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3Rs: from complexity to predictivity

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The application of the 3Rs principle, Reduce, Refine, Replace (Directive 2010/63 EU), asks for scientific innovation with a continuous development of methodologies. Non Animal Methods (NAMs), from cell cultures to tissue-based assays, from in vitro epithelial barriers for oral, respiratory and topical exposure (i.e. alveolar, dermal, intestinal barrier) to 3D cultures and organoids and/or spheroids, are useful predictive tools, in order to answer to the requirements of biological complexity. Moreover it is clear that the new approach is looking to a strategy, integrated or tiered, through combined tests, instead of stand alone methods, that are a few and with limited application, like in skin irritation (OECD 439) or corrosion (OECD 431).

Considering systemic toxicity like carcinogenicity, genotoxicity, reproductive toxicity or the multiple mechanisms of Endocrine Distuptor Chemicals (EDCs), new alternative methods are necessary to solve complex endpoints.

If the new vision implies Integrated Testing Strategies (ITS), Integrated Approaches for Testing and Assessment (IATA) or Defined Approaches for Testing and Assessment (DA), on the other hand research is looking to advanced technologies like Microfluidic Perfusion Systems (MPS), which could expand their applicability from toxicity testing to biomedical research.

A predictive 3Rs interdisciplinary approach, addressed to investigate different aspects of a multilevel science, considering humans, animals and environment through a One health vision, is the future goal.

Keywords:
3Rs; Non Animal Methods; Predictivity; Complexity.