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OECD ADVERSE OUTCOME PATHWAY

Project Submission Form

(Revised 14 October 2014: the Secretariat information to send the form was modified)
If you require further information please contact the OECD Secretariat
Return completed forms to Lisa Savary (Lisa.SAVARY@oecd.org) and Camilla Francis
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PROJECT TITLE

Inhibition of tyrosinase leads to decreased population in fish

SUBMITTED BY (Country / European Commission / Secretariat)

South Korea

DATE OF SUBMISSION TO THE SECRETARIAT

20/05/2019

DETAILS OF LEAD COUNTRY/CONSORTIUM

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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

Other, please specify below

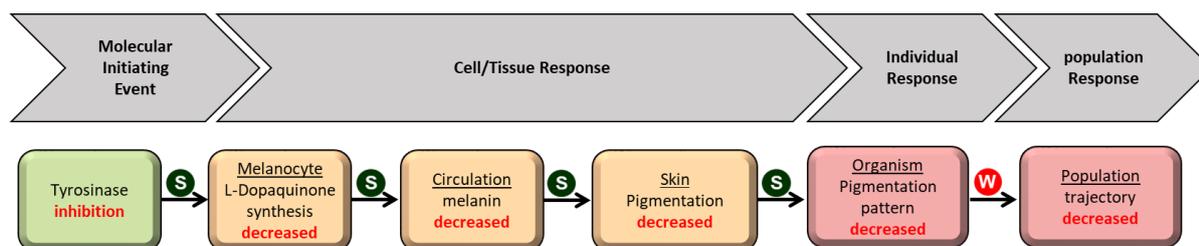
If other category, please specify:

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.

The present AOP shows a tyrosinase (TYR) inhibition-mediated adverse outcome (AO) in fishes. TYR is the rate-limiting enzyme controlling the induction of melanogenesis in diverse colored patterns in aquatic organisms. The significant reactions of TYR can be explained as followings; First, TYR can convert L-tyrosine directly to L-3,4-dihydroxyphenylalanine (L-DOPA) which is a precursor of (2S)-2-Amino-3-(3,4-dioxocyclohexa-1,5-dien-1-yl)propanoic acid (L-Dopaquinone) synthesis; Second, TYR catalyzes the oxidation of L-DOPA to the L-Dopaquinone which is the reactive intermediate for the eumelanin and pheomelanin synthesis. Inhibition of TYR can be caused by chemical inhibitors such as 1-phenyl 2-thiourea (PTU), sesamol, arbutin, Kojic acid, bis(4-hydroxybenzyl) and etc. (J. Karlsson et al., 2001; W. C. Chen et al., 2015; Baek and Lee, 2015; S. H. Cha et al., 2011). TYR inhibition, the MIE for the present AOP, results in reduction of L-Dopaquinone level in the melanocyte via inhibition of L-DOPA oxidation moreover, it results in attenuation of eumelanin and pheomelanin biosynthesis (T. S. Chang, 2012; J. Choi and J. G. Jee, 2015; S. Y. Lee, 2016; A. J. Winder and H. Harris, 1991; W. C. Chen et al., 2015). The lowered level of melanin biosynthesis by TYR inhibition simultaneously leads to depigmentation in skin tissue and diminished pigmentation pattern in the fish body (L. E. Jao et al., 2013; S. Y. Wu et al., 2015; S. H. Baek and S. H. Lee, 2015; W. C. Chen et al., 2015; D. C. Kim et al., 2017).

Pigment patterns in common fishes usually play a significant role to communicate within species, intersexual interactions, escape potential in the eyes of predators and finding shoal mate (Price et al., 2008; C. L. Peichel et al., 2004; R. E. Engeszer et al., 2004). Accordingly, it is considered that the tyrosinase inhibitor-induced depigmentation reduces the trajectory of fishes. Although several studies regarding agonistic behaviour, loss of visual performance, changed survival rate and spawning performance in depigmented fishes have been performed over the past decades (O. Slavík and M. Wackermannová, 2016; J. Q. Ren et al., 2002; O. Slavík et al., 2015; U. L. Onyia et al., 2016; K. Bondari, 1984; J. O. A. Q. U. I. N. Pérez-Carpinell et al., 1992), these studies have not been clarified the exact mechanism of the decreased trajectories of fish population by specific tyrosinase inhibitor.



Weight of evidence [WoE]

- S** Strong
- W** Weak

This AOP is designed to estimate changes in trajectory of fishes resulted from the TYR inhibition by potential inhibitors. Decreased trajectory resulted from reduced pigmentation pattern in the fish body is potential endpoint for eco-toxicity. The proposed end point will provide useful high throughput risk assessment screening tool for potential chemicals. Consequently, this AOP can be applied to the prediction of eco-toxicity caused by the inhibition of TYR.

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.

This AOP is under development supported by the National Research Council of Science & Technology (NST) grant by the Korea government (MSIP) (No. CAP-17-01-KIST Europe).

	<u>To do</u>	<u>Expected duration</u>
Building the AOP frame	Development of KEs	3 month
	Production of experimental data	18 month
Overall assessment of the AOP	Biological domain of applicability	3 month
	Essentiality of all KEs	3 month
	Evidence supporting all KERs	5 month
	Quantitative WoE considerations	5 month
	Quantitative understanding for each KER	6 month

References

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