NEW OECD GUIDANCE DOCUMENT ON GOOD *IN VITRO* METHOD PRACTICES (GIVIMP) FOR THE DEVELOPMENT AND IMPLEMENTATION OF *IN VITRO* METHODS

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In vitro data need to be of high scientific relevance and quality, reproducible and internationally accepted if used in a regulatory context. Therefore, recently, a guidance document (GD) on Good *In Vitro* Method Practices (GIVIMP) has been developed. It should be applied for the development and implementation of *in vitro* methods for regulatory use in human safety assessment aiming at reducing the uncertainties in cell and tissue-based *in vitro* method derived predictions.
The development of the GIVIMP guidance is coordinated by the European validation body EURL ECVAM and has been accepted on the work plan of the OECD test guideline programme as a joint activity between the Working Group on Good Laboratory Practice (GLP) and the Working Group of the National Coordinators of the Test Guidelines Programme (WNT). The GIVIMP GD is divided into 10 sections covering: (1) Roles and responsibilities, (2) Quality considerations, (3) Facilities (4) Apparatus, material and reagents, (5) Test systems, (6) Test and reference/control items, (7) Standard operating procedures (SOPs), (8) Performance of the method, (9) Reporting of results, (10) Storage and retention of records and materials.
The scope of the GIVIMP document includes the principles of good cell culture practice (GCCP) for the greater international harmonization, standardization, and rational implementation of laboratory practices. GCCP principles have to be strictly applied to *in vitro* systems to deliver robust cellular models for toxicity testing. Failure to adopt GCCP principles in laboratories significantly increases the risk of generating erroneous data as well as risking worker health issues and legal liabilities.

New approach methods (NAM) in toxicology with a focus on in vitro developmental neurotoxicity testing".

Current approaches for generating data relevant to developmental neurotoxicity hazard evaluation according to the OECD TG 426 are entirely based on complex animal testing that is time- and resource-consuming, therefore rarely performed. As a result, there is a lack of information concerning the developmental neurotoxicity (DNT) hazard posed by industrial and environmental chemicals. New testing approaches based on batteries of alternative and complementary (non-animal) tests are badly needed to identify chemicals with DNT potential. The need for more effective DNT screening is driven by the scientific fact that the developing nervous system is more sensitive to exposures of some chemical classes of hazardous substances. In addition, recent societal concerns have been raised linking the rise in children's developmental learning disabilities to chemical exposures.

To facilitate the use of alternative methods in DNT regulatory decision making process the Adverse Outcome Pathway (AOP)-informed and key neuro-develop-mental processes-driven an Integrated Approaches to Testing and Assessment (IATA) will presented. IATA should be

customised for the chemical/class of chemicals and the specific regulatory need, using various sources of information (non-testing methods, in vitro approaches, in vivo animal and human data). For generation of new data the proposed IATA framework should be based on a set of *in vitro* test methods that can be used in a flexible combination (fit-for-purpose), anchoring the assays against molecular initiating events, the selected set of key events identified in the existing DNT AOPs and key neurodevelopmental processes (including neural precursor cell proliferation, migration, neuronal differentiation, neuronal network formation etc). The advantage of such types of assays is that they capture toxicants with multiple targets and modes-of-action.

Such IATA would facilitate an application of mechanistic knowledge into DNT evaluation produced by in vitro methods, increasing scientific confidence in decision making process, delivering data that could contribute to screening for prioritization, hazard identification and characterization and possibly safety assessment of chemicals, speeding up evaluation of thousands of compounds present in industrial, agricultural and consumer products that lack safety data on DNT potential.