University of Naples Federico II
Department of Pharmacy
Doctoral Course in Pharmaceutical Sciences XL Cycle

EVALUATION OF NEW APPROACH METHODOLOGIES — NAMS, AND THEIR APPLICATION IN THE REGULATORY FRAMEWORK, AS TOOLS FOR AN INTEGRATED PREDICTIVE APPROACH WITHIN THE NEXT GENERATION RISK ASSESSMENT FOR HUMAN AND ENVIRONMENTAL HEALTH.

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Risk assessment and regulatory toxicology are experiencing profound changes. At a global level, institutions, regulatory agencies and the scientific community have embraced the objective of revolutionizing the paradigm of the evaluation of regulated products. The new policies of sustainability, green and circular economy, and "one substance, one assessment" have also contributed to raising awareness on these issues.
For these reasons, combined with ethical issues and scientific validity, the classic strategies that made massive use of animals, are gradually replaced by alternative approaches, known as New Approach Methodologies (NAMs). These models based on stand-alone or integrated in vitro, in chemico, in silico and ex vivo methods guide the transition towards the Next Generation Risk Assessment – NGRA. Nonetheless, NAMs have the advantage of providing a precise and mechanistic understanding of the properties of substances/products, being more focused on the human species and better considering susceptible populations. Thanks to the integration of these approaches with computational methodologies, analytical techniques based on multiomics and non-testing methodologies that consider the Weight of all Evidence (WoE), a deeper understanding of the mode of action, as well as the associated uncertainties and data gaps, can be achieved.
In this context, and taking on the challenge of the development, validation and regulatory acceptance of NAMs, the activities within this doctoral project aim to evaluate the regulatory relevance of alternative tests and strategies, considering the different regulatory needs within the various legislations. Using methods based on WoE and integrated methodologies such as Adverse Outcome Pathways, the impact of NAMs in the current regulatory framework will be analysed. Furthermore, comparative in vitro studies to evaluate the relevance and reproducibility of alternative models (e.g., 3D models) will be conducted.
The results of the doctoral project may have great relevance at the regulatory and institutional level and be a valuable support to public government agencies (e.g., Istituto Superiore di Sanità), in collaboration of which the doctoral project will be carried out and which work in the field of regulatory toxicology and Next Generation Risk Assessment.

References

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