

## AOP Coach Checklist and Final Review Report

### COACHES CHECKLIST AND REVIEW REPORT

ver. 2022-11-29

#### AOP Information

AOP number/title: **AOP 460: Antagonism of Smoothened receptor leading to orofacial clefting**

Author: Jacob I. Reynolds<sup>1</sup> , Brian P. Johnson<sup>1,2</sup>

<sup>1</sup>Department of Biomedical Engineering, Institute for Quantitative Health Science and Engineering, Michigan State University, East Lansing, MI

<sup>2</sup>Department of Pharmacology and Toxicology, Michigan State University, East Lansing, MI

Associated wiki page: <https://aopwiki.org/aops/460>

#### Coach Information

Coach Information

Name: Judy Choi

OECD Country/Organisation: Germany

E-mail: [judy.choi@bfr.bund.de](mailto:judy.choi@bfr.bund.de)

Final review/Compliance check before AOP acceptance for journal review

Name: Sonja von Aulock

Compliance review conducted as editor of ALTEX

E-mail: [editor@altex.org](mailto:editor@altex.org)

#### Review Information

Date this checklist has been filled: 24.10.2024

Date of final draft PDF snapshot proposed for external review: 2023-06-14

#### General Observations and Conclusions of the Coach(es)/Reviewer(s)

Description of major changes compared to the AOP outlined in the original submission/proposal by authors:

## AOP Coach Checklist and Final Review Report

Summary of coach comments and author responses:

Potential regulatory significance of AO could be specified. Typos should be corrected to improve clarity. Some sections on Quantitative Linkage were not filled owing to lack of information or combined with sections on Uncertainties and Inconsistencies. These minor points will be fed into the scientific review.

### Checklist

The following tables are checklists for the overall AOP and for the individual KEs and KERs.

<b>Overall AOP</b>	<i>Yes</i>	<i>For revision</i>	<i>Revision agreed</i>	<i>Not applicable</i>
<i>Does the title of the AOP follow the correct convention (MIE or first KE leading to AO)?</i>	x			
<i>Does the title of the AOP reflect its content/domain?</i>	x			
<i>Is a graphical representation included?</i>	x			
<i>Is it clear who the authors/developers of the AOP are? Contact information for one or more corresponding author(s) should be included.</i>	x			
<i>Is the status of the AOP described?</i>	x			
<i>Does the abstract concisely describe the main content of the AOP in a standalone manner?</i>	x			
<i>Have prototypical stressors been identified for the MIE?</i>	x			
<i>Has the regulatory relevance of the AO been described?</i>	x			
<i>Is the domain of applicability of the AOP defined in accordance with the OECD AOP Handbook?</i>	x			
<i>Is the level of support for essentiality of the KEs described and assessed in accordance with the OECD AOP Handbook?</i>	x			
<i>Has consideration been given to the level of support for the calls on the Overall WoE and the Quantitative Understanding?</i>	x			

## AOP Coach Checklist and Final Review Report

<b>KE number, title: MIE 2027</b>	Yes	For revision	Revision agreed	Not applicable
Has the KE already been used in other AOPs?				x
Has the KE been reviewed according to OECD requirements?				x
If an existing KE is being adapted, have the previous authors been informed?				x
Is the KE described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is the biological context (level of organization, terms) specified?	x			
Are KE components defined using structured ontology terms (Process, Object, Action)?	x			
Is the KE description clear?	x			
Are measurement methods specified, described and referenced?	x			
Is the domain of applicability described?	x			

<b>KE number, title: KE 2044</b>	Yes	For revision	Revision agreed	Not applicable
Has the KE already been used in other AOPs?				x
Has the KE been reviewed according to OECD requirements?				x
If an existing KE is being adapted, have the previous authors been informed?				x
Is the KE described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is the biological context (level of organization, terms) specified?	x			
Are KE components defined using structured ontology terms (Process, Object, Action)?	x			
Is the KE description clear?		x*		
Are measurement methods specified, described and referenced?	x			
Is the domain of applicability described?	x			
*Explain abbreviation: ciliary localization sequence (CLS); its instead of its'				

## AOP Coach Checklist and Final Review Report

<b>KE number, title: KE 2028</b>	Yes	For revision	Revision agreed	Not applicable
Has the KE already been used in other AOPs?	502			
Has the KE been reviewed according to OECD requirements?				x
If an existing KE is being adapted, have the previous authors been informed?				x
Is the KE described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is the biological context (level of organization, terms) specified?	x			
Are KE components defined using structured ontology terms (Process, Object, Action)?	x			
Is the KE description clear?		x*		
Are measurement methods specified, described and referenced?	x			
Is the domain of applicability described?	x			
* oncogene instead of onocogene; primary instead of primarily; its instead of its'; SMO is then instead of SMO this then				

<b>KE number, title: 2040</b>	Yes	For revision	Revision agreed	Not applicable
Has the KE already been used in other AOPs?	491 & 502			
Has the KE been reviewed according to OECD requirements?				
If an existing KE is being adapted, have the previous authors been informed?				x
Is the KE described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is the biological context (level of organization, terms) specified?	x			
Are KE components defined using structured ontology terms (Process, Object, Action)?	x			
Is the KE description clear?	x*			
Are measurement methods specified, described and referenced?	x			
Is the domain of applicability described?	x			

## AOP Coach Checklist and Final Review Report

* oncogene instead of onocogene; primary instead of primarily; its instead of its'; SMO is then instead of SMO this then; genes that are instead of genes have are				
--	--	--	--	--

KE number, title: KE 1262	Yes	For revision	Revision agreed	Not applicable
Has the KE already been used in other AOPs?	many			
Has the KE been reviewed according to OECD requirements?	x			
If an existing KE is being adapted, have the previous authors been informed?				
Is the KE described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x*			
Is the biological context (level of organization, terms) specified?	x			
Are KE components defined using structured ontology terms (Process, Object, Action)?	x			
Is the KE description clear?	x			
Are measurement methods specified, described and referenced?	x			
Is the domain of applicability described?	x			
*description is not fully independent of an AOP, but this KE has been reviewed and used in multiple AOPs				

KE number, title: 2043	Yes	For revision	Revision agreed	Not applicable
Has the KE already been used in other AOPs?	491 & 502			
Has the KE been reviewed according to OECD requirements?				
If an existing KE is being adapted, have the previous authors been informed?				
Is the KE described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is the biological context (level of organization, terms) specified?	x			
Are KE components defined using structured ontology terms (Process, Object, Action)?	x			
Is the KE description clear?	x*			

## AOP Coach Checklist and Final Review Report

Are measurement methods specified, described and referenced?				
Is the domain of applicability described?	x			
*consider use of "normal" and "other" ; introduce all abbreviations				

KE number, title: KE 1821	Yes	For revision	Revision agreed	Not applicable
Has the KE already been used in other AOPs?	man y			
Has the KE been reviewed according to OECD requirements?	263			
If an existing KE is being adapted, have the previous authors been informed?				
Is the KE described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is the biological context (level of organization, terms) specified?	x			
Are KE components defined using structured ontology terms (Process, Object, Action)?	x			
Is the KE description clear?	x			
Are measurement methods specified, described and referenced?	x			
Is the domain of applicability described?	x			

KE number, title: KE 2041	Yes	For revision	Revision agreed	Not applicable
Has the KE already been used in other AOPs?	491 & 502			
Has the KE been reviewed according to OECD requirements?				x
If an existing KE is being adapted, have the previous authors been informed?				
Is the KE described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is the biological context (level of organization, terms) specified?	x			
Are KE components defined using structured ontology terms (Process, Object, Action)?	x			
Is the KE description clear?	x			

## AOP Coach Checklist and Final Review Report

Are measurement methods specified, described and referenced?	x*			
Is the domain of applicability described?	x			
*correlating instead of corelating				

KE number, title: AO 2042 (including MIE and AO; copy this table for each KE)	Yes	For revision	Revision agreed	Not applicable
Has the KE already been used in other AOPs?	491 & 502			
Has the KE been reviewed according to OECD requirements?				x
If an existing KE is being adapted, have the previous authors been informed?				
Is the KE described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is the biological context (level of organization, terms) specified?	x			
Are KE components defined using structured ontology terms (Process, Object, Action)?	x			
Is the KE description clear?	x*			
Are measurement methods specified, described and referenced?	x#			
Is the domain of applicability described?	x			
(Only for AO) Is Regulatory Significance of the AO described?	x*			
*birth defects instead of births; etiology of OFCs is complex and includes instead of etiology of OFCs are complex and include #affected instead of effected; its instead of its' *consider specifying: and could result in regulatory measures in the context of developmental and reproductive toxicity (DART) testing.				

KER number, title: 2734 (copy this table for each KER)	Yes	For revision	Revision agreed	Not applicable
Has the KER already been used in other AOPs?				x
Has the KER been reviewed according to OECD requirements?				x

## AOP Coach Checklist and Final Review Report

If an existing KER is being adapted, have the previous authors been informed?				x
Is the KER described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x*			
Is biological plausibility described/discussed?	x			
Is empirical evidence presented, referenced and discussed?	x			
Are uncertainties and inconsistencies described?	x			
Is Quantitative Understanding of the Linkage described?	x			
Is Domain of Applicability described?	x			
Is Evidence Collection Strategy described?		x <sup>#</sup>		
*mouse instead of mice; including instead of inculding; #Described overall in accompanying journal manuscript				

KER number, title: 2735 (copy this table for each KER)	Yes	For revision	Revision agreed	Not applicable
Has the KER already been used in other AOPs?				x
Has the KER been reviewed according to OECD requirements?				x
If an existing KER is being adapted, have the previous authors been informed?				x
Is the KER described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is biological plausibility described/discussed?	x			
Is empirical evidence presented, referenced and discussed?	x			
Are uncertainties and inconsistencies described?	x			
Is Quantitative Understanding of the Linkage described?	x			
Is Domain of Applicability described?	x			
Is Evidence Collection Strategy described?		x <sup>#</sup>		
its instead of its' #Described overall in accompanying journal manuscript				

KER number, title: 2721 (copy this table for each KER)	Yes	For revision	Revision agreed	Not applicable

## AOP Coach Checklist and Final Review Report

Has the KER already been used in other AOPs?				x
Has the KER been reviewed according to OECD requirements?				x
If an existing KER is being adapted, have the previous authors been informed?				x
Is the KER described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is biological plausibility described/discussed?	x			
Is empirical evidence presented, referenced and discussed?	x			
Are uncertainties and inconsistencies described?	x			
Is Quantitative Understanding of the Linkage described?	x			
Is Domain of Applicability described?	x			
Is Evidence Collection Strategy described?		x <sup>#</sup>		
#Described overall in accompanying journal manuscript				

KER number, title: 2731 (copy this table for each KER)	Yes	For revision	Revision agreed	Not applicable
Has the KER already been used in other AOPs?	491			
Has the KER been reviewed according to OECD requirements?				x
If an existing KER is being adapted, have the previous authors been informed?				x
Is the KER described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is biological plausibility described/discussed?	x			
Is empirical evidence presented, referenced and discussed?	x*			
Are uncertainties and inconsistencies described?	x			
Is Quantitative Understanding of the Linkage described?		x <sup>#</sup>		
Is Domain of Applicability described?	x			
Is Evidence Collection Strategy described?		x <sup>#</sup>		
*are instead of is				
*included in Uncertainties section				
#Described overall in accompanying journal manuscript				

## AOP Coach Checklist and Final Review Report

<b>KER number, title: 2732 (copy this table for each KER)</b>	Yes	For revision	Revision agreed	Not applicable
Has the KER already been used in other AOPs?	491			
Has the KER been reviewed according to OECD requirements?				x
If an existing KER is being adapted, have the previous authors been informed?				x
Is the KER described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is biological plausibility described/discussed?	x			
Is empirical evidence presented, referenced and discussed?	x			
Are uncertainties and inconsistencies described?	x			
Is Quantitative Understanding of the Linkage described?		x*		
Is Domain of Applicability described?	x			
Is Evidence Collection Strategy described?		x <sup>#</sup>		
*no information available but this is not stated explicitly #Described overall in accompanying journal manuscript				

<b>KER number, title: 2724 (copy this table for each KER)</b>	Yes	For revision	Revision agreed	Not applicable
Has the KER already been used in other AOPs?	491			
Has the KER been reviewed according to OECD requirements?				x
If an existing KER is being adapted, have the previous authors been informed?				x
Is the KER described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x			
Is biological plausibility described/discussed?	x			
Is empirical evidence presented, referenced and discussed?	x			
Are uncertainties and inconsistencies described?	x			
Is Quantitative Understanding of the Linkage described?		x*		
Is Domain of Applicability described?				
Is Evidence Collection Strategy described?		x <sup>#</sup>		

## AOP Coach Checklist and Final Review Report

* no information available but this is not stated explicitly				
#Described overall in accompanying journal manuscript				

<b>KER number, title: 2726</b> <b>(copy this table for each KER)</b>	Yes	For revision	Revision agreed	Not applicable
Has the KER already been used in other AOPs?	491			
Has the KER been reviewed according to OECD requirements?				x
If an existing KER is being adapted, have the previous authors been informed?				x
Is the KER described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x*			
Is biological plausibility described/discussed?				
Is empirical evidence presented, referenced and discussed?				
Are uncertainties and inconsistencies described?	x			
Is Quantitative Understanding of the Linkage described?	x*			
Is Domain of Applicability described?	x			
Is Evidence Collection Strategy described?		x <sup>#</sup>		
*palatal shelf instead of palatal.				
¥included in Uncertainties section				
#Described overall in accompanying journal manuscript				

<b>KER number, title: 2792</b> <b>(copy this table for each KER)</b>	Yes	For revision	Revision agreed	Not applicable
Has the KER already been used in other AOPs?	491			
Has the KER been reviewed according to OECD requirements?				x
If an existing KER is being adapted, have the previous authors been informed?				x
Is the KER described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?	x*			
Is biological plausibility described/discussed?	x			
Is empirical evidence presented, referenced and discussed?	x			
Are uncertainties and inconsistencies described?	x			

## AOP Coach Checklist and Final Review Report

<i>Is Quantitative Understanding of the Linkage described?</i>	x			
<i>Is Domain of Applicability described?</i>	x			
<i>Is Evidence Collection Strategy described?</i>		x <sup>#</sup>		
<i>*mouse instead of mice; two medial nasal processes instead of two medial nasal process; two mandibular processes instead of two mandibular process; fuse intermaxillary process (missing words?)</i>				
<i>#Described overall in accompanying journal manuscript</i>				

<b>KER number, title: 2882</b> <i>(copy this table for each KER)</i>	Yes	For revision	Revision agreed	Not applicable
<i>Has the KER already been used in other AOPs?</i>				x
<i>Has the KER been reviewed according to OECD requirements?</i>				x
<i>If an existing KER is being adapted, have the previous authors been informed?</i>				x
<i>Is the KER described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?</i>	x*			
<i>Is biological plausibility described/discussed?</i>	x			
<i>Is empirical evidence presented, referenced and discussed?</i>	x			
<i>Are uncertainties and inconsistencies described?</i>	x			
<i>Is Quantitative Understanding of the Linkage described?</i>	x			
<i>Is Domain of Applicability described?</i>	x			
<i>Is Evidence Collection Strategy described?</i>		x <sup>#</sup>		
<i>*two medial nasal processes instead of two medial nasal process; two mandibular processes instead of two mandibular process; fuse intermaxillary process (missing words?)</i>				
<i>#Described overall in accompanying journal manuscript</i>				

<b>KER number, title: 2894</b> <i>(copy this table for each KER)</i>	Yes	For revision	Revision agreed	Not applicable
<i>Has the KER already been used in other AOPs?</i>				x
<i>Has the KER been reviewed according to OECD requirements?</i>				x

## AOP Coach Checklist and Final Review Report

<i>If an existing KER is being adapted, have the previous authors been informed?</i>				x
<i>Is the KER described in a way that allows its reuse in other AOPs (i.e. independent of this AOP)?</i>	x*			
<i>Is biological plausibility described/discussed?</i>	x			
<i>Is empirical evidence presented, referenced and discussed?</i>	x			
<i>Are uncertainties and inconsistencies described?</i>	x			
<i>Is Quantitative Understanding of the Linkage described?</i>	x			
<i>Is Domain of Applicability described?</i>	x			
<i>Is Evidence Collection Strategy described?</i>		x <sup>#</sup>		
<i>*its instead of its'</i>				
<i>#Described overall in accompanying journal manuscript</i>				