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CONSIDERATIONS ON APPLYING ORGAN-ON-CHIP FOR REGULATORY PURPOSES

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The regulatory landscape

The European Union (EU) has over 30 pieces of key legislation put in place over the last 50 years to regulate a vast range of chemicals in a multitude of industrial sectors. Apart from facilitating the EU's single market and supporting the innovation and competiveness of EU industry, the EU's chemical acquis has also the important aim of protecting human health and the environment from potential adverse effects of chemicals and products made from them. An essential provision for EU legislation is its continual adaptation in order to remain efficient and relevant, including up-take of scientific and technical advances in hazard and risk assessment practice, with a strong emphasis on shifting to non-animal methods. For example, the EU's Cosmetics Regulation imposes a marketing ban on cosmetic products that have cosmetic-specific ingredients tested on animals since the regulation came into force in 2013. In addition, the REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) Regulation strongly encourages registrants to consider alternatives to animal testing and has established extensive guidance on how a registrant may adapt standard information requirements where possible. There is a clear impetus therefore to evolve toxicological hazard assessment not only to address ethical concerns surrounding animal testing but also to provide enhanced levels of protection for humans and the environment.

Exploiting Organ-on-Chip for regulatory purposes

Whether it is ensuring the safe use of pharmaceuticals, food additives, or plant protection products, regulatory frameworks typically require producers or suppliers to provide information on toxicological properties of their chemicals for the purposes of risk assessment. Animal testing has been the primary means of providing such data, particularly for complex health effects such as systemic organ toxicity and cancer. Apart from the societal pressure to move away from animal testing, there is a growing scientific impetus for more human-relevant approaches such as Organ-on-Chip (OoC). As the technology advances however, a significant challenge has emerged for solution-providers i.e. how to optimally combine novel experimental and computational methods in a way that delivers the comprehensive information set needed for regulatory decision-making. To this end, the OECD has led efforts to design an overarching framework known as Integrated Approaches to Testing and Assessment (IATA) that has a primary aim of bringing non-animal methods to bear in regulatory domains [1]. Thus positioning OoC as a central element of an IATA is likely to provide a pragmatic and effective means of demonstrating utility and application for regulatory purposes.

Building confidence to gain regulatory acceptance

As scientists, end-users and regulators engage in developing and applying OoC-enabled IATA, a number of issues will have to be grappled with. These include, for example, how to strike the right balance between flexibility on one hand, to embrace the rapid evolution of the scientific toolbox, and formality on the other hand, motivated by expectations for validation [2] and standardisation to aid implementation. In addition, efforts will be needed to understand how to best characterise sources of uncertainty within IATA stemming from OoC and how best to establish the scientific credibility of proposed OoC approaches to ensure the willingness of others to actually use them to inform safety decisions [3].

References

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