

# **Update on Review of Skin Sensitization Non-Animal Methods Received by OPPT in the TSCA New Chemicals Program**

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PETA/EPA/PCRM (PEP) Webinar

May 27, 2020

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# Topics Covered

- OCSPP 2018 Skin Sensitization Policy
- Overview of Information Received by OPPT
- Next Steps



# Skin Sensitization: Replacement of Laboratory Animal Testing

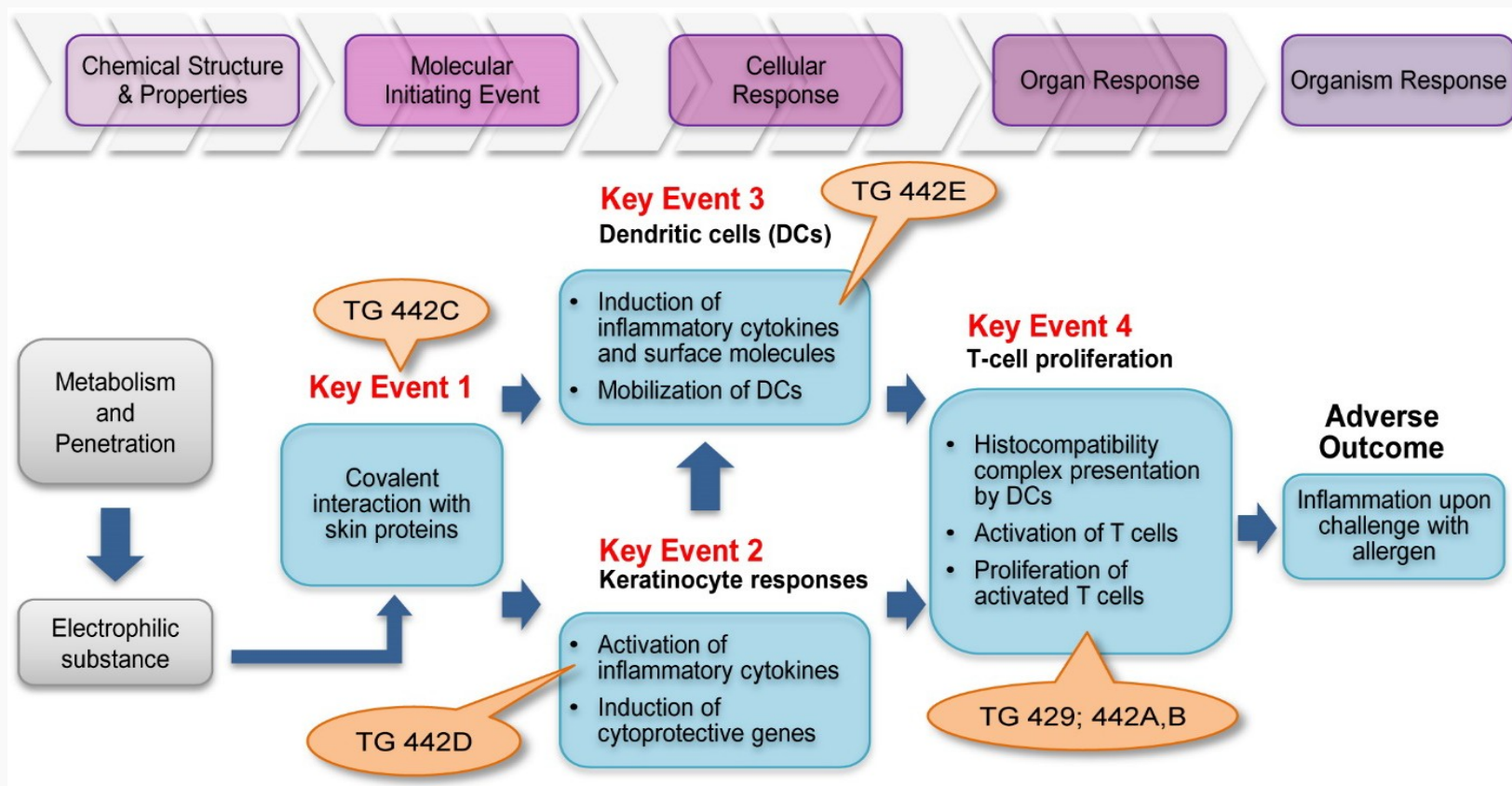
## *Draft Interim Science Policy: Use of Alternative Approaches for Skin Sensitization as a Replacement for Laboratory Animal Testing*

<https://www.regulations.gov/document?D=EPA-HQ-OPP-2016-0093-0090>

- Announced April 10, 2018 and describes the science that supports a policy to accept alternative (*in silico*, *in chemico*, and *in vitro*) approaches for identifying skin sensitization hazard in place of animal studies.
  - Multiple non-animal testing strategies - *in silico*, *in chemico* and *in vitro*, inputs demonstrate comparable or superior performance to one of the most widely used laboratory animal studies for this endpoint, the local lymph node assay (LLNA).
- The draft interim policy is the result of collaboration between a number of entities working on alternative methodologies, including ICCVAM, NICEATM, ECVAM, and Canada PMRA
- This is a joint policy for use by EPA OPP and OPPT

# Adverse Outcome Pathway (AOP)

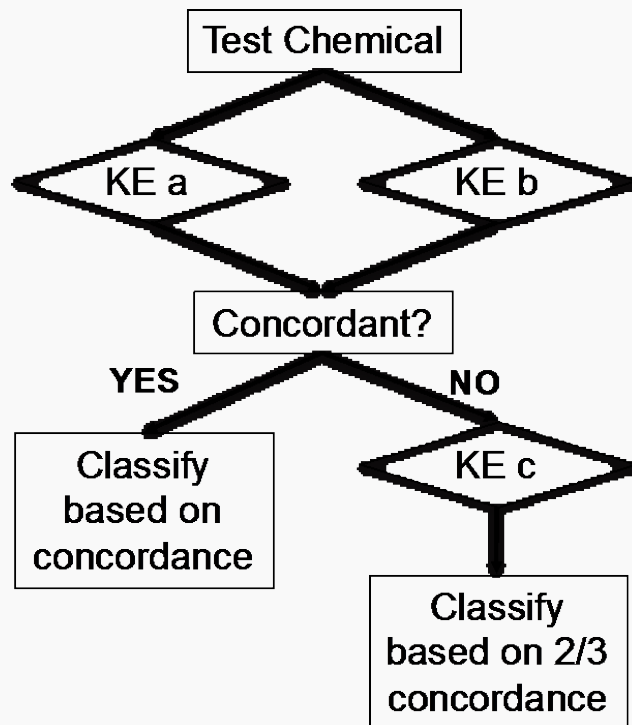
*(adapted from Strickland et al., 2018)*



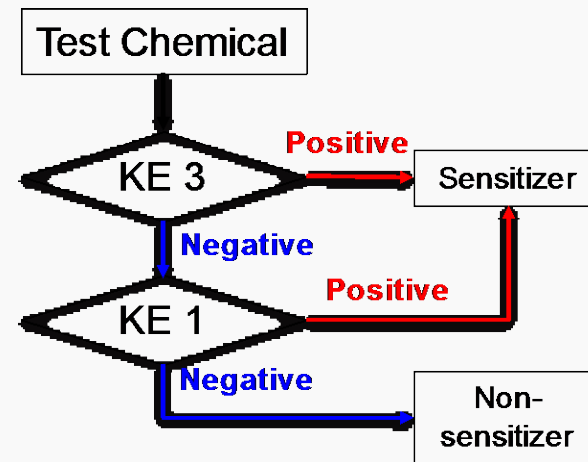


# The Two Defined Approaches (DA's) in the Policy

*"Two out of Three"*



*Key Event 3/1 Sequential Testing Strategy*





## **Overview of Information OPPT Has Received Since October 1, 2015 (All Information Claimed CBI; Only Non-CBI Information is Presented)**

- OPPT has received 49 submissions with skin sensitization NAMs since the beginning of FY 2016 and April of 2020 as part of new chemicals submissions
- The submissions were received from 24 different companies
- The work was performed by 16 different laboratories



## Overview of Information OPPT Has Received Since October 1, 2015 (Only Non-CBI Information is Presented)

<b>Fiscal Year</b>	<b>Submissions with NAMs Only</b>	<b>Submissions with NAMs Plus <i>in vivo</i></b>	<b>Submissions with NAMs plus RIPT*</b>	<b>Submissions with NAMs, <i>in vivo</i> and RIPT</b>	<b>Totals</b>
2015	2	2	3	1	6
2016	5	2	5	2	10
2017	1	-	1	-	2
2018	3	6	2	1	10
2019	9	-	1	-	10
2020	7	4	1	1	11
<b>Totals</b>	<b>27</b>				<b>49</b>

\*RIPT = Human Repeated Insult Patch Test



## Overview of Information OPPT Has Received Since October 1, 2015 (Only Non-CBI Information is Presented)

Fiscal Year	Defined Approach (DA) Method			No DA Used	TOTAL Submissions
	“2 out of 3”	Key Event Sequential Testing Strategy	Other		
2015	1	-	-	5	6
2016	2	-	-	8	10
2017	-	-	-	2	2
2018	2*	-	-	8	10
2019	1	-	1	8	10
2020	2	-	-	9	11
<b>TOTALS</b>	<b>8</b>	<b>0</b>	<b>1</b>	<b>40</b>	<b>49</b>

\*In both cases, 2/3 suggested positive results and an *in vivo* study was performed. The *in vivo* result was negative.





## Overview of Information OPPT Has Received Since October 1, 2015 (Only Non-CBI Information is Presented)

Information Type Submitted	Number Submitted
Key Event 1: OECD 442C	41
Key Event 2: OECD 442D	39
Key Event 3: OECD 442E	19
LLNA (OECD 429, 442A, 442B)	11
Guinea Pig (OECD 406)	3
RIPT	13

*OPPT is evaluating the submitted studies to inform both comparisons/results for TSCA-specific chemicals and to finalize the draft policy.*



## Next Steps: Other Activities

- On-going work at NICEATM to evaluate use of skin sensitization NAMs on formulations/mixtures/TSCA chemicals
- Case study to develop approach for quantitative risk assessment using isothiazolinone class of preservatives. Collaborative project with IT task force, NICEATM, OPP, and IIVS. (Just released on 5/14/20 - <https://www.regulations.gov/document?D=EPA-HQ-OPP-2014-0160-0009>)
- Comments were received on the draft interim policy in the summer of 2018



## Next Steps: Road to Finalizing Policy

1. Consider the comments received on the 2018 Draft Policy
2. Evaluated the NICEATM TSCA Specific Data on Skin Sensitization NAMs
3. Review of information received (OPPT and OPP)
4. Recognize and incorporate appropriate recent OECD activity

1 + 2 + 3 + 4 = Finalize OCSPP Skin Sensitization Policy



# Acknowledgements

- Todd Stedeford, US EPA

**THANK YOU!**

QUESTIONS?

