Replacing Animal Research

Reducing animal testing in the health sector through strategic investment

Guide for Investors

Stewart Investors

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Research Team

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About the authors

ISF is an independent research institute within the University of Technology Sydney. We conduct transdisciplinary, project-based research in line with our vision of creating positive change towards sustainable futures.

The University of Adelaide has research strengths at the intersection of animal research, public understanding of science, and ethical consumption as reflected in this report.

Replacing Animal Research (formerly the Fund for the Replacement of Animals in Medical Experiments or FRAME) is a charity based in the United Kingdom which develops and promotes alternatives to animal testing by funding research, education, and policy work.

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Summary of key issues for investors

Significant changes could be made in the healthcare sector with increased corporate transparency and greater awareness of investor interest in responsible corporate practices relating to animal research and non-animal based approaches. This Guide contains detailed background information and points for investors to consider when engaging with companies about their practices in this important domain.

Investors should focus on the following key issues when engaging companies in this sector:

- What are your **current animal testing practices,** including numbers and types of animals used on an annual basis, and what has been the general pattern of usage over the past 10 years?
- Are you investing in, developing, or using any **non-animal methods,** and if so, what are your current targets and timelines for implementation?
- What are your processes for **ensuring compliance with the 3Rs** including replacement in research performed for you by external suppliers such as Contract Research Organizations (CROs)?
- Is your company involved in petitioning regulators or working with others in the health sector to promote **greater use of non-animal methods along with the necessary changes in regulation** to support them?

Whenever engaging with companies, investors should emphasize that animal testing and transitions to non-animal methods are important issues for them that are likely to materially affect their investment decisions and the reputation of the companies in question.

The issue: animal testing

What is animal testing?

The term ‘animal testing’ generally refers to a range of types of procedures performed on living animals. It is associated with a number of types of research including focus on fundamentals of biology, understanding of diseases, assessment of the adverse effects and effectiveness of new medicinal products including pharmaceuticals and therapeutics, and testing toxicity including human health effects and/or environmental safety of consumer and industrial products.

Where is it conducted?

Animal experimentation is conducted in a range of settings including universities, research institutes, pharmaceutical companies, and commercial facilities that provide animal testing services to industry.

Why is animal testing used?

It tends to be used when human experimentation would be unfeasible, difficult to perform in a standardized manner, or unethical. However, critics are concerned that animal testing is overutilized and without sufficient consideration of alternatives that utilize fewer animals, no intact animals, or non-animal approaches.

What type of animals are used and how many?

The overwhelming majority of experimental animal research is done using rodents (mice and rats), fish, amphibians, and reptiles. The global annual rate of vertebrate animal experimentation–with organisms ranging from zebrafish to non-human primates–was estimated to be 192 million as of 2015, although accurate numbers are difficult to obtain in many locales and settings.

Although efforts to reduce animal use have been implemented in many institutions and countries, these are widely thought to have been offset by increasing use of mice due to popularity of standardised, genetically modified strains as well as regulatory requirements that compel use of animal testing. Hence many countries including Canada, Australia, Israel, South Korea, and Germany have reported rising numbers of animals used for research in recent years particularly mice and fish, but declines in the use of cats, dogs, non-human primates, rabbits, guinea pigs, and hamsters. Publications on animal testing also continue to increase in number.

What are the concerns?

Research using non-human animals is often credited with considerable successes: its supporter argue that it has made fundamental contributions to basic knowledge in many biological and medical fields, and served as the basis for developing effective therapeutics such as drugs and surgical interventions as well as vaccines. However, critics question its reliability and replicability, pointing to relatively high rates of failures of translation between animal models and humans, the potential suffering and other harms caused to experimental animals, our lack of knowledge or agreed metrics for measuring pain and suffering, and the limits of our understanding of sentience in various types of animals.

Animal welfare is a long-running issue of concern for consumers. Recent research by the Responsible Investment Association Australia (RIAA) notes that consumer concern around animal cruelty has increased in the past two years: animal cruelty topped the list of concerns, coming in ahead of human rights and environmental issues. In 2024, 74% of Australians reported that they wanted to avoid animal-related issues, 66% cited animal cruelty as important to avoid when investing their money, and 54% wanted to avoid animal testing for non-medical purposes. However it is important to note that only 11% of Assets Under Management in Australia are negatively screened for animal testing.

The context: legislative requirements and voluntary initiatives

Regulation and oversight

Animal testing practices are significantly shaped by regulation in the jurisdictions in which they occur, with the European Union and the United Kingdom having more stringent legislative requirements than most other locales. The U.S. Food and Drug Administration (FDA) is a key driver of practices in this space as the United States is the most significant market for many drugs. The FDA recently has signalled that animal testing is no longer strictly required for pharmaceutical market approvals, but also has not accepted alternative evidence to date.

Cosmetic testing on animals has been banned or is in the process of being banned in many locales including the European Union, United Kingdom, Norway, Australia, India, and Canada, but not the United States. The European Union has recently implemented regulations to eliminate use of animal testing in toxicology and other regulatory research, with the United States expected to soon follow suit.

Many companies have facilities or subsidiaries in more than one jurisdiction in part to be able to conduct what they view as the necessary animal experiments despite regulatory and ethical limitations in some locales. They also often employ external entities to perform animal testing, again in more regulatory favourable settings, particularly in some parts of Asia and the United States. These patterns make it difficult to fully track the numbers of animals utilized, the purposes for which they are used, and any one company's total portfolio of animal and related forms of experimentation.

Specific processes associated with approvals for animal testing differ according to locale, but generally involve review and oversight by some form of institutional ethics committee, and compliance with the 3Rs.

The three Rs

The Three Rs (3Rs)—Replacement, Reduction, and Refinement—have become widely used guiding principles associated with animal research in most places:

- **Replacement** refers to the use of non-animal methods over animal methods whenever it is possible to achieve the same scientific aims.
- **Reduction** requires use of methods that enable researchers to obtain comparable levels of information with fewer numbers of animals.
- **Refinement** emphasizes the need to develop and utilize methods to improve animal welfare including to more effectively alleviate or minimize potential pain, suffering, or distress to animals used in experimentation.

Alternatives to animal testing have long been proposed, together with recognition of the need to improve animal welfare and scientific rigour especially where use of animals cannot be avoided, but until recently replacement has presented the most significant challenges in relationship to implementing the 3Rs.

Voluntary initiatives

Voluntary pledges by companies in the healthcare sector also shape their animal testing practices. For instance, many companies in the United Kingdom are signatories to the *Concordat on Openness on Animal Research* which has enhanced disclosure on animal testing but has also been critiqued by some as being a form of 'humane washing.' Similar voluntary agreements exist in other locales including Belgium, Spain, Portugal, and Australia. Supporters argue that more transparency and openness will result in increased public trust and help to legitimize animal research practices where they remain required. However, despite disruptive animal rights activism having declined significantly in recent years, many companies remain concerned that making information about animal research public will increase exposure to such activism and create reputational damage. Others find openness compacts too demanding and in conflict with company requirements to maintain this type of information as commercial-in-confidence.

Alternatives to animal testing in the health sectors

Replacement techniques

Replacement techniques are often grouped under the descriptor of 'new approach methodologies' or NAMs. Such approaches can include:

- computer modelling, simulations, and mathematical calculations
- in-vitro techniques using cells, tissues, or organoids
- imaging
- biochemical analyses
- genetics and gene profiling
- use of human research subjects
- reuse of existing data via meta-analysis or similar

In some cases, replacement of higher-level organisms and vertebrates in particular is taken as the most important goal, with solutions including use of lower-level, non-vertebrates, whereas other types of NAMs include use of animals together with non-animal methods. In this guide, we use the terminology of 'non-animal' methods or models to distinguish such hybrid systems categorised as NAMs from those that do not involve any intact animal testing.

Barriers to development and adoption of alternatives

Despite increasing awareness of the importance of developing replacement methods, progress in this domain has been slow. For instance, recent research by NC3Rs, exploring use of 3Rs approaches in World Health Organization (WHO) guidelines for animal use in quality control and batch release testing in vaccines, found that although overall awareness of the 3Rs is high, animals are still widely used, and development and uptake of non-animal technologies is very low.

Factors that will influence company action include regulatory requirements particularly in key markets where products are intended to be sold. In addition, animal testing associated with some types of products is more likely to be reduced or replaced by non-animal models: for instance cosmetic and personal care products typically do not need to meet standards of efficacy but only requirements associated with safety, whereas pharmaceuticals and therapeutics require higher levels of testing to meet typical regulatory standards. Finally, reducing or eliminating animal use is likely to be much easier for companies with well-established product lines that no longer require extensive animal testing, but may not represent actual development of alternative approaches.

It is widely recognized that institutional ethics reviews processes in universities, research institutions, or companies often do not encourage researchers to develop alternatives. Other significant barriers to development and adoption of alternatives include: regulatory requirements for animal testing, particularly for pharmaceuticals; lack of training and expertise in using alternatives in the context of biomedical and other forms of testing; institutional patterns that reinforce use of animals (particularly rodents), including widespread commercial availability of strains and ready access to experimental animals; and uncertainties about what standards should be utilized in relation to many of the newer techniques. There is some evidence that the topic of animal testing is considered by some companies to be immaterial or lower risk when compared to other ethical, social, and governance issues. The issue of adoption of non-animal approaches is therefore not currently prioritised. Finally, consumers tend to be more accepting of the use of technologies or animal experimentation when directed at developing medical applications aimed at treating or curing diseases, and hence development of alternatives may not be viewed as a priority by them in this context.

Issues for investors

Recent research on a sample of 21 companies in the health sectors found that there is an overall lack of transparency and disclosure on use of animal testing and non-animal methods (or NAMs). It is difficult to obtain accurate and robust data on any aspect of animal testing, including basic data on numbers and types of animals used, or patterns of usage over time (i.e., whether they are increasing or declining). Outsourcing of animal testing to Contract Research Organisations (CROs) often in different regulatory jurisdictions adds to the lack of transparency about basic data and increases companies' risk and reputational exposure.

This lack of transparency is at odds with consumer interests in animal welfare. In the absence of disclosures, investors have no visibility about companies' exposure to animal welfare risks and limited data to inform their investment decisions particularly in the healthcare sector.

Current best practice includes:

- public commitment to the 3Rs;
- participation in established audit and accreditation schemes for animal testing;
- requirements that CROs or other outside suppliers implement the 3Rs in procurement guidelines or Supplier Codes of Conduct; and
- public disclosure of commitments and practices associated with animal testing, and efforts at developing non-animal methods in some detail including timebound targets, recognising that some information may be commercial-in-confidence.

How can investors improve practices and disclosure?

This guide can be used to support investor engagement with companies on this topic. It can be used by investors to help identify if, where, and how to engage with companies to address animal testing and use of non-animal testing approaches in the following key areas:

1. internal and supply chain action to reduce animal testing and promote use of non-animal approaches;
2. influence on regulation of animal testing and use of non-animal approaches; and
3. disclosure of data, practice, and progress toward reduction in numbers of animals used and efforts at replacement.

For the three areas above, this guide sets out investor expectations and checklists of best practices.

High-level investor expectations

Investors should expect companies to:

- implement actions in line with the 3Rs;
- engage with regulators and other interested parties to shift the regulatory landscape to reduce and replace animal testing wherever possible;
- disclose use of animal testing and details about investment in and development of non-animal approaches internally and in supply chains; and
- monitor and publicly report on progress made, including against timebound targets to reduce and replace animal testing.

Investors should stress that animal testing and transitions to non-animal methods are important issues to them that can materially affect their investment decisions and the reputation of the companies in question.

Internal and supply chain action to reduce animal testing and promote use of non-animal approaches

Investor expectations

- Public commitment to the 3Rs and standards for their implementation both internally and with external contractors such as CROs and universities via procurement guidelines and Supplier Codes of Conduct
- Time-bound targets for reduction and replacement
- Appropriate staff training about the 3Rs and practices associated with them including non-animal approaches
- Participation in established audit and accreditation schemes in relation to animal testing both internally and in the context of external contracted research

Checklist of practices

Expected best practices	Disclosure
Transparent policies committing the company to implementation of the 3Rs across its supply chain	Yes
Establishment of timebound targets for implementing non-animal approaches to reduce or replace the use of animals in testing across the company's supply chain	Yes
Investment in training on non-animal approaches across the company's supply chains to the extent permitted by current local regulations, and in the required technologies associated with such approaches	Yes
Use of methods to ensure the accuracy and reliability of non-animal testing approaches	Yes
Participation in established audit and accreditation schemes in relation to animal testing for internal operations and across the supply chain	Yes
Incorporation of consideration of non-animal approaches in procurement guidelines or Supplier Codes of Conduct	Yes

Engagement questions

- Has your company implemented any non-animal methods that have reduced or replaced the use of animals in the last 10 years? If so, for what types of research? If no, can you please explain why not?
- Has your company established any timebound targets for implementing non-animal methods that could reduce or replace the use of animals? If so, how is your company tracking against these targets? If there are no targets but you have implemented some non-animal methods, what has been the impact in terms of reducing the numbers of animals used?
- How are staff trained to be aware of non-animal methods and be able to use them successfully? Does your company employ methods to ensure the accuracy and reliability of non-animal testing methods?
- Is your company part of any audit/accreditation schemes in relation to animal testing, for example AAALAC?
- In relation to CROs or other external entities that carry out animal testing for you, do you include consideration of non-animal methods or reducing animal numbers in Supplier Codes of Conduct?
- Does your company require CROs or other external entities with which you work to participate in audit or assurance schemes, or require some other form of company-directed independent oversight of animal research and related practices?

Influence on regulation and environment of animal testing and use of non-animal approaches

Investor expectations

- Sharing of data on use of and standards associated with non-animal methods with regulatory agencies
- Efforts to petition regulators to change requirements associated with the use of experimental animals to promote non-animal approaches
- Sectoral leadership and collaboration on non-animal approaches
- Public outreach to promote commitment to the 3Rs and transparency about continued animal testing where required

Checklist of practices

Expected best practices	Disclosure
Data on non-animal approaches is made available to the regulatory agencies within the limits of commercial-in-confidence requirements	Yes
Efforts to petition regulators or similar to change requirements associated with the animal testing to promote experimental approaches that reduce the numbers of animals used or replace the use of animals	Yes
Collaboration or leadership within the healthcare sector to develop and implement methods that could reduce numbers of animal used or replace the use of animals	Yes
Outreach programs designed to inform the public about the company's commitments to and activities associated with reducing and replacing animal testing	Yes

Engagement questions

- Is data on non-animal methods, for example when run in parallel to animal testing, made available to the regulatory agencies such as the FDA within the limitations of commercial-in-confidence requirements?
- Is your company engaged in efforts to petition regulators or similar to change requirements associated with the use of experimental animals in order to promote non-animal approaches that reduce numbers of animals used? If so, what types of research or species of animals are being prioritised in these efforts?
- In what ways is your company collaborating or leading within the healthcare sector to develop and implement non-animal methods that could reduce or replace the use of animals?
- Does your company have any outreach programs designed to inform the public about your commitments to reducing or replacing animal testing, or your current practices in this domain?

Disclosure of data and practices

Investor expectations

In addition to the disclosures above, companies should disclose

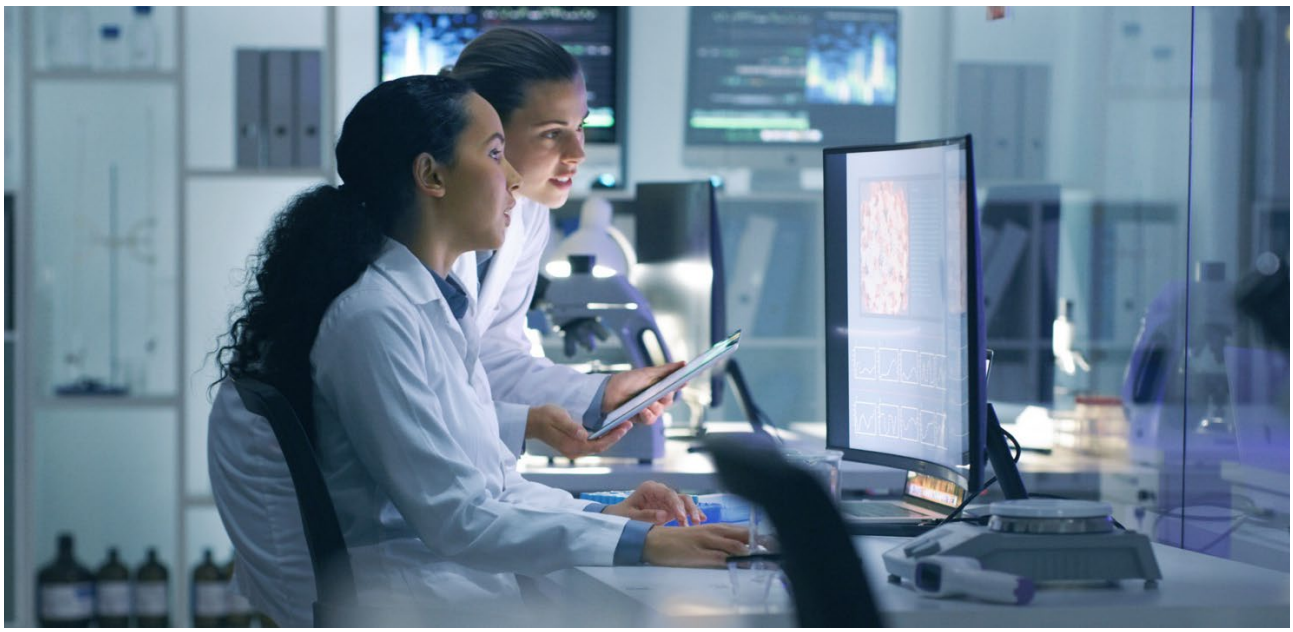
- Details on company engagement in animal testing as part of internal operations, through subsidiaries, or use of external contractors such as CROs: when, how, and why animals are used in testing
- Approximate numbers of animals (by species) per year used in testing by the company, its subsidiaries, or external contractors such as CROs utilised by them
- Progress on actions and targets including year-on-year changes in the number of animals used in testing by the company, its subsidiaries, or external contracts such as CROs over the last 5 years
- Details about product types where testing on animals is mandated by an approval agency before the product can go into human clinical trials and efforts to reduce numbers of animals where possible
- Legal jurisdiction(s) in which animal testing takes place within the company, its subsidiaries, or on its behalf by external contractors such as CROs

Checklist of practices

Expected best practices	Disclosure
Inclusion of disclosures and progress reporting on all elements identified above at least annually in Annual Reports, Sustainability Reports, and/or equivalent status company reporting	Yes
Publicly available policy on commitment to 3Rs with particular attention to Reduction and Replacement	Yes

Engagement questions

- Would you consider including more data on animal testing and non-animal testing in your Annual, Integrated, and/or ESG (Environmental, Social, and Governance) Reports?
- If you have been unable to disclose information on animal testing or development of non-animal methods due to commercial sensitivity, what are the barriers to being able to disclose such information publicly?



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