Measuring Success

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All stakeholders should endeavor to identify <u>appropriate metrics</u> for prioritizing activities, monitoring progress, and measuring success.

- A challenge faced by all 3Rs efforts, including those conducted internationally, is determining the actual impact on the stated objective, whether it be reducing animal numbers or improving human relevance. The difficulty of measuring the impact on animal usage, in particular, is exacerbated in the United States due to limitations imposed by the Animal Welfare Act.

- Despite these difficulties, agency-specific mechanisms often exist that can be used to estimate the impact of a given activity, such as tracking the number of waivers granted for a particular animal test.

- In order to assess the impact of this national strategy, effective mechanisms need to be created to track progress and identify objective criteria for measuring success.

Common Approaches

- # animals used by industry
- # animals used for tests submitted to agencies
- # methods approved

US legal requirements for documenting animal use by species, number and test type

Animal Welfare Act (AWA, 7 U.S.C. 2131)

- Covers all animal species *with the exception of rats, mice, and birds*, which are not considered animals for the purposes of the Act. Rats and mice are the species most commonly used for toxicity testing. USDA Animal and Plant Health Inspection Service (APHIS) is responsible for the enforcement of the AWA.

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PHS Policy on Humane Care and Use of Laboratory Animals

- Covers any research or testing on vertebrate animals (*including mice and rats*) conducted at facilities that receive PHS funding and compliance is monitored by NIH Office of Laboratory Animal Welfare (OLAW).

- OLAW requires annual reporting of average daily census of each species held at a facility, but these numbers do not reflect the purpose or actual numbers used for testing (i.e. numbers are estimates and include breeding colonies).

- Rats and mice account for ~90% of animals used for toxicological testing
- In the United States, there is no legal requirement to report the number of rats and mice use in toxicological testing
- There is no legal requirement to report the type of test conducted on any animal species.

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- Animal data for products that fail during development are not generally submitted.

Challenges

- Would require significant resources from both agencies and industry
- Unlikely to yield information that is timely or actionable
- Animal use may fluctuate based on situational need (i.e., DOD), and therefore does not allow for an accurate comparison over time.
- Lack of international harmonization will result in continued use of animal testing even when approved alternatives exist.

How can we measure success?

EPA Office of Pesticide Programs From Dec, 2011 to January, 2017

Type of Study	Total # of Requests	Waivers Granted	Required Studies
Inhalation	288	222	66
Neurotoxicity	186	163.5	22.5
Dermal	57	50	7
Developmental	48	39	9
DNT	18	15	3
Subchronic Dog	14	11	3
Reproductive	38	32	6
Immunotoxicity	223	207	16
Chronic/ Carcinogenicity	28	24	4
Subchronic Rat	12	10	2

Submitted Acute 6-Pack Studies

	Guideline	2012	2013	2014	2015
Acute oral	870.1100	324	248	328	268
Acute dermal	870.1200	292	257	313	255
Acute inhalation	870.1300	264	217	248	254
Eye irritation	870.2400	291	261	273	251
Skin irritation	870.2500	270	254	268	258
Skin sensitization	870.2600	247	237	262	267

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  - LLNA for potency categorization of skin sensitizers (refinement and reduction of animal use)

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- Target zero animal use - in many cases, there are tractable targets for the complete replacement of animal testing (i.e., biologics).
- Standardized electronic reporting could enable the future application of analytics