999, and has been accepted by nine federal regulatory agencies, including CPSC, EPA, OSHA, and FDA.

Corrositex replaces the “Draize” skin irritancy test that is performed on rabbits and guinea pigs. In the Draize tests, researchers apply chemicals to the backs of rabbits or guinea pigs and wrap the area for the first day to keep the chemicals in close contact with the skin. These tests are highly painful and can last for up to six hours a day, with tests on a single animal lasting up to three weeks. Corrositex has many advantages over the Draize test: it is easier and takes less time to perform.

1834.9(a) (2006) might be seen as an exception because it purports to require the use of alternatives that have been validated, although there appear to be large loopholes in this legislation. For a discussion of the legislation generally, see Stacy E. Gillespie, A Cover-Girl Face Does Not Have to Begin with Animal Cruelty: Chapter 476 Gives Legal Force to Alternative Testing Methods, 32 McGeorge L Rev 461 (2001).

See, for example, Francione, Introduction to Animal Rights at 34 (cited in note 9) (noting that the Congressional Office of Technology Assessment stated that “[e]stimates of the animals used in the United States [for research] each year range from 10 million to upwards of 100 million” but “concluded that ‘all these data are unreliable’ because ‘every estimate of animal use stands as a rough approximation’”).

In addition to Corrositex, the three other non-animal alternatives to the Draize skin irritancy tests that have been partially validated by ICCVAM are Murine Local Lymph Node Assay (“LLNA”), EpiSkin, and Epiderm. NIEHS, About ICCVAM: Overview (cited in note 88).

The “Draize” tests were named after their inventor, John Draize, a toxicologist who headed the United States Dermal and Ocular Toxicity Branch of the FDA and developed the tests in the early 1940s.

Francione, Introduction to Animal Rights at 45 (cited in note 9).

Id.

Draize skin irritancy tests can take up to two to four weeks to return the desired results, whereas Corrositex can provide a determination of corrosivity in approximately four hours. See Institute for In Vitro Sciences, Inc, Corrositex Continuous Time Monitor Assay, available at <http://www.iivs.org/methods/CORROSTX_symbol.pdf> (last visited Jan 7, 2006); E-mail from Martin Wolf, Chemist at Seventh Generation, to Nikia Fico.
less expensive to perform,\textsuperscript{125} yields generally equivalent results,\textsuperscript{126} and eliminates animal use. Yet few of the large consumer products companies that perform corrosivity tests use or rely on Corrositex or other non-animal alternatives, while many still use the Draize tests.\textsuperscript{127}

In addition, several non-animal alternatives to eye irritancy testing have shown great promise for replacing the Draize eye testing.

\textsuperscript{125} MB Research Laboratories, which performs product safety testing for manufacturers, charges $950 for one kit of Corrositex, which provides testing supplies to replace ten Draize skin irritancy tests. MB Research Labs, \textit{2006 Capabilities and Prices}, available at <http://www.mbresearch.com/capabilities.pdf> (last visited Apr 30, 2006). By comparison, it charges $1,750 to perform the same amount of testing on albino rabbits. Id. Further, a recent evaluation done by InVitro International, a large provider of non-animal testing methods, found that one of their customers saved up to $50,000 annually in shipping costs for a single compound by using Corrositex instead of animals. InVitro International, \textit{Corrositex}, available at <http://www.invitrointl.com/products/corrosit.htm> (last visited Feb 24, 2006).

\textsuperscript{126} Corrositex has an accuracy rate of 79\% when compared to the rabbit skin corrosivity tests. ICCVAM, \textit{Corrositex: An In Vitro Test Method for Assessing Dermal Corrosivity Potential of Chemicals} 19 (NIH 1999). While this figure may appear to make Corrositex a less desirable test than rabbit tests, this is not necessarily the case. Corrositex, because it uses human skin cells, may produce better results than the rabbit tests in some cases, and this could explain why there is not better or perfect correlation between the two. See, for example, \textit{Siharath v Sanders Pharmaceuticals}, 131 F Supp 2d 1347, 1366 (N D Ga 2001) ("Extrapolations from animal studies are not considered reliable in the absence of a credible scientific explanation of why such extrapolation is warranted.").


On the other hand, companies such as Seventh Generation, Tom's of Maine, and Ecover exclusively use alternatives to the Draize tests. Wolf E-mail (cited in note 124); Murphy E-mail (cited in note 124); E-mail from Caroline Broeckx, Ecover Belgium, to Nikia Fico (Dec 23, 2005) (on file with author) (stating that Ecover never uses Draize testing but does use the non-animal alternatives).
irritancy test and are now in the ICCVAM validation process. These include EpiOcular, an in vitro model produced by the company MatTek. EpiOcular replaces the Draize eye irritancy test that is performed on rabbits, often albinos because of their large, clear eyes. In the Draize tests, rabbits are physically restrained while and after chemicals are applied to their eyes. Rabbits have fewer tear ducts than do humans, and they do not have blink reflexes, so they cannot flush out the chemicals. These tests are highly painful, and rabbits have been known to break their backs struggling to escape their restraints. Like Corrositex, EpiOcular has many advantages over the Draize eye test: it is easier and takes less time to perform, yields generally equivalent results, and eliminates animal use. Unlike Corrositex, however, EpiOcular is currently more expensive to perform than the Draize test. Despite its net advantages, few of the large

---

128 Alan M. Goldberg and Thomas Hartung, Protecting More Than Animals, Scientific Am 84, 91 (Jan 2006):

The replacement effort faced a major setback in the early 1990s, when six large validation trials for alternatives to the Draize eye test failed. The outcome was puzzling, since some of the alternatives were being used in the cosmetics industry without apparent problems. Having reviewed other data, we now understand why the alternatives failed: their results were being compared with those of the Draize test itself, which, it turns out, yields many false positives. ICCVAM ... [is] now reviewing existing information on the Draize test and its alternatives. The study will form the basis of a statement of validity or, if necessary, another validation trial of Draize alternatives, and this time we are reasonably confident of success.


130 See Francione, Introduction to Animal Rights at 45 (cited in note 9) (“Albino rabbits are normally used for these tests because their eyes are large, clear, and easily observable, and because the tearing of their eyes, appreciably less than that of other animals’ eyes, does not wash away or dilute the substance to be tested.”).

131 EpiOcular results can usually be obtained in three minutes to an hour, as compared to three to eighteen days using the traditional Draize eye irritancy test. See MatTek Corp, Ocular Irritation Protocol: Neat Method (MTT ET-50) for Use with EpiOcular™ Tissue Model (OCL-200) 2 (2005) (on file with MatTek) (MatTek unpublished protocol method); Wolf E-mail (cited in note 124) (noting relative ease of performing alternative tests); Murphy E-mail (cited in note 124) (same).

132 EpiOcular has up to a 93% correlation rate with the Draize eye irritancy test and can even be used to differentiate between materials which are too mild for the Draize test to distinguish. MB Research Labs, The EpiOcular Prediction Model: In Vivo Versus In Vitro Draize Scores for Consumer Products, available at <http://www.mbresearch.com/epi-pre.htm> (last visited Apr 30, 2006) (finding that when a single outlier is excluded from the calculation, the correlation rate between EpiOcular and the Draize eye irritancy test raises from 85% to 93%).

133 For a full assay done with EpiOcular, MB charges $2,100, whereas the equivalent
consumer products companies that perform corrosivity tests use or rely on EpiOcular or the other non-animal alternatives, while many still use the Draize tests.\textsuperscript{134}

It is unclear why large consumer products companies still use the Draize animal tests to measure corrosivity. In researching this Article, many of these companies were contacted in an attempt to shed light on this, but none responded.\textsuperscript{135} The publicly available information from company websites and other sources are sparse on details of animal testing, for obvious reasons.\textsuperscript{136}

Perhaps these companies still use the Draize test only to fill in the holes left by the imperfections of non-animal alternatives,\textsuperscript{137} or because in some instances animal tests are still required by law.\textsuperscript{138} More likely reasons, however, are comfort with the traditional animal model, the vested interests of institutional players in animal research,\textsuperscript{139} fear of deviating from the status

\textsuperscript{134} See sources cited in note 127. But see MatTek Corporation, \textit{In Vitro Alternative to Draize Test}, available at <http://www.mattek.com/pages/products/epiocular/draize_alternative> (last visited Jan 5, 2006) (claiming that Colgate-Palmolive, Procter & Gamble, and Unilever all use their EpiOcular alternative “to replace some/all of their traditional Draize (rabbit) ocular irritation testing”).

\textsuperscript{135} E-mail from Nikia Fico to Abbott Labs, contacted through their website (Dec 23, 2005) (on file with author); E-mail from Nikia Fico to Bristol Myers Squibb, contacted through their website (Dec 23, 2005) (on file with author); E-mail from Nikia Fico to Colgate-Palmolive, Co, contacted through their website (Dec 23, 2005) (on file with author); E-mail from Nikia Fico to Gillette, contacted through their website (Dec 23, 2005) (on file with author); E-mail from Nikia Fico to Johnson & Johnson, contacted through their website (Dec 23, 2005) (on file with author); E-mail from Nikia Fico to Pfizer, contacted through their website (Dec 23, 2005) (on file with author); E-mail from Nikia Fico to Proctor & Gamble, contacted through their website (Dec 23, 2005) (on file with author); E-mail from Nikia Fico to The Clorox, Co, contacted through their website (Dec 23, 2005) (on file with author); E-mail from Nikia Fico to Unilever, contacted through their website (Dec 23, 2005) (on file with author).

\textsuperscript{136} Johnson & Johnson provides more information than most. See <http://www.jnj.com/community/policies/animal_testing/statement.htm> (last visited Jan 28, 2006) (“We have modified the standard test method for eye irritation, the Draize eye test, to reduce the number of animals per test. We have modified the standard Draize skin irritation test to require fewer animals, and we rely heavily on studies in human volunteers.”).

\textsuperscript{137} Carmen Fleetwood, \textit{In Vitro Testing is the New Guinea Pig}, Wall St J B2B (Sept 29, 2004) (“One limitation of MatTek’s tests is that they don’t demonstrate how a drug or treatment will interact with other organs, according to Mitch Klausner, vice president of scientific affairs at MatTek. This limitation is on of the reasons the company’s tissue models are unlikely to fully replace animal testing.”).

\textsuperscript{138} For example, the law still requires animal tests for substances classified as a “pesticide.” 40 CFR 158.34 (2005). But the question remains why a cleaning product from one company, for example, receives this classification when more progressive companies are developing products that accomplish the same purpose and avoid it.

\textsuperscript{139} Balls, \textit{Replacement of Animal Procedures} at 200 (cited in note 32) (“The mainte-
quo and the legal liability that may accompany that decision, and irrational insistence on high-fidelity models. For academic researchers, the pressure to publish may be a factor, as far more papers can be published in a given time period if animal experiments are used. It is also the case that viable alternatives do not yet exist for many experiments and tests involving animals. Here, the research community and the federal government can be criticized for lax funding for alternatives compared to the funding they devote to animal research.

140 Id at 201 ("Validation is difficult and the hurdles placed in the path of replacement alternatives must be high . . . if mistakes are to be avoided."). On the issue of legal liability, see, for example, Sibarath, 131 F Supp 2d at 1367 (noting that a "few courts have been more amendable to the use of animal studies in proving causation, at least pre-Daubert" but rejecting the use of animal studies for that purpose in that case).

141 Balls, Replacement of Animal Procedures at 203 (cited in note 32) (noting in 1994 that "what Russell and Burch said about the emotional weight acquired by the high fidelity fallacy when the demands of public health and safety are involved . . . remains as true today as it did in the 1950s!"). See also notes 38-41 and accompanying text.

142 Greek and Greek, Sacred Cows and Golden Geese at 79 (cited in note 32): Not only [are they] easier, animal experiments are also much quicker than human studies. A rat's generation time is weeks, not decades. By the time a clinician publishes one good paper, an animal experimenter can publish at least five. The easiest way to publish is to take a concept already published and change something, the type of animal used, the dose of the drug, the method of assessing the results, or some other variable. This way, the concept has already been milled and all the researcher has to do is follow the template with new grist.

For a discussion of the resistance to the Three R's among the academic research community, see note 58 and accompanying text.

143 For instance, the Wall Street Journal reports that Proctor & Gamble devotes only one percent of its annual research budget to alternatives. See Fleetwood, In Vitro Testing is the New Guinea Pig, Wall St J at B2B (cited in note 137) (noting, seemingly with favor, that Proctor & Gamble devotes $10-$13 million of its annual $1 billion research budget to the development of alternatives). Government funding in the U.S. is also woefully deficient. See Goldberg and Hartung, Protecting More Than Animals at 90 (cited in note 128). Goldberg an Hartung state:

Finding funds for research specifically directed at alternatives has been difficult, at least in the U.S. The National Toxicology Program, which coordinates all toxicological testing programs within the federal government, together with the National Institutes of Environmental Health Services, provides the bulk of government funding for alternatives. Although the U.S. government's agencies are interested in humane science, they have spent less than $10 million over the past decade on validating alternatives for regulatory use. Id.

Government funding is only moderately better in Britain, where there is significantly more opposition to the use of animals in experiments than in the U.S. For example, although a negative report on laboratory animal use and treatment prompted the British government to award three million pounds to the National Centre for the Replacement, Refinement and Reduction of Animals in Research for the years 2006-2008, even moderate animal welfare organizations described this funding as a "drop in the ocean." See
C. The Three R’s Have No Application to New and Emerging Technologies

The third major deficiency of the Three R’s is that they were not designed with new and emerging technologies in mind. The Three R’s attempt to reduce, refine, and replace existing and archaic uses of animals that are no longer needed given a non-animal alternative. They were not designed to apply to “cutting-edge” technologies that will be first tried out on animals.

This design deficiency in the Three R’s manifests itself through the way in which potential replacements are evaluated. Non-animal alternatives are typically evaluated by comparing data produced by using the alternative with data produced by traditional animal tests.\(^{144}\) For instance, the ICCVAM has to date validated only sixteen alternatives and partially validated only four non-animal alternatives, including Corrositex.\(^{145}\) The applications for each of these alternatives compared data produced by the alternative with data produced by traditional animal tests, with the alternatives yielding generally equivalent results.\(^{146}\)

This method of evaluating non-animal alternatives is problematic on multiple levels, all of which suggest that the accep-

---

\(^{144}\) See 42 USC § 2851-4(b) (2000) (stating that alternatives to be promoted and encouraged “if such test methods are found to be effective for generating data, in an amount and of a scientific value that is at least equivalent to the data generated from existing tests”); Andrew Rowan, *The Alternatives Concept*, available at <http://www.nal.usda.gov/awic/alternatives/rowan.htm> (last visited Jan 12, 2006) (“[A]ny valid alternative system must provide data which leads to the same conclusion with at least the same degree of confidence as that obtained from the system being replaced.”). The exception is where a body of data from human experiments is available for comparison purposes, but this is uncommon.

\(^{145}\) See *About ICCVAM: Overview* (cited in note 88) (discussing alternatives to certain toxicity tests); E-mail from Brad Blackard to Nikia Fico (Jan 12, 2006) (on file with author).

\(^{146}\) The Murine Local Lymph Node Assay (“LLNA”), an alternative to guinea pig assays to determine the potential of chemicals to cause allergic reactions, performed equivalently with the traditional animal test for identification of strong to moderate chemical sensitizing agents, correlating with the guinea pig assays 88% of the time. ICCVAM, *The Murine Local Lymph Node Assay: A Test Method for Assessing the Allergic Contact Dermatitis Potential of Chemicals/Compounds* 13 (NIH 1999). Corrositex, discussed earlier, had an accuracy rate of 79% when compared to the rabbit skin corrosivity tests. ICCVAM, *Corrositex: An In Vitro Test Method for Assessing Dermal Corrosivity Potential of Chemicals* 19 (NIH June 1999). EpiSkin and EpiDerm, *in vitro* human skin cell culture modeling systems for dermal corrosivity testing, both had a 83% correlation rate to the Draize skin irritancy test. ICCVAM, *Recommended Performance Standards for In Vitro Test Methods for Skin Corrosion* 27 (NIH May 2004). As discussed in note 126, *in vitro* tests using human cells may produce better results than animal tests in some cases by removing the extrapolation difficulties present in the latter. This could help to explain why there is not better or perfect correlation with animal tests.
tance of an alternative will be the exception rather than the rule. First, it is far from certain that the benchmark for comparison, the animal data, is reliable due to extrapolation problems. Many scientists, animal advocates, and even courts have lodged this objection.\textsuperscript{4} Second, while toxicity testing often lends itself to this evaluation process, biomedical research does not. As Rowan explains:

Diagnosis and toxicity testing are somewhat different activities from basic and applied research. In both diagnosis and toxicity testing, the techniques used are not subject to much change. . . . However, in basic and applied research, the investigator is likely to vary the technical approach considerably from one project to the next. In addition, the investigator may need to use more than one technique to resolve a particular question to the satisfaction of his or her peers. As a result, it is usually much easier for those who are promoting the idea of alternatives to focus on such areas as diagnosis and toxicity testing.\textsuperscript{48}

Third, animal data will not be available for comparison purposes in new and emerging fields of research. As one commentator states, “where a new method is developed to identify new effects not previously tested or well defined, there is no paradigm

\textsuperscript{147} See, for example, Kathy Archibald, Animal Testing: Science or Fiction, available at <http://www.theecologist.co.uk/current_issue/ animal_testing.htm> (last visited Jan 5, 2006) (stating that the Handbook of Laboratory Animal Science admits that “uncritical reliance on the results of animal tests can be dangerously misleading and has cost the health and lives of tens of thousands of humans”); Marlene Cimons, Cancer Drugs Face Long Road From Mice to Men, LA Times A1 (May 6, 1998) (The article quotes Dr Richard Klausner, former director of the U.S. National Cancer Institute (“NCI”): “The history of cancer research has been a history of curing cancer in the mouse. We have cured mice of cancer for decades, and it simply didn’t work in humans.”); Sabin, Remarks, Statement before the subcommittee (cited in note 32) (“[The polio vaccine was long delayed by the erroneous conception of the nature of the human disease based on misleading experimental models of [it] in monkeys.”); Regan, The Case for Animal Rights at 371 (cited in note 102) (“Animal toxicity tests of products can be, and have been, challenged on the basis of their limited scientific validity. The problem of extrapolating test results from animals to human is notorious.”) (citation omitted); Greek and Greek, Sacred Cows and Golden Geese at 58-76 (cited in note 32) (questioning validity of animal-modeled drugs); Siharath, 131 F Supp 2d at 1366-67:

First, extrapolating from animals to humans is difficult because “differences in absorption, metabolism, and other factors may result in interspecies variation in responses.” . . . Second, the “high doses customarily used in animal studies requires consideration of the dose-response relationship and whether a threshold no-effect does exist.” (citations omitted).

\textsuperscript{148} Rowan, Of Mice, Models, & Men at 271 (cited in note 5).
with which to compare the effectiveness of the alternative.\footnote{149} Underlying these problems is the fact that the evaluation of non-animal alternatives typically requires a stable usage situation—in other words, a well-developed technique that many researchers employ.

A stable usage situation will not be present in new and emerging areas of research, including the use of animals for stem cell research, cloning, xenotransplantation, genetic modification, and bioterrorism defense.\footnote{150} These areas of research have the potential to greatly escalate the use of animals in experiments and the suffering that these animals are made to endure.\footnote{151}

Stem cell research promises to be a focal point of biomedical research in the twenty-first century. This research will involve surgically inserting human and animal stem cells into animals to monitor the effects.\footnote{152} What will happen to the recipients of the stem cells is unknown, which is why animals will be the first experimental subjects. As a 2005 opinion piece in the \textit{New York Times} stated, “[c]learly it is unethical to study the unknown actions of stem cells in human subjects. One obvious solution is to insert the cells into animals and watch how they develop.”\footnote{153}

\footnote{149} Gallagher, \textit{Toxicity Testing Requirements} at 264 (cited in note 80).

\footnote{150} While some of these technologies have been explored in the past (for example, xenotransplantation and the use of animals for bio-agents research), this Article refers to them as “new” technologies because they are becoming prominent or widely studied only now.

\footnote{151} See Rudacille, \textit{The Scalpel and the Butterfly} at 205 (cited in note 5). Rudacille explains:

[A] group of new technologies that necessarily involve extensive use of animals has the potential to reignite the [animal experimentation] debate. Xenotransplantation, in which organs and tissues from animal donors are transplanted into human hosts, and transgenic technology, which adds or deletes genes or transfers genetic material between species, are two types of research that have raised questions and concerns among some scientists and bioethicists. Even more controversy surrounds a related development, still in its infancy but already a source of considerable discussion: somatic cell nuclear transfer, popularly known as cloning. All of these use significant numbers of animals in research programs that deserve careful scrutiny. But most of the debate thus far, both within the scientific community and among bioethicists and policymakers, has focused on the possible implications of these evolving technologies for human beings, with relatively little discussion of their impact on animals or the linkages between the two.

\footnote{152} See, for example, Jamie Shreeve, \textit{The Other Stem-Cell Debate}, NY Times 6-42 (Apr 10, 2005) (describing invasive stem cell experiments being performed on monkeys on the Caribbean island of St. Kitts in the hopes of curing Parkinson's disease, and stating “[d]riving the surge in chimeric experimentation is the enormous but still untested promise of human stem cells”).

\footnote{153} Id.
While some animal advocates view stem cell research as an alternative to animal experimentation,\(^{154}\) that is an inaccurate characterization. Stem cell research will involve the use of hundreds, thousands, or potentially even millions of animals in experiments as it develops. However, the ethics of using animals in these experiments, and a discussion of whether the suffering of animals will outweigh the benefits to humans, has so far been a footnote to religious objections over destroying human embryos.\(^{155}\) Any objections that have been made have focused on the possibility of producing "chimeras"\(^{156}\) with human-like consciousness, which could be viewed as an anthropocentric concern.\(^{157}\) Indeed, only the chimera concern is reflected in the *Guidelines for Human Embryonic Stem Cell Research* recently published by the National Academy of Sciences.\(^{158}\)

Cloning is another new and rapidly emerging technology that will involve significant animal use. As Rudacille states, "all... possibilities [for cloning] must be extensively researched\(^{159}\)"

---

\(^{154}\) See Jean Swingle Greek and C. Ray Greek, *What Will We Do If We Don't Experiment on Animals? Medical Research for the Twenty-first Century* 95-101 (Trafford 2004) (describing stem cell research as a "new frontier in *in vitro* technology"); *Stem Cell Research: Moving Beyond Vivisection*, available at <http://www.peta.org/mc/factsheet_display.asp?ID=128> (last visited Apr 30, 2006) (supporting stem cell research, but recognizing that it "currently involves animals"). See also Kim Stallwood, *Editor's Agenda, Animals' Agenda* 5 (Sep/Oct 2001). Stallwood states:

> Curiously, throughout this very public discussion about science and ethics [over stem cell research], there was mostly silence from the animal rights community, at least with regard to media reports and congressional debate. No organization (that I heard of) interjected an opinion about whether stem-cell research might ultimately reduce the use of animals in similar research, or whether vivisection might even increase based on efforts to "prove" in animals what might first be observed in stem-cell tests.


\(^{156}\) See Shreeve, *The Other Stem-Cell Debate*, NY Times at 6-42 (cited in note 152) (The article explains that a chimera is "an organism assembled out of living parts taken from more than one biological species. The word comes from the monstrous creature of Greek mythology—part lion, part serpent and part goat.").

\(^{157}\) See, for example, Nicholas Wade, *Chimeras on the Horizon, But Don't Expect Centaurs*, NY Times F1 (May 3, 2005) (discussing potential moral issues raised by creation of chimeras).

and tested in animals before being applied to human populations. Cloning is directly related to stem cell research and to xenotransplantation, which is discussed below. Despite much time, effort, money, and animal use by researchers, cloning remains an extremely inefficient process with an average survival rate of a mere 0.5%-4.0%, even for previously cloned species.

Cloning also causes significant animal suffering, both for the cloned animals and their mother-carriers. In a 2001 New York Times article, a researcher described her cloning portfolio as a “gallery of horrors” that provided “a seldom-heard cautionary tale.” Cloned embryos often grow excessively large in the mother’s uterus and require a caesarean section operation. This mutation occurs so often that it has been dubbed “large offspring syndrome.” It has also been observed that “cloned embryos frequently carry profound deformities which result in markedly high rates of abortion. Cloned animals also appear to exhibit serious health problems, including early death and serious failures of their organs as they grow.” As with stem cell research, Ru-

159 Rudacille, The Scalpel and the Butterfly at 206 (cited in note 5).

160 See Guidelines for Human Embryonic Stem Cell Research at 2 (cited in note 158). The advantage of using [cloning] to derive hES [human embryonic stem cells] is that the nuclear genomes of the resulting hES cells would be identical with those of the donors of the somatic cells. One obvious benefit is that this would avoid the problem of rejection if cells generated from the hES cells were to be transplanted into the donor. Id.

161 See notes 167-74 and accompanying text.

162 See Lesley Paterson, et al, Application of Reproductive Biotechnology in Animals: Implications and Potential Applications of Reproductive Cloning 79 Animal Reproduction Sci 137, 142 (2003) (“Four years since [the cloning of Dolly] ... cloning remains an inefficient process with typically 0.5-5% of embryos becoming viable offspring.”); Gina Kolata, In Cloning, Failure Far Exceeds Success, NY Times F1 (Dec 11, 2001) (“A vast majority of [cloning] efforts fail, even in species that have at one time or another been cloned.”).


The animal is made to lactate early with hormone treatment and thereafter is kept lactating permanently in order to keep up production. The protein the animal has to produce is in addition to all the normal proteins in her milk, which in transgenic sheep like Tracy [a genetically-modified forerunner of Dolly] ... is more than twice as much protein as in ordinary sheep milk. So she is under permanent metabolic stress. Id.

This kind of overproduction is known to cause mastitis, lameness, general malaise and exhaustion in dairy cows.

dacille notes that "the issue of animal welfare has largely been ignored in public discussions about cloning."\(^{166}\)

A third new technology, xenotransplantation, seeks to harvest animal organs and transplant them into humans to replace defective human organs. Animals are used in this process because of a lack of human organ donors.\(^{167}\) Inter-animal transplants are often used to develop and refine the process.\(^{168}\) However, the experiments have not yet been successful because human immune systems consistently reject the animal organs, treating them as invading organisms.\(^{169}\) Efforts have shifted to producing cloned and transgenic animals, such as pigs altered with human DNA, in the hopes of tricking the human body into accepting the animal organ.\(^{170}\) The "end goal is to create a living production line of these partially humanized pig organs to use as spare parts for humans."\(^{171}\)

Xenotransplantation can cause significant animal suffering. For example, reports tell of one baboon "which had a piglet heart transplanted into its neck and for several days was observed holding the heart, which was swollen and seeping blood and pus as a result of infections from the wound. The animal also suffered body tremors, vomiting, [and] diarrhea."\(^{172}\) Notably,

\(^{166}\) Rudacille, *The Scalpel and the Butterfly* at 229 (cited in note 5).


\(^{169}\) See Rudacille, *The Scalpel and the Butterfly* at 228 (cited in note 5) ("By using transgenic technology, it might be possible to transfer rat genes into [a] mouse before xenotransplantation, to ‘trick’ the rat’s body into accepting the foreign tissue indefinitely."); Gary Francione, *Cloning Breeds Contempt and Adulation*, Chi Trib 23 (Mar 7, 1997) ("With complete knowledge of the genome sequence, companies . . . will acquire an even broader range of profitmaking applications, such as the ability to combine greater genetic knowledge with the cloning process to produce animals with ‘human’ organs. These ‘animals’ could then serve as ‘organ factories’ for xenografts and cross-species transplants."); Kolata, *In Cloning*, NY Times at F1 (cited in note 162) ("They also are cloning to genetically modify animals so that humans can use their organs."). See also Frontline, *Organ Farm: Synopsis*, available at <http://www.pbs.org/wgbh/pages/frontline/shows/organfarm/etc/synopsis.html> (last visited Jan 12, 2006) ("Because a human body would immediately reject a pig organ as foreign, these ‘transgenic’ pigs are genetically altered with human DNA in the hope that a human recipient’s body will be fooled into thinking the organ is human.").

\(^{170}\) Id.

\(^{171}\) Id.

xenotransplantation is unique among the new technologies because it *inherently* requires high-volume animal use for success.\(^{173}\) Therefore, the Three R's would have little or no application to xenotransplantation even if one day it were to present a stable usage situation.\(^{174}\)

Researchers are genetically modifying animals for purposes ranging from those discussed above to use of transgenic animals in artwork.\(^{175}\) Commentators observe that “it is vital that particular attention be paid to proposals to develop and use transgenic animals as models for human disease. [As] this rapidly-developing field affords great scientific opportunities, but also threatens to greatly increase laboratory animal suffering.”\(^{176}\) Also, they note that “techniques used in biomedical research for the production of transgenic animals have several implications for animal welfare in terms of the Three Rs of Russell & Burch . . . [a]ll of these actual and potential implications for animal welfare demand serious consideration within a broad ethical analysis of the technology.”\(^{177}\)

Finally, researchers are dramatically increasing the use of animals in bioterrorism experiments after the terrorist attacks of September 11, 2001 and subsequent anthrax attacks. HSUS reports that the number of grants for bioterrorism research in-
creased from 338 in 2003 to 661 in 2004. According to HSUS, these experiments will subject "tens of thousands" of animals to "Category A" pathogens including "anthrax, botulism, tularemia, smallpox, [and] plague." Many of these animals will be nonhuman primates. According to two scientists, "a[n] increased demand for nonhuman primates will undoubtedly characterize the new era in which bioterrorism has become a reality." Like the stem cell, cloning, xenotransplantation, and genetic modification experiments discussed in this section, bioterrorism research may produce few actual human benefits yet cause a large number of animals to experience tremendous suffering. But the Three R's cannot be used to police any of these experiments, which are newly emerging and thus do not present a stable usage situation.

CONCLUSION

Animal experimentation provides a good test of whether animal use can be meaningfully regulated. In the past twenty years, the Three R's have become the primary mechanism for that regulation, having been incorporated into both federal law and research policy. This Article has taken a systematic look at the Three R's and has concluded that they fail in several respects. These failures will become even more apparent as researchers escalate the use of animals for stem cell research, cloning, genetic modification, xenotransplantation, and bioterrorism defense.

In her recent book on the history of animal experimentation, Deborah Rudacille observed that "the war between antivivisection and animal research has given way to a tenuous truce—at least between the parties willing to accept the Three R's solution proposed by Russell and Burch." Animal advocates should break that truce and seek to abolish animal experimentation on moral grounds, rather than ceding the practice and attempting to


179 Id.


181 Rudacille, The Scalpel and the Butterfly at 269 (cited in note 5).
regulate it. Regulation is ineffective, even under favorable conditions—it provides false comfort that we can use animals for our purposes without them suffering in the process. An abolitionist approach, while more of an uphill battle, is the only way to prevent animals from suffering in our laboratories and beyond.