New approach methods in toxicology with a focus on *in vitro* developmental neurotoxicity (DNT) testing

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The new approach methods (NAM) are being developed to make the use of chemicals safer and to reduce the need for animal testing**.** They include a variety of new testing tools and new concepts to improve the mechanistic understanding of the toxic effects of chemicals.
Taking as an example the current requirements for generating data relevant to DNT hazard evaluation according to the OECD TG 426, they 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 DNT hazard posed by industrial and environmental chemicals. Therefore, a new testing paradigm based on batteries of alternative and complementary (non-animal) tests are badly needed to identify chemicals with DNT potential. Additionally, 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 neurodevelopmental disorders of children (autism, learning disabilities, ADHD) to chemical exposures.

To facilitate the use of alternative methods in DNT regulatory decision making process the Adverse Outcome Pathway (AOP)-informed and key neurodevelopmental processes-driven an Integrated Approaches to Testing and Assessment (IATA) will be proposed. IATA should be customised for the specific regulatory need, using various sources of information. Generation of new data 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.

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.