Methods2AOP: An International Collaboration to Integrate Assay Annotations into the AOP Key Event Descriptions

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One of the fundamental principles for the Adverse Outcome Pathway (AOP) framework is that AOP Key Events (KE) must be detectable and have appropriate measurements to be acceptable and substantiate proper linkage(s) between possible real-life stressors and effects on a particular KE. AOP authors must provide method-related information in a "how it is measured or detected" section for each KE entered in the AOP-Wiki to justify how the test method provides a measurement of an underlying biological process. However, this free text description field does not reflect the importance of the link between a given KE and a test method used to measure it (and vice versa) nor enables a consistent description of the methods across different KEs. The role of test method linkages in the AOP-Wiki must become more explicit and visible, and the Methods2AOP initiative aims to make this possible.

Facilitated by the European Commission's Joint Research Centre (JRC, EURL ECVAM), the Methods2AOP initiative is an international collaboration that also includes NIH NICEATM, US EPA, Environment and Climate Change Canada, and others. To date, the collaboration has adapted ~30 key fields from existing efforts such as OECD guidance document (GD) 211 and divided them into two levels to facilitate the association of test method with KEs (level 1) in a simple but FAIR (Findable, Accessible, Interoperable, Reusable) manner while also integrating enough real-life assay details (level 2) to annotate the technical implementation and enable interpretation of outputs within the AOP context. To promote FAIR principles, fields are restricted to terms from existing ontologies whenever possible and new information will be captured as tables in the AOP-Wiki. Eventually, test methods would be a new primary entity within the AOP-Wiki linking AOP descriptions to external sources of information regarding the associated test methods.

Challenges encountered throughout the process of identifying appropriate fields on both levels include delineating meaning and which aspects of methods are captured between levels and keeping the information requirements straightforward and non-prescriptive. It is a priority to encourage adoption among information providers while collecting requisite details on test methods to increase the overall trustworthiness and utility of a methods annotated AOP.

This annotation framework is established in full transparency and alignment with requirements from the OECD Extended Advisory Group on Molecular Screening and Toxicogenomics

(EAGMST, the body governing the AOP Framework), and other affected stakeholders to advance the integration of experimental definitions into AOP frameworks and facilitate the increased regulatory uptake of AOP knowledge.

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