Getting closer to non-animal approaches in science?

Lessons from around the world



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Animal use in Canadian laboratories 1975 – 2016



SOURCE: ANNUAL ANIMAL DATA REPORTS - CCAC.CA





Insanity is repeating the same mistakes and expecting different results."







Is it time to retire the 3Rs and change the paradigm?



 $\mathsf{B}^{\mathsf{Z}}\mathsf{\Box}\mathsf{M}\mathsf{E}\mathsf{D}^{\mathsf{Z}}$



'Animal models' attempt to recreate human disease artificially in the laboratory



High failure rates for candidate drugs that appear safe & effective in animals



Data: USFDA, PhRMA

"Most of this failure is due to the limited predictive value of preclinical models."

CREDIT: ASIA NEWS

PLENGE ET AL. NAT REV DRUG DISCOV. 2013; 12: 581-94; KOLA & LANDIS. NAT REV DRUG DISCOV. 2004; 3; 711-15





HSI's BioMed21 Collaboration » critical reviews & strategic roadmaps



Autism Spectrum Disorders (Muotri, 2015)



Funded reviews have identified poorly predictive models & suggested novel roadmaps

- Alzheimer's disease
- Amyotrophic lateral sclerosis
- Asthma
- Autism spectrum disorder
- Autoimmune disorders
- Cardiovascular disease
- Diabetes type II
- Liver disease
- Parkinson's disease
- Tuberculosis
- Zika virus

... others in development



International workshop series

- Europe (Brussels, Dec. 2015)
 - Langley et al. Drug Discov. Today 2017
- Latin America (Rio de Janeiro, May 2017)
 - Triunfol et al. Drug Discov. Today 2018
- North America (Washington, June 2017)
 - Marshall et al. Drug Discov. Today 2018



"We have moved away from studying human disease in humans... The problem is that **it hasn't worked**, and it's time we stopped dancing around the problem... We need to refocus and **adopt new methodologies** for use in humans, **to understand disease biology in humans**."







Modern, human-relevant tools » organ-on-a-chip



CREDIT: NIH / NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES





CREDIT: WYSS INSTITUTE / HARVARD UNIVERSITY



Modern, human-relevant tools » multi-organ human-on-a-chip





CREDIT: TISSUSE / TECHNICAL UNIVERSITY OF BERLIN



Modern, human-relevant tools » high-throughput / high-content in vitro



CREDIT: NIH / NATIONAL CHEMICAL GENOMICS CENTER







Modern, human-relevant tools » understanding complex disease biology





CREDIT: HUMANTOXICOLOGYPROJECT.ORG



Modern, human-relevant tools » computational modeling





What's driving animal use? » regulatory testing







Addressing the problem » 1 test / regulation / country at a time



Deletion of 1-year dog test

- First scientific redundancy analysis published in late 1990s
- Test requirement deleted in US, India, EU & Canada between 2007-16
- Japan & S Korea took action in 2018
- Brazil is the last major market to move
- → 20+ years to remove 1 test in 1 industry sector!



Addressing the problem » 'mandatory alternatives' laws

European Union

 Requirement to use available alternatives established in 1986 Animal Experiments Directive and subsequent regulations

Brazil

 2014 CONCEA Resolution establishes 5-year mandatory phase-out for animal tests with government-recognized replacement

United States

• 2016 revision of Toxic Substances Control Act introduced unprecedented animal protective language in a US national chemical law

South Korea

 2017 'K-REACH' Reform Bill introduced established first-in-Asia animal protective language in a national chemical law



South Korean politicians propose K-REACH animal testing reduction principles

Environment ministry sees amendment as positive

12 October 2017 / Alternatives assessment & substitution, K-REACH, South Korea, Test methods





What's driving animal use? » basic & biomedical research







Addressing the problem » redirect funding to human-based models

Eliminating poorly predictive models	Developing new improved models	Replacing animals with better <i>in vitro</i> & <i>in silico models</i>	Alternative tools
 Parkinson's Disease Diabetes Asthma Chronic Pain Schizophrenia Depression Autism 	 Parkinson's Disease Diabetes Asthma Chronic Pain Schizophrenia Depression Autism 	 Diabetes Cancer Schizophrenia Chronic pain Drug safety Parkinson's Disease 	 Biomarkers Novel cell lines 2D and 3D cell cultures Imaging Computation Simulation Pooling & novel analysis of existing data

Addressing the problem » redirect funding to human-based models

116th CONGRESS 1st Session



To amend the Public Health Service Act to ensure that non-animal methods are prioritized, where applicable and feasible, in proposals for all research to be conducted or supported by the National Institutes of Health, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

February 13, 2019

Ms. ROYBAL-ALLARD (for herself and Mr. CALVERT) introduced the following bill; which was referred to the Committee on Energy and Commerce

A BILL

- To amend the Public Health Service Act to ensure that non-animal methods are prioritized, where applicable and feasible, in proposals for all research to be conducted or supported by the National Institutes of Health, and for other purposes.
- 1 Be it enacted by the Senate and House of Representa-
- 2 tives of the United States of America in Congress assembled,

3 SECTION 1. SHORT TITLE.

4 This Act may be cited as the "Humane and Existing
5 Alternatives in Research and Testing Sciences Act of
6 2019" or the "HEARTS Act of 2019".

Humane and Existing Alternatives in Research & Testing Sciences (HEARTS) Act acknowledges that:

- "A great deal of research that has utilized animal studies yielded no benefits for humans"
- "Oversight is generally week and little heed is paid to the use of non-animal methods or the avoidance of duplication"
- A system of active incentives is needed to encourage researchers to utilize humane, costeffective, and scientifically suitable non-animal methods"



Bringing it all together » adopting strategies that work







