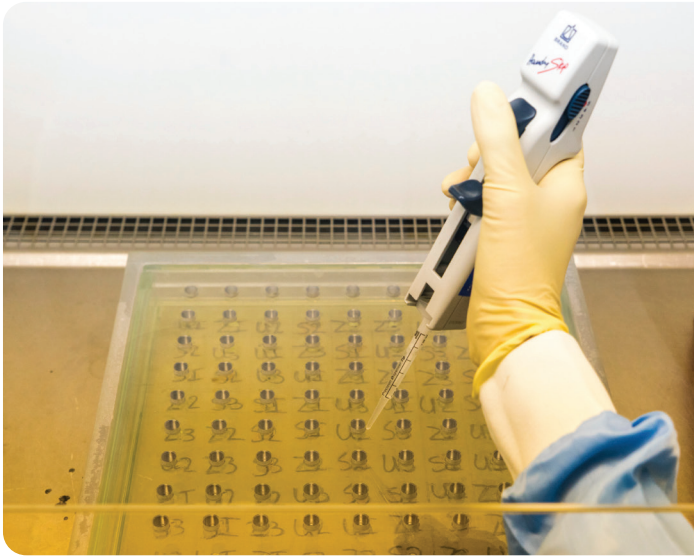
Phasing out animal testing in chemical safety assessments

The animal health sector's perspective

AnimalhealthEurope developed a detailed sector–specific Roadmap identifying the main challenges, both technical and regulatory, faced by the animal health industry in the implementation of new approach methodologies (NAMs). The animal health sector strongly supports the accelerated development, validation and uptake of technologies and methods to reduce reliance on animal–based tests in the research, manufacturing and authorisation of veterinary medicines.

International harmonisation in the regulatory acceptance of NAMs is an essential element for successful outcomes globally.



Our Commitment to the 3Rs approach

In the EU, animal health companies are required by law to demonstrate that all veterinary medicines are effective and safe for the animal patient, the user, the consumer and the environment. This evidence is generated using a range of testing techniques, including chemical, physical, *in silico*, *in vitro* and *in vivo.*

Our members are committed to the phase–out of animal–based tests, wherever and whenever possible, under the 3Rs approach — Replacement, Reduction and Refinement — and the science–based phase–in of new approach methodologies (NAMs).

Whilst there is no single replacement for animal testing, and various tests are required by legislation, we will work together with all stakeholders involved to drive forward the phase–out of animal testing where scientifically feasible. The final stages of safety and efficacy testing for veterinary medicines will, however, always need to be conducted in the target species.

The Animal Health Industry is committed to replacing animal use with new approach methodologies, though animal patients will still be needed for final clinical efficacy and safety tests



Mapping of existing alternative tests and approaches

AnimalhealthEurope built on the *'3 baskets'* classification system previously developed by EFPIA to map existing alternatives, with a few nuances to allow for differentiation on certain points, e.g. where NAMs exist and are accepted, or where new data is not requested.

BASKET 1:

(a) Animal testing with validated and accepted NAM; used in dossier submissions or batch release.

(b) Animal testing which is considered unnecessary (no new data being requested) or should be deleted.

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Regulatory acceptance to be secured.

BASKET 2:

Animal testing with non-validated NAMs, which can be prioritised for short-term R&D.

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Secure regulatory acceptance and scientific validation.

BASKET 3:

(a) Animal testing for which there is still no concept for a NAM, and prioritised for long-term R&D.

(b) Animal testing which cannot be replaced, except by a 'Next Generation Risk Assessment' route. Refinement still possible.

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Work on technical options based on the impact of the requirements (frequency of use, number of animals used, severity).

The need for a global regulatory approach

Scientific evolution, national and regional regulation, the ethical responsibilities of companies and regulators, and public rejection of animal testing are all drivers for broad replacement of *in vivo* methods with new approach methodologies (NAMs). Significant efforts in research and development, along with substantial time and resources, are dedicated to developing new alternative methods.

However, the animal health market is relatively small, with high market entry costs, so accessibility to the global market is generally considered critical.

The absence of a global approach to the replacement of animals used for regulatory purposes with New Approach Methodologies remains a major hurdle

Hurdles can arise from **discrepancies in timing** on the regulatory acceptance of NAMs around the world, impacting on the global marketing of veterinary medicines. Such discrepancies, which reflect differing levels of knowledge, skill and familiarity between territories, include:

- → no acceptability of NAMs at all in some countries;
- → acceptability with additional local regulatory requirements, or if direct correlation studies with the historical *in vivo* assay can be provided;
- → acceptability of the regulatory dossier, but with requirement for local additional *in vivo* re-testing, either by the companies or the local authorities;
- → differences in acceptability between existing registered products and new products;
- → no specific timelines for acceptance in some countries; and
- → when and if international guidelines (such as VICH guidelines) are in place: implementation and additional requirements depend on the individual countries.

Many animal health companies operate globally, and a lack of regulatory harmonisation may lead to an unscientific and unethical situation in which NAMs and animal studies are conducted in parallel for different regions. Global regulatory acceptance is therefore a key requirement: all parties involved need to feel confident with NAMs, so thorough establishment and validation of methods is a mandatory pre-requisite.

Current challenges for the animal health industry

In the current regulatory environment, animal health companies can face some or all of the following challenges:

- Increased demand for R&D resources to comply with EU requirements and to develop and validate NAMs;
- Additional human and financial resources, administrative burden, time and effort to develop the knowledge and skills to apply NAMs and to understand requirements for their regulatory acceptance in other countries;
- Additional tests on animals in parallel to *in vitro* assays, with the related ethical questions, brand perception concerns, etc.; and
- Requests for "correlation studies" comparing NAMs with historical *in vivo* methods, with limitations not well understood or accepted outside the EU.

For global regulatory acceptance, NAMs need to be validated by international organisations like the OECD and defined in respective Guidelines (e.g. OECD or VICH). Without such regulatory uptake, there is a risk of NAMs not being accepted by an authority, resulting in a refusal of the marketing authorisation for the veterinary medicine. This means not only delays and additional expenses for the company, but also a lost opportunity for the country in question to have timely access to the medicine.

Our Recommendations



We welcome the European Commission's Roadmap towards phasing out animal testing for chemical safety assessments, and we call for mutual recognition to be encouraged globally.

The EU should lead in actively promoting acceptance of NAMs worldwide, and leverage its influence and resources to help facilitate the transition in other geographies.

AnimalhealthEurope developed an animal health sector-specific Roadmap for the transition to non-animal safety testing. The actions indicated overleaf are not exhaustive, but provide a high-level outline of what needs to be achieved in the short, medium and long term.

The animal health sector will continue to invest in the research and development of NAMs, and will adopt and use NAMs wherever viable and legally accepted. Delivering on these objectives can only be fulfilled through close cooperation and collaboration with all relevant stakeholders within the health sector, and with good dialogue between related sectors.

We count on EU regulators to establish guidance on regulatory validation and acceptance of NAMs, and to encourage early dialogue with industry on novel approaches, regulatory expectations and evidence needs. Further support will be needed from the EU institutions and international organisations such as VICH for both research and legislative change.

Roadmap towards phasing out animal testing in chemical safety assessments

Short term *within 2 years*

- Continued mapping, planning and 'preparing the ground'
- Develop a more detailed planning and milestones for the Roadmap
- Identify opportunities for collaboration across sectors
- Identify areas where our sector needs funding support to fill research gaps
- Identify funding opportunities for the prioritised research gaps
- Identify regulatory barriers caused by technical guidelines and monographs
- Identify legal barriers in key export markets
- Develop indicators to monitor progress
- Participate in international events to promote global uptake of NAMs
- Initiate plans to complete validation of NAMs in Basket 2
- Initiate activities to develop NAMs for prioritised areas in Basket 3
- Develop a communication strategy to raise awareness (including internally)
- Initiate plans to remove technical and regulatory barriers within EU

Medium term *within 5 years*

- Implement a detailed plan with actionable short to long term objectives
- Establish sources funding
- Establish collaborative projects
- Enact plans to remove technical and regulatory barriers within EU
- Enact plans to increase regulatory acceptance of validated NAMs in Basket 2
- Continue with research to develop NAMs for prioritised areas in Basket 3
- Initiate plans to remove technical and regulatory barriers globally
- Prepare an interim progress report with agreed indicators

Long term *within 10 years*

- Complete activities initiated and carried over from earlier phases
- Ongoing: continually assess scientific advancements and progress in regulatory science with an eye on tests in basket 3
- Develop a report on progress made with NAMs for tests in basket 3, and identify what is needed to complete a full transition of our sector to animal–free testing
- Collaborate in work to develop a new approach to regulatory risk assessment that is completely free of animal–based testing
- Achieve demonstrable progress in the removal of regulatory barriers globally
- Achieve demonstrable progress in regulatory acceptance of NAMs globally
- Provide training in the application of NAMs in animal health drug development