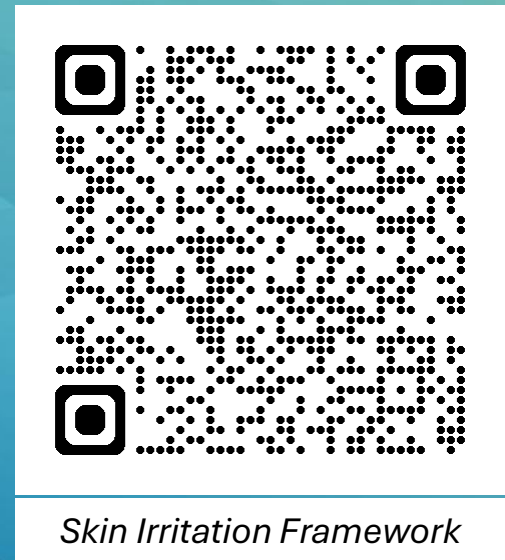




Implementation of a New Approach Methods (NAMs)-based Framework to Evaluate Skin Irritation of New Chemicals under TSCA

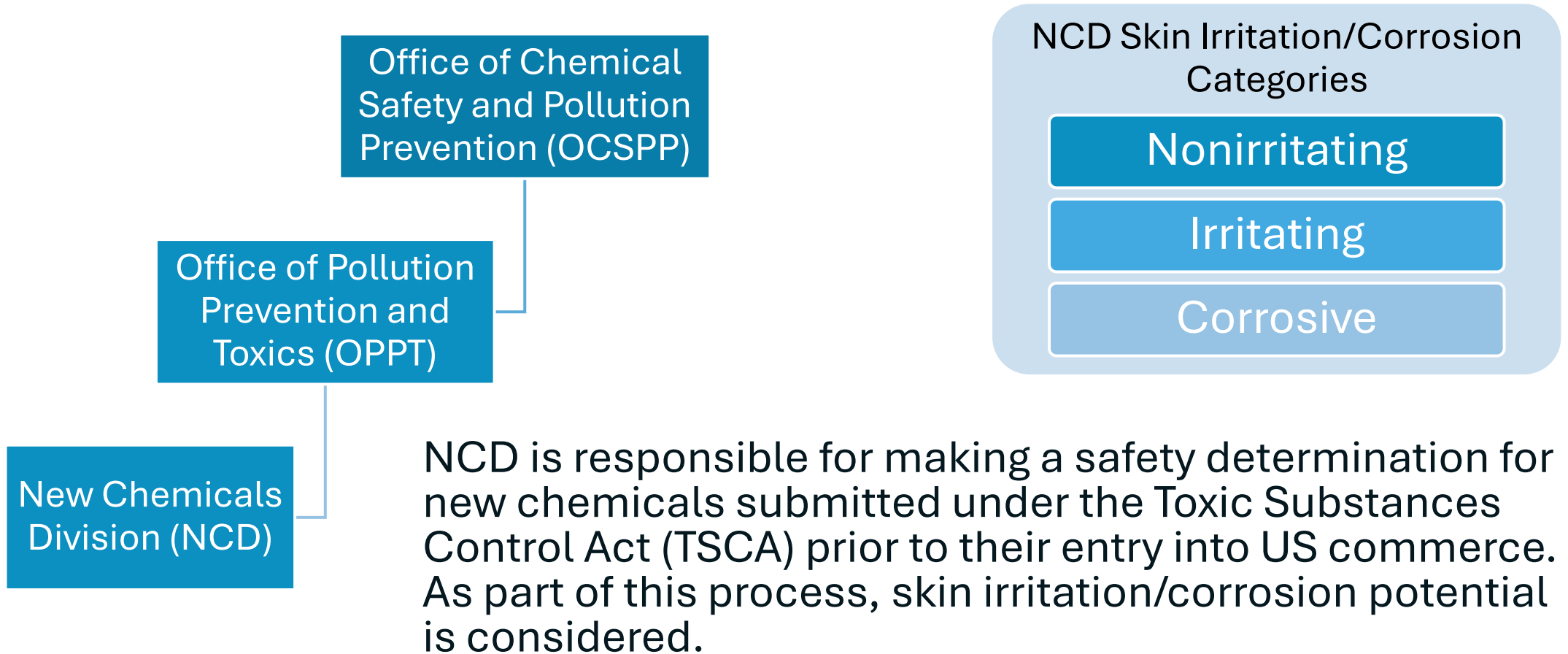
EPIC Webinar
Rachel Brunner
March 17, 2026



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Assessment of Skin Irritation/Corrosion Potential for New Chemicals



Prioritization of data based on reproducibility and relevance to human skin irritation/corrosion

Limitations of rabbit study

The in vivo skin irritation test in rabbits lacks reproducibility¹, particularly in the mild to moderate range of irritancy².

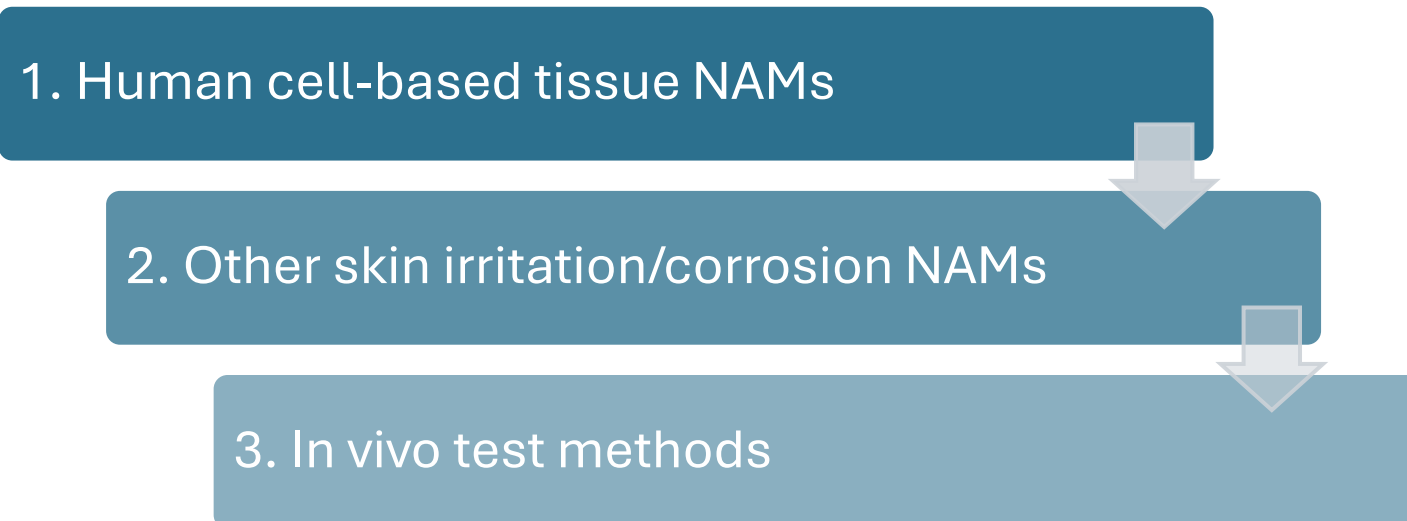
Advantages of NAMs

NAMs for skin irritation/corrosion were found to perform as well as or better than the in vivo rabbit skin irritation test.³

1. Weil & Scala, 1971
2. Rooney et al., 2021
3. Raabe et al., 2025

Key Principle of Skin Irritation Framework

- Prioritization of data based on reproducibility and relevance to human skin irritation/corrosion



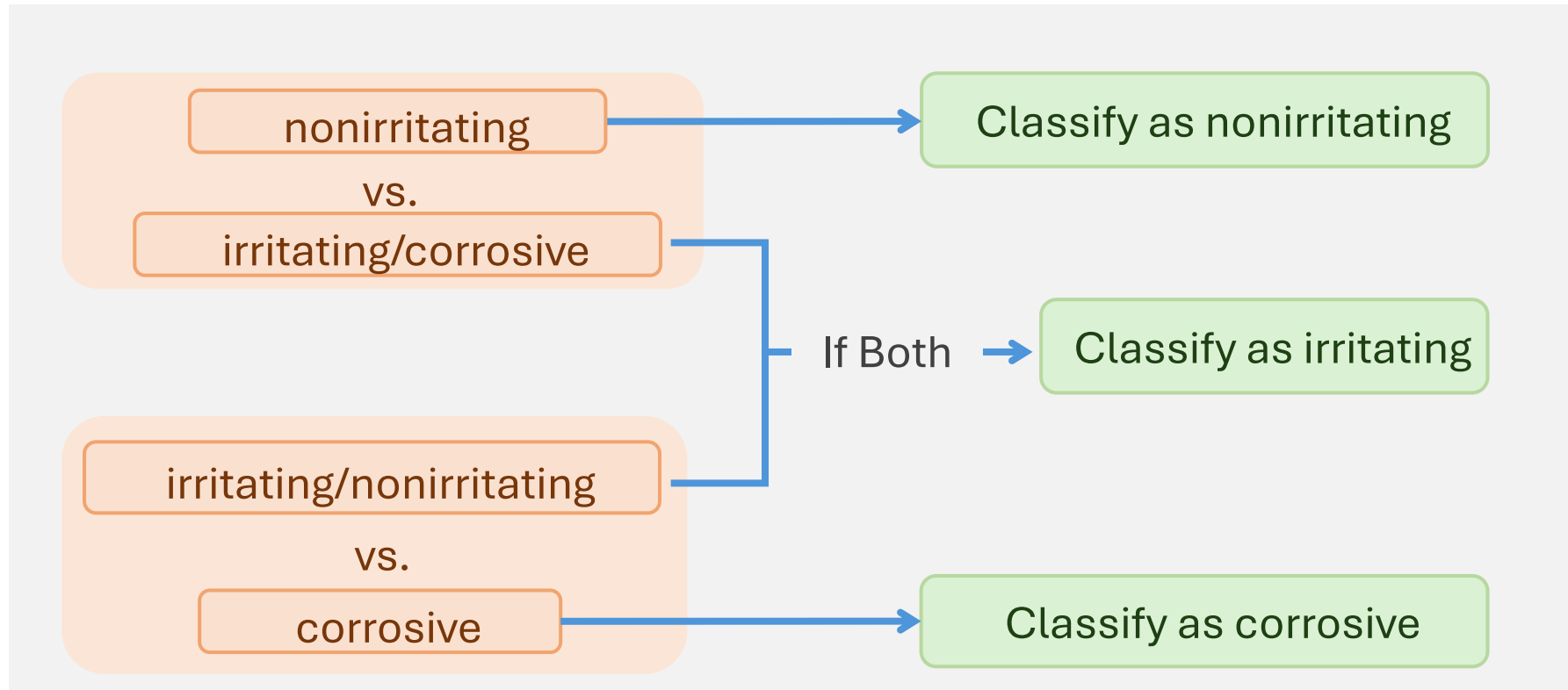
Reduction of Vertebrate Animal Testing

- These NAMs provide superior reproducibility and greater biological relevance to mechanisms of human skin irritation/corrosion when compared to testing using animals.
- This framework supports EPA’s [Recommitment to Reducing Animal Testing and Eliminating Mammalian Testing by 2035](#).
- This is consistent with the [Strategic Plan to Promote the Development and Implementation of Alternative Test Methods Within the TSCA Program](#), developed by EPA in 2018 in response to TSCA section 4 (h)(2)(A) which states that EPA must:
“develop a strategic plan to promote the development and implementation of alternative test methods and strategies to reduce, refine, or replace vertebrate animal testing and provide information of equivalent or better scientific quality and relevance for assessing risks of injury to health or the environment [···]”
- This skin irritation and corrosion framework fulfills, in part, the long-term goal of the Strategic Plan to integrate and prioritize NAMs in the TSCA decision process for risk evaluation to reduce and eventually replace the use of vertebrate animal testing.

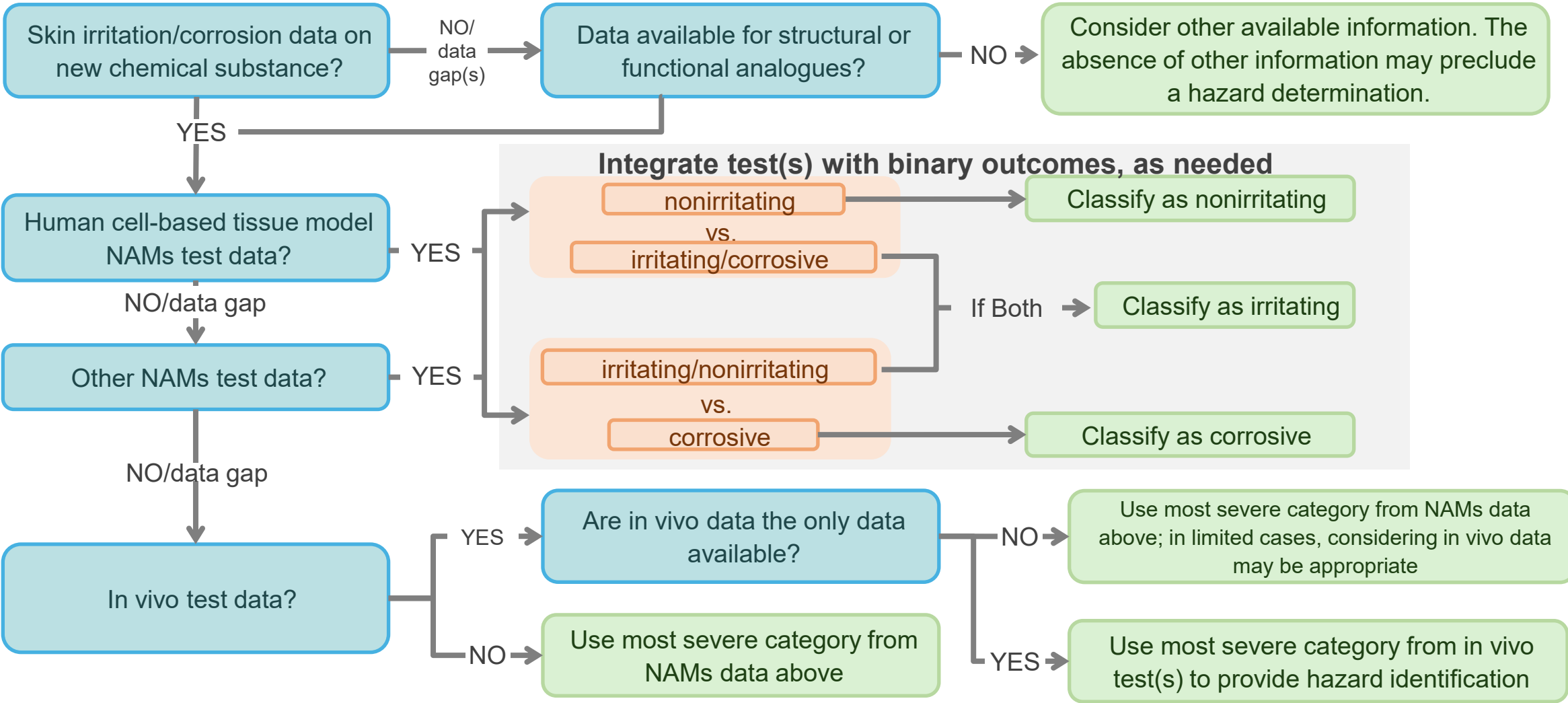
Hazard Identification Capability of Some OECD Test Guidelines

Guideline	Test Method	Hazard Classification Based on Percent Tissue Viability		
		Nonirritating	Irritating	Corrosive
Human Cell-Based Tissue Model NAMs based on In Vitro Reconstructed Human Epidermis (RhE)				
In Vitro Skin Irritation: Reconstructed Human Epidermis Test Methods (OECD TG 439)	RhE model	Nonirritating	Irritating or Corrosive	
In Vitro Skin Corrosion: Reconstructed Human Epidermis Test Method (OECD TG 431)	EpiSkin™ prediction model	Nonirritating or Irritating		Corrosive
	EpiDerm™			Corrosive
	SkinEthic™			
	RHE epiCS®			
LabCyte EPI-MODEL24 SCT				
Other NAMs				
In Chemico Membrane Barrier Test Method for Skin Corrosion (OECD TG 435)	Corrositex (in chemico)			Corrosive

Integration of NAMs with binary outcomes to classify across the 3 NCD categories

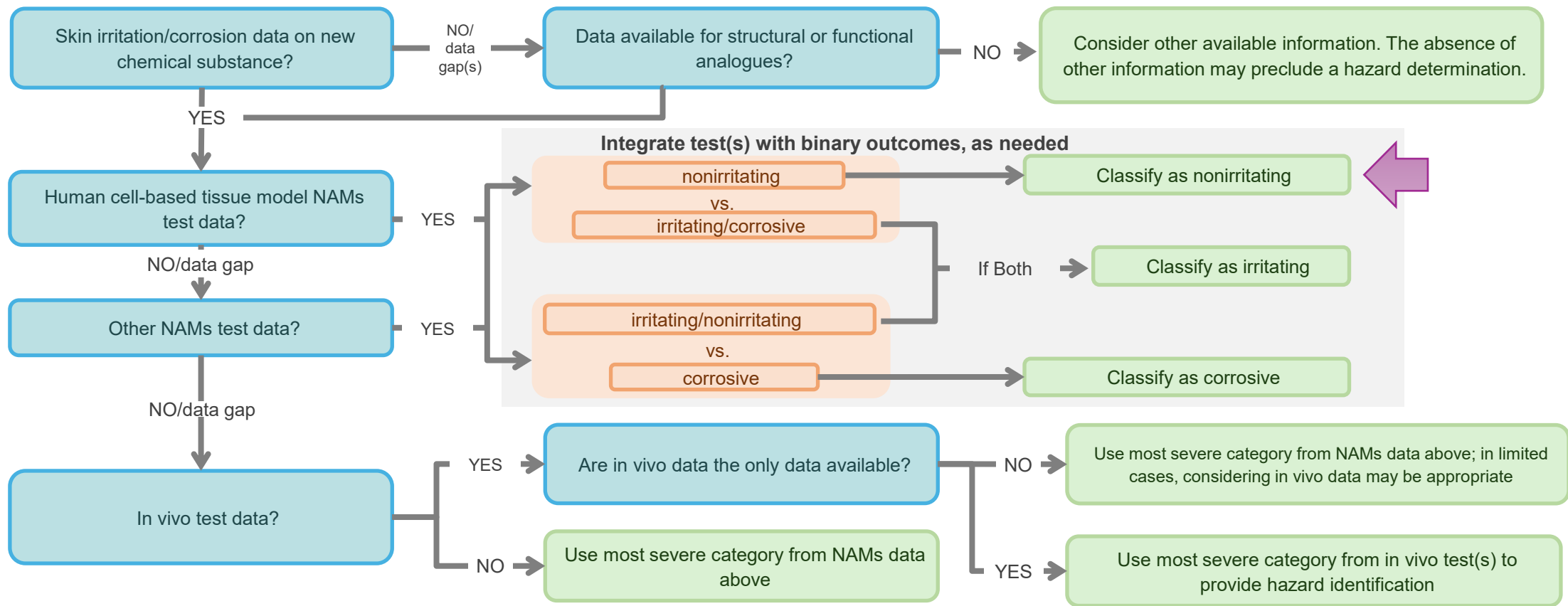


Decision Framework



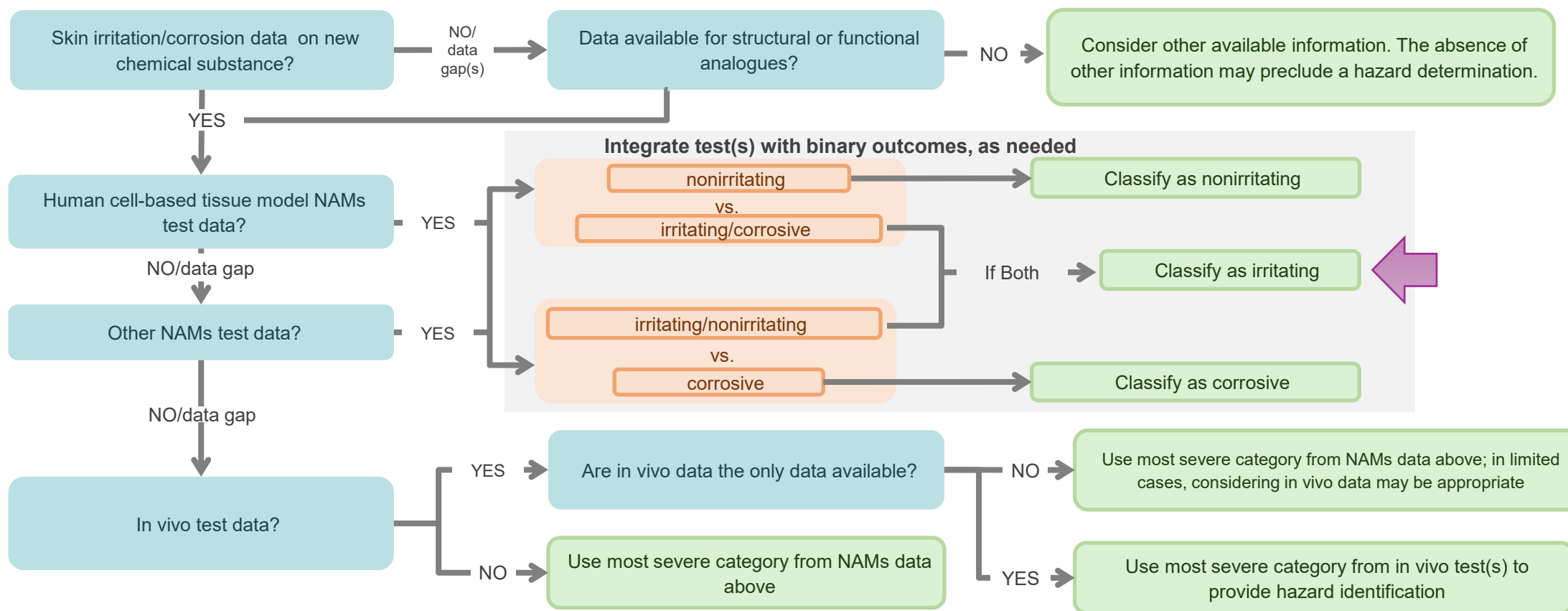
Example 1

Study	Type of Data	Result
In Vitro Skin Irritation: Reconstructed Human Epidermis Test Methods (OECD TG 439)	Human cell-based tissue model	Nonirritating
In Chemico Membrane Barrier Test Method for Skin Corrosion (OECD TG 435)	Other NAM	Nonirritating/irritating
[In Vivo] Acute Dermal Irritation/Corrosion (OECD TG 404)	In vivo	Nonirritating



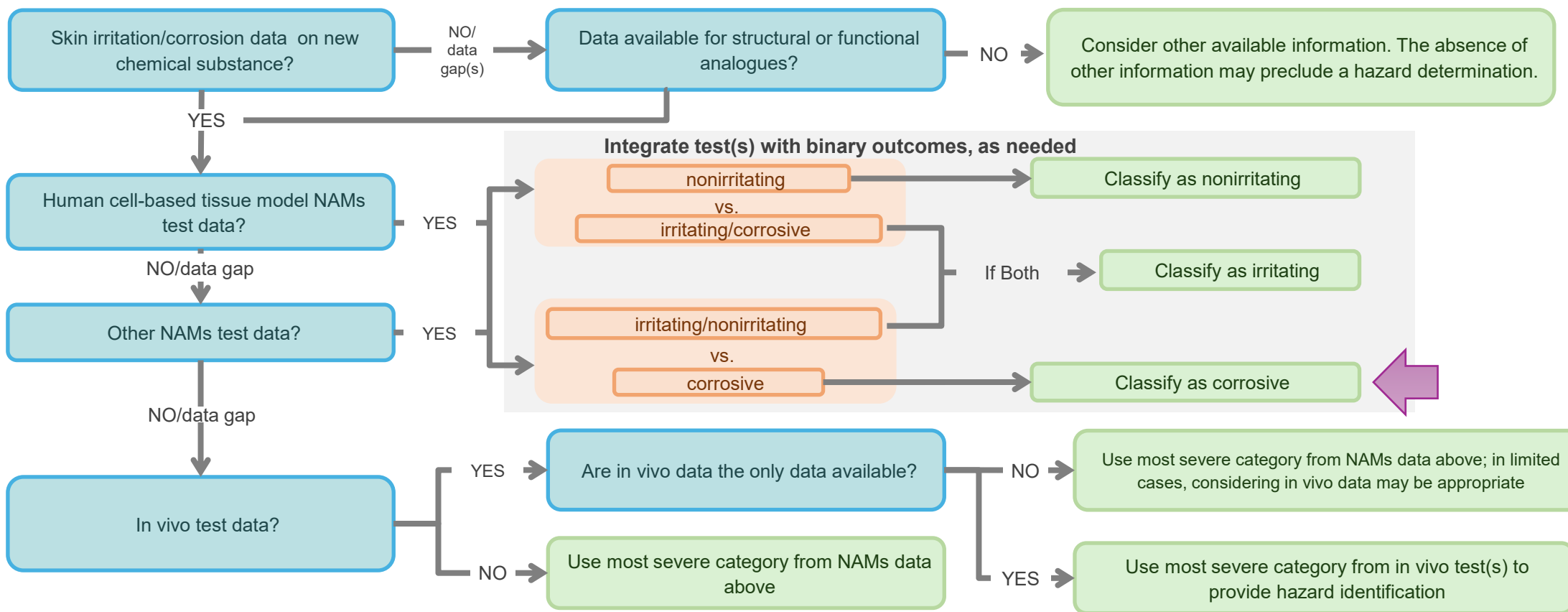
Example 2

Study	Type of Data	Result
In Vitro Skin Irritation: Reconstructed Human Epidermis Test Methods (OECD TG 439)	Human cell-based tissue model	Irritating/corrosive
In Vitro Skin Corrosion: Reconstructed Human Epidermis Test Method (OECD TG 431)	Human cell-based tissue model	Nonirritating/irritating



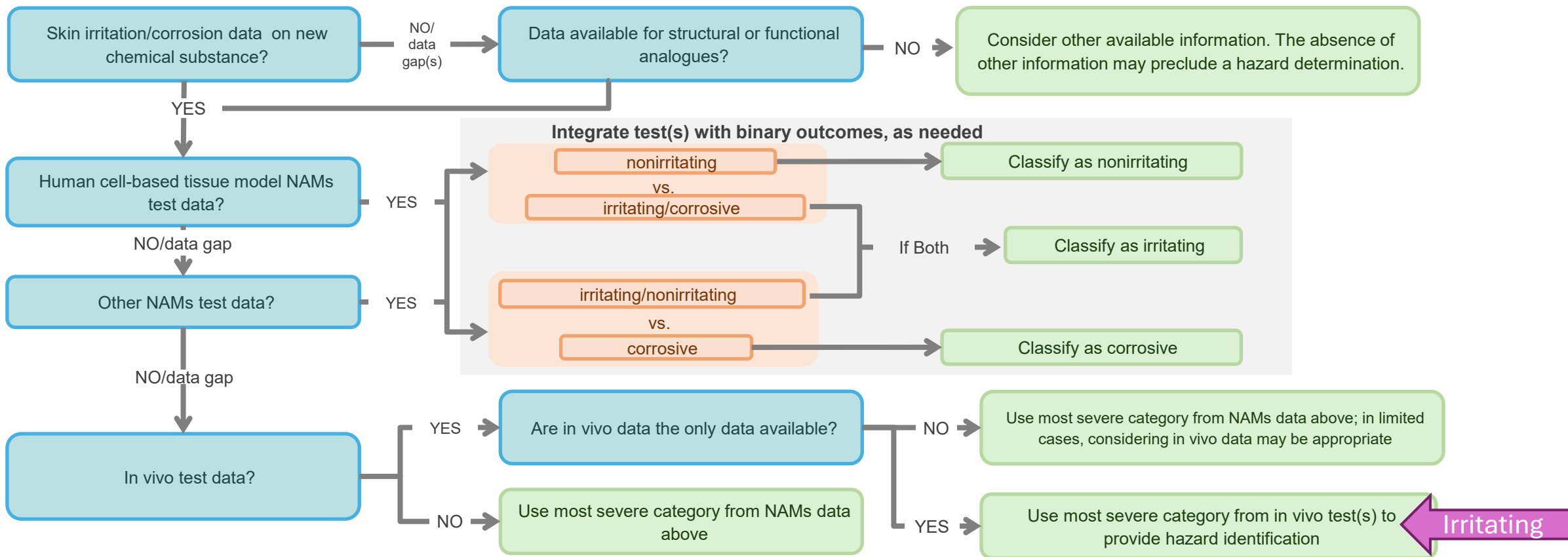
Example 3

Study	Type of Data	Result
In Vitro Skin Irritation: Reconstructed Human Epidermis Test Methods (OECD TG 439)	Human cell-based tissue model	Irritating/corrosive
In Chemico Membrane Barrier Test Method for Skin Corrosion (OECD TG 435)	Other NAM	Corrosive
[In Vivo] Acute Dermal Irritation/Corrosion (OECD TG 404)	In vivo	Irritating



Example 4

Study	Type of Data	Result
[In Vivo] Acute Dermal Irritation/Corrosion (OECD TG 404)	In vivo	Irritating



Conclusions

This approach:

- ✓ Prioritizes reproducible and human-relevant data for assessing skin irritation/corrosion potential.
- ✓ Is expected to encourage new chemical submitters to provide more NAMs data, in turn resulting in reduced vertebrate animal testing.
- ✓ Improves the efficiency, consistency, and transparency of the assessment of skin irritation/corrosion potential within NCD.
- ✓ Serves as a resource for stakeholders preparing new chemical submissions to EPA under TSCA.

Acknowledgments – Thank you!



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This is just part of a growing landscape of NAMs work for use in EPA OPPT new chemicals assessments...

NAMs for Read Across

Extensive use of analogue data from both internal TSCA chemicals and publicly available databases

Category assessments from other national and international hazard and risk assessment entities

2010 TSCA New Chemicals Program Chemical Categories

Structural Alerts

In silico tools | e.g., OncoLogic™ and OECD QSAR Toolbox

Recent and Upcoming NAMs

New Chemicals Program Decision Framework for Hazard Identification of Eye Irritation and Corrosion (released in 2024)

Respiratory sensitization
OECD detailed review paper

Framework for read across using EPA's ChemInformatics Modules

Threshold for Toxicological Concern (TTC) Approach

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Supplemental Slides

Hazard Identification Capability of Some Established Test Methods

Guideline	Test Method	Hazard Classification based on Percent Tissue Viability		
Human Cell-Based Tissue Model NAMs based on In Vitro Reconstructed Human Epidermis (RhE)				
OECD TG 439 (Irritation)	RhE model	Nonirritating	> 50%	
		Irritating/corrosive	≤ 50%	
OECD TG 431 (Corrosion)	EpiSkin™ prediction model	Corrosive	< 35% after 3 min, OR	
			≥ 35% after 3 min exposure AND < 35% after 60 min, OR	
		≥ 35% after 60 min exposure AND < 35% after 240min		
	EpiDerm™ SkinEthic™ RHE epiCS® LabCyte EPI-MODEL24 SCT	Corrosive	< 50% after 3 min, OR ≥ 50% after 3 min AND < 15% after 60 min	
		Irritating/nonirritating	≥ 50% after 3 min AND ≥ 15% after 60 min	
Other NAMs				
OECD TG 435	Corrositex (in chemico)	Acid/Alkaline Reserve	High	Low
		Corrosive	≤ 240 min	≤ 60 min
		Irritating/nonirritating	> 240 min	> 60 min