

SOT 2018 San Antonio
★ March 11-15 ★

★ *In Vitro* Lecture and Luncheon ★

Sponsored by the Colgate Palmolive Company



More Than Skin Deep:

When Alternative Approaches
Outperform Animal Tests



2018 *In Vitro* Lecture
Nicole Kleinstreuer
Speaker





Schedule



11:30 AM–12:00 Noon	Lunch
12:00 Noon–12:10 PM	Welcome: Dr. Reynolds, Education Committee Recognition: Dr. Ganey, SOT President
12:10 PM–12:20 PM	Presentation: Dr. Nicole Kleinstreuer
12:20 PM–12:45 PM	Discussion at Tables
12:50 PM–1:00 PM	Summary/Wrap up



Welcome



Mindy F. Reynolds
Education Committee Chair





Host: Education Committee



- * **Mindy F. Reynolds**, Chair
- * **Deb Hoivik**, Co-chair
 - Aaron B. Bowman
 - Azita (AJ) K. Cuevas
 - Rebecca J. Dearman
 - Sakina Elzebair Eltom
 - Michael K. Peterson
- Michael K. Peterson
- Angela Slitt
- Courtney Jamison, Graduate Representative
- Priya Tripathi, Postdoctoral Representative
- Tao Wang, Council Contact
- Mary Beth Genter, Co-Council Contact

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In Vitro Lecture Planning Group



Mindy Reynolds
Nicole Kleinstreuer
Kevin Beggs
Deb Hoivik

Agnes Karmaus
Priya Tripathi
Larissa Williams

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In Vitro Lecture Goals



- * Feature important research using *In Vitro* and alternative techniques to study basic mechanisms
- * Illustrate how these test methods benefit animal welfare by replacing animal use whenever it is feasible
- * Encourage students and postdoctoral scholars to use alternative techniques in their research

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More Than Skin Deep: When Alternative Approaches Outperform Animal Tests



Nicole C. Kleinstreuer
Deputy Director, NICEATM
NIEHS, DNTP

SOT 2018 *In Vitro* Lecture and Luncheon



National Toxicology Program
U.S. Department of Health and Human Services



Skin Sensitization

“Allergic Contact Dermatitis”

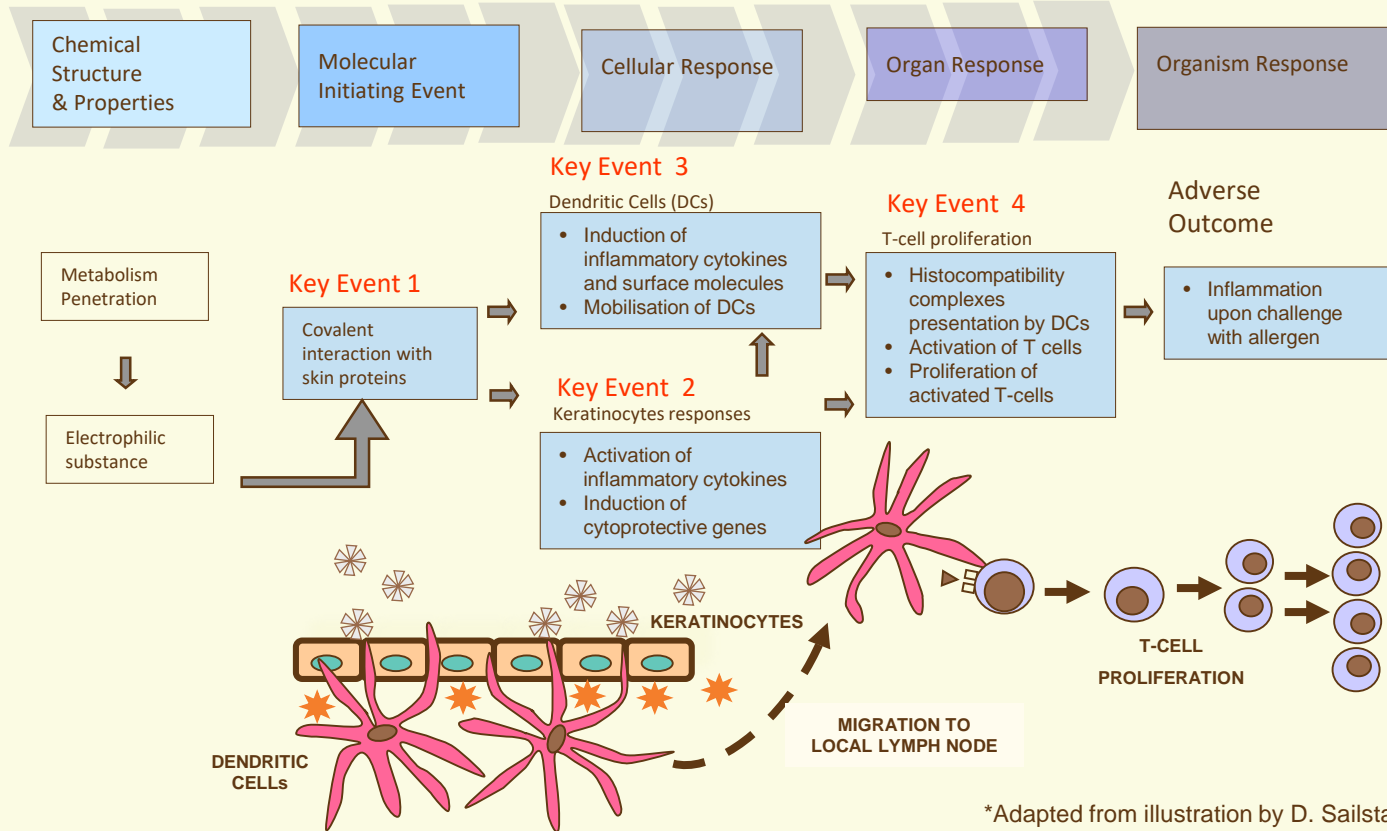
- ✦ Accounts for 10-15% of all occupational disease (*Anderson et al. 2010*)
- ✦ Major testing requirement for cosmetics, pesticides, industrial chemicals, etc.



**NOT TESTED
ON ANIMALS**

Adverse Outcome Pathway (AOP)

Skin Sensitization OECD (2014)



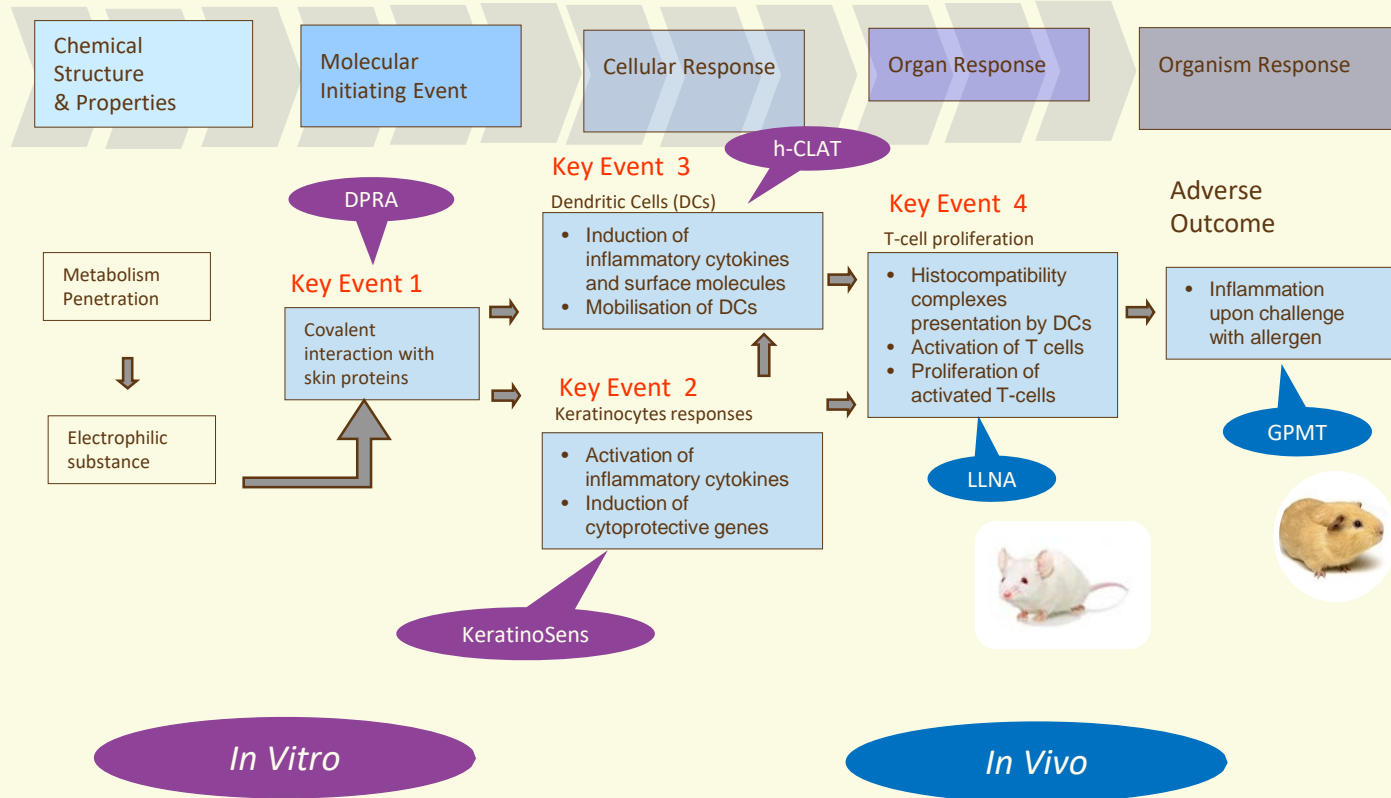
*Adapted from illustration by D. Sailstad












Adverse Outcome Pathway for Skin Sensitization



Test Methods



US Regulatory Requirements/Considerations

		Reference Animal <u>Method</u>	Classification <u>Criteria</u>
	Pesticides, Industrial chemicals	 LLNA	Non Sensitizer  Hazard
	Household Products	 LLNA	Non Weak Strong  Potency
	Dermatological Products	 GPMT	Quantitative  Potency*

Daniel et al. 2018 in press

*preference



Accuracy of Animal Tests Against Human Data



GPMT / Buehler



Hazard
~72%

Potency (GHS)
~60%

LLNA



Hazard
72%-82%

Potency (GHS)
54% - 60%

ICCVAM. 1999. NIH Publication No. 99-4494
ICCVAM. 2010. NIH Publication No. 11-7709
Urbisch et al. 2015. *Reg Tox Pharm* 71:337-351.
Dumont et al. 2016. *Tox In Vitro* 34: 220-228
Hoffmann et al. 2018 *Crit Rev Tox* in press

Reproducibility of Multiple Tests

Hazard
~78%

Potency
~62%



Global Skin Sensitization Project

- ✳ Objective: analysis of non-animal defined approaches (DA)

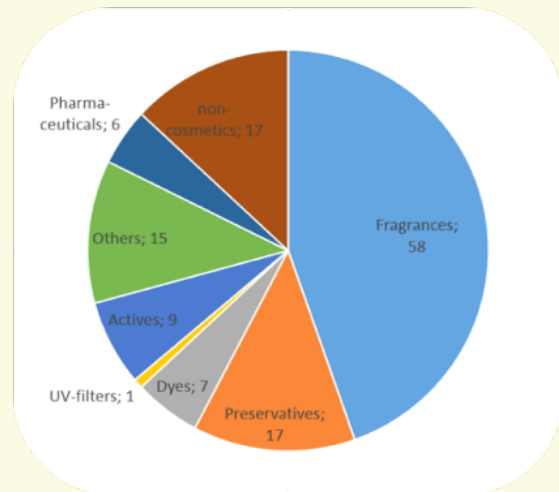
- OECD submitted case studies

- ✳ Collaboration with Cosmetics Europe

- 128 substance dataset
- Animal (LLNA) data
- Clinical human data
- Curation/generation of *in vitro* data
 - Covering all key events of the AOP

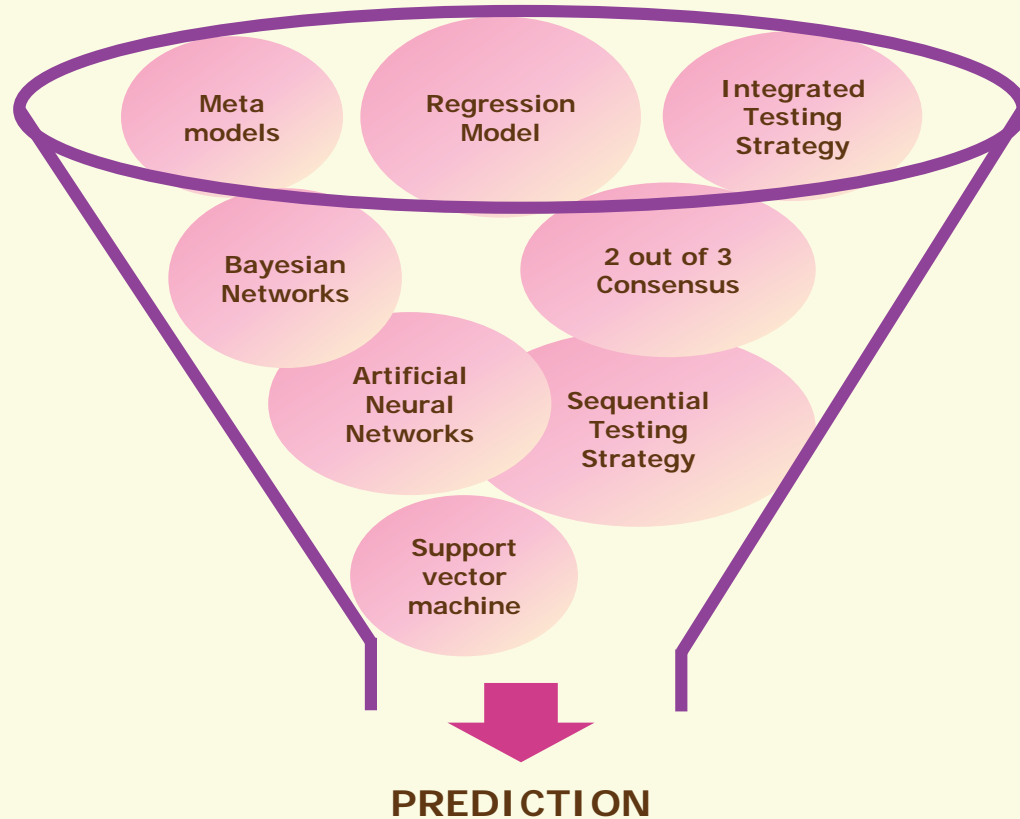
- ✳ Analyze non-animal DAs in an open source and transparent way

- ✳ Evaluate performance against the LLNA and human hazard/potency categories



**Spectrum of 128 substances
(largely cosmetic ingredients)**

Different Defined Approaches (DAs)





DA Performance Evaluation



Most non-animal defined approaches evaluated so far perform **better** than the LLNA at predicting human skin sensitization hazard and potency.

(And when compared to the LLNA, are equivalent in performance to the LLNA at predicting itself.)



CASE STUDY



Is this non-animal defined approach
ready to replace the LLNA?



Case Study Discussion

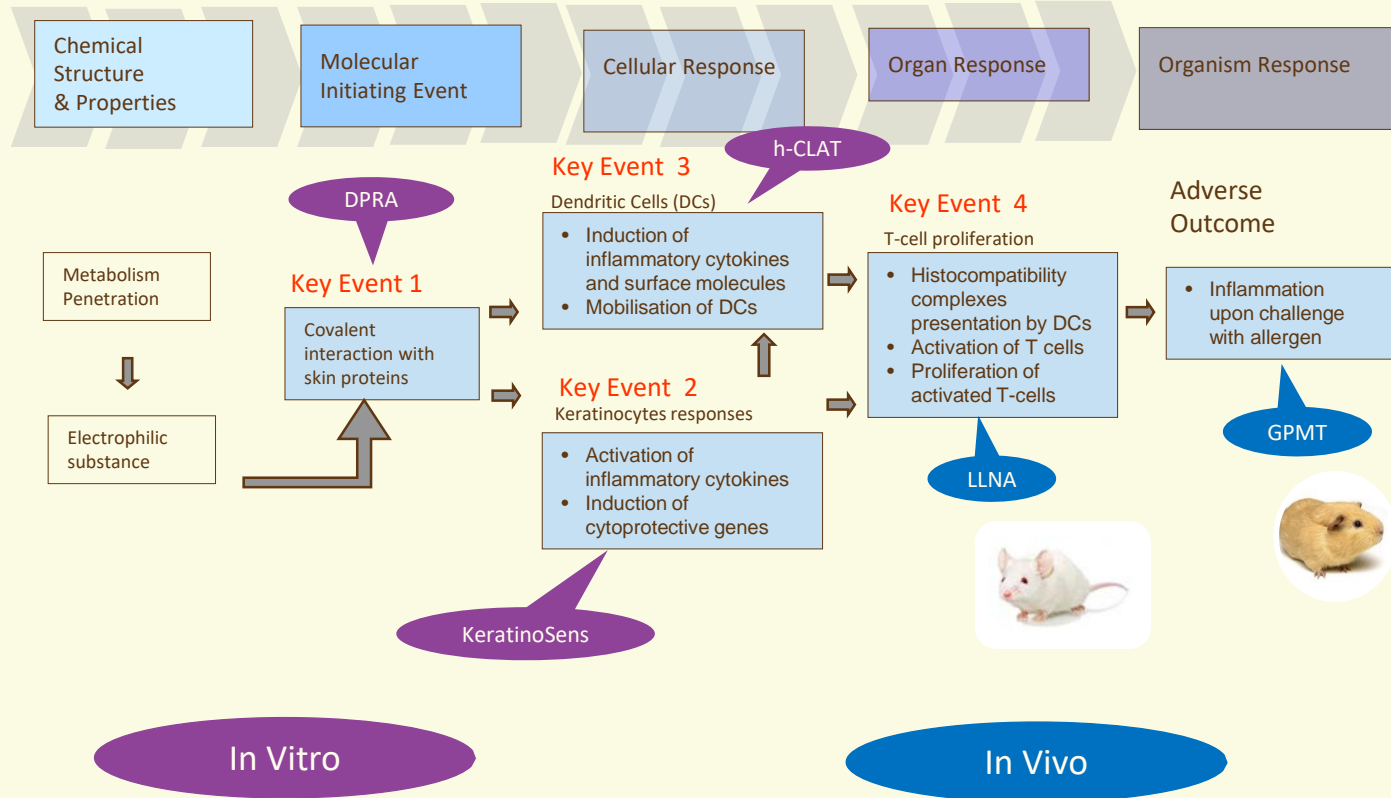




Adverse Outcome Pathway for Skin Sensitization



Test Methods



CASE STUDY



Is this non-animal defined approach
ready to replace the LLNA?



Closing Remarks





International and Domestic Progress



- ✦ OECD proposal (SPSF) co-led by US, EU, and Canada submitted November 2016
 - Create a performance-based test guideline for non-animal defined approaches to skin sensitization testing
 - Included in OECD work plan April 2017
- ✦ Special session of the WNT met in December 2017 to review progress and discuss next steps
 - Achieved consensus on evaluation framework for DA assessment

Thanks to...



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Carsten Goebel



Erwin Van Vliet



Nikki Gellatly**



Petra Kern



Pierre Fabre
Derma-Cosmétique

Elodie Clouet



Jochen Kuehnl



Masaaki Miyazawa



COLGATE-PALMOLIVE

*currently JaCVAM, **currently NC3Rs



Key Message

With testing advances, we continue to improve research and reduce reliance on animal models.





Thank you for your participation!

