Method description template

[*METHOD NAME*]

*Please send your method description (or your questions) to* *torben.osterlund@ed-pepper.eu* *or* *celine.boudet@ed-pepper.eu*

*Do not hesitate to contact Torben or Céline in case you have questions.*

*Developers can be guided in assessing the readiness of the method by using the ReadEDTest questionnaire (*[*https://readedtest.u-paris-sciences.fr*](https://readedtest.u-paris-sciences.fr)*). The main use is to identify strength and weaknesses. Please note that even if the method does not meet all the criteria from ReadEDTest, this is not an obstacle for Pepper to consider it for validation, depending of course of which part is to be improved. Do not hesitate to contact us to discuss it further.*

This document is based on the OECD GD 211 and EURL ECVAM Test pre-submission form

# PURPOSE OF THE DOCUMENT

This Method description template lists the information needed to assess the fitness of the method to Pepper’s constraints. The document will allow Pepper to perform a preliminary assessment of the status of development of the methods and its potential relevance. If the outcome of the assessment is positive, the method will be submitted to a ranking vote of Pepper’s Relevance Committee. The methods with the higher ranking will be validated by Pepper.

# ELIGIBILITY

This call addresses methods for the characterisation of endocrine disruptors. It will not consider *in silico* methods or long-term *in vivo* methods, method covering pathways or endpoints which are already covered by standardised methods such as OECD or US EPA Test Guidelines, Methods which are already in an ongoing validation elsewhere. It will consider, but is not limited to, methods allowing the identification of an endocrine mode of action (MoA), an endocrine-related adverse outcome (AO), or linking a MoA to an AO are in the scope of Pepper.

Good submissions would be methods that:

* Were developed in Europe
* Are mature enough, which includes having an established protocol (ideally a Standard Operating Procedure with acceptance criteria and prediction model), and available historical reference compounds.
* Respond to an identified need (with regard to regulatory identification of EDCs). Its potential integration into a testing strategy/integrated approach to testing and assessment will be considered1
* Have a positive impact on 3Rs
* Are likely to be accepted by international institutions (such as the OECD)
* Are applicable easily in many labs (i.e. not requiring a very specific/expensive type of equipment)
* Do not face legal or logistical obstacles to a broad use of the method.

The method developer must be prepared to commit to a validation exercise (including human resources devoted to the project)2.

The template to describe the method is provided here.

Alternatively, the method can be described using a template such as the OECD Guidance Document 211 (GD211) on method documentation for the purpose of safety assessment, or the ToxTemp (described in Krebs *et al* 2019, ALTEX 36(4), 2019).

1 However, a testing strategy or IATA does not need to be submitted

2 Pepper will provide financial contribution, but the developer needs to be aware that a validation requires time to test substances, answer questions from Pepper/participating labs, draft/modify the SOP, gather historical data, organize a training ...

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| TEMPLATE FOR METHOD DESCRIPTION |
| 1. General information |  |
| 1.1 Assay name (title) |  |
| 1.2 Assay developer(s)/Laboratory and contact details | *Name, address, email address, phone number* |
| 2. Test Method Definition |  |
| 2.1 Scientific principle of the method | *A summary description of the scientific principle including the biological/physiological basis and relevance (e.g. modeling of a specific organ) and/or mechanistic basis (e.g. modeling a particular mechanism by biochemical parameters) should be described. If possible, indicate what the**anchor point is within an AOP.* |
| 2.2 Intended toxicological use of the method | *Does the method addresses/informs on** *Human Health effects,* ☐*Environmental effects,* ☐*Other (explain)*
 |
| 2.3 Purpose of the test method | *Briefly describe the intended purpose (i.e. practical use) of the method (e.g. regulatory or non-regulatory) and whether it is intended to be used alone or in combination with other methods (e.g. within an Integrated Approach to Testing and Assessment (IATA)).**The response measured in the assay should be put in the context of the biology/physiology leading to the in vivo response or effect (apical effect)* |
| 2.4 Test system: Tissue, cells, extracts utilised in the assay (and the species source) or experimental animals | *Describe the biological material and constraints to be applied (Biosafety level, etc).**Indicate whether cryopreserved biological material can be used or only freshly prepared.**Provide information on whether materials are readily available commercially or whether materials are developed in the laboratory (e.g. cell suspensions from tissue). Indicate source/manufacturer of biological**material used.* |
| 2.5 Metabolic competence of the test system |  |
| 2.6 Description of the experimental system exposure regime | *Indicate dosage and exposure time including observation frequency. (number of doses/concentrations tested or testing range, number of replicates, the use of control(s) and vehicle).**Indicate whether there might be potential solubility issues with the test**system, and solutions proposed to address the issue* |
| 2.7 Standard Operating Procedure | *Is there a defined protocol describing step-by-step the method, including a list of all necessary reagents and instruments*Yes/No/Partially |
| 2.8 Quality/acceptance criteria | *Are quality criteria for the test system (e.g. cell line, tissue model) being used and are they specified in the protocol?* |
|  | *Are there acceptance criteria for the data obtained for the test substances and controls, and are they specified in the protocol? (e.g; the E2 reference standard concentration-response curve should be sigmoidal in shape and have at least three values within the linear portion of the concentration-**response curve)* |
| 2.9 Known technical limitations and strength | *e.g. The assay may not be technically applicable to certain types or class of chemicals*Limitations:-Strengths:- |
| 2.10 Technical requirements | *e.g. luminometer with 2 injectors* |
| 2.11 Information about the throughput of the assay | *indicate the throughput of the assay to provide an indication of likely resource intensity, and qualify with e.g. approximate number of chemicals/concentrations per run\*.**Specify the duration of a run* |
| 2.12 Cost of application | *Provide an estimation of the cost (consumables, workforce time, other materials) of a run\** |
| 2.13 Status of the method development and uses | *State whether the method is used in other laboratories*Regulatory use: *Provide details of any potential regulatory application and of the toxicological hazard endpoint being addressed by the assay*. |
| 2.14 Availability of information about the assay in relation to proprietary elements | *Describe if the test method includes components, equipment or other scientific procedures that are covered (or pending) by Intellectual Property Rights (IPR) (e.g., patents, patent applications, industrial designs and trademarks). Information should be provided on the overall availability of the IPR-protected components including whether they are commercially available or require a Material Transfer Agreement (MTA) or other licensing agreements* |
| 3. Data interpretation and prediction model |  |
| 3.1 Data analysis | *Does the method require a procedure for deriving, on the basis of the raw data, the method endpoint results? Describe how the data are summarised and expressed (e.g. normalisation to negative control, derivation of score value, . IC50 using modified Hill equation)* |
| 3.2 Explicit prediction model | *Is there a prediction model/data interpretation procedure available for translating the method results into predictions of human health,**environmental and/or other biological effects? (if yes provide it)* |
| 3.3 Software name and versionfor algorithm/prediction model generation |  |
| 4. Test method performance |  |
| 4.1 Robustness of the method | *Information on within-laboratory repeatability and reproducibility, and between laboratory transferability and reproducibility, should be reported**if available.* |
| 4.2 Reference chemicals/chemical libraries, rationale for their selection andother available information | *List the chemicals tested (data obtained with these chemicals will have to be provided to Pepper if the method enters pre-validation).* |
| 4.3 Performance measures/predictive capacity (if known) | *Report any goodness-of-fit statistics or results of goodness-of-fit testing (including if relevant a rationale for selection/use of a particular function) that might be available for the assay and/or its prediction (e.g. r2, r2 adjusted, standard error, sensitivity, specificity, false negative and false**positive rates, predictive values, etc).* |
| 4.4 Applicability domain | *Describe the types of substances in terms of their physical properties or similar (e.g. specific types of substances) for which the assay is appropriate.* |
| 5. Potential regulatory applications |  |
| 5.1 Context of use | *For example, support category formation and read-across; Priority setting; Screening level assessment of a biomarker or mechanistic activity or response; Integrated approaches to testing and assessment (IATA)* |
| 5.2 Endocrine disrupter identification | *What aspect of the WHO definition on endocrine disrupter$, does the method inform on? (endocrine activity, adverse effect, biological plausible link)* |
| 6. References |  |
| 6.1 References on method development | *List publications describing the method (and its development)* |
| 6.2 References on method application | *List publications describing the use of the method* |
| 7. Supporting information |  |
| 7.1 Ethical issues and contributions to 3Rs |  |
| 7.2 Ethical regulations applicable | *Does the method fall under the Directive 2010/63 on the protection of animals used for scientific purposes or other regulation on bioethics?* |
| 7.3 Comparisons with other methods | *e.g what is the added value of this method compared to existing one(s)? Is it an enhancement of an existing method?* |

\* a run is an independent experiment characterized by a new set of solutions and controls

$ An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations (IPCS/WHO, 2002)