LERU and EU-LIFE foresee many negative consequences if the ERA Proposal *'animal approaches in biomedical research and testing of pharmaceuticals'* is accepted in its current form

EU-LIFE and LERU bring together some of Europe's most prominent life science institutes and research universities. We have been working with the European Commission and Member States representatives in the drafting of the ERA proposal '*Animal approaches in biomedical research and testing of pharmaceuticals*' initially proposed by the EC as a reply to the European Citizens Initiative "Save Cruelty Free Cosmetics - Commit to a Europe Without Animal Testing". While we are not convinced that an ERA action is an efficient tool to advance the development of animal and non-animal methodologies in research, **we welcome the openness of the EC and the leading Member States to include representatives of the scientific community in the design of the action** through the formal participation of EU-LIFE and we thank the drafting group for the constructive conversations.

LERU and EU-LIFE and the members it represents remain committed to the 3Rs principles, and the replacement of animals in scientific research where possible to do so[1,2]. We strongly acknowledge the considerable positive evolution of the proposal from the first to the current proposal. It has proven a challenging task, owing to differing interests and the complex nature of the topic. Indeed, whilst the proposal looks good at first glance, **we remain concerned about the general tone of the final version of the proposal namely by giving an unjustified positive portrayal of NAMs.**

Animal experimentation is governed by the 2010 directive. This includes an NCP network that meets regularly with the Commission. This directive is regularly amended by means of delegated acts, after consultation with SCENHIR and public consultation (Scientific Committee on Emerging and Newly Identified Health Risks), as was the case again this year. Ahead of the discussion on the ERA action proposal in the ERA Forum meeting on 14th December 2023, we outline our thoughts on the proposal and offer some guiding principles for further work in this area.

- The action needs to be realistic regarding the **coexistence of NAMs *and* animal methods, as *complementary* technologies.** The text maintains that NAMs and animal-based approaches are *alternatives* and that the NAMs should always be chosen. It doesn't even mention reduction and refinement (as the other two 3R

[1] https://www.leru.org/news/joint-press-release-leru-and-eu-life-applaud-the-european-commission-for-a-sensible-approach-regarding-animal-research
[2] https://www.leru.org/news/joint-statement-on-the-request-to-phase-out-the-use-of-animal-experimentation-in-europe

technologies). We would like the reference to elimination of animal research to be removed as there are many areas which we believe animal use will remain vital for the foreseeable future, even with NAMs. **A focus on 3Rs in general is therefore needed to be more realistic.**

- Further refinement of the **terminology of NAMs** is needed. At present the term NAM can mean several things, and it is confusing when several definitions exist. In our view, it should refer to New Approach Methodologies - which also includes animals where appropriate. In contrast, in this proposal, it refers to the total replacement of animals, i.e. animal-free.

- A more positive description of the role of researchers in the development and uptake of NAMs is needed. It still depicts the scientific community as inactive and wary of changing their work practice without reasonable motive. On the contrary, **the scientific community is leading developments and is aware of the latest methodologies, contributing to better and novel models with and without animals.** Researchers are attentive to animal welfare and take seriously their responsibility for reducing the use of animals in research whenever viable alternatives are available, at the same time as being willing to contribute to solving important and urgent societal and health challenges.

- Many of the assumptions and statistics used in the proposal are questionable and **highly speculative** and **may paint NAMs as more effective than they are** (and perhaps can ever be). In some cases, the document runs counter to existing EC policies in this area. The numbers used in the document do not agree with official EC figures (see the ALLURES database). For example, it is unrealistic to state that "*this action would cover over 90% of animals used in the EU for scientific purposes, which might exert a significant impact on their reduction*". Furthermore, the statement '*NAMs could also bring innovations that use human-based methods, allowing to a better translation for medical applications accurate, reproducible, and sustainable, allowing to better understand, prevent and treat diseases, especially in areas where animal models represent a limited translational value*' is highly speculative.

- We urge caution regarding monitoring mechanisms – especially regarding statements implying that successfully implementing NAMs will directly impact on animal use reduction as some NAMs are not animal free.

- We **welcome the initiative to address the barriers for dissemination and uptake of NAMs** because of lack of resources and to create more awareness amongst the younger generation through education and training.

- The scientific validation of a NAM is a well-regulated process, involving numerous players (eg EMA), and we do not believe a new forum would have added value - while adding to the administrative burden at a time when there is no budget for the ERA.

We also consider that:

- The action should bring together a fair representation of different research domains and research topics to ensure that the representation includes **researchers heavily relying on animal methods for some of their hypotheses but also using NAMs**.

- **It is necessary to ensure that the proposal is aligned with existing and planned EC initiatives.** For example, for WG4 on education and training of researchers, it is necessary to align this activity with the EC's Open Science agenda and already existing initiatives at JRC, as datasets have already been published[3].

We believe that:

- The remit of the ERA action is very large. "*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*". We are concerned that it will require a correspondingly large budget. We believe that **patients would benefit far more from the same resources addressed to serious biomedical research that uses (and develops) NAMs in parallel with, as a complementary approach to, the use of animals.**

- The level of description requested for the ERA action does not allow to address this complex subject with the level of detail necessary to avoid any inadvertent negative impact on Europe's scientific quality, impact, and productivity. **Detail and nuance are essential in this very controversial area.**

We propose the following guiding principles for future work on this proposal, and on NAMs in general.

- There is an **absolute need to involve researchers from academia and industry in all levels of co-creation of policies and decisions, both at national and European level and in any subsequent steps.** We very much welcome the effort made for the inclusion of researchers in working groups and bodies relevant for developing policies for NAMs within this ERA action. This should continue.

- It is **vital to complement and not duplicate other initiatives that are already being developed by the European Commission**, e.g. the roadmap for the regulatory testing of chemicals.

- **The potential for using NAMs in scientific research and in regulatory testing fundamentally differ.** Separating research and regulatory testing into two different working groups and to foresee the interplay between them, is therefore very

[3] https://publications.jrc.ec.europa.eu/repository/search?query=Advanced%20Non-animal%20Models%20in%20Biomedical%20Research&sort=relevance

welcome. However, there are still places within the proposal this distinction is not clearly made, and as a result, it leaves the reader with the false impression that what is true for regulatory testing, is also true for research.

In summary, EU-LIFE and LERU remain fully available and actively engaged in developing this ERA action further. We fully support further funding for NAMs, and a progressive step by step reduction in animal experiments when scientifically possible to do so, but we do not feel that this proposal in its current form is the best way to do this.

Please do not hesitate to contact the following people if you have any questions:

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