

Andrew N. Rowan, D.Phil.
President
April 14, 2020

Why is Animal Research such a Charged Issue?

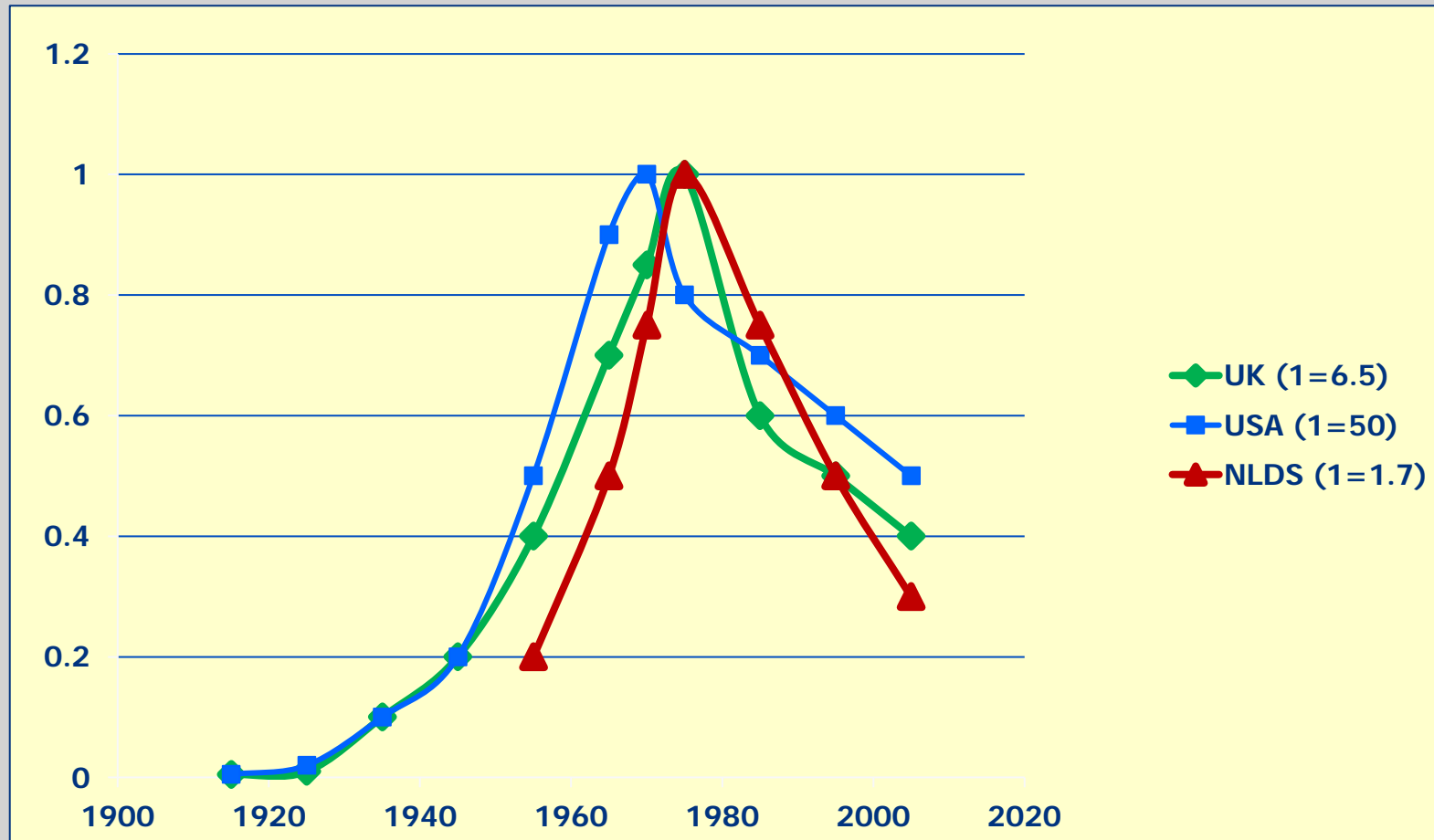


OUTLINE

- **Laboratory animal use**
- **Personal journey & insights from 1976 to today -
Joining FRAME, Feb 1976**
- **RD French (1975) volume – *AV & Med Sci in the
19th century*, Princeton University Press**
- **HSUS 1978-1982**
- **TUSVM 1983-1997**
- **HSUS 1997-2018**
- **Attitudes**
- **Concluding comments**

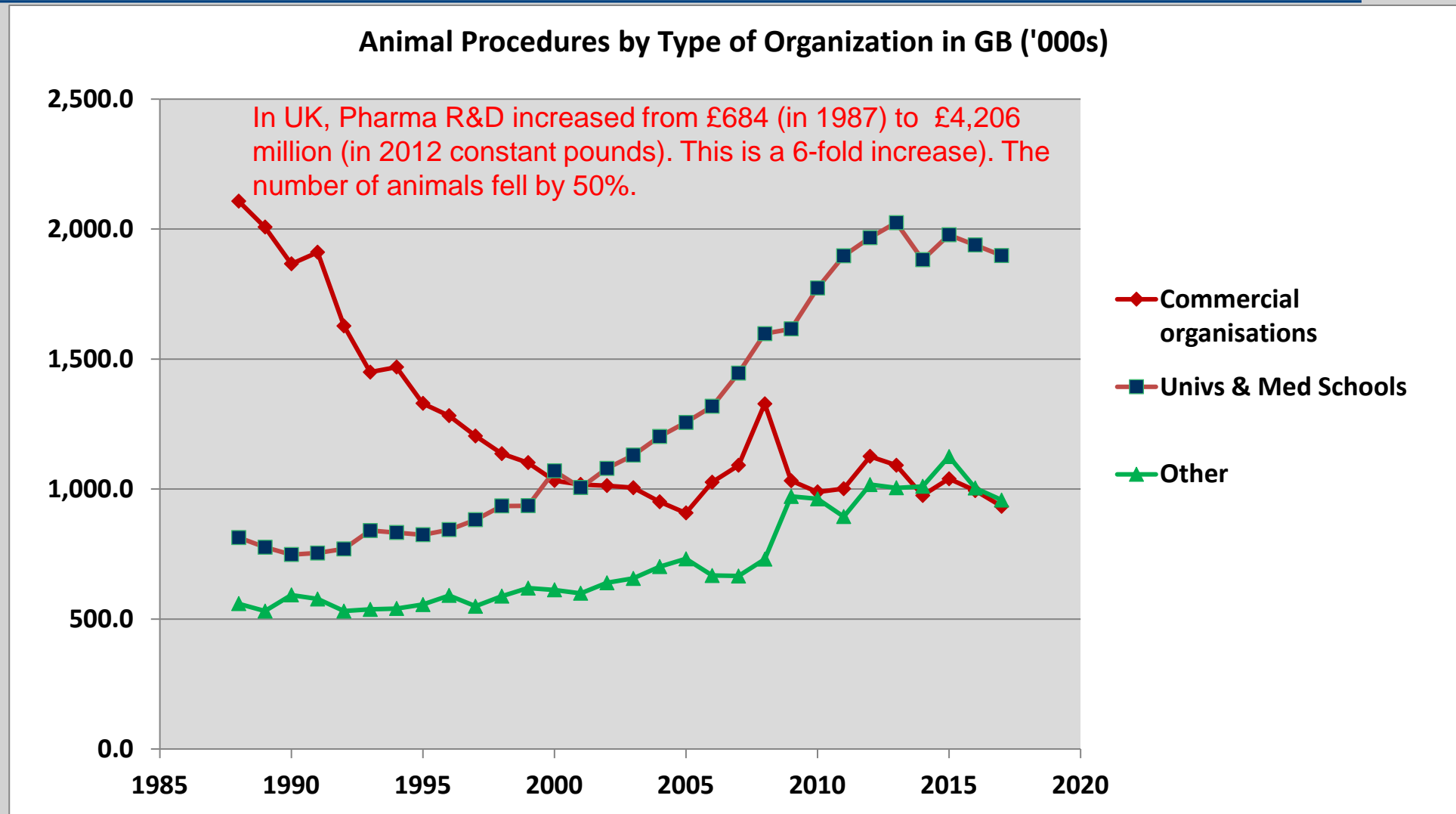
April 14, 2020

UK/USA/Netherlands: Laboratory Animal "Use" Trends



BARS ARE NORMALIZED TO RECORD HIGHPOINT OF ANIMAL USE AS 1.0 - ROUNDED TO NEAREST TENTH

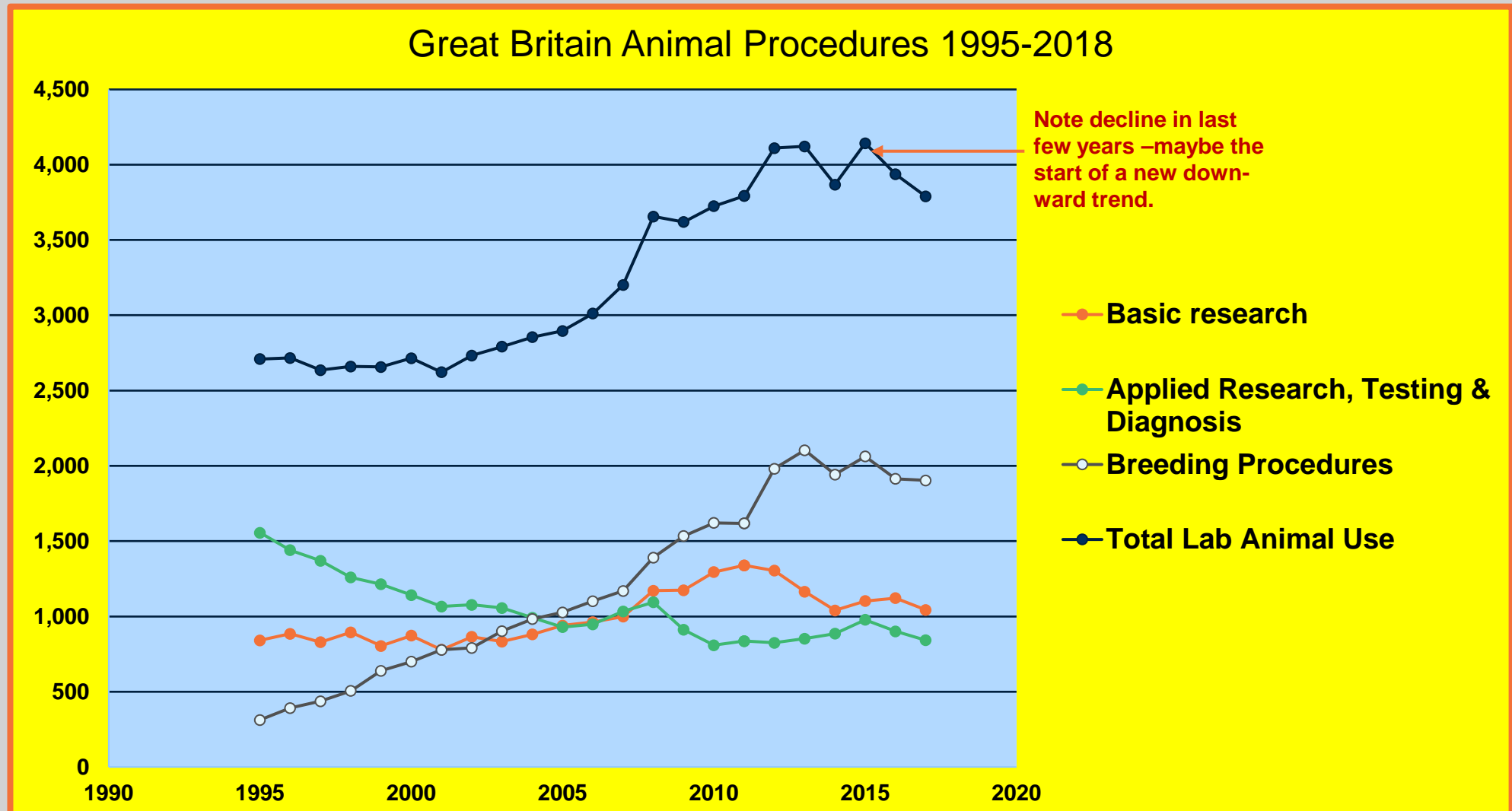
University/Med School vs Corporate Animal Use (GB)



April 14, 2020

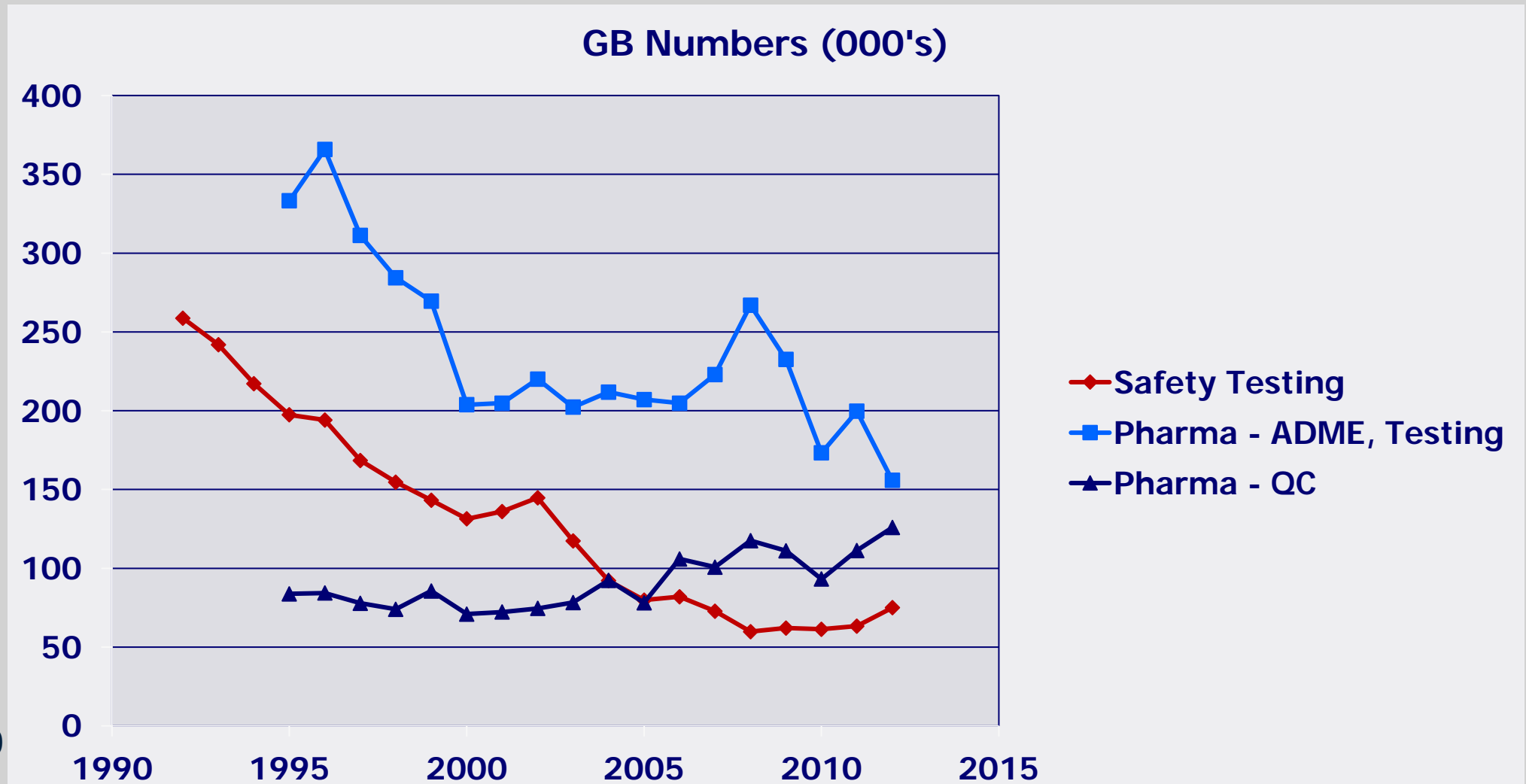
Trends in Types of Research/Use (GB)

(From UK Home Office Annual Reports)



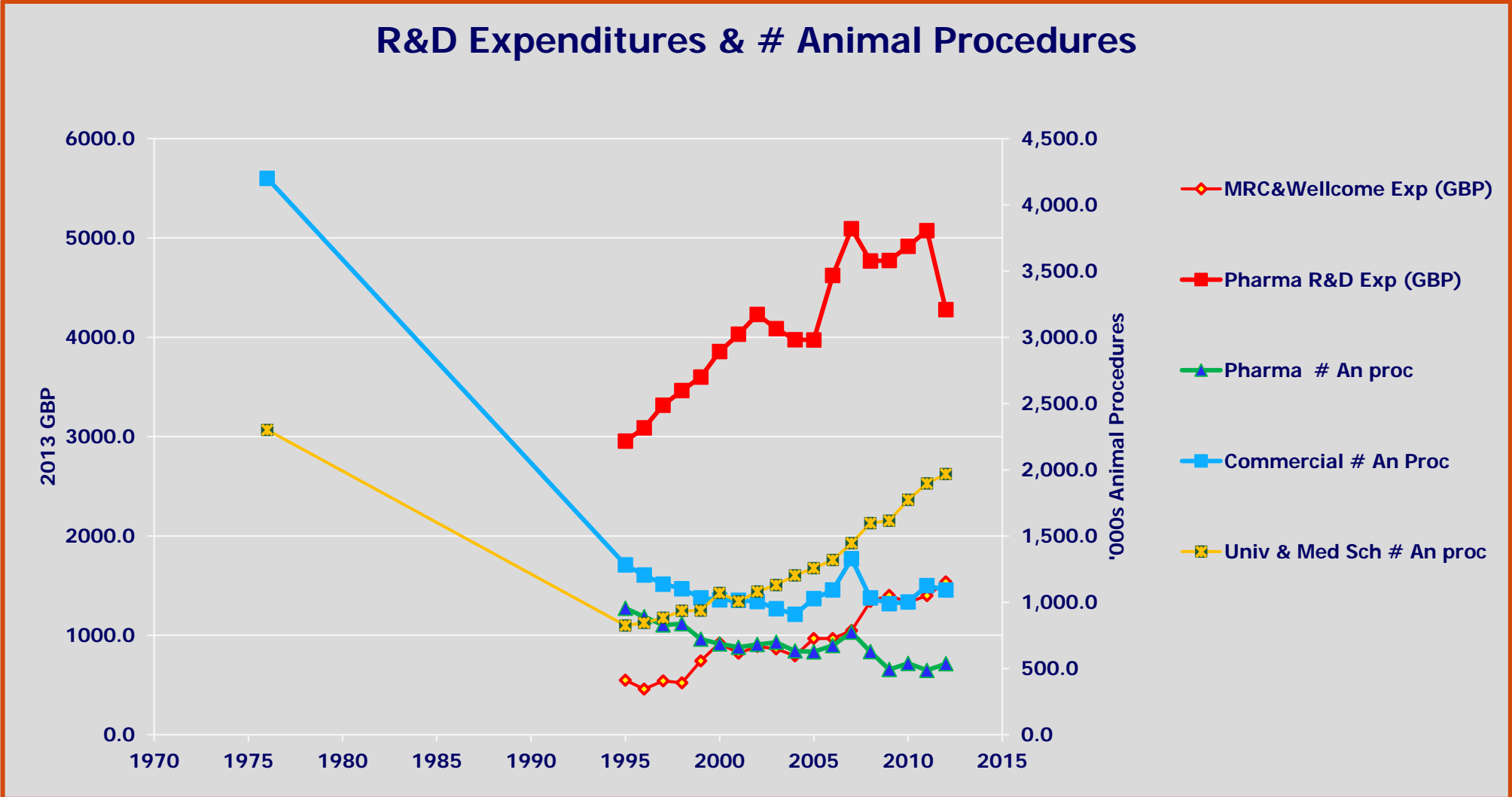
April 14, 2020

Toxicity/Safety Testing Trends



April 14, 2020

Funding & Animal Use (GB)



April 14, 2020

OUTLINE

- Laboratory animal use
- Personal journey & insights from 1976 to today -
Joining FRAME, Feb 1976
- RD French (1975) volume – *AV & Med Sci in the 19th century*, Princeton University Press
- HSUS 1978-1982
- TUSVM 1983-1997
- HSUS 1997-2018
- Attitudes
- Concluding comments

April 14, 2020



FRAME, 1976-1978

- Looking to engage in **science policy**
- FRAME opportunity – decided message not all crazy – interesting challenges
- Early trips to university & corporate labs – each told me other was problem
- Push for “alternatives” center (eventually launched by MRC in 2004)
- LD50 & Home Office case



OUTLINE

- Laboratory animal use
- Personal journey & insights from 1976 to today
- Joining FRAME, Feb 1976
- RD French (1975) volume – *AV & Med Sci in the 19th century*, Princeton University Press
- HSUS 1978-1982
- TUSVM 1983-1997
- HSUS 1997-2018
- Attitudes
- Concluding comments

April 14, 2020

Richard French analysis of AV

(a superb history!)

- RD French
 - *Antivivisection & Medical Science in Victorian Society* (1975), Princeton University Press.
 - Darwinian Revolution – animals now viewed as different in degree, not in kind
 - Anatomists threatened by Physiologists (early 19th cent.)
 - Medical researchers “plan” research that “deliberately” harms animals
 - Public health “a better approach?”
 - Victorian “Sensitive Man” ideal
 - Philosophical trends – expand circle of moral concern – Bentham & clerical protagonists
 - Religious influences – Wesley & Methodists, Cardinal Manning
 - Temperance union in USA
 - Suffragettes & Feminist influence?

(see also AWH Bates 2017, *AV & Profession of Medicine*, Palgrave MacMillan – a focus on the character/virtue of the experimenter)

Some comments from French (1975) & Bates (2017)

- 19th century campaigners against “vivisection” viewed it as a different issue than using animals for meat & leather.
 - The suffering from vivisection was not illegal because it was not a “wanton” cruelty
 - Experiments carefully planned – forethought & purpose
 - Carried out by educated professionals – the sort of people that society expected to engage in exemplary standards of conduct
 - “Expected duty” to cultivate objectivity and to suppress any feelings of compassion was deeply problematic.
 - Some medical professionals argued that anyone prepared to inflict pain on helpless animals must be lacking in empathy.
 - “callous for the sake of greater compassion”
 - Experimenters’ & AV paradox – animals so similar to be good models for humans but were then likely to feel as humans did

The 19th century debate

- Medical research – utilitarian arguments: the predicted benefits to medicine outweighed any suffering & viewed opponents as tender-hearted but profoundly ignorant.
- AV – belabored the point that anyone experimenting on animals was callous and insensitive character traits associated with the lower classes & undesirable in a medical professional.



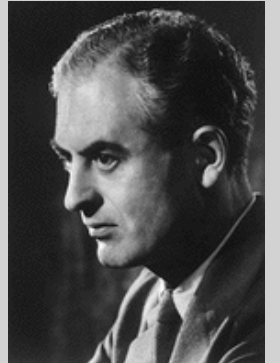
FRAME, 1976-1978

- Toxicity Testing
 - LD50 Review by Home Office - 1976
 - Expert advisor – “the LD50 is the cornerstone of modern toxicology.”
 - Draize test campaign
 - FRAME Toxicity Committee developed out of symposium at Royal Society.

FRAME, 1976-1978

- Medawar Insights

- Sir Peter Medawar – British immunologist, philosopher/commentator on science, Nobel Prize winner (Medicine, 1960)



- In mid-1950s, argued research technol. had advanced to the point that one could focus on “improvements in animal care” as a welfare goal.
- He persuaded the Univ. Fed. on Animal Welfare to launch project that produced - *The Principles of Humane Experimental Technique* by Russell & Burch, 1959.



Medawar & Animal Research

- Ten years later - 1969 speech by Medawar
- “The use of animals .. to enlarge our understanding of nature is part of a far wider exploratory process, ... but this does not imply that we are forevermore, and in increasing numbers, to enlist animals in the scientific service of man. I think that **the use of experimental animals** on the present scale is a temporary episode in biological and medical history, and that **its peak will be reached in ten years time**, or perhaps even sooner. In the meantime, we must grapple with the paradox that nothing but research on animals will provide us with the knowledge that will make it possible for us, **one day, to dispense with the use of them altogether.**”

OUTLINE

- Laboratory animal use
- Personal journey & insights from 1976 to today
 - Joining FRAME, Feb 1976
- RD French (1975) volume – *AV & Med Sci in the 19th century*, Princeton University Press
- HSUS 1978-1982
- TUSVM 1983-1997
- HSUS 1997-2018
- Attitudes
- Concluding comments

HSUS 1978-1982

- Considerable exchange between APOs and Lab Animal community (AALAS, AAALAC, NSMR, ABR)
- Draize campaign launched – connected with Spira
- Taub case and legislative initiatives in Congress – leading to 1985 AWA Amendments – primarily promoting alternatives, control pain & distress, and establish IACUCs for self-regulation
- Maybe things rosier in the fog of memory – but definitely remember more dialogue

OUTLINE

- Laboratory animal use
- Personal journey & insights from 1976 to today
 - Joining FRAME, Feb 1976
- RD French (1975) volume – *AV & Med Sci in the 19th century*, Princeton University Press
- HSUS 1978-1982
- TUSVM 1983-1997
- HSUS 1997-2018
- Attitudes
- Concluding comments

April 14, 2020



TUSVM 1983-1997

- PRIM&R IACUC meetings – launched in 1983 – Rachlin and I developed early programs then handed on to a planning committee that eventually consisted just of lab animal veterinarians. Today, no representatives from APOs attend the PRIM&R Conferences.
- EPA Alternatives project – Dialogue among APOs, Environmentalists, Corporations, Consumer Groups, Government Regulators
- Arluke Ethnography of animal research – occurred over four or so years and led to number of talks and published papers.



TUSVM 1983-1997 Arluke Ethnography

- Reaction of lab techs versus lab animal veterinarians
 - Asked for open commentaries on article
- Ca. 20% of interviewees compared animal experiments to Holocaust
- Uneasiness most common among newcomers; among seasoned workers, most common in animal caretakers and rare among veterinarians and scientists
- For most part, interviewees did not have elaborate moral justifications and appeared “ethically inarticulate”

April 14, 2020

OUTLINE

- Laboratory animal use
- Personal journey & insights from 1976 to today
 - Joining FRAME, Feb 1976
- RD French (1975) volume – *AV & Med Sci in the 19th century*, Princeton University Press
- HSUS 1978-1982
- TUSVM 1983-1997
- HSUS 1997-2018
- Attitudes
- Concluding comments

HSUS 1997-2018

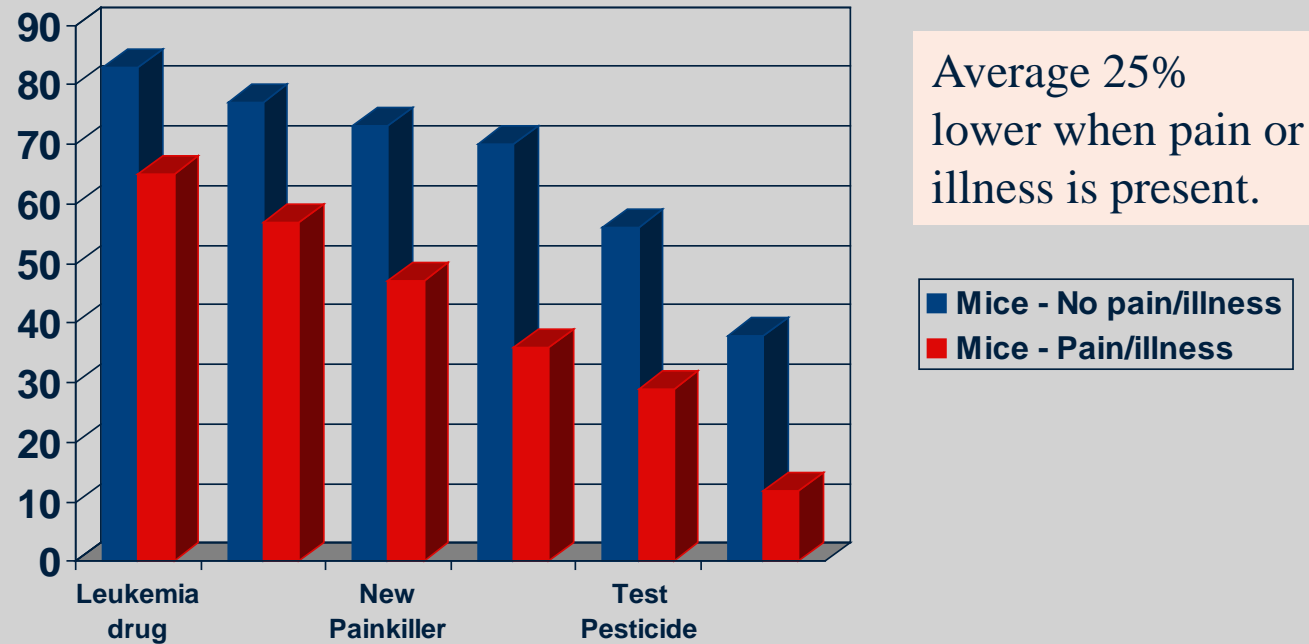
- For one to two years after rejoining HSUS, still invited to speak at universities – then dried up until 2011 invitation from UWisc.
- 2012 PRIM&R IACUC Meeting – asked to participate in a panel on PCRM’s criticism of Ivy League universities. Other panelists said they would not participate and were astonished to learn I was on PRIM&R Board!
- Attempted a dialogue program – HSUS teamed with Charles River to launch at PRIM&R. Criticized because no scientists in group. Eventually fell apart without any results.

OUTLINE

- Laboratory animal use
- Personal journey & insights from 1976 to today
 - Joining FRAME, Feb 1976
- RD French (1975) volume – *AV & Med Sci in the 19th century*, Princeton University Press
- HSUS 1978-1982
- TUSVM 1983-1997
- HSUS 1997-2018
- Attitudes
- Concluding comments

April 14, 2020

ATTITUDES TO ANIMAL RESEARCH UK - 1999



From New Scientist, 22 May, 1999, pp. 26-31

April 14, 2020

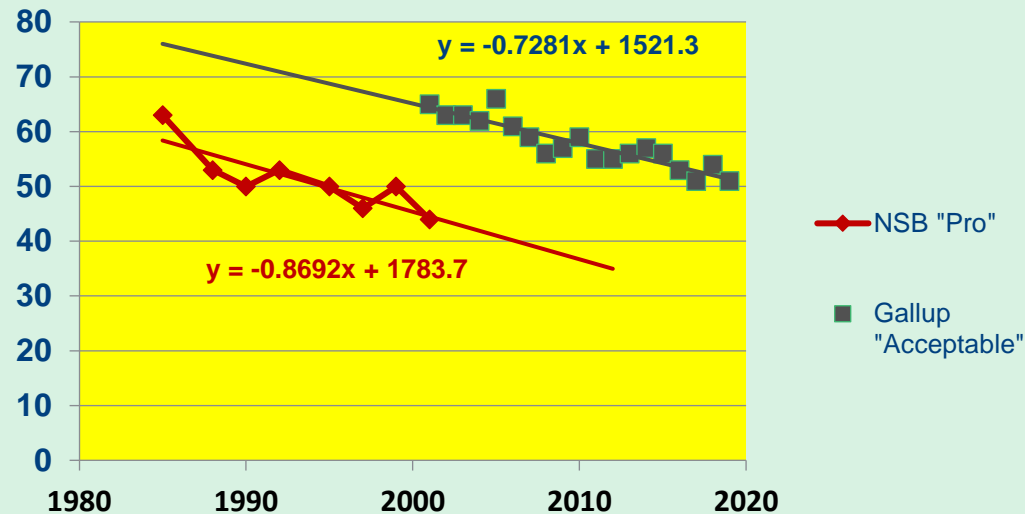
HSUS SURVEY (2001) – Disapprove/Approve Research Causing Pain & Distress

	Severe	Moderate	Little/No
Strongly disapprove	57	37	20
Somewhat disapprove	18	23	13
Total Disapprove	75	60	33
Strongly approve	8	11	30
Somewhat approve	13	23	32
Total Approve	21	34	62

April 14, 2020

Shifting US Public Attitudes

US Public - % Favorable to Animal Research



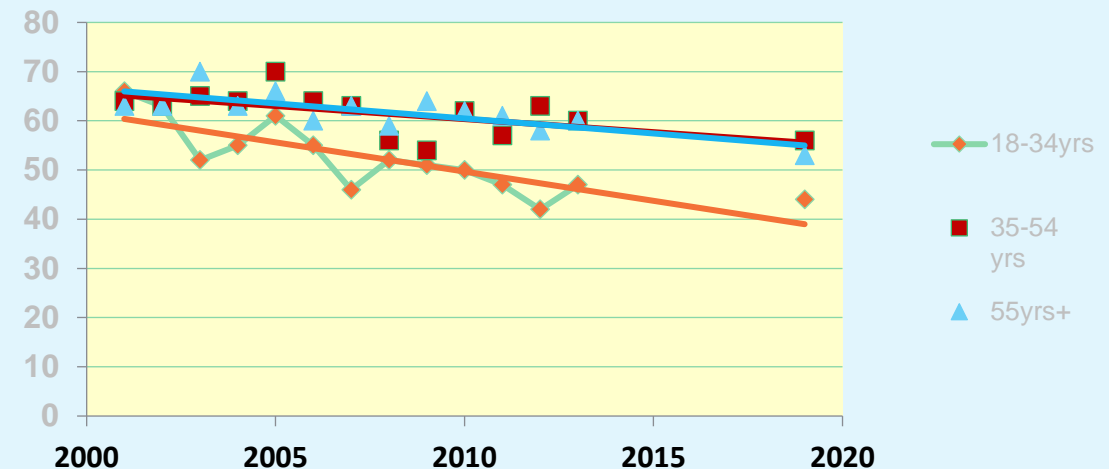
➤ Gallup Surveys

- It is "morally acceptable" to do medical testing on animals - Poll in May of each year. <http://www.gallup.com/poll/1681/Moral-Issues.aspx>

• NSB Surveys

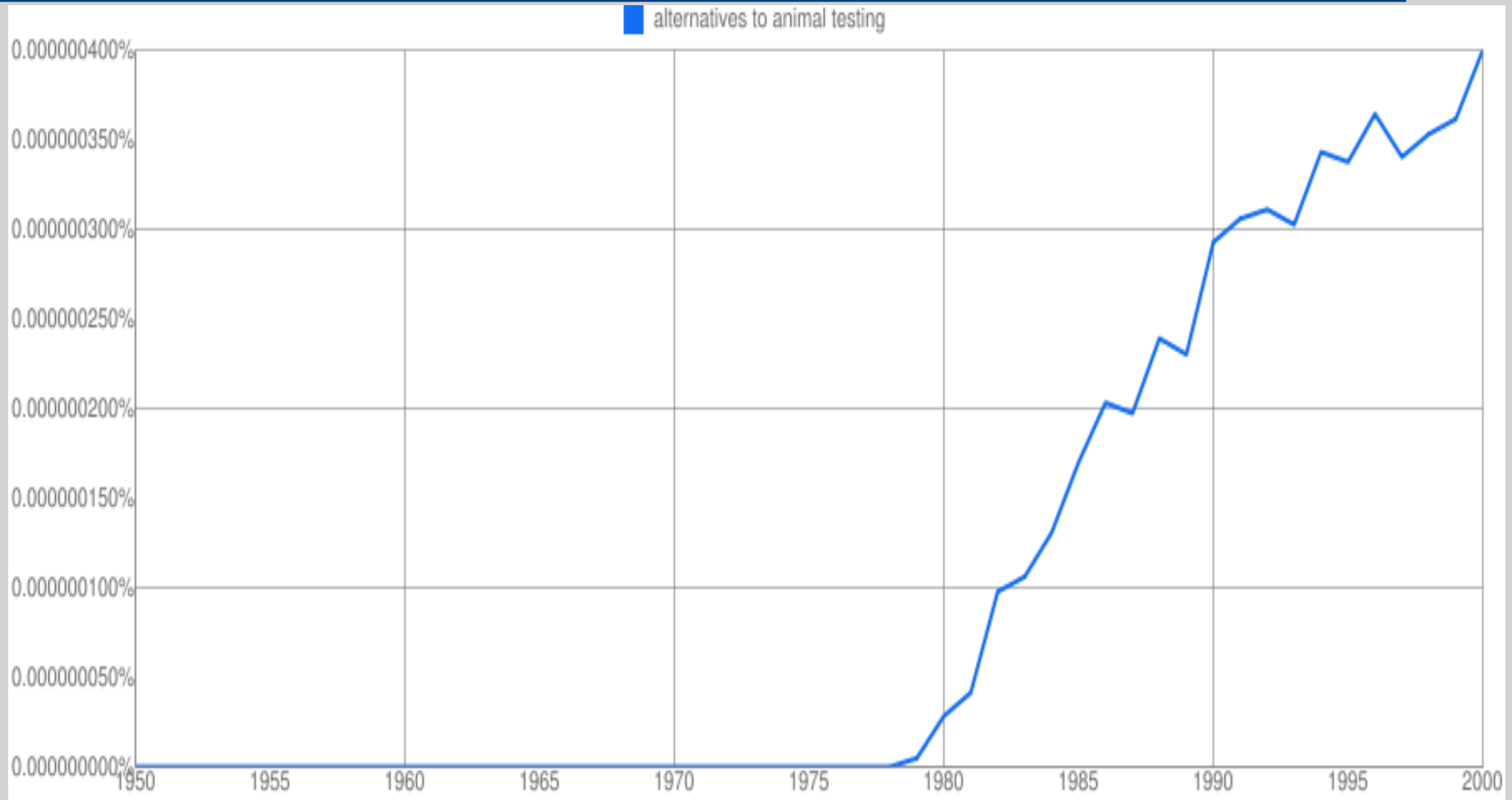
- "Scientists should be allowed to do research that causes pain and injury to animals like dogs and chimpanzees if it produces new information about human health problems." (National Science Board, 2002).

Age Cohorts in Gallup Poll



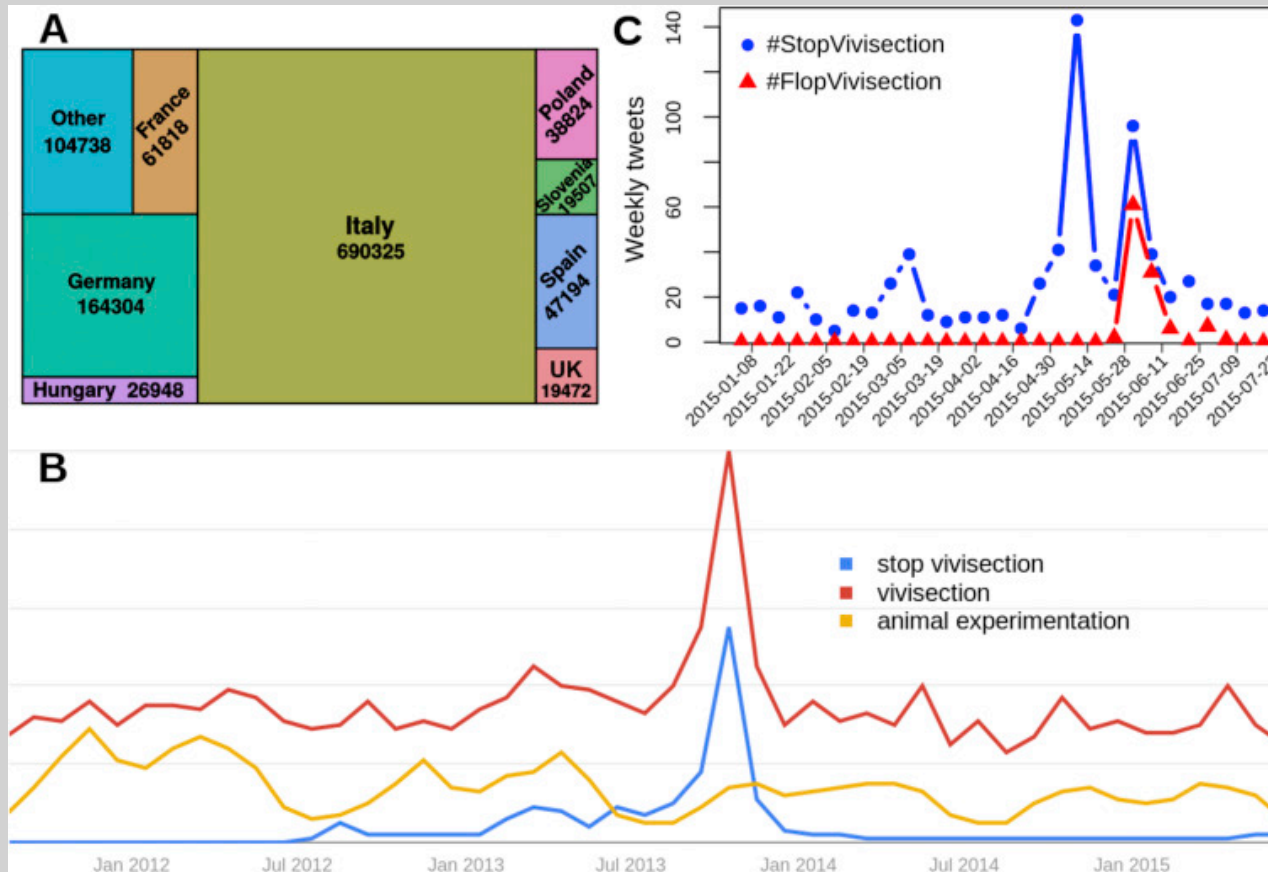
n-Gram - “Alternatives to Animal Testing”

(L’Oreal, Unilever, P&G spent perhaps \$1 billion on Alternatives R&D since 1981. Unilever & P&G now part of political campaign to end the sale of animal-tested cosmetics.)



April 14, 2020

European Citizen's Initiative: "Stop Vivisection"



- Italy Focus

- 19th century – sadistic scientist to 21st century – scientist making money

- From Victorian Era

- Link feminist politics to AV via vulnerable subject
- Victorian “sentiment” challenges utilitarian arguments
- Science secluded – in secrecy by men whose obsession sets apart – Magician not Mechanic

April 14, 2020

OUTLINE

- Laboratory animal use
- Personal journey & insights from 1976 to today
 - Joining FRAME, Feb 1976
- RD French (1975) volume – *AV & Med Sci in the 19th century*, Princeton University Press
- HSUS 1978-1982
- TUSVM 1983-1997
- HSUS 1997-2018
- Attitudes
- Concluding comments

1950 – 2000 Unusual

- In past 420 years, only two periods where science was viewed with favor by public – namely post-Newton (1600-1650) and 1950-2000 (e.g. Vannevar Bush's Endless Frontier)
- Thus emerging from period where science was granted special privileges – greater suspicion in future.
- We are currently experiencing the consequences of too little respect for expertise and recommendations of experts

Can scientists talk to critics?

- They do not understand
- Science is too complex
- Criticism purely emotional
- I could become a target
- What would it benefit?
- Can they ever be satisfied?

Compare 1870 to 2020

Issue	1870	2020
Animal Status	Darwin influence: animals differ in degree	Animal Sentience much bigger issue today
Anatomists vs Exp. Physiol.	Significant issue	Non-issue today
Sadistic researcher	Important trope	Rel. minor today – now profit-seeking scientist
Public Health	Important	Minor issue
Philosophy	Important	Important
Religion	Important	Minor
Feminist infl.	Victorian “sensitive”	Important
Question models	An issue but double-edged	Important development today

April 14, 2020

Animal Model Challenges – Comments by Last 2 NIH Directors

- **Dr Elias Zerhouni:** “We have moved away from studying human disease in humans... We all drank the Kool-Aid on that one, me included. The problem is that it hasn’t worked, and it’s time we stopped dancing around the problem...We need to refocus and adapt new methodologies for use in humans to understand disease biology in humans.”
- **Dr Francis Collins:** “The average length of time from target discovery to approval of a new drug currently averages ~13 years, the failure rate exceeds 95%, and the cost per successful drug exceeds \$1 billion, after adjusting for all of the failures. The use of animal models for therapeutic development and target validation is time consuming, costly, and may not accurately predict efficacy in humans. With earlier and more rigorous target validation in human tissues, it may be justifiable to skip the animal model assessment of efficacy altogether. www.ScienceTranslationalMedicine.org 6 July 2011
- NCATS Established at end of 2011.

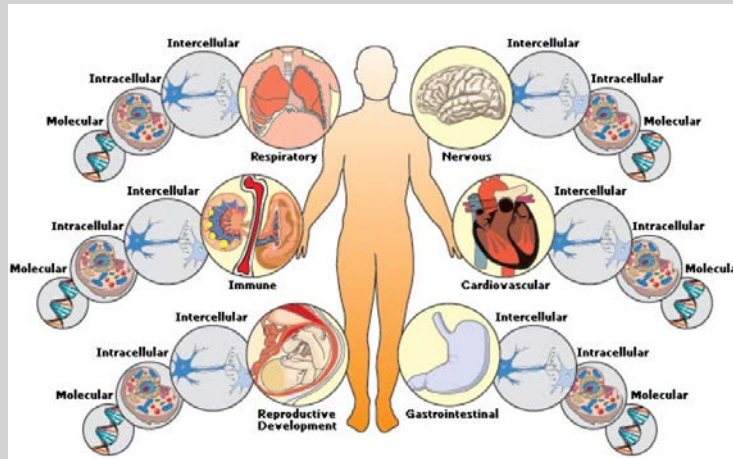


April 14, 2020

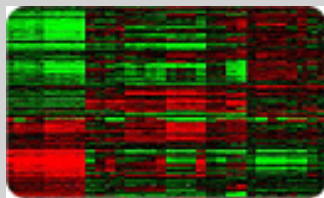
Medawar's "Art of the Soluble"

New tools make new approaches possible.

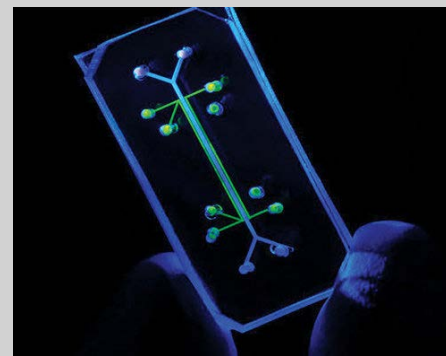
Systems biology



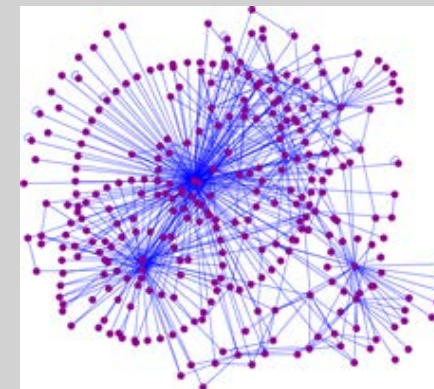
Ultra-HTS



Omics, high-content



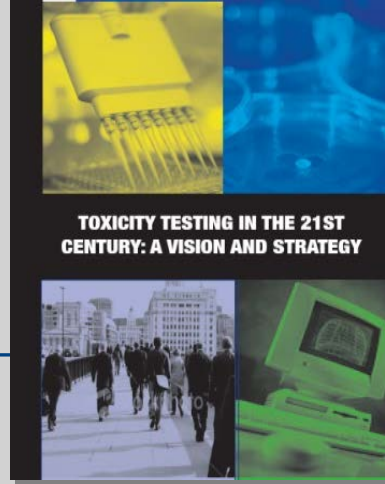
Organ-on-a-chip



bioinformatics

US National Academies Report: 2007

- Commissioned by US EPA
- Presentations & workshops overcome initial scepticism
- Government launched programs (e.g., Tox21, ToxCast, NextGen)
- “21st Century Toxicology” – Human Toxicology Project (Consortium)
- SoT’s 2014 FutureTox Symposium – talked about **when** animal tests will be replaced – not **if**.
- **UK announces closure of two major GMO Mice units in 2019**



DARPA/NIH: \$140 million for “Human-on-a-chip” Technology

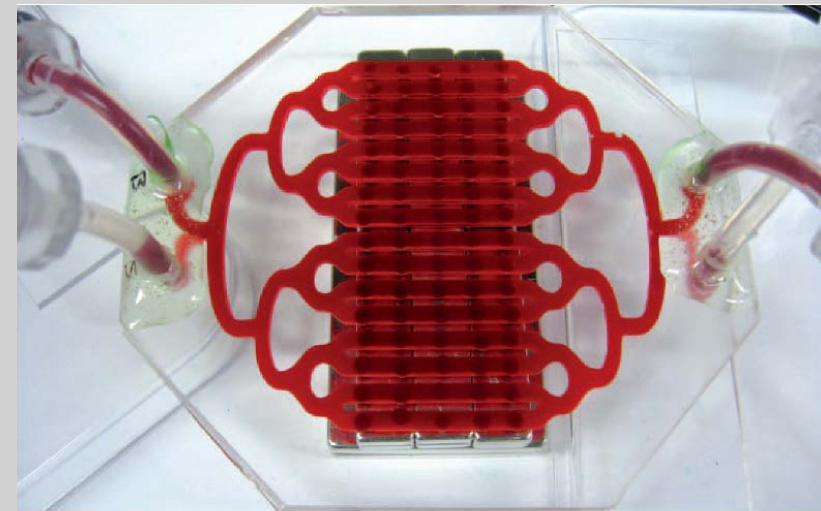
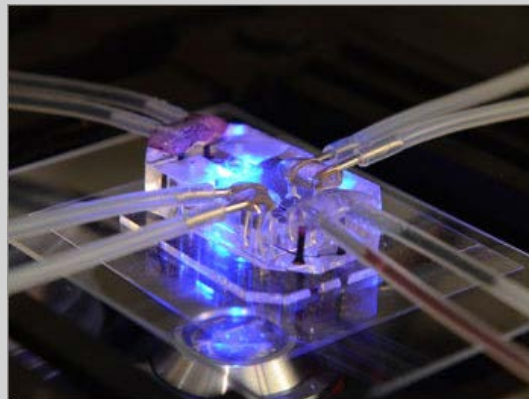
TECHNOLOGY FEATURE

A LIVING SYSTEM ON A CHIP

For years, scientists have struggled to reconstruct tissues and organs by combining cells and nanotechnology. These devices are now edging from cool concept to practical application.

<http://wyss.harvard.edu/viewpage/265>

“... replace animal testing in drug development,...”

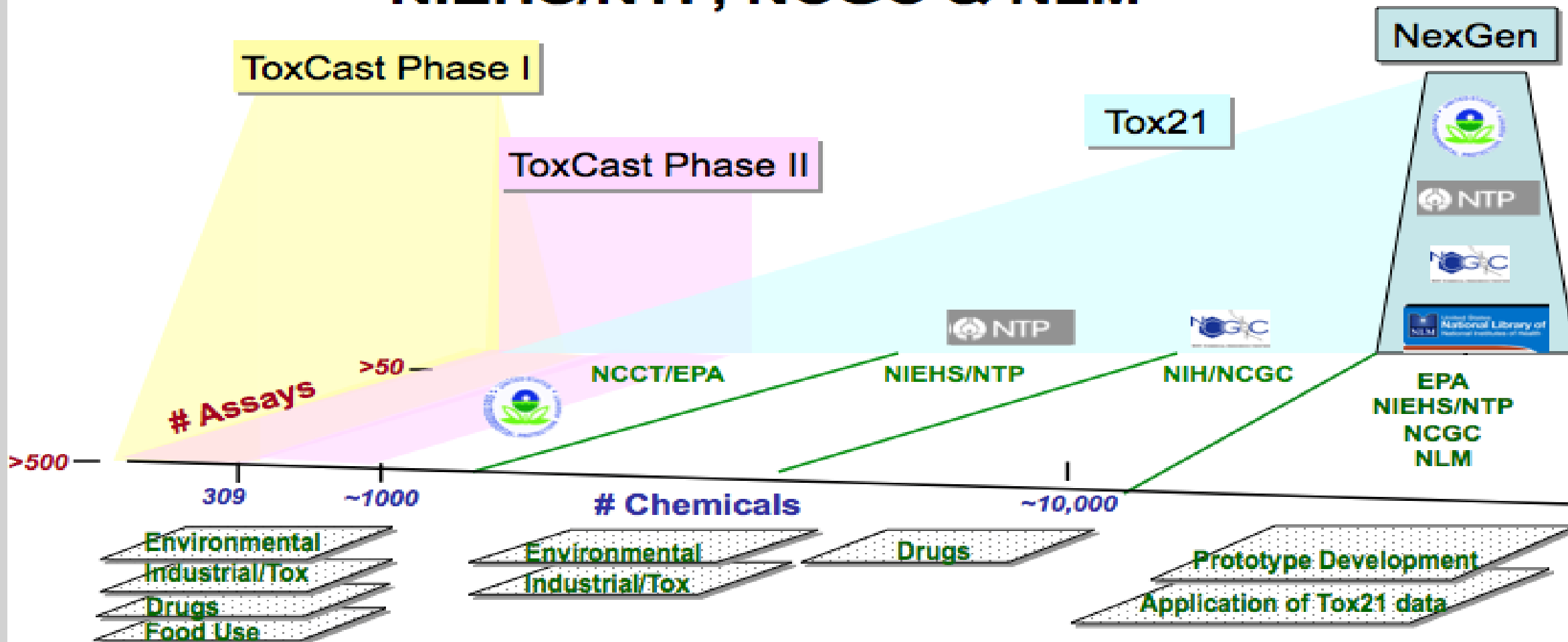


Researchers are making miniature versions of organs such as the spleen (above). Such organs on chips could speed tests of drugs and toxicity.

US EPA "NexGen" Initiative

S. Barone, EPA NCEA, Regional Risk Assessors Conference, June 9, 2010

A Collaboration: EPA Labs/Centers, NIEHS/NTP, NCGC & NLM



3R Initiatives – As of 2012

- EPAA & EU initiative on alternatives (\$10-20 mill/a.)
- EU-COLIPA project on chronic tox (\$10 mill/a.)
- AXLR8 – EU Coordination Project (ended 2012)
- ToxCast (EPA) & NIH/NTP (\$15-20 million a year)
- MLI Initiative (\$70 million a year)
- TRND Initiative (\$24 million a year)
- NTP (\$130 mill/a. – part on HTS & other technologies)
- FDA & NIH Reg. Science Initiative (\$2.25m/ann.)
- HTP Consortium (HSUS/HSI, Corporations & Hamner)
- **Ca. \$200 mill/a. already being spent**

The Power of the New Approach

- *For one-fifth the cost of a single rodent cancer test (that takes 3-4 years to complete), NIH can screen 1,408 chemicals in 200 different cell tests, at 15 different concentrations in 2 weeks .*



- *Produces 10s of millions times the data generated from animal studies – **and already about as relevant/useful!!***
- *Much needs to be done to apply new “pathways” and “translational sciences” approaches but potential already apparent .*

April 14, 2020

Sturla et al, 2014 Chem. Res. Toxicol.

<http://pubs.acs.org/doi/pdfplus/10.1021/tx400410s>

- “We stand at the edge of an unprecedented transformation in the conduct of toxicological evaluations. “ **(and biomedical research)**
- **Enabled by several factors**
 - “the increasing power and availability of molecular measurement tools able to probe ... inside organisms”
 - “the increasing affordability of high-throughput and high-content characterization approaches that can be applied to thousands of chemicals in short time periods rather than the chemical-by-chemical approach that involves thousands of animals and perpetual high costs and years of duration”
 - “the increasing computational power, data-storage capacity, and information-management tools now available”
 - “the acceleration in the development of adequate in vitro test systems to complement and gradually replace animal models”
 - the “significant resource investment by governments throughout the world”

Implications of New Approach

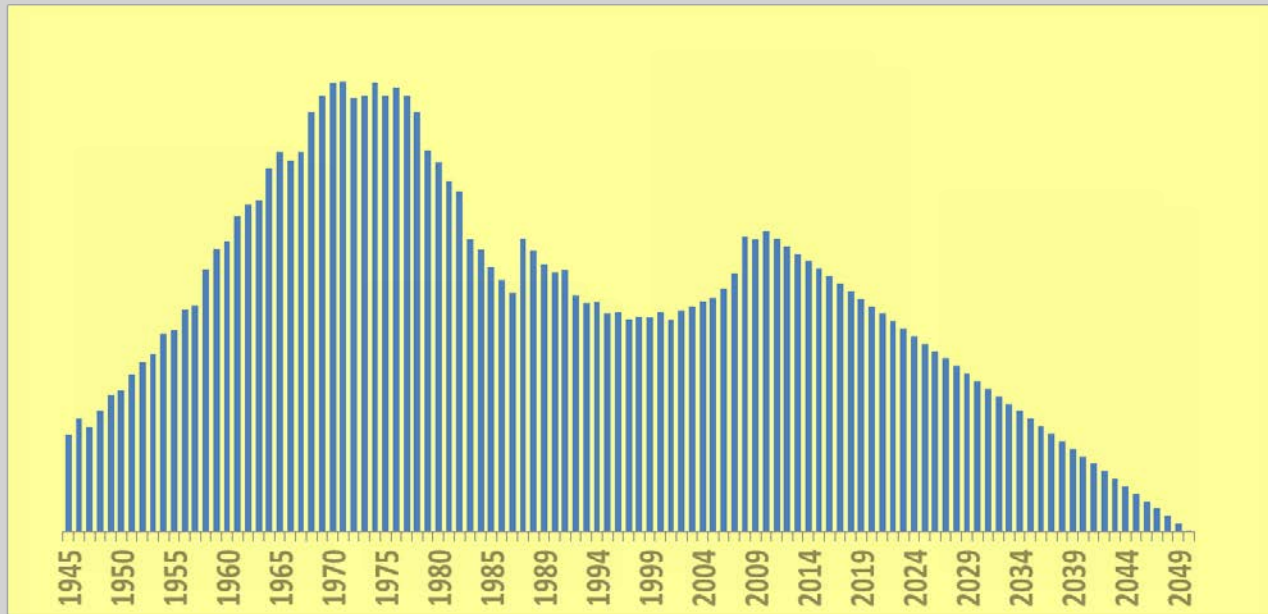
- Safety assessment to be made:
 - Of a much larger number of substances and mixtures than is currently possible (10,000s per year vs 1-200)
 - More rapid, efficient, and cost-effective than at present (answers reached in weeks vs. years, at a cost 1000-fold lower)
 - In systems that are more relevant to humans
 - Using fewer or no animals
- But challenges because:
 - animal testing is a legal requirement in most regulated product sectors
 - In basic research difficult to deliver “off the shelf” alternatives to animal experiments.
 - Big geo-political differences across globe

Thinking Big – Replace most/all animal studies

President John F. Kennedy

Delivered in person before a joint session of Congress
May 25, 1961

“I believe we possess all the resources and talent necessary. But the facts of the matter are that we have never made the ... decisions or marshaled the ... resources required for such leadership. We have never specified long-range goals on an urgent time schedule, or managed our resources and our time so as to ensure their fulfillment.”



WellBeing International

www.wellbeingintl.org

