

THE HUMANE SOCIETY
OF THE UNITED STATES

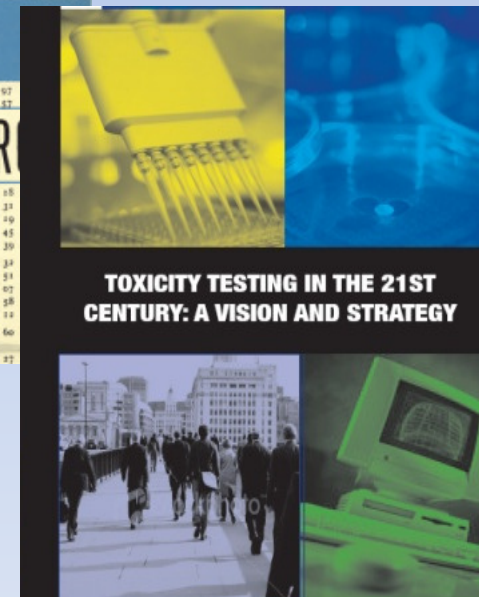
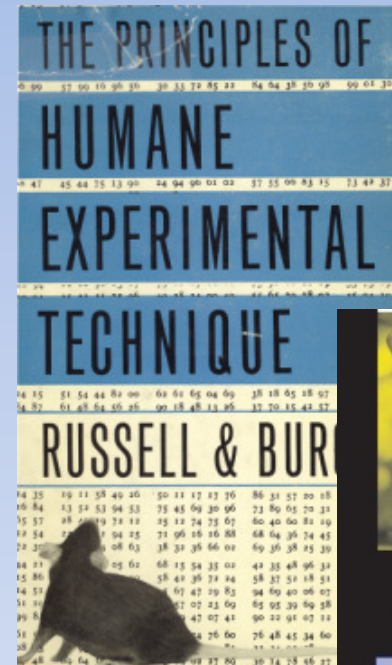
Animal Testing & Alternatives: *What Animal Welfare Organizations in the United States Expect in the Future*

Martin Stephens, Ph.D
HSUS Vice President for Animal Research Issues

20th Anniversary of ZEBET at the BfR
Berlin, October 26-27, 2009

Presentation Outline

- Take-home message
- HSUS
- HSUS + ZEBET
- HSUS' perspective on the Way Forward



Resolution on 21st Century Toxicology Adopted by Animal Protection Organization at the WC7

*Call for a new approach to toxicity testing & risk assessment
to move away from animal use & better protect
health, safety & the environment*

Rome, August 2009

Whereas animal-based toxicity tests are often decades old, time-consuming, expensive, seldom formally validated, of questionable reliability and relevance scientifically, and responsible for the suffering and death of millions of animals annually;

Whereas the scientific limitations of animal tests are clearly evident in the current 92% failure rate for new drugs (due to safety concerns and inefficacy observed in human trials yet unforeseen in animal studies¹), while practical considerations preclude reliance upon animal tests to clear the backlog of tens of thousands of existing chemicals to be adequately safety tested;

Whereas recent years have seen unprecedented scientific and technological advances, which hold great promise for advancing the scientific foundation of toxicity testing and risk assessment²;

Whereas leading scientists from Europe and North America have called for a move away from conventional animal tests in favour of a “21st century” approach based on sophisticated cellular and computational methods that assess chemicals’ effects on critical biological processes³;

Whereas available human data, e.g. from clinical drug trials, represent the “gold standard” for human safety assessment and if made widely available would further the development and evaluation of 21st century approaches.

Therefore, be it resolved that the undersigned call upon governments, regulators, corporations, academic scientists, public interest NGOs, and other stakeholders to actively and cooperatively support a global transition to a humane 21st century approach³ in toxicological risk assessment in the interests of generating data more relevant to evaluate health risks to people, generating data on a larger number of substances and mixtures, reducing testing costs, while progressively replacing animal testing.

¹ US FDA (2004). *Challenge and Opportunity on the Critical Path to New Medical Products*. Washington, DC.

² EPAA (2008). *New Perspectives on Safety – Workshop Report*. Brussels.

³ US National Research Council (2007). *Toxicity Testing in the 21st Century: A Vision and a Strategy*. Washington, DC.





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About The HSUS

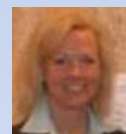
- Founded in 1954
- 400+ full time staff
- 2009 budget: \$134M
- 11M members & supporters
- Address full spectrum of AP issues
- No administrative connection to...
 - US government
 - local humane societies
- HSUS family of organizations includes...
 - Humane Society International (HSI)
 - Humane Society Legislative Fund (HSLF)



HUMANE SOCIETY
INTERNATIONAL



HUMANE SOCIETY
LEGISLATIVE FUND



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HSUS & Animal Experimentation

- The HSUS wants to see the day when animals are no longer used in harmful experimentation
- Advocate for the 3Rs
- Have a long history of building partnerships with other stakeholders
- Reject violence and harassment as tactics



Examples of HSUS's [Co-]Contributions to the Three Rs



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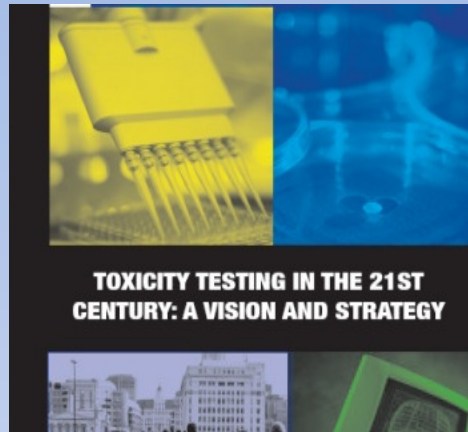
ZEBET & HSUS



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The Beginnings of a Revolution



... envisions a not-so-distant future in which virtual routine toxicity testing would be conducted in human cells or cell line in vitro by evaluating cellular responses in a suite of toxicity pathways using high-throughput tests, that could be implemented with robotic assistance. --Andersen & Krewski (2009)



TOXICOLOGY

Transforming Environmental Health Protection

Francis S. Collins,^{1*} George M. Gray,^{2*} John R. Bucher^{3*}

We propose a shift from primarily in vivo animal studies to in vitro assays, in vivo assays with lower organisms, and computational modeling for toxicity assessments.



“Animal testing won’t disappear overnight, but the agencies’ work signals the beginning of the end.”

--E. Zerhouni, NIH Director (USA Today, 2/15/08)



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Is the NRC Vision **The Holy Grail*** for Three Rs in Toxicology?

- Vision for complete replacement
- Unifying conceptual framework
- “Vindication” of claims about
 - Limitations of animal testing
 - Concordance between good science & Three Rs
- Toxicity testing:
 - 8-15% of animal use
 - Several million animals
 - Disproportionate share of severe suffering



* “any greatly desired and sought-after objective; ultimate ideal or reward” (Dictionary.com)

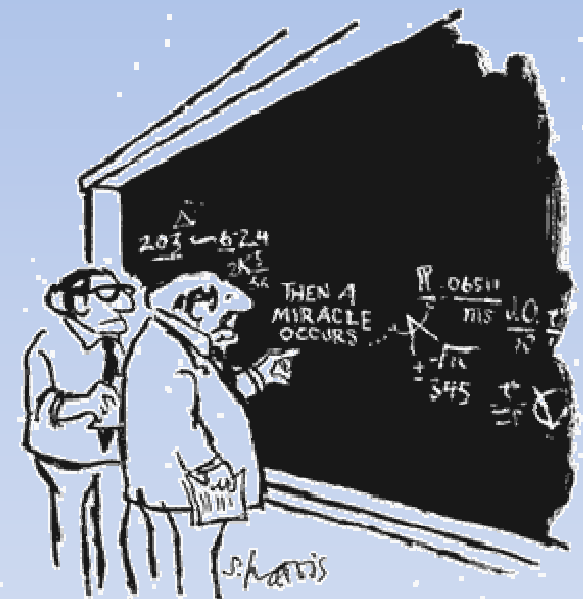
Encouraging signs

- Tox 21
- EPA Strategic Plan
- Attention at ...
 - 7th World Congress
 - Society of Toxicology
- Related efforts
 - ASAT(Netherlands)
 - EPAA



Challenges to Implementation

- Long-term process
- Expensive
- Vision & strategy not fully elaborated
- “Validating” a completely new approach
- Difficulties with supplanting an entrenched system

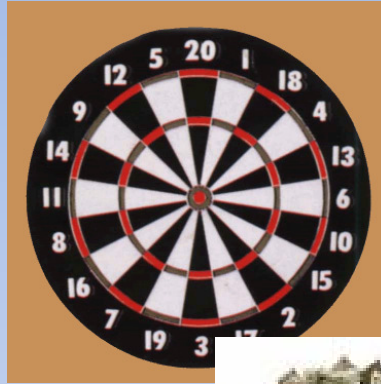


"I THINK YOU SHOULD BE MORE EXPLICIT HERE IN STEP TWO."



Implementing the NRC Vision

- Strategic focus
- Adequate funding
- International cooperation



I. Strategic Focus

- We need a big biology project a la Human Genome Project
 - “Human Toxicology Project”
- We’re aiming to predict outcomes in humans
 - Not in high dose animal studies
- We need high-quality human data
 - Pfizer – EPA agreement
- Progressive elaboration and implementation
 - Modular approach with proof of principle

II. Funding

- EU government
- US Government
- Industry/Trade Associations

III. International Coordination

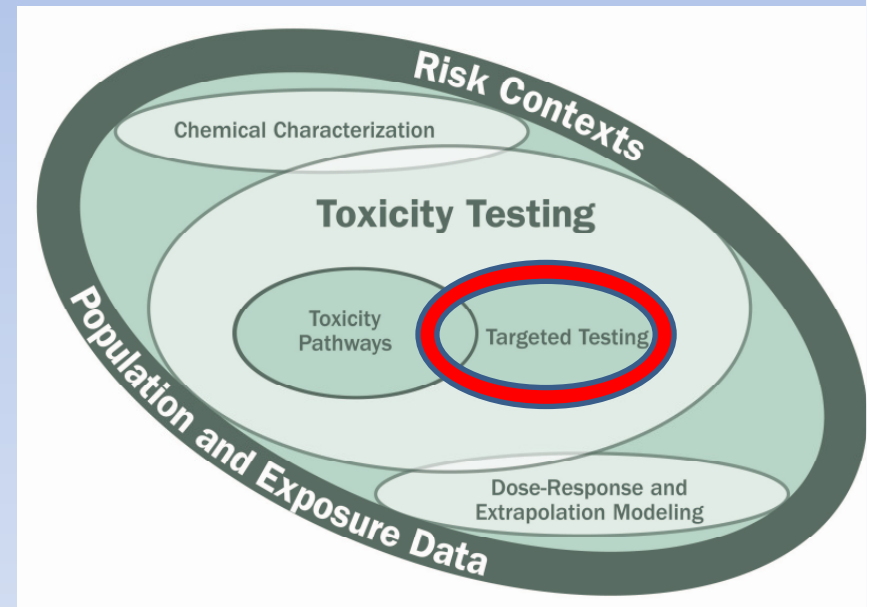
- Within EU
 - AXLR8
- Within US
 - Tox21
 - ToxCast
- Transatlantic
 - CAAT & T4
 - OECD?

Concerns with Implementation

- Implementation in animals first??
 - “We need to learn how to walk before we can run”
- Lip service to “NAS vision” in 21st century tox
- No coordinating entity in charge
- “Come back in 20 years when you’ve sorted it all out”
- Tox21 valuable but not full story
- Top-down versus bottom-up approaches

Targeted Testing (TT): Changing to Fit the Times

- Short term:
 - Limited pathway testing (PT)
 - Extensive TT, mostly in vivo & integrated testing strategies (ITS)
- Medium term:
 - Balance between PT & TT
- Long term:
 - Mostly PT
 - TT itself mostly in vitro
 - organotypic models, etc.



Human Toxicology Project Consortium



- Aims:
 - Facilitate global implementation of the recommendations of the NRC report
 - Promote dialogue, information sharing, and establishment of an R&D roadmap
 - Lobby for, coordinate, & provide resources for transatlantic efforts**
 - Engage in collaborative outreach to all sectors
 - Urgently develop a targeted research program to jumpstart the transformation**
- Current partners:
 - Industry: Dow, Exxon-Mobil, Johnson & Johnson, Procter & Gamble, Unilever
 - NGOs: HSUS
 - Research Institutions: Hamner

The **AXLR8** Project

- HSI is the driving force behind a forthcoming EU FP7 Coordination Action
 - 3.5 year, >550,000€ project aimed at laying the groundwork in Europe for a transition toward a mechanistically-driven approach in toxicology
 - **Key functions:**
 - Coordinating the work of EU-funded 3Rs research projects through annual scientific workshops (including transatlantic participation)
 - Guiding future EU research/funding priorities
 - Promoting active engagement by regulatory authorities & other stakeholders
 - **Partners**
 - Free University of Berlin
 - VITO

AltTox.org: Website and Interactive Forums Devoted to Non-Animal Testing Methods

- Designed for professionals in industry, government, academia & NGOs
- >5,000 visitors per month to the website
- >200 registered forum users
- ~ 50 essays written on the “The Way Forward” by invited experts in various fields
- Managed by The HSUS and Procter & Gamble



Other Issues

- Work to discourage US complaint at WHO against Cosmetics Directive
- Ensure the relevant sector-specific regulations require full use of available 3Rs methods and include scope for '21st century' approaches
 - E.g. TSCA, antimicrobials/biocides
- Strengthen public policy frameworks mandating acceptance and use of available, valid 3Rs methods
 - E.g., ICATM



Thank You!

For further information, contact:

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