



Food for Thought...

Criticizing Animal Experimentation, at My Peril

Stephen F. Eisenman

Professor of Art History, Northwestern University, Evanston, IL, USA

Summary

Initiatives leading to even modest reduction in animal use at major U.S. universities are likely to continue to face strong opposition. At least, that's the conclusion the author draws from his efforts at Northwestern University. In fact, despite a growing body of evidence that animal-based research is flawed at best and misleading or un-scientific at worst its use is growing at Northwestern and elsewhere. Moreover, recent discoveries concerning animal consciousness and emotion have not led to notable improvements in the conditions in which AWA protected animals live at the Chicago vivarium. There, animals languish in featureless rooms or sterile cages without access to daylight and with little opportunity to express their natural behaviors and aptitudes. The writer's public exposure of these conditions led to a fierce backlash. Unless there is a significant change in laboratory and university culture, reform will only come when the marketplace and funding agencies demand better and more reliable, non-animal models for the testing of drug toxicity and effectiveness.

Keywords: animal testing, antibodies, IACUC, vivisection, Northwestern

1 Antibody follies

Though I'd for a long time wondered what went on in the basements of large biomedical research buildings on university campuses, my serious interest in animal experimentation began just two years ago after I was elected Faculty Senate President at Northwestern University (NU) in Evanston, Illinois. In late October 2013, I received an email from an acquaintance formerly employed by PETA (People for the Ethical Treatment of Animals), asking me to sign a letter requesting that my university sever its purchasing agreement with a company in violation of the Animal Welfare Act (AWA). I agreed to look into it. Nothing I have done in my 30-year academic career – and I have been in faculty governance for about half that time – created more antagonism than my subsequent inquiries into biomedical experiments on live animals and my visit to the university basements where they are carried out. What I saw and learned was very disturbing and persuaded me that things need to change, a lot.

The company in question was Rockland Immunochemicals, located some 50 miles northwest of Philadelphia. One of hundreds of commercial producers of research antibodies and other biomedical materials in a multibillion-dollar global industry, Rockland was cited by the USDA for almost two dozen violations of the AWA.¹ They included dirty and unsafe cages, lethal blood draws, rough handling of animals, poor veterinary oversight, and a number of more gruesome transgressions including one involving premature cervical dislocation.²

The organizers of the campaign wanted to punish Rockland as well as bring attention to the broader question of the ethics and efficacy of animal-based research. But because signing the letter might suggest assent by the Faculty Senate as a whole, I decided instead to instigate a general review of NU's antibodies procurement policy. My first step was to find out what an antibody was – no small question for a professor of art history. My second was to ask members of the Senate Research Committee if they would take up the issue at their next meeting. The committee chair however, a physician experienced in animal experimenta-

¹ http://www.aphis.usda.gov/foia/enforcement_actions/2014/June/AWA/Stipulations/PA130022_AC_SA_Rockland_final.pdf. There were additional, prior violations as well: See: <http://www.care2.com/causes/and-the-winner-of-2013s-worst-lab-for-animal-violations-is.html>

² Standard euthanasia protocols require that CO₂ poisoning be followed by "a physical method from which the animal cannot recover such as cervical dislocation, bilateral thoracotomy, decapitation, removal of vital organs or exsanguination..." (Northwestern University Euthanasia Policy, Effective Date 3/18/2013). Prior to having its neck broken, a rabbit destined for euthanasia is supposed to be rendered unconscious with CO₂. Apparently a number of rabbits at Rockland woke up during gassing and the technicians went ahead and broke their necks anyway.

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tion, demurred. He said it was none of our business, that such an inquiry was nothing but a way for animal rights activists to harass researchers, that existing animal welfare standards were nothing more than philosophical posturing, and finally that I was possibly a spy sent by PETA.

After considerable back and forth, the committee at last proposed that I direct the inquiry to the head of NU purchasing and the Vice President for Research. Eight months later, the research VP sent an email to concerned faculty (a group of about 50) stating that Santa Cruz Biotech (a second company identified as an AWA violator) was being put on probation for its transgressions of law. Rockland in the meanwhile paid its \$32,071 fine and remained in the university's good graces.³

In the year between my receipt of the petition letter and the notice sent to faculty by the research VP I tried to assemble, and put in proposal form, information about best-practices in the manufacture and use of animal-derived mono- and polyclonal antibodies, recombinant antibodies, antigens, phage display and the rest. It was a foreign land. I read articles that required me to search the definition of every other word or phrase, and relearn some of the basic cell biology I was taught in high school. I also wrote to researchers in Europe and the US to clarify certain points, and reviewed the modern history of the antivivisection movement. (It began in England in 1875 with the National Antivivisection Society founded by Francis Power Cobbe.) In May 2015, at the penultimate Senate meeting of the year and nearing the end of my term as President, I distributed a draft paper with the dry title, *Report to the Faculty Senate Concerning the Procurement and Use of Research Antibodies*, proposing that the university move to replace animal-based monoclonal antibodies (mAbs) with non-animal, recombinant-based antibodies (rAbs).⁴ The latter I learned, in addition to being cruelty-free, offer better scientific results because each antibody is generated from a unique code and is therefore identical, enabling precise replication. In my report, I summarized the case as follows:

“rAbs are now widely acknowledged to be superior to mAbs in 1) speed of production; 2) target avidity/specificity; 3) convertibility into any antibody isotype; 4) reproducibility; and 5) ethical sourcing – no animals suffer or die in their production.”⁴

I was hardly alone in making such a proposal. Just before I released my report, the journal *Nature* published an extended opinion by two prominent researchers, signed by about 50 others, that argued much the same thing (Bradbury and Pluchthun, 2015).

The response to my paper was not what I expected. Initially, I received a couple of letters of support, but within a few days the tide of opinion turned and the emails became negative, personal, and even threatening. A couple of scientists wondered who really wrote the report despite seeing my name on the title

page. Some suggested it was the product of a sinister outside force – presumably PETA. (The organization is the *bête noir* of animal researchers at NU. They attribute to the group an almost occult power – like people once did the Freemasons.) But after persuading critics that I was in fact the paper's author, and that I was not a PETA spy, they shifted tack and claimed that I had unethically presented the report as the product of the Senate as a whole, despite my published disclaimer to the contrary. At the final Senate meeting in June, a group of about a dozen demonstrative animal researchers (“How dare you? I love animals!” one exclaimed), succeeded in getting the body to vote in favor of removing the antibodies paper from the Senate website. (I was censored!) They had taken my sober, narrowly framed proposal supporting a gradual change in procurement policy as a full throttle attack on animal-based science and their research prerogatives. The faculty Committee on Animal Resources (CAR) eventually posted on their website a long, critical and highly technical response to my proposal, to which I replied. (The full debate is now available on Altweb⁵.) Then, in late October 2015, to my pleasure and surprise, I received a letter from CAR indicting that 1) Santa Cruz Biotech was being removed from the NU preferred vendor list and that the committee would be sending the USDA a letter criticizing the company; and 2) that the VP for research would investigate the need for a rAb production facility. I had at least succeeded in opening the door to change.

I learned a lot from these antibody follies: 1) that the number of faculty and advanced graduate students at NU who experiment on animals is large – probably numbering in the hundreds; 2) they are a very well organized constituency, with committees, subcommittees, blogs, and lots of supporters among staff, faculty and administration; and 3) that they vehemently oppose anybody from outside their ranks looking over their shoulders, but that when sufficient pressure is brought to bear (buttressed by sound science) reform is possible.

2 Animal testing on campus

From the anger generated by my modest proposal, I drew the inference that what might be called “the animal question” was more than just a matter of a faulty antibody procurement policy. Animals are used in thousands of experiments at NU every year at a cost to the university in the millions of dollars, and yet the research scientists are deeply averse to oversight by anyone outside their ranks. Of course, a certain chauvinism is natural within any discipline – would the art history department want a chemist to review its PowerPoint lectures? – but the initial, shrill response to my paper suggested more than that. Did the researchers have something to hide? So, in late May 2015, I decided to broaden my review of animal experimentation. My first

³ http://www.aphis.usda.gov/foia/enforcement_actions/2014/June/AWA/Stipulations/PA130022_AC_SA_Rockland_final.pdf

⁴ http://altweb.jhsph.edu/news/2015/antibodies_proposal.html

⁵ http://altweb.jhsph.edu/news/2015/antibodies_proposal_reply.html



step was to read William Russell and Rex Burch's book, *The Principles of Humane Experimental Technique* (1959). It established the 3Rs protocols – Replacement, Reduction and Refinement – that were later mandated by the National Institutes of Health (NIH), and became the global standard. “Replacement” means avoiding the use of animals in experiments and relying instead upon human volunteers, mathematical or computer models, or other non-animal methods. “Reduction” is minimizing the number of animals. This can be done by improving experimental design, using better statistical models, and sharing data between researchers. “Refinement” means reducing to a minimum the pain and suffering of lab animals.⁶

“Replacement” is obviously the most important and controversial of the three Rs. If it is achieved, the rest are unnecessary. Though several respected and well-funded organizations promote “a world where non-animal methods are accepted as scientific best practice,”⁷ animal-based research in the US and globally is rising, not declining. In 2014, there were in the United Kingdom over 4 million scientific experiments using animals, a small rise from the previous year, but a more than 30% increase from a decade before.⁸ In the US, the total number of yearly animal experiments is about 20 million and also appears to be rising. Globally, the number is 115 million (Taylor et al., 2008). And while experimentation upon AWA protected animals in the US has declined significantly in the last decade, other animals – chiefly mice and rats but also fish – have more than taken their place.⁹ (The AWA does not offer protection to birds, rats, mice, farm animals or any cold-blooded animals.) The coming expansion of NU's animal lab by some 50,000 sq ft suggests it is anticipating further growth in animal research.

The second step in my inquiry into the use of animals in experimental research was to arrange a visit to the Center for Comparative Medicine (CCM) also known as the Chicago Vivarium¹⁰ or animal lab. I knew from the website of the NU-IACUC that tours were given rarely and generally for purposes such as training, scientific collaborations and vendor visits. They are also allowed “to promote awareness of the importance of working with animals in research.”¹¹

In my application letter to the center's chief administrators, I said that my interest was not casual but based upon my roles as 1) NU professor of art history and author of two books about animals and art; 2) scholar in the field of Animal Studies pre-

paring a paper to be delivered at a conference on animal research at the Oxford Centre for Bioethics in Oxford, UK; and 3) President of the Faculty Senate and author of a controversial report concerning the procurement and use of research antibodies. They agreed to my visit – they'd escort me themselves – with the usual stipulation that no visual or audio recordings were allowed. (Though common among animal labs, the prohibition nevertheless raises suspicions. I know of nowhere else on campus where photography is prohibited.)

My June 30, 2015 tour was brief – not more than about an hour. In addition to being forbidden from taking photographs or making audio recordings, I was strongly discouraged from taking notes. Thus my description must rely upon memory and jottings made later that afternoon. Moreover, I was denied access to large parts of the facility, including the primate lab. I neither saw any experiments being performed on animals nor any animals being euthanized. All of the animals I saw were in cages or small rooms or – in the case of mice – in shoebox-sized plastic containers. Here is what I experienced and saw, followed or preceded by brief reflection, analysis and comparison:

Access to the vivarium in the Searle Medical Research Building on Lake Shore Drive is circuitous. After leaving the CCM office, we take an elevator down to the lobby, then walk along some corridors, through some doors, more corridors, and then take another elevator heading down. After that are some more hallways, and at least one security door. Once inside the vivarium, but not yet in the area where the animals live, I put on hospital scrubs: gown, mask, gloves and booties. After going through another security door, we are in what feels like a cross between a hospital and a high school – a long, fluorescent lit corridor with yellow, ceramic brick walls, polished floors, and rooms of various sizes left and right. Some have large glass walls exposing metal tables and racks – clearly intended for some kind of preparation – and others are small rooms with windows in the doors. Many of the animals are housed in these modest-sized rooms. I am guided to look through the nearest door. It contains a single sow in a bare room lit entirely by artificial light. I'm told the pig has no opportunity for social interaction of any kind because she is radioactive. She's lying on the

⁶ See the materials collected by the U.K. National Center for the Replacement, Reduction and Refinement of Animals in Research: <https://www.nc3rs.org.uk/the-3rs>

⁷ FRAME (Fund for the Replacement of Animals in Medical Experiments), <http://www.frame.org.uk/frame-at-a-glance/>, In the U.S., CAAT (Center for Alternatives to Animal Testing), based at the Johns Hopkins, Bloomberg School of Public Health, describes its mission to: “Promote and support research in the development of *in vitro* and other alternative techniques.”

⁸ <http://www.theguardian.com/science/2014/jul/10/animal-experiments-rise-again-uk-genetic-research>. Also see: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/327854/spanimals13.pdf

⁹ http://www.aphis.usda.gov/animal_welfare/downloads/7023/Animals%20Used%20In%20Research%202014.pdf. Also see the reports on animal usage by the Anti-Vivisection Society (<http://www.navs.org/science-first/animal-research-numbers-continue-downward-trend-according-to-newly-released-report>) and PETA (<http://www.peta.org/issues/animals-used-for-experimentation/fish-laboratories/>)

¹⁰ The word vivarium is euphemistic. It has generally been used to describe an enclosure in which animals are kept in an environment that mimics their natural one, or else a location where food animals are held, especially fish. It has recently begun to be used to describe an animal research lab.

¹¹ <http://www.research.northwestern.edu/oprs/acuc/policies-procedures/documents/2014/91161POLICY-VivariumVisitorPolicy.pdf>



floor, motionless – it takes me a minute to be sure I see her breathing. I feel bad for her because pigs are highly sociable animals.

Please note I could have written “pigs like company” or “pigs enjoy having friends,” but the tendency to employ scientific or animal welfare newspeak was nearly irresistible. The place was clean and orderly, and run by scientists with exemplary academic records. We all dressed in scrubs to prevent compromising the health and research worth of the animals, and we talked – when we talked at all – in low tones if not quite whispers, as if we were surrounded by sleeping and sick patients. Any sentiment or anthropomorphizing was out of place. Here, the ethic of research prevailed.

Any treatment of lab animals is permitted under US law if there is “an acceptable justification,” or if the treatment is validated by “necessary clinical reasons,” or “experimental purposes.”¹² But long-term solitary confinement of a pig seems at the very least a violation of the spirit of the Animal Welfare Act and 3Rs principles.

The *IACUC Guidebook* (one of the US gospels of care) states that in general:

“Cages should allow for conspecific social interaction within or between enclosures, adequate ventilation, and observation of animals with minimal disturbance of them and provide a safe and secure environment that permits the normal physiologic and behavioral needs of the animals to be expressed;”¹³

The highly respected *UFAW Handbook on The Care and Management of Laboratory and other Research Animals* specifically forswears pig solitary:

“Pigs being curious and agile animals, will suffer from boredom if not given the opportunity to engage in a range of activities. Common enrichment items include the provision of hanging chains or objects in the pens.... Socialization within groups and the establishment of a social hierarchy are behavioral traits typical of free ranging pigs and should be taken account of when housing pigs in pens.” (Hubrecht and Kirkwood, 2010, p. 478)

My follow-up inquiry about why the pig was irradiated was never answered, but it is probably research concern about the danger of low doses of radiation. Finding mutations in cancer-specific genes in irradiated tissues might provide a clue about safe versus unsafe levels of radiation – at least in pigs (Abbott, 2012). But given the enormous pool of people subjected to ra-

diation every day – from CAT scans, x-rays, airport security, radiation therapy, and radon – it would seem that animal models are superfluous at best, especially given the high animal welfare cost. The unstated 3Rs calculus has always been that great suffering can only be justified by great research rewards.

After a few minutes observing the radioactive pig, I was ushered down the hall and prompted to stop in front of another windowed door.

At first, I don't see any animals at all, just two rows of gray-pink volumes, receding at left and right. Then I discern movement – a quiver, a subtle inflation and deflation, and a slight shift of position. These also are pigs, and I am observing their rear ends. I feel a bit embarrassed for them and for myself. Why won't they turn and show me their faces? How long is it proper to stare? I remember visits to the Central Park Zoo when I was a child and disappointment that the animals never displayed themselves the way they were supposed to: the gorilla always turned away and the polar bear stayed at the far end of his pool. One of my hosts tells me the pigs are part of an obesity study and my shame grows.

Pigs have been used for obesity studies since the 1960s. In 1979, a team of authors argued that the pig was an ideal model for the study of obesity because of “general physiological similarities to humans”. While granting that Rhesus monkeys and other primates might be better models, they “are not tractable lab animals” because they generally have to be “chained” – forced into a sitting position with neck and head restrained – in order to be experimented upon whereas pigs are more compliant (Bliss-Moreau et al., 2013; Houpt et al., 1979). So was convenience the main reason for selecting this animal model? Or was the choice of pigs based also on the long, vernacular association of obesity with pigs and hogs? These particular pigs in the vivarium are research subjects for scientists from the Northwestern Comprehensive Center on Obesity, “formed in 2008 to understand and address the global epidemic of obesity.”¹⁴ But given the vast number of obese humans of all ages, genders, ethnicities and nationalities who are active/sedentary, smokers/non-smokers, drinkers/teetotalers, meat eaters/vegans, is there really a paucity of human research models?

Soon I am led to another windowless room (except for the rectangular glass portal on the door) that contains four or five cats lying in cages; another cat is out of a cage, passing just below me, her upraised, question-mark tail moving in and out of view. The room appears sterile

¹² AREANA and OLAW *Institutional Animal Care and Use Committee Guidebook*, p. 85; *Guide for the Care and Use of Laboratory Animals*, p. 30, 61. See: http://www.aphis.usda.gov/publications/animal_welfare/2014/fsc_research_oversight.pdf

¹³ *IACUC Guidebook*, p. 44. In addition to the *IACUC Guidebook*, the published standards that bind all federally funded research institutions are the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* (<http://grants.nih.gov/grants/olaw/references/phspol.htm#PublicHealthServicePolicyonHumaneCareandUseofLaboratory>) and the *Guide for the Care and Use of Laboratory Animals* (<http://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf>).

¹⁴ <http://www.ncco.northwestern.edu>



and lacking in any cat toys, boxes, paper bags, scratching posts, catnip or other common feline diversions.

I was surprised to see cats. They are used with decreasing frequency in biomedical research – their numbers in labs have declined by about two thirds in the last generation – and they are pet animals that elicit great sympathy. If the public knows you are messing with a kitten, there will be trouble. (In fact, kittens are often used in studies of blindness because they have binocular vision and frontal eyes, like humans.) The sterility of the environment was shocking. House cats have a way of inflecting a space – unraveled balls of yarn, toy mice, frayed upholstery – but here there was none of that.

The *UFAW Handbook* states:

“Good laboratory housing for cats should include a range of shelving at different heights, and a choice of resting and hiding places...[and provide] opportunities for climbing...[and] semi-hidden spaces to explore or to withdraw from the group.” (Hubrecht and Kirkwood, 2010, p. 456)

The *European Convention for the Protection of Vertebrate Animals* adds:

“Outside runs provide an environmental enrichment opportunity for cats in both breeding and user establishments and should be provided where possible. Pseudo-predatory and play behavior should be encouraged.” (CoE, 2006, p. 30)

As any human companion knows, cats are happiest when they can go outside. Indoor-cats will thrive only with a great deal of attention, affection and play – “pseudo-predatory behavior.” The cats in this sterile environment however must live lives of quiet desperation. But the end of their lives is even worse. They are likely doomed to suffer the fate of the two Column E cats in 2014: subjected to laminectomies (removal of the back part of the vertebra) and spinal transection. (The USDA and National Institute of Health regulate the imposition of pain by means of a lettered scale from B to E, with the latter signifying painful procedures for which no analgesics are administered. Column E pain must be specifically approved by the IACUC.)

The purpose of those operations, according to documents submitted to the USDA and the NU-IACUC, is to induce bilateral hind limb paralysis and thereby “elucidate how substances function to facilitate the recovery of hind limb locomotion.”¹⁵ Given the regulatory high hurdle of Column E experiments, the justification is poor. Cats have been used for spinal cord

research since the 1970s after it was discovered they recover some hind leg movement on a treadmill days or weeks after their spinal cord was severed (Forssberg et al., 1975; De Leon et al., 1999).¹⁶ The idea therefore arose that if the impulse for locomotion resides in the spinal cord itself and not in the brain, some combination of chemical and kinetic therapy may be able to restore lost movement in humans suffering spinal cord injury. Unfortunately, decades of cat experiments have not produced a single drug that helps patients with spinal cord injury (Hadley et al., 2002; Hadley and Walters, 2013; Tator et al., 2012). Indeed, profound differences in cat and human physiology, neurochemistry and kinetics may render translational medicine useless in this case¹⁷, like many others. Direct research on humans on the other hand, has produced a number of very promising discoveries, including a motorized exoskeleton that enables some paraplegics to walk.¹⁸

The next room contains dogs. It is about the same size as the one for cats – perhaps 12 by 16 feet – with cages on the long walls and an alley in between. (Most doors are open.) Once again, it is windowless. As we approach the portal, the dogs erupt in barking. I can't see any toys, platforms, chewable treats or other playthings, (no squeaky toys?) though it is possible that a few are outside my view. A chart on the door indicates the period of daily exercise for each dog – generally about 15 minutes. I realize at once that the dogs are never taken outside and never see or feel daylight.

In the *UFAW Handbook*, we read:

“Dogs are naturally inquisitive and actively seek information about their environment. The use of a raised platform and ramp is especially beneficial allowing some privacy from neighboring dogs but also allowing good vision of the surroundings. Since dogs naturally chew, objects which are safe and possibly flavored, such as rawhide or other commercially produced chews, may be suspended within the pen enclosure.” (Hubrecht and Kirkwood, 2010, p. 436)

The *European Convention* notes the obvious:

“Outside runs provide an environmental enrichment opportunity ...and should be provided where possible.” (CoE, 2006, p. 30)

The dogs I saw in the vivarium are members of the same species, *Canis familiaris*, as the animals I have lived with and closely observed for the past 35 years. First there were the

¹⁵ https://acissearch.aphis.usda.gov/ACIS_Export/faces/pdfpage.jspx?anmluce=190151215310973

¹⁶ In fact, for at least 150 years, researchers have been severing the spinal cord of cats in order to study locomotion and the sources of convulsions (Wood, 1873).

¹⁷ A new drug therapy, partially effective in rats, was recently made public. Its translational significance remains to be seen: Lang et al., 2015.

¹⁸ <http://www.pcrm.org/research/animalstalt/animaltesting/spinal-cord-injury-experiments-on-animals>; <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm402970.htm>



pugs Smiley and Connie, then the Jack Russell Terrier Asta, quickly joined by the Rhodesian Ridgeback Nisa; then came the mutt Pepper, and now Echo, a mix of German Shepherd and Blue Heeler. My dogs were morose if they were left alone (without their human companions) for more than a few hours. They would be jumping out of their skins if they didn't have a chance to run and play for an hour or more per day: Asta liked to chase down and tear the covers off tennis balls; Nisa loved long, leisurely runs; Echo plays Frisbee at least twice a day and loves to swim in Lake Michigan. All my dog companions have had strong food preferences: Smiley shelled and ate the walnuts that fell from the tree in our Los Angeles backyard – he grew fat on them; Pepper ate strawberries and other fruits. Echo is a diffident eater and will never dine alone – her humans must stand or sit beside her. In the winter, they all loved to lie indoors in the sun, light pouring through the window until they got so warm they began to pant. Any of us who have had companion dogs can tell similar stories – we are all ethologists when it comes to our pets. (The plural of anecdote, the motto goes, is data.) Among NU-IACUC approved procedures for these dogs was ventricular tachypacing to induce congestive heart failure. After three weeks, atrial fibrillation was evaluated by means of “open chest mapping.”¹⁹ An NIH grant for this work lasts until 2019.

I asked the CCM administrator conducting my tour if the dogs were ever adopted out. She told me no, and later briefly elaborated they are euthanized because “their tissues are needed for the research.” I doubt the need. Tissue samples can obviously be obtained (think biopsies) – even from major organs – without killing the whole animal. I think the reason is simply convenience. Some U.S. state legislatures agree with me. Minnesota, Connecticut and Nevada have all passed bills requiring universities to adopt out cats and dogs used in research. California and New York have bills pending in their legislatures that would do the same.²⁰ Even without an Illinois law, Northwestern could easily establish an adoption program.²¹ But that wouldn't change the nature of the research. Would such a program simply function as an alibi for cruel and invasive experiments – allowing researchers to claim that their treatment of dogs and cats is acceptable because a percentage are eventually adopted? When I visited the Vivarium in June there were three or four dogs. According to the August 4 USDA-APHIS inspection report there was only one. What happened to the others? What will become of the last dog? Is he alone in his cell more than 23 hours per day or will other dogs soon join him?

In another windowless room, rabbits are housed in cages on two tiers. The tops of the cages are barely high enough

for their ears when the animals are sitting up or on all fours. The animals have no room to hop. Their days must be impossibly tedious, except for when they are sent to have surgery. Their free relatives can often hide from hawks, owls, coyotes and human hunters, but these animals have no defense against the hands that seize them. They must possess both a terror and a certainty about death (or at least the unknown fate outside their cages) unusual among their species.

The UFAW Handbook states:

“During the last 10-20 years the approach to housing rabbits has changed considerably, and group housing in floor pens has been introduced in many laboratories and countries... Housing in pens enables rabbits to express social behaviors and to exercise... Floor pens should be large enough for the rabbits to be able to carry out basic behaviors such as locomotion, rearing, grooming and avoiding cage mates.” (Hubrecht and Kirkwood, 2010, p. 404-405)

Last year, Northwestern experimented upon 293 rabbits, of which 286 were Column D procedures in which the animals experienced “pain or distress... [but were given] anesthetics, analgesics or tranquilizers appropriate to prevent or alleviate pain or distress.”²² Among the procedures that receive designation D are “surgery, including biopsy, gonadectomy, neurophysiological manipulations or preparations such as the implantation of electrodes and recording devices.” Can the animals call for a nurse when the post-operative analgesic proves inadequate? Can they press the button that self-administers narcotics? Rabbits like cats are relatively undemonstrative when they experience pain – how can researchers know when the D threshold passes over to E?

Finally, there are the mice and rats. Almost unnumbered, they are the archetypal lab animal, unmonitored by the USDA. But by virtue of their ubiquity, researchers have learned a tremendous amount in recent years about rodent behavior and even about the rodent mind. For example: we now know that they play, laugh and feel empathy (Panksepp, 2000; Underwood, 2015).

The population of mice at the NU vivarium numbers more than 20,000 and as many as 50,000. (I am given both statistics.) They live in shoebox sized plastic (polycarbonate) enclosures with bedding materials and a single cardboard lean-to for hiding. The boxes are placed side-by-side on shelves stacked some five or six high. I get to see these close-up and marvel at the ability of the animals

¹⁹ <http://1.usa.gov/1kyE910>; on open-chest mapping see: Lemery, 2002.

²⁰ <https://www.nysenate.gov/legislation/bills/2015/s98>; <http://animallaw.foxrothschild.com/2014/06/17/adoption-of-research-animals/>

²¹ A model placement program is the Beagle Freedom project which as so far received more than 75,000 adoption pledges: <http://www.beaglefreedomproject.org>

²² http://oacu.od.nih.gov/ARAC/documents/USDA_Reports.pdf



to build shelters out of their bedding and cardboard. I am shown one mouse with babies – they are naked and called “pinkies.”

The *UFAW Handbooks* tells us:

“Mice are active, highly exploratory animals, which in the wild, spend considerable time foraging, seeking a wide variety of food. They construct elaborate nests and burrows and form complex social structures. All these behaviors, which they remain strongly motivated to perform, are still present in the laboratory mouse. Housing systems for laboratory animals have often been designed on the basis of economic and ergonomic aspects... with little or no consideration of animal welfare... leading to frustration and suffering. [With mice], increasing the complexity of the cage is more important than increasing floor area as such.” (Hubrecht and Kirkwood, 2010, p. 284)

3 What about the IACUC?

The current IACUC chair has held the position for more than nine years. He told me a long tenure in the job was valuable because of the “steep learning curve.” I brooded over that, wondering if a nearly decade-long term might foster complacency regardless of the chair’s individual merit. What was the administrative and psychological toll of supervising from a distance, year after year, the suffering and deaths of tens of thousands of animals? Could the chair still fathom, as was his responsibility, the life and death significance of each IACUC application? Could he ever reject the protocols of men and women who were for so many years his close friends and colleagues, in the name of animal protection and good science?

The IACUC chair also has the chief responsibility for determining membership of the committee. I asked him if he was intending to ask any animal ethicists to join.²³ He said no because they might be biased against animal research. We debated that a while until he volunteered that there were probably some ethicists who could keep an open mind and do a good job. (He added that I was unlike the activists he had met because we could discuss things amicably even if we disagreed. He didn’t ask me to join the IACUC.) He added his preference to bring in a statistician – a useful addition in my view since many animals die because of poor statistical models (Festing et al., 2002).

The current NU-IACUC has 23 members. Of these, 17 are actively engaged in animal based research, including the mandated veterinarian. Three others are NU administrators (two

IACUC staff, and one biological safety officer). That makes 20 out of 23 members who are either regular applicants to the IACUC or its administrators. The IACUC chair himself regularly submits animal research protocols to his own committee. The two required unaffiliated members have careers in marketing and finance with no apparent expertise in animals, animal care, ethics or law; one is a Northwestern alum. The person required by law to “represent general community interests in proper care and use of animals” has served that role for nine years and is the spouse of a physician. It is unlikely this individual represents “general community interests.” A recent US Gallup poll indicates that 67% of people surveyed were “concerned or very concerned” about the treatment of animals in laboratory research, and 32% believe that “animals deserve exactly the same rights as people to be free from harm or exploitation.”²⁴ A Pew poll shows that just 47% of Americans believe that animals should be used in research experiments, while 50% disapprove. On the other hand, 89% of U.S. scientists (including physicians) approve using animals in experiments.²⁵

The potential bias of IACUCs has attracted the attention of scholars. A recent study found that at 21 of 25 top NIH funded institutions (insufficient data was available for four), 67% of members were animal researchers and another 15% were veterinarians who conducted animal experiments. In addition, 93% of IACUC chairs themselves conducted animal research with the result that 98% of in-house research protocols were approved. (At Northwestern I was told, the figure is 100% though some research plans are significantly modified.) The phrase “rubber-stamp” is unavoidable here. What is even more remarkable is that when the same protocols were submitted blind to other institutions, 61% were determined to be “not understandable at all”, “not very convincing” or “not convincing at all” and lacking justification for the type and number of animals used (Plous and Herzog, 2001; Hansen, 2012; Hansen et al., 2012; Leslie, 2006).

The issue of IACUC bias should be viewed in the context of increasing doubts about the validity of animal experimentation itself (for a critical review of animal based research see Andregg et al., 2006). Though still widely believed to be essential for both basic and applied research (especially for pre-clinical drug trails), a minority of researchers are now challenging that faith.²⁶ A peer-reviewed, systematic review from 2007 published in the venerable *BMJ* (formerly *British Medical Journal*) found that clinical drug trials for head injury, respiratory distress syndrome, osteoporosis, stroke, and hemorrhage conformed with animal results only half the time, meaning that animal trials were no more predictive than a coin flip (Perel et

²³ Some other countries – notably Germany and Sweden – recruit a portion of their members from the animal welfare or animal rights communities. In Germany, one third of members must come from animal welfare organizations. In Sweden, half of the 12-person committees must be from the general public, and two of the laypersons from animal protection organizations. See: Physicians Committee for Social Responsibility, “Animal Care and Use Committee – Structural Problems Impair Usefulness”: http://www.pcmr.org/sites/default/files/pdfs/research/testing/exp/ae_iacuc.pdf

²⁴ <http://www.gallup.com/poll/183275/say-animals-rights-people.aspx>

²⁵ <http://www.pewinternet.org/2015/01/29/public-and-scientists-views-on-science-and-society/>

²⁶ There is a significant body of research raising doubts about validity. See for example Perel et al., 2007; Pound and Bracken, 2014; Godlee, 2014; Akhtar, 2015.



al., 2007; Akhtar, 2015). In 2004, the US FDA estimated that at least 92% of drugs that passed preclinical animal trials did not make it to market, primarily due to safety issues and lack of effectiveness.²⁷ Toxicity tests in animals are notoriously unreliable. A pair of studies from 1996 and 2000 evaluated 68 methods for determining the toxicity of 50 chemical compounds and found that animal tests predicted human toxicity only 59% of the time; human cell tests conducted *in vitro* however, had an 83% accuracy rate (Clemenson et al., 1996, 2000).

There are many reasons animal trials may fail to be predictive, the most obvious of which are physiological and genetic difference between humans and animals. Beyond that, the impact of lab conditions – contingent upon the different standards of care in each laboratory and the psychology of each animal – can affect an animal's behavior, physiology, chemistry and neurobiology leading to anomalous research results. Even the particular supplier of a lab animal of the same genetic strain can lead to conflicting results in tests of drug or other therapies (Mogil, 1999). The result is that many drugs found to be useful in animals are shown to be valueless in people, and equally significant – but often overlooked – many discovered to be ineffective or toxic in animals are beneficial to humans. Two examples of blockbuster drugs that failed animal trials are Tamoxifen, a now essential drug in the treatment of breast cancer, and Gleevec, an equally valuable tool against certain forms of leukemia (Anon., 2003; Akhtar, 2015). (If Aspirin or Tylenol had been tested on cats – for whom it can be deadly – we might all be taking morphine for headaches.) If the critics of animal testing are correct, the cost in animal lives, dollars lost, and human suffering and death is almost incalculable.

4 What is to be done?

Though NU was cited for two AWA violations in March 2014, it has generally maintained a good record of compliance for the last decade or so. (In 2003 it was cited for numerous, serious violations, and the Humane Society of the United States alleged several cases of substandard care and possible AWA violations between 2003 and 2006.²⁸) In addition, the many layers of research oversight – documented on the CAR, CCM and IACUC websites – suggest an institutional commitment to abide by the letter of federal law and university rules.

But it is one thing to follow the letter of the law, and another to ensure humane treatment of animals and abide by the ethic of the 3Rs. My research and observations suggest that the standard of animal care at Northwestern is significantly below that set forth in the highly respected *UFAW Handbook* (Hubrecht and Kirkwood, 2010) and the *European Convention for the Protection of Vertebrate Animals* (CoE, 2006). Given emerging doubts about the scientific efficacy of animal research and testing, widespread and growing public concern over animal welfare, and the new scientific consensus regarding animal consciousness and suffering, universities such as Northwestern – with extensive biomedical research facilities and very healthy endowments – should be leaders in improving the care of research animals (“Refinement”) and more importantly, in the search for non-animal research alternatives (“Replacement” and “Reduction”).²⁹ An example of such leadership is provided by the Center for Alternatives to Animal Testing (CAAT) at the Johns Hopkins Bloomberg School of Public Health and the Wyss Institute at Harvard. CAAT is a clearing house and proving ground for new, non-animal based research models. The Wyss at Harvard, (along with MIT, Vanderbilt, Yale, Cornell and a few other universities) has pioneered the development of “biomimetic microsystems,” three-dimensional models of human organs that can mimic cells and blood vessels and thus replace animal testing in the study of disease or toxicity (Wenner Moyer, 2011; Eisenstein, 2015).³⁰ This year, the NIH awarded \$70 million to 17 universities to further develop Tissue Chip Drug Screening.³¹ (Northwestern was not among the award recipients.)

Despite the well-documented failures of the existing research paradigm, and despite progress in developing non-animal models for basic and applied science, vivisection remains the rule in university biomedical labs. Notable careers and great fortunes have been made from drugs and therapies tested on animals, and the university professor who challenges the system does so at some professional risk. After I spoke on the radio about the NU vivarium and published a short, critical essay about it, all 20 members of the Committee on Animal Resources (CAR) wrote to the incoming Faculty Senate President (a physician on the faculty of the business school) that I had tricked them into giving me a tour and endangered researchers by the publicity I brought. They demanded I be censured or removed from the Senate. The new President agreed to quickly hold an informal

²⁷ “Currently available animal models, used for evaluating potential therapies prior to human clinical trials, have limited predictive value in many disease states. Better predictive nonclinical screening methods are urgently needed” (FDA, 2004).

Also see: Harding, 2004. On low-predictivity in animal studies of inflammation (corroborating similar findings concerning sepsis, neurodegeneration, and stroke), see: Leist and Hartung, 2013.

²⁸ http://www.humanesociety.org/news/press_releases/2010/04/northwestern_university_animal_research_042910.html

²⁹ See the 2012 Cambridge Declaration on Consciousness, signed by more than a dozen leading neuroscientists, neuropharmacologists and neuroengineers including Christof Koch, Philip Low, and Jaak Panksepp (<http://fcmconference.org/img/CambridgeDeclarationOnConsciousness.pdf>) and the Declaration of Lisbon, supporting reduction in animal testing, composed by Philip Low and others and issued on May 8, 2015 (<http://infospedh.wix.com/spedh#!>)

³⁰ <http://wyss.harvard.edu/viewpage/461/>; <http://www.ncats.nih.gov/tissuechip/projects>

³¹ CAR's recent published statement is dispositive concerning its attitude toward these developments: “It is true that non-animal techniques, such as cell cultures and computer simulations, are important and play a part in our advances. However, these methods cannot yet mirror the complex and sometimes unpredictable interactions within a living system.” <http://www.research.northwestern.edu/oprs/acuc/?src=or-hdr>

trial and prepared a motion of no-confidence to send to the Senate Research Committee when it reconvened in October. Rather than be a part of this, I resigned the Senate in mid August, two weeks after my term as president had ended. Thus concluded my association with a faculty body I helped create in 2008, whose statutes and bylaws I co-authored, and which I had served as first and fifth president. At NU, you criticize vivisection at your peril.

But whatever the current opposition to reform, the changing ethical and scientific landscape suggests that experimentation on animals must dwindle and then disappear. New scientific understanding of animal awareness and consciousness – not just pleasure and pain but also anxiety, distress, anticipation, hope, empathy and even love – has enormously raised the stakes in the debate (Panskepp, 2012; de Waal, 2009; Griffin, 2001). It is no longer possible to assert that even the lowly laboratory mouse hasn't the right to a life, or that its loss is a matter of indifference to it. Remarkably, these ideas – the result of developments in affective neuroscience and allied fields – have filtered down to the lay public faster than to most research scientists that work with lab animals. The result is growing pressure on universities to monitor, regulate, reduce and ultimately replace animals used in scientific experimentation. And the pressure on animal experimentation is not only from the public and the leaders of animal rights and welfare organizations; it is also from government and corporations – especially drug companies – that want safe, effective and profitable drugs produced quickly. The real question now concerns the speed of change and how many animal (and human) lives will be lost in the meantime.

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Conflict of interest

The author has no conflict of interest.

Correspondence to

Prof. Stephen F. Eisenman
5000 N. Marine Drive, 12A
Chicago, Illinois 60640, USA
e-mail: s-eisenman@northwestern.edu