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An Introduction to ECETOC's workshops on Point of Departure and IVIVE modelling

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'Omics technologies have been part of the research toolkit since the late 1990s. Right from the start there were predictions about how these technologies would revolutionize toxicology allowing greater insight into pathological changes, understanding of mechanisms, and in deriving points of departure. There were, however, several challenges identified including recording of metadata, processing of data, and finally interpretation. ECETOC was amongst the first to systematically explore the application of 'omics methods, now incorporated into the group of methods known as New Approach Methodologies (NAMs), to regulatory toxicology. Outputs have led to projects included in the workplan of the Extended Advisory Group on Molecular Screening and Toxicogenomics (EAGMST) group of the OECD and to the drafting of OECD Guidance Documents for omics data reporting. The workshop on the derivation of a Point of Departure (POD) from 'omics data, jointly with the one on PBPK models for in vitro-in vivo extrapolation provide a framework for the use of NAM data for quantitative risk assessment. Workshop presentations demonstrated that 'omics data developed within robust frameworks for both scientific data generation and analysis can be used to derive a POD. The issue of noise in the data was discussed as an important consideration for identifying robust omics changes and derive a POD. As such variability or "noise" can comprise technical or biological variation within a dataset but should clearly be distinguished from homeostatic responses. Adverse Outcome pathways (AOPs) were considered to be a useful framework on which to assemble omics methods, and several case examples were presented in illustration of this point. What is apparent is that high dimension data will always be subject to varying processing pipelines and hence interpretation, depending on the context they are used in. Yet, they can provide valuable input for regulatory toxicology, with the pre-condition being robust methods for the collection and processing of data together with a comprehensive description how the data was interpreted, and conclusions reached.

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Point of Departure, IVIVE, 'omics.