

Responsible Use of Laboratory Animals



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Director, Office of Animal Resources
Harvard University Faculty of Arts & Sciences
December 15, 2015

Animal Modeling Across Harvard

Allergy
Alzheimer's Disease
Anesthesiology
Artificial Organs
Atherosclerosis
Behavioral Neuroscience
Biomaterials
Bone Marrow Transplants
Burn Injury
Cancer
Congestive Heart Failure
Crohn's Disease
Deafness
Diabetes Mellitus

Drug Addiction
Gene Therapy
Genomics
Hepatitis
HIV/AIDS
Huntington's Disease
Inflammation
Laser Therapy
Limb Regeneration
Nerve Regeneration
Obesity
Organ Transplants
Orthopedics
Parkinson's Disease

Pharmacology
Plastic Surgery
Pneumonia
Radiation Therapy
Renal Failure
Sepsis
Shock
Skin Grafting
Stem Cells
Stroke
Trauma
Ulcerative Colitis
Vaccines
Vascular Surgery

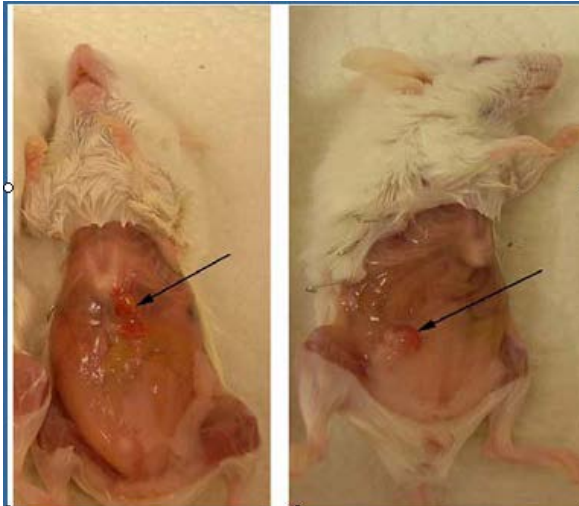
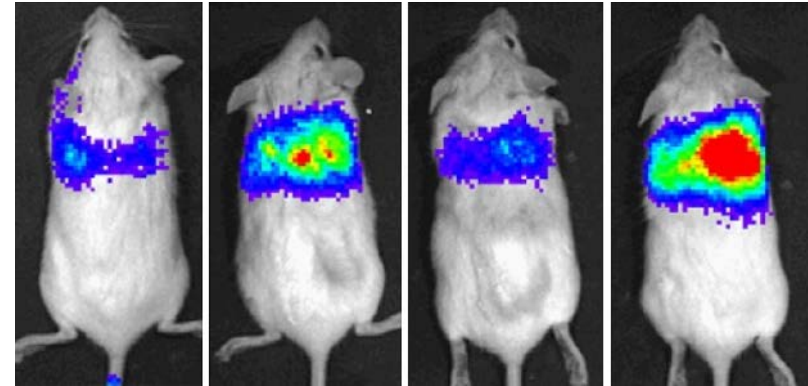


Today's Presentation

- Animal Research and the Public
- Animal Research Regulations
- Animal Research Compliance Lapses
- Animal Research Compliance Advice
- Harvard FAS Resources for Help

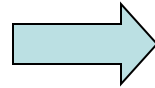
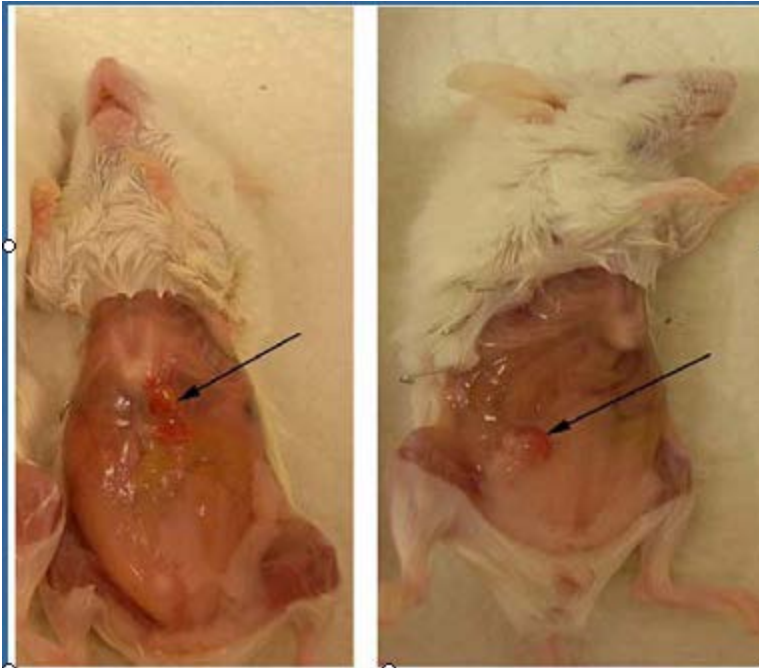


Published Mouse Photos



Bring In The Blogs

Xenografted SCID mice in a peer-reviewed scientific publication



All authors were
'featured' on an Animal
Rights blog site, with
statements such as:

*"We hope you die like
your animals died"*

Would This Have Mattered?



VS.



Bring In The Tweets





Have an account? [Sign in](#)

Get short, timely messages from Yale Kills Animals.

Twitter is a rich source of instantly updated information. It's easy to stay updated on an incredibly wide variety of topics. [Join today](#) and follow [@Yale_Kills](#).

[Sign Up >](#)

Get updates via SMS by texting **follow Yale_Kills** to **40404** in the United States
[Codes for other countries](#)



Yale_Kills

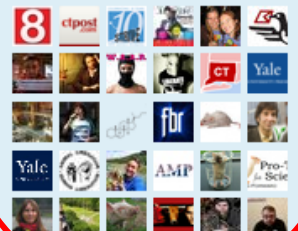
Name Yale Kills Animals
Location New Haven, CT
Bio Sharing details on who does what to animals in Yale's laboratories.

67 following 33 followers 1 listed

Tweets 14

[Favorites](#)

[Following](#)



[REDACTED] injects
rhesus monkeys with nicotine &
amphetamines ~ [REDACTED]

10:45 AM Sep 20th via web

[REDACTED] has intentionally caused
mice to develop cancerous tumors & has killed them by breaking
their necks.



Bring In The Tweets

(name deleted) “has intentionally caused mice to develop cancerous tumors & has killed them by breaking their necks.”

You Can't Win

AVMA Guidelines for the Euthanasia of Animals: 2013 Edition



“CERVICAL DISLOCATION

“Cervical dislocation is a technique that has been used for many years and, when performed by well-trained individuals, appears to be humane... This technique is used to euthanize poultry, other small birds, mice...”

Science Videos On-line

Journal of Visualized Experiments

Drawing Blood from Rats through the Saphenous Vein and by Cardiac Puncture

[Christine Beeton](#), Adriana Garcia, K. George Chandy
Department of Physiology and Biophysics, University of California, Irvine



0:00	Title
0:05	Introduction
0:21	Subscription Lock
1:12	Drawing Blood from the Saphenous Vein
2:40	Blood Draw by Cardiac Puncture
5:06	Conclusion
5:24	Credits

Science Videos On-line

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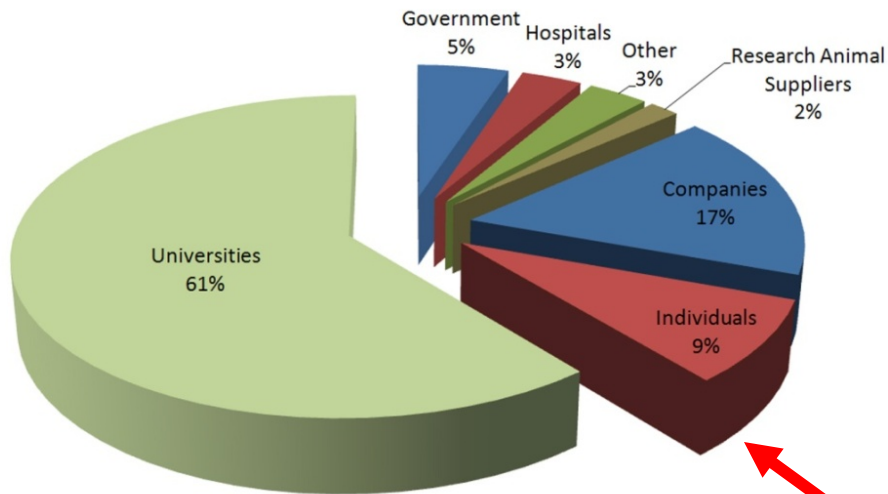


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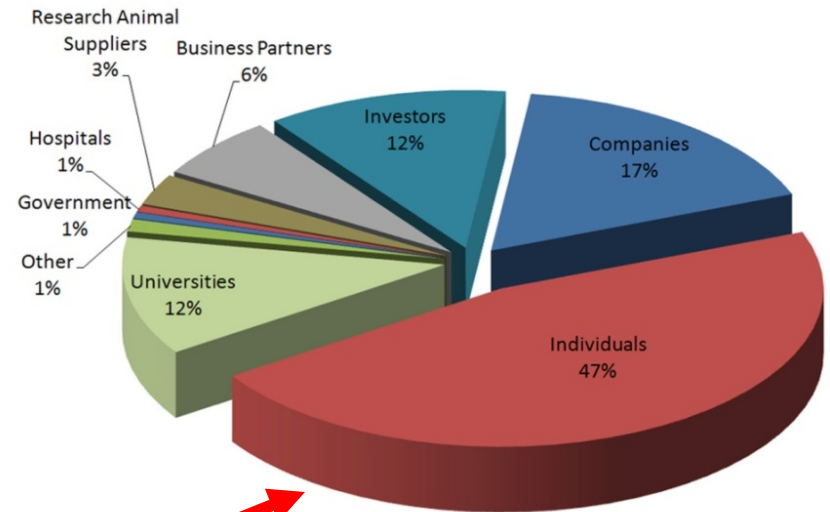
Individuals Increasingly Targeted

Targets of Illegal Actions from 1990-2009

1990-1999



2000-2009



Based on approximately 216 reported illegal incidents

It's Getting Worse

*Nearly one-quarter of
biologists say they
have been affected by
animal activists. A
Nature poll exposes the*

BATTLE SCARS

BY DANIEL CRESSEY

Nature 470:452-3, 2011

Science Videos On-Line

Journal of Visualized Experiments

Homing of Hematopoietic Cells to the Bone Marrow

Massachusetts General Hospital



Free Access

On-line Amateurs

You Tube B

Seed tumor at liver of mouse-Suture□□□□□-□□□(□)

miss9ch 276 videos



On-line Professionals

Journal of Visualized Experiments

Principles of Rodent Surgery for the New Surgeon

Kathleen R. Pritchett-Corning, Yiyi Luo, Guy B. Mulder, William J. White
Charles River, Research Models and Services



0:05	Title
1:25	Understanding Aseptic Technique
2:32	Preparing the Work Area for Surgery
4:14	Preparing the Instruments for Surgery
5:12	Preparing the Animal for Surgery
7:00	Preparing the Surgeon for Surgery and Proper Surgical Practice
8:41	Post-operative Considerations
9:40	Representative Results
10:00	Conclusion

The Whole World Is Watching

-----Original Message-----

From: [redacted]

Sent: Monday, [redacted] 2:04 AM

To: [redacted]

Subject: Unable to access [redacted] website

I have been unable to access the [redacted]
[redacted] website [redacted] to report a severe
breach of the [redacted] regulations for care of
research animals.



Could you please forward the attached pdf file to the [redacted]
[redacted] so that they are aware of experiments being
carried out by researchers that claim to have approval by their
committee?

Yours sincerely,

[redacted]

(Could you also please reply to this message to confirm that you have received it?)

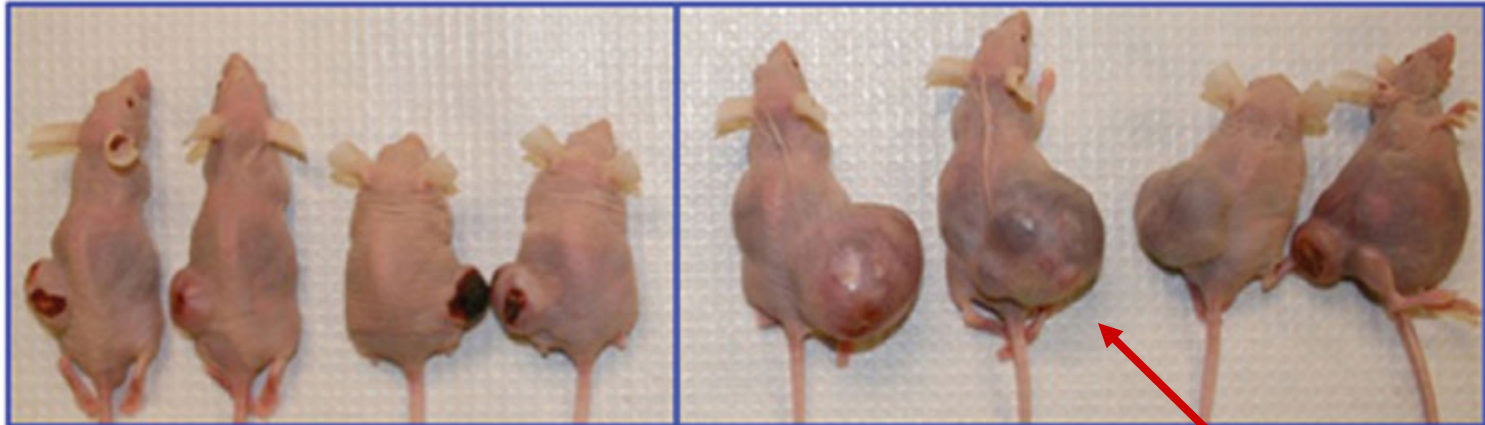
The Whole World Is Watching

Not approved



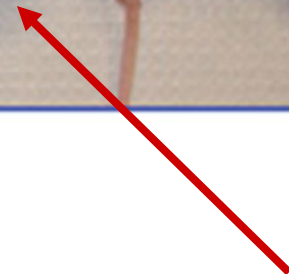
-treated

Vehicle-treated



nature

Supplementary Fig.



Larger than allowed

Career Consequences

From: Marte, Barbara [<mailto:B.Marte@nature.com>]

Sent: Friday, 8:23 AM

To:

Subject: RE: update

Dear

I just wanted to update you, as promised, on the course of action we have decided on:
We will be issuing a corrigendum from the authors, stating that the these experiments were not performed in compliance with the regulations of the Institutional Animal Care and Use Committee at , and will therefore be withdrawn from the paper.

With kind regards,

Barbara

Dr Barbara Marte

Senior Editor, Nature

4 Crinan Street

London N1 9XW, UK

tel + 44 (0)20 7843 4584

Fax + 44 (0)207 843 4596

e-mail: b.marte@nature.com

Laws and Regulations

- Animal Welfare Act (7 U.S.C. §§2131 et. seq.)
 - Covers all warm-blooded species **except laboratory mice, rats, birds**
 - USDA institutional registration, annual reports
 - Unannounced inspections of facilities, records, protocols
- City of Cambridge Laboratory Animal Ordinance
 - Applies to all vertebrate species
 - Unannounced inspections of facilities, records, protocols
- Information available to public via FOIA

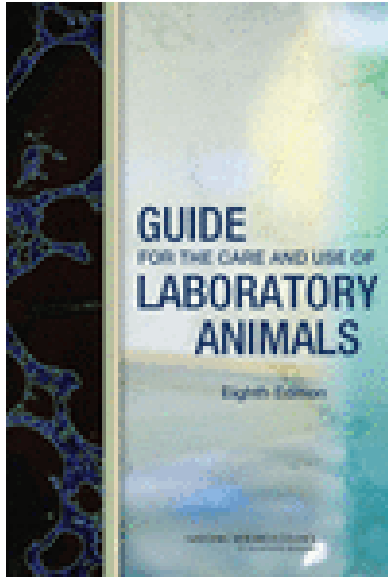


Federal Grants and Contracts

- All PHS-funded vertebrate animal use subject to Public Law 99-158
- Annual Letter of Assurance to NIH's Office of Laboratory Animal Welfare
- Self-reporting of major incidents or violations
- Inspections if serious violations suspected
- Grant suspensions/revocations if not fixed
- Information available to public via FOIA



“The Guide”



- National Academy of Sciences
- most recent edition 2010
- dominant reference document

http://www.nap.edu/openbook.php?record_id=12910&page=1/

Internal Animal Welfare Oversight

- Institutional Animal Care & Use Committee
 - required by USDA, NIH, AAALAC
 - approves protocols and amendments; dissenting votes recorded
 - reviews entire program and all animal locations every 6 months; deficiency correction required
 - investigates animal welfare concerns
 - can suspend or revoke animal research privileges



True Story

- Post-doc has a new idea, performs a “quick-and-dirty pilot” study on ~30 mice
- Mice get ill when they’re not supposed to
- Post-doc consults with veterinarian
- Veterinarian consults NIH-funded protocol for more details, discovers pilot procedure not in protocol...

Federal Grants and Contracts

“Institutions are required to report such situations to the Institute/Center (IC) supporting the award and to OLAW. In cases where charges have been made for unauthorized animal activities, appropriate adjustments must be made to the grant to remove those charges.” (NOT-OD-10-081, April 15, 2010)



Federal Grants and Contracts

- “...no costs for activities with live vertebrate animals may be charged to NIH if there is not ...Institutional Animal Care and Use Committee (IACUC) approval.” (NOT-OD-07-044, January 26, 2007)
- “Absence of IACUC approval includes failure to obtain IACUC approval, expiration, or suspension of IACUC approval.” (NOT-OD-10-081, April 15, 2010)



True Story Con\$equence\$

Expenses refunded to grant:

- Allogeneic cell transfers from donor mice to experimental mice (@ \$200 each = \$6,000)
- Cells isolated from experimental mice and labeled for FACS (time & mtl\$)
- Cells cultured for bacterial contamination (time & mtl\$)
- Cage per diems (\$1.13/cage/day)...

→ NIH notified 2X

Institutional Animal Care and Use Committee (IACUC)

- Members: 7 Harvard faculty scientists who use vertebrates, 2 veterinarians, 3 non-scientists, 1 community representative
- Committee appointed by Dean Kirwan
- Meets 6x/year (approximately once every 2 months)
- Responsibilities:
 - Review and approve protocols/amendments
 - Review facilities and program at least every 6 months
 - Investigates and resolves allegations of mistreatment or noncompliance



Animal Protocol Review Process

1. PI submits protocol to IACUC Admin Office
2. Protocol previewed by IACUC Admin Office for missing, unclear or obviously incorrect information, resolve with PI
3. Protocol reviewed by IACUC
 - possible outcomes: full approval, provisional approval with modifications, defer, withhold approval
4. Modifications/revisions reviewed by IACUC
5. Full approval = animal orders permitted



Another True Story

- Animal care technician performs end-of-day checks, notices 1 animal in cage is groggy
- Reviews animal's record, discovers surgery earlier that day with entry checked off for post-op analgesics (per protocol) later that evening
- Facility electronic access data and surveillance video cannot identify anyone on that protocol entering facility since early afternoon...

What Can Go Wrong?

- Anything done to animals that's **not** IACUC-approved
- Anything not done to animals that's IACUC-**required**
- Working under an expired protocol
- Working under the wrong protocol
- Outdated drugs & other medical materials
- Inadequate documentation for every surgery, anesthesia, analgesia, treatment
- Leaving an anesthetized animal unattended
- Aseptic technique not followed

Animal Protocol Tips

- Pre-submission
 - Consult with OAR veterinarian for technical details
 - Consult with IACUC Admin Office for format details
- Post-approval
 - Familiarize everyone on the protocol with protocol
 - Submit amendments **before** doing anything different



Help with Lab Animals at FAS

IACUC Admin Office

Contacts:

- Denise Moody, denisemoody@fas.harvard.edu, 617-496-3090
- Ellyn Lane, lane@fas.harvard.edu, (617) 495-1510
- Kathy Meunier, kmeunier01@fas.harvard.edu, (617) 496-4678
- Steve Crowley scrowley@fas.harvard.edu , (617) 495- 3589

Information:

- General questions - iacuc@fas.harvard.edu
- IACUC website - <http://iacuc.fas.harvard.edu/icb/icb.do>
- eProtocol website - <https://harvard.keyusa.net/userLogin.do>



Help with Lab Animals at FAS

Office of Animal Resources

- Steve Niemi, DVM, Director
sniemi@fas.harvard.edu, (617) 384-9576
- Kate Pritchett-Corning, DVM, Senior Clinical Veterinarian
pritchettcorning@fas.harvard.edu, (617) 384-9563
- Mary Ann (“Mimi”) Crowley, Manager of Animal Care
 - mcrowley@mcb.harvard.edu, (617) 496-4603



POLICY ON REPORTING ANIMAL WELFARE CONCERNS

The use of live animals in research and teaching is a privilege that includes a responsibility to report concerns about how animals are treated or if their treatment is in compliance with applicable federal, state, and local laws and regulations and university policies. Any concerns or questions about the care and use of laboratory animals should be directed promptly to any of the following contacts listed below.

In accordance with the University's Whistleblower Policy, the University will protect from retaliation members of the Harvard community who make good faith reports of suspected violations of law or University policy. The University's Compliance Hotline is a resource for members of the Harvard community who are uncomfortable reporting through the recommended contacts and prefer to anonymously report any suspected violations of law or Harvard policy.

University Contacts

- Craig P. Hunter, PhD, Professor of Molecular and Cellular Biology and Chair, HU/FAS Standing Committee on the Use of Animals in Research and Teaching: (617) 495-8309 or craig_hunter@harvard.edu
- Leslie A. Kirwan, Dean for Administration and Finance of the Faculty of Arts and Sciences, Institutional Official: (617) 496-8729 or leslie_kirwan@harvard.edu
- Steven M. Niemi, DVM, Attending Veterinarian and Director, Office of Animal Resources: (617) 384- 9576 or sniemi@fas.harvard.edu
- Denise M. Moody, Director of Research Compliance: (617) 496-3090 or denisemoody@fas.harvard.edu
- Institutional animal care and use committee administrative office: iacuc@fas.harvard.edu
- Compliance Hotline: <https://www.integrity-helpline.com/HarvardUniversity.jsp> or 877-694-2275

Revised 2/10/14





Restoring faith in the research enterprise – a call to action

Malcolm Macleod

Professor of Neurology and Translational Neurosciences

University of Edinburgh

and

Honorary Consultant Neurologist, NHS Forth Valley

**Collaborative Approach to Meta-Analysis and Review of
Animal Data from Experimental Studies**

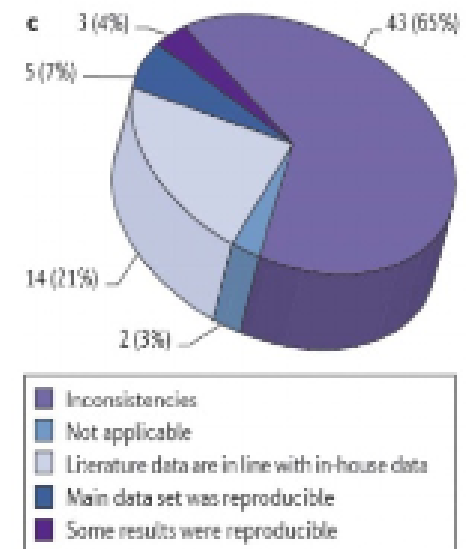
CAMARADES: Bringing evidence to translational medicine



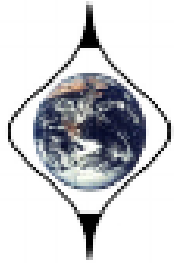
What happens when pharma tries to replicate academic findings?



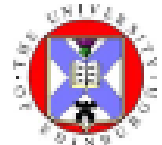
- Bayer, Berlin
- In-house target identification and validation projects over 4 years
- Womens' health, cardiovascular disease, oncology
- 67 projects



Prinz et al, Nature Reviews Drug Discovery, 2011



Most studies are at risk of bias



Disease	Randomisation (%)		Blinding (%)		Power calculation (%)	
	Yes	No	Yes	No	Yes	No
Stroke	37	63	37	63	3	97
Alzheimer's	16	84	22	78	0	100
Parkinson's	16	84	15	85	0	100
Multiple Sclerosis	9	91	16	84	0	100
Pain	12	88	26	74	0	100

Questions?

