NEW ERA ACTIONS FOR THE ERA POLICY AGENDA 2025-2027

TEMPLATE FOR NATIONAL CONSULTATION PROCESS

This template follows up on the debate in the ERA Forum on 25 May, in which Forum representatives agreed on a coordinated approach towards the definition of new actions for the ERA Policy Agenda 2025-2027. It builds on a gap analysis exercise in which the ERA Forum assessed, which parts of the Pact for Research and Innovation are already covered by the Policy Agenda 2022-2024 and where there should be additions.

Forum representatives are invited to distribute this template among actors at national level to collect input for potential new actions for the ERA Policy Agenda 2025-2027. The priority areas of the Pact for Research and Innovation and content of the Policy Agenda 2022-2024 should be taken into account when filling in this template.

The results of the national process should be then fed into the gap analysis document by Forum representatives. This will help to prepare the overall assessment for the ERA Forum.

Action title *(Please use as a maximum two lines.)*	Non-animal approaches in biomedical research and testing of pharmaceuticals
Description of the action *(Please explain the proposed action in a simple, clear and communicable narrative.)*	Animal–free New Approach Methodologies (NAMs) have a great potential to reduce animal testing in biomedical research and safety and efficacy assessment of pharmaceuticals (human and veterinary medicinal products and medical devices). In comparison to animal studies, NAMs could also bring innovations that are more human-relevant, accurate, reproducible, and sustainable, allowing to better understand, prevent and treat diseases, especially in areas where animal models are of limited translational value. The development, acceptance and implementation of NAMs are a high priority for the European Commission and several Member States, which have invested substantially in their development; for the European Parliament, as exemplified by its 2021 resolution to accelerate transition to innovation without animals in research, regulatory testing and education; for the pharmaceutical and medical technology industry in need of improved tools to bring innovative treatments to patients; and for the civil society, as illustrated by the recent 2023 European Citizen's Initiative ''Save cruelty free cosmetics", calling to move towards a regulatory system for safety assessment without animal testing and for a gradual ban of animals in research. Despite the huge interest in NAMs from a broad range of stakeholders, their acceptance and implementation by end-users and regulators have been relatively slow for a variety of reasons, including: 1) insufficient availability of NAMs to cover all aspects of biomedical research or the complex regulatory endpoints 2) lack of coordinated investments in Member States to fund and prioritize further development of NAMs and dedicated research infrastructures 3) Insufficient resources in most Member States to qualify, standardize and validate NAMs

4) disparities between Member States in education and training programmes on the use of NAMs in schools, universities, and research institutes
5) varying awareness of, and lack of confidence in NAMs from the EU and national regulators, as well as from industry

As the EU does not have legal mechanisms to force the development and validation of NAMs, the solutions to all these hindering factors would be optimally addressed in a coordinated and harmonized manner with Member States and with all relevant stakeholders through an ERA policy action.

As this ERA policy action, apart from improving the tools for biomedical research and effective innovation in pharmaceuticals, will focus on the areas where most animals are used in Europe, it is also an important driver to sustainably reduce the number of animals used in research and regulatory testing. According to the latest Commission report on the statistics on the use of animals for scientific purposes, about 8 million animals were used in 2020. 72% of animals were used for basic, translational, and applied research. 17% were used for regulatory testing, of which 80% for pharmaceuticals[1]. By Focusing on these areas, in addition to routine production (blood-based products, antibodies, etc.) that accounts for 5% of animals, this action would cover over 90% of animals used in the EU for scientific purposes, which might exert a significant impact on their reduction.

This ERA-action proposes a harmonized approach to address the above-mentioned challenges, share best practices between Member States, and coordinate the development, validation, acceptance and implementation of NAMs, thereby contributing to ethically and socially responsible innovation.

The action will setup an EU-wide forum consisting of relevant ministries, regulatory agencies, research funding organisations, academia, pharmaceutical and medical technology industry, Contract Research Organisations (CROs), to align national and regional policies for speeding up the development, validation, acceptance, and implementation of NAMs.

The forum will be supported by four working groups (WGs), which focus on the following themes:

<u>WG1: Development of NAMs and common European infrastructures</u>

Experts from biomedical research, pharmaceutical and medical technology industry, regulatory agencies, and other relevant stakeholders collaboratively identify key areas where new NAMs are most needed and expected to have the highest impact, for instance in certain disease or

[1] Summary Report on the statistics on the use of animals for scientific purposes in the Member States of the European Union and Norway in 2020, European Commission (2023)

	biological areas, or specific safety and efficacy assessment endpoints for pharmaceuticals. Based on the needs and knowledge gaps identified, experts subsequently provide insight and priorities to governments and industry for the further coordinated development of NAMs, taking into consideration the complementarity of scientific strengths and available expertise in the different Member States and regions. The development and sustainability of key European infrastructures that can be utilised for NAMs (high throughput "omics" equipment, biobanks, super computers, complex multi-organ cultures, production facilities for therapeutic antibodies, databases, etc.), as well as their access, is also addressed, and opportunities for synergies across Member States are identified. **<u>WG2: Validation, acceptance and implementation of NAMs</u>** Developers and users of NAMs, regulatory agencies, and other relevant stakeholders, identify the minimum criteria that NAMs need to meet to enable their acceptance and implementation in the contexts of basic and applied biomedical research, and for the regulatory assessment of pharmaceuticals. They propose priorities for the qualification and validation of NAMs in the two different contexts of use. Member States take the decision to jointly support the validation of a certain number of NAMs earmarked for acceptance and implementation in regulatory testing of pharmaceuticals. **<u>WG3: Education and training</u>** Relevant education and training programmes on NAMs in Europe and other continents for students, researchers, technicians, and regulators are mapped, and their quality and outreach assessed. Based on this exercise, which incorporates the best practices identified in the most advanced Member States or countries outside of Europe, the working group makes suggestions to Member States for jointly developing, in close collaboration with education directors at knowledge institutes, NAMs education and training modules that will target not only the current professionals (researchers, regulators), but also their next generation. **<u>WG4: Openness & awareness</u>** Ministries, regulators, competent authorities, researchers, journal editors, and other stakeholders develop common policies to improve the openness of research, especially for publishing available NAM protocols, and results from animal experiments, even if these are negative/neutral, to avoid unnecessary duplication of animal testing. The data should be shared in all Member States. The working group reflects on how to share best practices to make sure that different ethical committees, funding assessment committees, reviewers, and regulators have a similar level of awareness of the latest

	scientific breakthroughs on available NAMs, and propose actions to improve the confidence of regulators in NAMs. The working group identifies opportunities for raising awareness of NAMs in the civil society and patients
Actors *(Please explain who would take part in the action and who would benefit from it.)*	- European Commission - Relevant national and regional ministries, regulatory agencies, funding organisations - European Medicines Agency (EMA) - Academia - Pharmaceutical and medical technology industry, Small and Medium size Enterprises (SME), Contract Research Organizations (CROs) - Citizens and patients might also be included on an ad-hoc basis
Expected impact *(Please describe the expected impact of the action (including outside the scientific community), paying attention to the fact that it needs to focus on concrete results and reachable deliverables.)*	The ERA action aims to accelerate and harmonize, through an aligned and coordinated approach across Member States, the development, validation, acceptance, and implementation of NAMs in biomedical research and regulatory testing of pharmaceuticals. Short- to medium-term expected impacts and deliverables are: 1) A framework in which national and regional ministries, funding organisations, regulatory agencies, academia, and industry, propose solutions to improve the coordination and harmonization of the use of NAMs in biomedical research and regulatory testing of pharmaceuticals 2) A NAM European development and infrastructure agenda identifying the areas where NAMs are most needed and expected to have the highest short- to medium-term impact. Member States identify actions they might jointly support, taking into consideration the complementarity of their scientific strengths and available expertise 3) A European NAM validation, acceptance and implementation strategy which identifies criteria for the validation, qualification and acceptance of NAMs. Member States decide to jointly support the validation of NAMs that are intended to be accepted and implemented in regulatory testing of pharmaceuticals 4) A European NAM education and training plan, identifying the various opportunities to better inform researchers and regulators on NAMs. Member States engage to develop common programmes based on best practices identified in the most advanced European or non-European countries 5) A European harmonized NAM openness and awareness programme that ensures open access to NAM protocols and all results of animal experiments. It also provides guidance to harmonize the awareness of NAMs in all ethical committees, funding committees, reviewers, and regulators, based on best

	practices in the participating Member States. It proposes concrete actions to increase the confidence of regulators in NAMs 6) Monitoring and evaluation mechanisms to assess the progression of acceptance and implementation of NAMs, in relation to the proposed action. Longer term expected impacts might include the followings: 7) Availability of NAMs that would drive progress in biomedical research and innovation 8) Novel and harmonised animal-free strategies for regulators (extending in other sectors beyond pharmaceuticals) to ensure the highest level of protection of human and animal health in the EU 9) Sustained decrease of animal use in biomedical research and regulatory testing 10) Strengthened international leadership of the EU in biomedical research and regulatory testing of pharmaceuticals without animal testing 11) Increased public trust in, and societal acceptance of scientific innovation 12) A European platform where expertise, data, infrastructures and other resources are shared and international scientific collaboration is optimally facilitated
Why do we need this action? *(Please indicate the need for this action in view of implementing the Pact for R&I and achieving the ERA objectives and explain why its objective cannot be reached through existing programmes/ activities. What is the action's added value at national and European level as well as for stakeholders? How does it make a change and how is co-creation ensured?)*	Animal testing raises ethical and societal concerns, as recently illustrated by the European Citizen Initiative "Save cruelty free cosmetics", calling to move towards a regulatory system for safety assessment without animal testing and for a gradual ban of animals in research. The initiative also invited the Commission and the Member States to strengthen the development of alternatives to animal testing (NAMs). This point was unanimously supported by scientists and scientific societies taking a public position regarding the initiative. Although Member States are bound by Directive 2010/63/EU that calls for the replacement of animal procedures as soon as valid alternative approaches become available, there is no coordination mechanism for the development of NAMs that are fit-for-purpose for different applications. It is also the case for the acceptance and implementation of NAMs. Despite the considerable support from the European Commission to the development and validation of NAMs during the last two decades, NAMs are far from being able to replace animal testing in most areas of biomedical research or for safety and efficacy testing of pharmaceuticals. Equally, the number of NAMs that are regulatory accepted or commercially available remain modest, and the number of test animals in the EU is decreasing only marginally. Support from the European Commission alone does not seem to drive the move towards acceptance of innovative NAMs. Proper harmonization and coordination between Member States is crucial to achieve this move and the consequent reduction of animal testing. Therefore, coordinated efforts on the

	development, validation, acceptance, and implementation of NAMs should be intensified, which is the challenge this ERA action proposes to address. Within the chemicals sector, considerable efforts to reduce animal testing in safety assessment were recently launched, as shown by the proposed development of a roadmap to phase out animal testing in chemical safety assessment (including industrial chemicals, pesticides, biocides and medicinal products) by the European Commission, or by the work of the European Partnership for Risk Assessment of Chemicals (PARC). However, these initiatives do not focus on biomedical research, which uses 72% of all animals in the EU. Safety and efficacy assessments of pharmaceuticals account for 13% of animal testing. Therefore, this ERA action focuses on these two areas, in addition to the routine production (5%), where the impact on the reduction of animals would be the highest. To genuinely support effective innovation in biomedical research and testing of pharmaceuticals with NAMs, all actors need to be actively involved, including Members States, regulators, academia and industry. The various programmes from the European Commission alone will not be sufficient to drive the move towards this complex and holistic goal. By launching this ERA action, the EU would show its global leadership in promoting responsible research and innovation and fostering scientific advances. The collaboration between Member States and their complementarity in different fields would enhance the effectiveness of research initiatives and reduce redundancy. It would create a unified and open research and innovation hub, which would attract talents and innovators, and boost research capabilities within the Member States. This ERA action would strongly contribute to the Pact for Research and Innovation, as it would align with its three values and principles: "upholding values", "working better" and "working together". It fosters collaboration among Member States, research institutes, industry, regulators, and stakeholders in a strategic area where coordination is missing. It promotes the sharing of knowledge, data, resources, and best practices in developing, validating and implementing NAMs. It also contributes to the promotion of responsible research and innovation by encouraging the development and adoption of innovative, verifiable and reproducible methods that will reduce the ethically sensitive use of animals in biomedical research and testing of pharmaceuticals. It seeks to ensure policy coherence and alignment across Member States, by working towards standardized and validated NAMs that would comply with evolving regulations. The possible active involvement of citizens and patients promotes transparency in the research and regulatory processes, fosters a better understanding of the scientific advancements, ethical considerations, and potential benefits of NAMs, and ultimately increases societal trust in science and innovation. The action positions Europe as a leader of NAMs development and implementation in the global research landscape while setting high

	standards for a paradigm change of regulatory testing of pharmaceuticals,
Additional information *(For example, timing and milestones, which already could be envisaged, can be indicated.)*	Timing Three years, ideally starting Q3 2025 Timeline and milestones 1) Q3 2025: Meeting of relevant ministries of MS and regions to decide on coordination of the action, and on structure, composition, governance, and operational rules of the four WGs. 2) Q4 2025: MS invite relevant stakeholders and experts to WGs. 3) Q1 2026: WGs are set and decide on the practicalities of their actions and tasks. 4) Q2 2026: WGs start working on their respective deliverables. 5) Q1 2027: Workshop with all WGs to discuss work progress, and increase synergy and alignment. 6) Q4 2027: Analyses, strategic agendas, recommendations of each WG are finalized and provided to the relevant actors. 7) Q1 2028: Coordinated joint actions are initiated. 8) Q3 2028: A symposium with all WGs discusses the key findings and the future steps for governments and stakeholders.
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