

April 2017

OECD ADVERSE OUTCOME PATHWAY

Project Submission Form

If you require further information please contact the OECD Secretariat Delrue
(Nathalie.delrue@oecd.org)

Return completed forms to our generic account (env.tgcontact@oecd.org), and Nathalie

PROJECT TITLE

Activation of estrogen receptors in immune cells exacerbates allergic responses

SUBMITTED BY (Country / European Commission / Secretariat)

Japan

DATE OF SUBMISSION TO THE SECRETARIAT

Nov. 30 , 2018

DETAILS OF LEAD COUNTRY/CONSORTIUM

Country/Organisation:	Japan
Agency/ministry/Other:	AOP Working Group, Testing Methodology Committee, The Japanese Society of Immunotoxicology
Contact person(s):	Yasuharu Otsubo
Mail Address:	2438 Miyanoura, Kagoshima 891-1394, Japan
Phone/fax:	+8199-294-2600
Email:	otsubo-yasuharu@snbl.co.jp

PROJECT CATEGORY

Development of an AOP - applicable to a chemical category

Select the development tool to be used

AOP-Wiki Effectopedia

Guidance document related to AOP development including its evaluation

Knowledge management tool for supporting AOP development including its evaluation

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Other, please specify below

If other category, please specify:

PROJECT DESCRIPTION

Please provide sufficient information to facilitate the review of the project submission by the OECD secretariat and the Extended Advisory Group with respect to its suitability to be included in the workplan of the AOP programme.

Immune disorders, such as, allergy and autoimmune disease are reported to occur more frequently in females, suggesting a possible role of estrogens and estrogen receptors (ERs) immune system function. Estrogen receptors are found in many types of immune cells and a documented action of estrogen is to alter immune responses toward an allergic Th2 phenotype. We propose to develop the AOP for the activation of estrogen receptors in immune cells leading to exacerbation of allergic responses.

Estrogen activate ERs in immune cells promoting the development of Th2 cells that secrete IL-4, IL-5, IL-10 and IL-13. The increased secretion of these Th2 cytokines contribute to the exacerbation of allergic responses.

Note: For AOP Development projects please indicate the extent of the pathway to be described (i.e. the anchor points), the intermediate events that are likely to be addressed, the state of current development, the degree to which this pathway is already understood and described in the literature, and the expectation on the availability of evidence to support the AOP. **Proposers should also indicate if and how the AOP is associated to any regulatory toxicological endpoints (e.g. acute or chronic toxicity, toxicity to reproduction etc.)** Please provide references, links or attachments for supplementary information.

PROJECT PLANNING

In this section, please provide an indication of when the project is likely to commence and the expected duration. Please also make reference to any particular milestones or external factors that will influence project planning, and if the project is linked to programmes of particular organisations or consortia.

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AOP Working Group of Testing Methodology Committee in the Japanese Society of Immunotoxicology will develop several AOPs for immunotoxicology in the next three years.

The timeline of the development of the present AOP is as follows:

Nov., 2018: to submit the AOP development

Jun., 2019: to complete AOP Wiki input and submit internal review of the AOP

Dec., 2019: EAGMST review

FLOW DIAGRAM

In this section, please provide a flow diagram of the proposed AOP, including the MIE, KEs at the various stages (molecular interaction, cellular response, organ response) and the AO.

