MethodsX 7 (2020) 101129

Contents lists available at ScienceDirect

MethodsX

journal homepage: www.elsevier.com/locate/mex

RE-Place: A local initiative to pave the road towards international recognition and promotion of new approach methodologies

M. Van Mulders[a,b,*], N. Liodo Missigba[a,b], V. Rogiers[b,1], B. Mertens[a,1]

[a] SD Chemical and Physical Health Risks, Sciensano, Brussels, Belgium
[b] In Vitro Toxicology and Dermato-cosmetology, Vrije Universiteit Brussel, Brussels, Belgium

ARTICLE INFO
Method name:
Keywords: 3Rs, Alternative methods, Replacement, Database, Open access, Knowledge sharing, NAM
Article history: Available online 5 November 2020

New and innovative technologies have been developed across the life sciences including computer modelling, artificial intelligence, biotechnology, sophisticated cell cultures, organ-on-a-chip and many more. In regulatory toxicology, methods based on these technologies have been successfully implemented, especially for local effects, thereby resulting in the use of less or even no experimental animals. For systemic toxicity and biomedical research questions, however, the situation is more complex. Nevertheless, cutting edge technologies are integrated in these domains as well, leading ideally to complete, but in practice rather to partial or limited replacement of experimental animals. Methods and strategies based on these new technologies are today referred to as 'New Approach Methodologies (NAM)'. They include different types of *in vitro, ex vivo, in silico* and *in chemico* assays, but they can also be based on the use of *in vivo* organisms that are not categorized as experimental animals according to European Directive EU/2010/63 [1].

As the development and practical use of NAMs is relatively new, (young) scientists may experience difficulties in retrieving relevant information, in particular on where they can acquire the skills for a specific NAM. In order to facilitate access to this type of information on a national level, the Flemish and Brussels governments jointly launched the project 'RE-Place' which aims to centralize the existing expertise on NAMs in Belgium in one database. As such, RE-Place stimulates the practical use of NAMs and thus, indirectly contributes to a reduction in animal experiments. Consequently, the RE-Place project meets the requirements of European Directive EU/2010/63, requesting that Member States (MS) shall promote the use and further development of NAMs [1]. The RE-Place project is coordinated by two Belgian partners, Sciensano and the Vrije Universiteit Brussel. Researchers from different disciplines are invited to submit their personal expertise to the RE-Place database, resulting in a

[1] Equally contributing authors.

https://doi.org/10.1016/j.mex.2020.101129
2215-0161/© 2020 Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

realistic overview of the NAMs that are actually used today. To collect specific information about the use of NAMs in a fast and consistent way, an online tool (available via the website www.RE-Place.be) has been developed. Via this online tool, experts can directly submit their knowledge into the RE-Place database.

One could argue about the added value of 'another database', as several initiatives already exist *e.g.,* AnimAlt ZEBET database in Germany [2], Norecopa databases in Norway [3], EUROECOTOX database of bioassays in Czech Republic [4], EURL ECVAM Database on Alternative Methods to Animal Experimentation (DB-ALM) at the European (EU) level [5] and many more. However, the unique feature of the RE-Place database is that it does not only contain a short description of the method itself, but also the names of the experts and centres that have expressed willingness to pass on their expertise to interested parties. In addition, the NAMs that are included in the RE-Place database are not limited to newly developed methods, nor to validated methods only, but capture all methods that are currently used.

The RE-Place project thus provides an answer to an existing need at national level as expressed in the recent EURL ECVAM report: 'Accelerating progress in the Replacement, Reduction and Refinement of animal testing through better knowledge sharing' [6]. Indeed, there is a lack of open access knowledge sources, and a lack of trust in these new types of methodologies, impeding their practical implementation [6]. In Belgium, RE-Place wants to tackle this hurdle by serving as a safe and reliable platform to exchange knowledge in order to accelerate the further use, development and validation of NAMs across different sectors and research areas. By sharing up-to-date knowledge on the available NAMs and by providing the opportunity to directly contact experts for more information, trust in these new methods can gradually grow within the scientific community. RE-Place will help to further strengthen local networking activities, and facilitate collaborations between various (research-) institutes. These networks can play an essential role in the dissemination of information on 3Rs, as personal contact has been identified as one of the preferred means of communication to exchange knowledge [6].

When proven successful, the RE-Place project could serve as a blueprint for other MS and could thus be a first step towards a uniform, harmonized bottom-up strategy across the EU. Local research initiatives like RE-Place are highly encouraged by the EU Commission as they allow to create partnerships and build collaborations between different stakeholders (scientific community, regulators, industry, animal welfare, consumer organizations). Information can be exchanged more easily, allowing experts from other application domains to benefit from the existing know-how.

For this Special Issue, the coordinators of RE-Place have carefully selected nine NAMs in the field of toxicology that have been submitted to the RE-Place database. By providing a detailed description of the research methodology, knowledge sharing on the current applications of NAMs in toxicology can be further improved, thereby also contributing to the philosophy of the MethodsX journal.

*Corresponding author at: SD Chemical and Physical Health Risks, Sciensano, Brussels, Belgium.
E-mail address: mieke.vanmulders@sciensano.be (M. Van Mulders)

References

[1] EU, Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes, Official Journal of the European Union L276 (2010) 33–79.
[2] BfR. 2020. AnimAlt ZEBET - database for alternative methods to animal experiments. Accessible at: https://www.bfr.bund.de/en/animalt_zebet___database_for_alternative_methods_to_animal_experiments-62822.html. Last accessed 19 October 2020.
[3] Norecopa. 2020. Databases of Norecopa. Accessible at: https://norecopa.no/databases-guidelines. Last accessed 19 October 2020.
[4] Research Centre for Toxic Compounds in the Environment. 2020. Euroecotox: alternative assays. Accessible at: http://projects.cba.muni.cz/euroecotox/index.php?pg=alternative-assays. Last accessed 19 October 2020.
[5] EC. 2019. EURL ECVAM database on alternative methods to animal experimentation. Accessible at: https://ec.europa.eu/jrc/en/scientific-tool/database-alternative-methods-animal-experimentation. Last accessed 19 October 2020.
[6] T. Holley, et al., Accelerating Progress in the Replacement, Reduction and Refinement of Animal Testing Through Better Knowledge Sharing, Publications Office of the European Union, Luxembourg, 2016 EUR 28234 ENISBN 978-92-79-63892-3, doi:10.2788/934083.