



# International Consortium for Innovation and Quality in Pharmaceutical Development (IQ) and the 3Rs Leadership Group

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# IQ Overview

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# Mission & Objectives

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- Mission: As a technically focused organization of pharmaceutical and biotechnology companies, IQ's mission is to advance science-based and scientifically-driven standards and regulations for pharmaceutical and biotechnology products worldwide.
- Objectives:
  - Share emerging knowledge through peer networks
  - Publicize and promote pertinent findings
  - Engage and collaborate with key stakeholders
  - Impact regulatory guidelines and expectations
  - Advance best practices leading to innovation and quality in pharmaceutical development



# 34 Current Member Companies

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AbbVie

Alexion Pharmaceuticals

Amgen

Astellas

AstraZeneca

Baxter

Bayer Healthcare

Biogen Idec

Boehringer Ingelheim

Bristol-Myers Squibb

Celgene

Cephalon

Daiichi Sankyo

Eisai

Eli Lilly

Endo

Genentech

GlaxoSmithKline

Incyte Corporation

Infinity Pharmaceuticals

Johnson & Johnson

Kythera

Merck (EMD) Serono

Millennium

MSD (Merck & Co.)

Novartis

Otsuka

Pfizer

Roche

sanofi-aventis

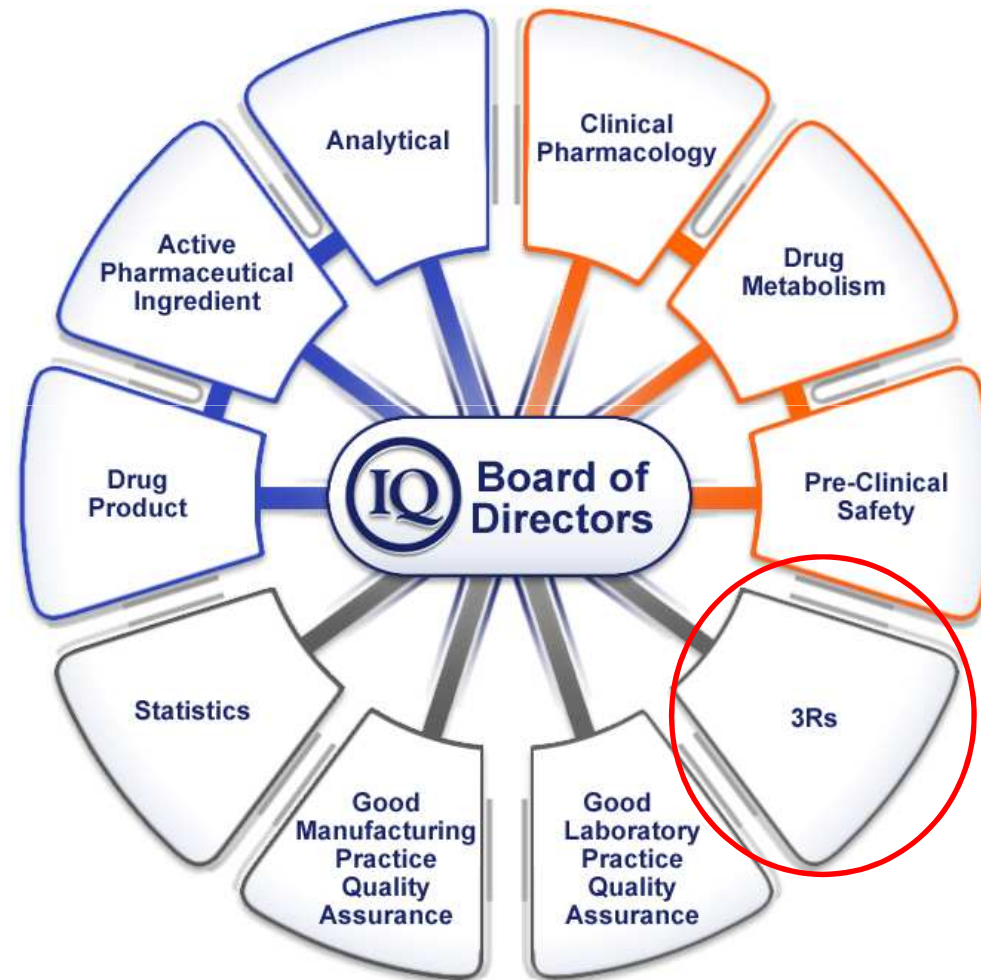
Sunovion

Takeda

Teva

Vertex

# IQ Organizational Structure



# 3Rs Leadership Group Overview

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# Mission and Structure

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- To promote sharing and integration of high quality scientific practices to advance the Reduction, Refinement and Replacement of animals used in the discovery and development of new medicines, vaccines, medical devices and health care products for humans and animals.



# 22 Current Members of 3Rs LG

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- AbbVie
- Amgen
- Astellas
- AstraZeneca
- Baxter
- Bayer
- Biogen Idec
- Boehringer Ingelheim
- Bristol-Myers Squibb
- Celgene
- Eisai
- Eli Lilly
- Genentech
- GlaxoSmithKline
- Johnson & Johnson
- Merck (EMD) Serono
- Millennium
- MSD (Merck & Co.)
- Novartis
- Pfizer
- Sanofi
- Vertex





# LG Activities

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- Formed January 2012
- 8 Working Groups under 3Rs LG
- Coordinating with *New Jersey Association of Biomedical Research* on 3Rs Programs
  - Co-Sponsored Spring 2012, Fall 2012, and Spring 2013 webinars on 3Rs
  - Co-Sponsored 3Rs Sharing Conference in 2012 and 2013
- Coordinating meeting of FDA, IQ 3Rs and CAAT\* in July 2013
  - Meeting Topics: Advancing Animal Welfare in Toxicology Studies and Optimization Strategies for Animal Studies

\* Johns Hopkins University Center for Alternatives to Animal Testing



# Current Working Groups (I)

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- Benchmarking WG
  - Conducted industry benchmarking survey on 3Rs activities in member companies in Summer 2012
  - Developing report on survey results
- Awards WG
  - Conducted benchmarking survey on awards given in member companies on 3Rs in Summer 2012
  - Developing a guide for IQ members to implement own internal awards program
- Position Paper WG
  - Draft position paper to communicate that animal research is essential but biopharma is committed to promoting 3Rs as good science and good business
- **European Liaison WG**
  - Establish working relationships with select European organizations (EFPIA, EPAA, Interpharma, NC3Rs)
  - Identify collaborations to promote the science of 3Rs



# Current Working Groups (II)

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- US Regulatory Outreach WG
  - Understand perspectives of agencies (e.g. FDA, USDA, ICCVAM) and 3Rs activities for collaboration.
  - Coordinated IQ comments on NICEATM-ICCVAM 5 year plan
- US NGO Outreach WG
  - Establish working relationships with NGO's that support use of animals in biomedical research.
  - ACLAM, ILAR, SCAW, NYAS, NJABR, NABR...others
- CRO Outreach WG
  - Explore 3Rs collaboration opportunities with CROs, who conduct a large percent of animal work in support of the biopharma industry.
  - Developing guidance documents on blood collection and dosing, site visit standards, standardized husbandry practices, and authority for attending vets
- IQ-wide Awards Proposal WG
  - Develop proposal to present to Board of Directors for the creation of an IQ Consortium sponsored external award for the 3Rs



# Conclusion

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- Exchange of 3Rs expertise
- Mutual willingness to share
- Numerous initiatives already started to apply and foster 3R projects
- IQ 3Rs LG wants to participate and contribute
- Mutual interest that US perspective is similar to the EU perspective
- IQ 3Rs seeks collaborations with mutual added value



# IQ 3Rs Leadership Group

## Benchmarking Survey: Strengths, Opportunities and Next Steps

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# Introduction

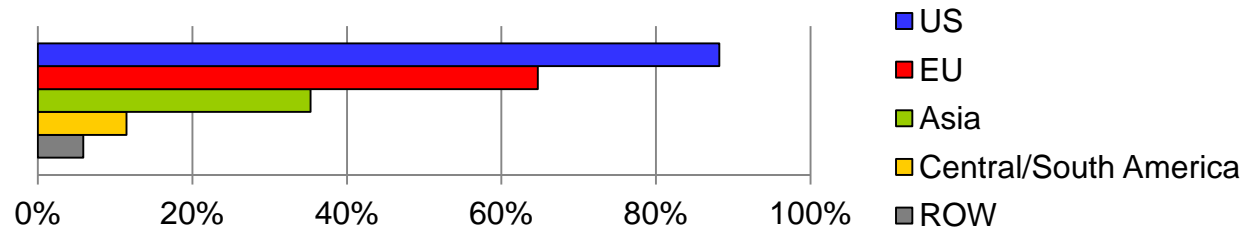
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- A benchmarking survey was created to assess a variety of 3Rs issues in the following categories:
  - Management of 3Rs, including the ethical review processes
  - Technical Applications of 3Rs
  - Scientific Applications of 3Rs
  - Promotion/Communications about 3Rs
  
- Purpose of the benchmarking Survey
  - Assess the overall commitment to the 3Rs
  - Attempt to assess current 3Rs practices
  - Identify 3Rs strengths across the industry
  - Identify 3Rs opportunities across the industry
  - Use this information to guide IQ3Rs LG strategies

# International Consortium for Innovation and Quality in Pharmaceutical Development (IQ)

- 20 member companies of IQ 3Rs LG were surveyed.
  - 75% of companies completed survey.

Note: One company submitted 3 responses by geographical location but 14 companies submitted one “global” response.

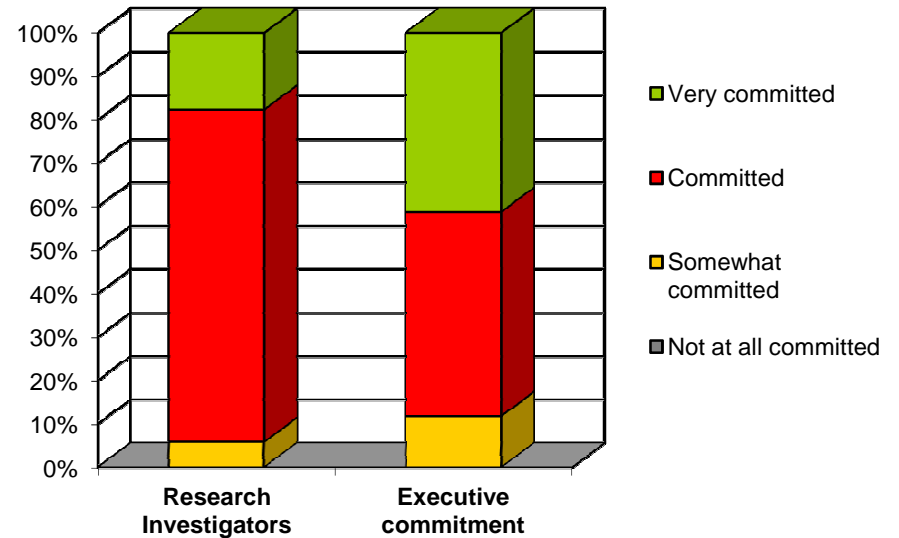


- Most are multinational biopharmaceutical companies.
- Size range of ~1.5-100K employees.
- Several don't conduct animal research internally.

Great diversity in the companies that responded to the survey

## Commitment to the 3Rs

- 80% have a corporate policy or standards.
- Researchers and Executives are committed.
- 76.5% indicated they have Executive level support



**3Rs Commitment Across the Industry is High**

**Opportunity: IQ should help ensure executive support for all 3Rs programs.**



# What are Your Greatest 3Rs Successes?

## Management

- Full-time 3Rs role established
- Corporate Animal Welfare Committee
- Global 3Rs Policy
- Executive management support 3Rs (corporate responsibility)

## Technology/Science

- Microsampling for PK studies
- Dried Blood Spot for better PK/PD data
- Jacketed external telemetry to eliminate the need for stand alone safety pharmacology studies
- Decreasing number of animals for device training
- Improved environmental enrichment
- Better anesthetics and analgesics

## Regulatory

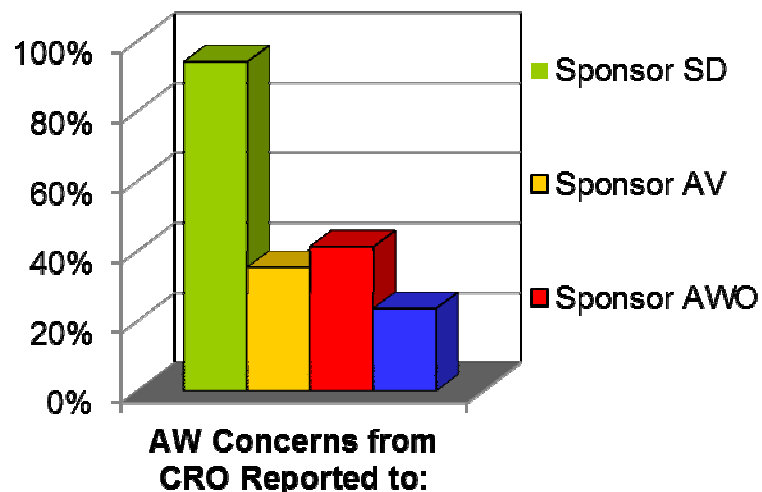
- Push for regulatory changes in vaccine and drug production and manufacturing - significant 3Rs, including replacement
- Reductions of dog use because of in silico methods to elimination of primates for regulatory submissions
- Replacement of monkeys with mice in vaccine testing

## Recognition

- Animal welfare awards tied to improvements in science.

# Authority, Assessment, Monitoring and Reporting of Contract Research Organizations

**>90% animal welfare concerns reported to Tox SD but only 30% reported to Attending Veterinarian of Sponsor company**



**Opportunity: Better communication about AW concerns at CROs with sponsor**

**AV's help to ensure consistent 3Rs practices.**



# Application of Statistical & Systematic Reviews

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- Statistical Review & Access to Statistical Expertise
  - 88% of companies ask questions about design and data analysis to statistically justify animal numbers.
  - 82% affirm their investigators have access to a statistician.
- Systematic Reviews for 3Rs in Animal Testing
  - A rigorous review, synthesis & meta-analysis of study data.
  - 26.7% of companies conduct formal systematic reviews.

**Opportunity: Systematic reviews may show real benefit in helping companies to adopt the 3Rs and may need to be promoted further.**



## Animal Reduction in IND Enabling Studies

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- 80% of companies surveyed have reduced the number of animals used per group for routine IND enabling studies.
- Many collaborations have enabled progress.

**For example: Challenging the regulatory requirement for acute toxicity studies in the development of new medicines: A NC3Rs workshop report (2007):**

This illustrates the benefits that can be achieved in implementing the 3Rs by a coordinated approach & sharing data to reach a common position based on evidence and science.



## Enrichment and Housing Refinements

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- Enrichment is consistently provided for all species on both GLP (>80%) and non-GLP (>88%) studies.
- 66% mandate solid-bottom caging for rodent housing.
- EU regulations require larger cages.
  - Current implementation of EU cage sizes:
    - 66.7% EU Only, 26.7% China & 20% US
  - Future adoption/implementation of EU cage sizes:
    - 33.3% will adopt internally & externally (CROs)
    - 20% will adopt internally only

**NOTE: More research data is needed on various cage sizes to determine effects on animal wellbeing.**

**Opportunity: Solid-bottom caging is a known best practice and should be implemented more widely across the industry.**



## Application of Best Practice

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- 80% of companies surveyed have banned a technique due to animal welfare concerns.
  - Techniques mentioned most often as being banned or slowly phased out since refined alternatives are available:
    - toe clipping for identification
    - retro-orbital blood collection
- 87% of respondents have adopted dried blood spot or microsampling methods to reduce animal numbers.

**Progress: Refinements in technology applied broadly can result in significant reduction of animal pain & distress, as well as numbers.**

# Application of Humane Endpoints

Application of humane endpoints:	Favorable responses	Number of responses (of 17)
Humane endpoints must be described in the animal care and use protocol	94%	16
★ <b>Veterinary staff are asked to help guide all decisions when there are questions about humane endpoints</b>	<b>88%</b>	15
Studies causing moderate-severe pain/distress are monitored by both research and veterinary staff	82%	14
<b>Special training is provided to staff for humane endpoints in challenging models</b>	<b>65%</b>	11
<b>A scoring sheet is used with certain challenging models to improve objective decision making</b>	<b>59%</b>	10

**Opportunity: Training for humane endpoints on challenging models and scoring sheets could enhance animal welfare.**



## Predictivity of Animal Models

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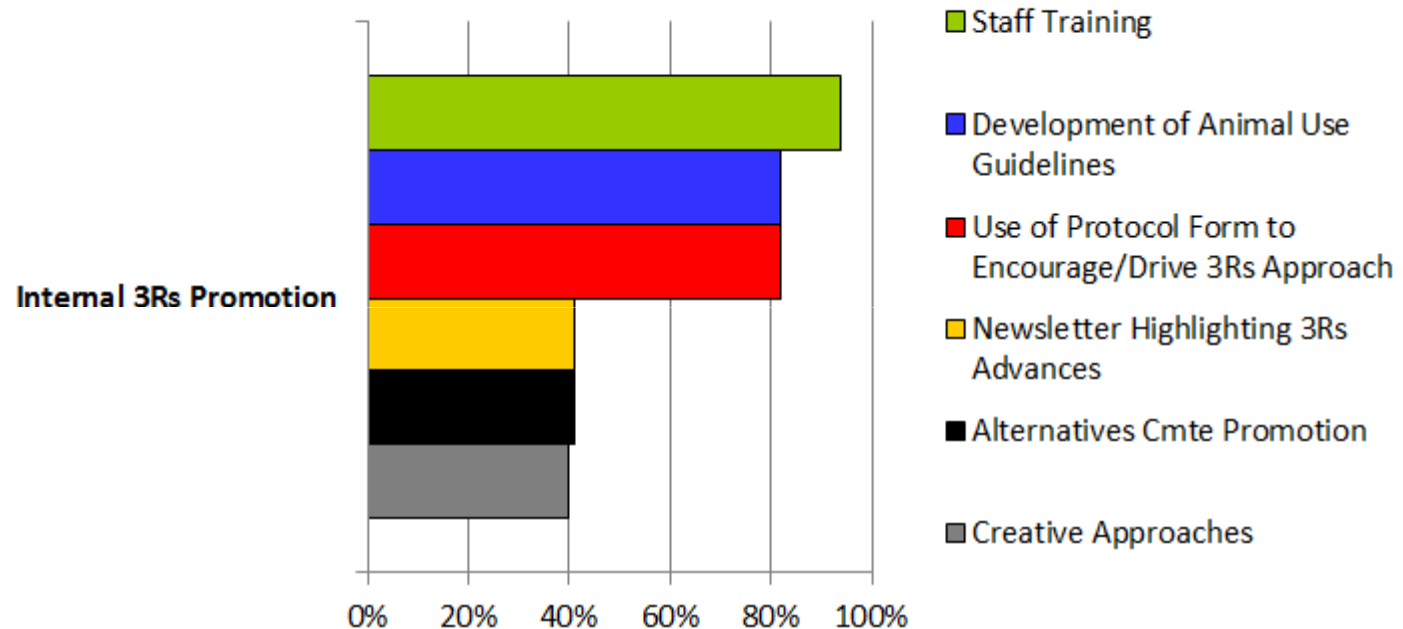
- 65% stated that they need better methods to characterize the predictivity of their efficacy models.
  - “Animal Models Framework” Pharma consortium has been used to evaluate efficacy during governance review.
- ~50% capture in-vitro screens prior to animal studies.
- 71.4% required studies in a lower species prior to NHP.

**Opportunity: Better characterized, more predictive animal models will advance the best science.**

**Opportunity: Use of in-vitro screens have been used broadly in drug discovery and development –clear evidence of 3Rs impact.**



# Promoting the 3Rs Internally



**Opportunity: Creativity in promoting the 3Rs internally can help enhance the corporate culture.**



## Determining Impact of Company Policies & Practices on the 3Rs

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- 41% currently utilize Key Performance Indicators (KPIs)
  - 3Rs award nominations
  - publications
  - program enhancements
  - animals spared/not used
  - qualitative measures (AAALAC, USDA, etc.)

**Opportunity: Consistent use of 3Rs KPIs could help to demonstrate our active commitment to ethical science.**



## Promoting the 3Rs Externally

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- 61.5% - Corporate Responsibility Reports
- 60% fund 3Rs in U.S. and 53% outside the US.
  - AALAS, ACLAM Foundation; NC3Rs; EPAA;
- Presentations on 3Rs advances
  - 60% National – AALAS, FELASA, PRIMR, ACLAM
  - 31% Local – NJABR, local AALAS meetings
  - 31% International meetings – World Congress on Alts.
- ~50% publish 3Rs advances in scientific journals.

**Opportunity: 3Rs LG should promote increased publication & presentation of science-based 3Rs advances by individual companies and consortia.**

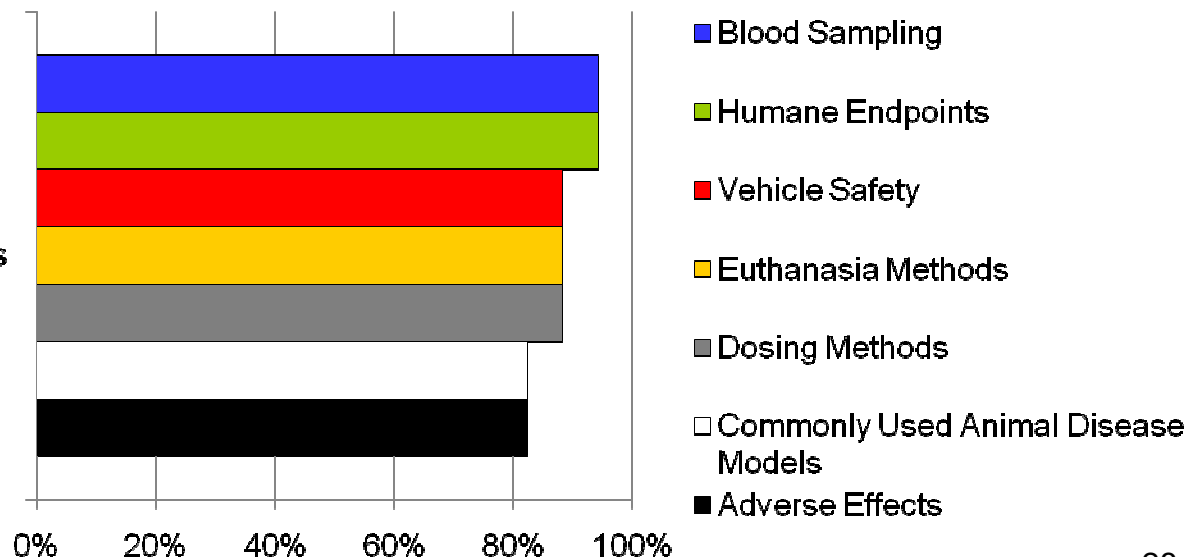
# Promoting the 3Rs Sharing

- All respondents felt there would be great benefit from sharing 3Rs information.

Comments included:

- Much to learn from each other
- Must break barriers to share precompetitive information
- Potential to extend reach of effective practices
- Substantial internal knowledge to be shared.
- Sharing will help all organizations

Would There Be Benefit to Sharing More 3Rs Information and Practices in the Following Areas?





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Thank you for your attention

Questions?



# Acronyms

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- AAALAC Association for Assessment and Accreditation of Laboratory Animal Care International
- AALAS American Association for Laboratory Animal Science
- ACLAM American College of Laboratory Animal Medicine
- EPAA European Partnership for Alternative Approaches
- ICCVAM Interagency Coordination Committee on the Validation of Alternative Methods
- ILAR Institute for Laboratory Animal Research
- NABR National Association for Biomedical Research
- NC3Rs National Centre for the 3Rs
- NICEATM National Toxicology Program Center for the Evaluation of Alternative Toxicological Methods
- NJABR New Jersey Association for Biomedical Research
- NYAS New York Academy of Sciences
- PRIM&R Public Responsibility in Medicine and Research
- SCAW Scientists Center for Animal Welfare