

# A systematic literature review for the determination of “negative” chemical compounds for developmental neurotoxicity (DNT) assay evaluation

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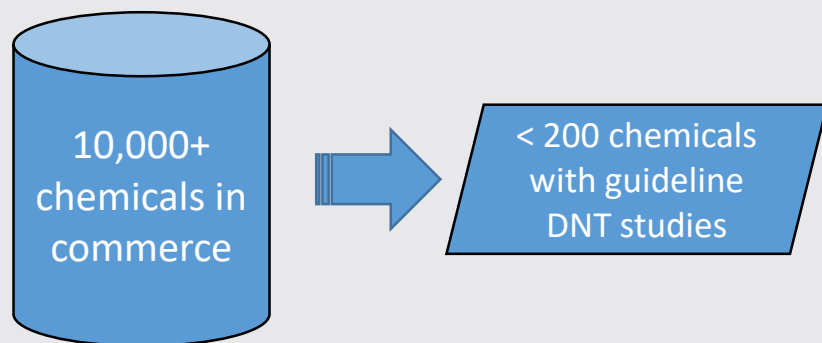
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Disclaimer: This abstract does not necessarily reflect EPA policy. Mention of trade names is not an endorsement or recommendation for use

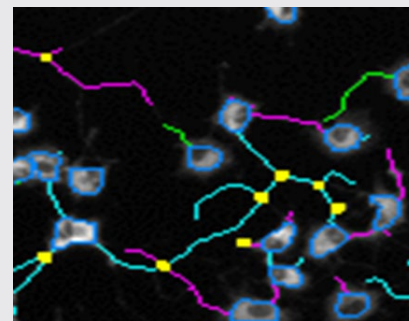


# Why create a list of “negative” chemical compounds for DNT assay evaluation?

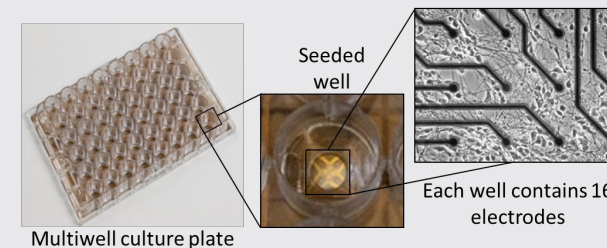
## Screening and prioritizing chemicals with putative DNT hazard



## Development of new approach methodologies (NAMs)



**High Content Imaging:** automated data acquisition of cell size, shape, location, fluorescence intensity



**Microelectrode Array:** Network Formation Assay

## How to evaluate the DNT prediction performance of these assay data?

		“Truth” (guideline DNT study)	
		Negative	Positive
Predicted using a NAM	Negative	True negative	False negative
	Positive	False positive	True positive

*Sensitivity and specificity*

Therefore, the aim of this study is to develop a curated list of negative DNT reference chemicals.

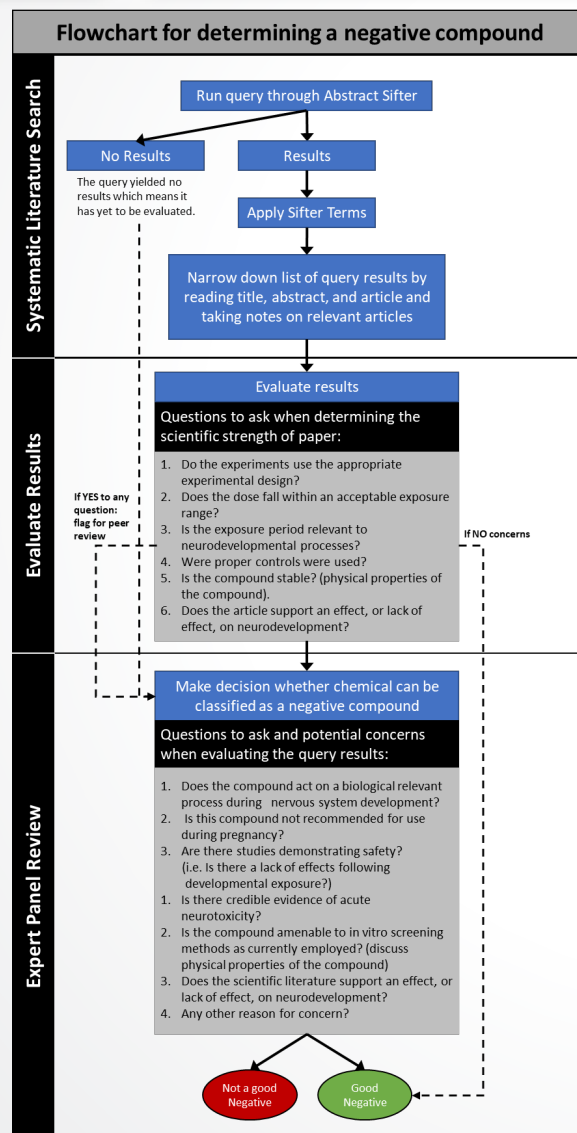


# Workflow Overview

## 1. Systematic Literature Search

## 2. Evaluate Results

## 3. Expert Panel Review



### Deliverables



Completed  
Abstract Sifter  
Files

Completed  
Score Card

Chemical  
Summary  
Write-Up

1. Is there a biological relevant process?
  - a. System by which chemical acts on.
  - b. Is this system present during development?
2. Pregnancy category (A-D, X)
3. Are there studies demonstrating safety? (i.e. Is there a lack of effects following developmental exposure?)
4. Is there credible evidence of acute neurotoxicity?
5. Is the compound amenable to in vitro screening methods as currently employed? (i.e. is it volatile, metabolically activated, does it degrade in DMSO or other solvents, have a low molecular weight, or have an extreme logP?)
6. Any other reason for concern?
7. Overall Score: 1-4

#### ACETAMINOPHEN

Synonyms: APAP, Paracetamol, Tylenol®, Calpol®, Panadol®, etc.

CAS Number: 103-90-2

DTXSID2020006

Formula: C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub>

Acetaminophen was first made in 1877 and is the most commonly used medication to treat fever and mild to moderate pain relief in the United States and Europe. When sold in combination with other medications, it can be used to treat more severe pain from cancer, surgery, etc. Acetaminophen is generally safe at recommended doses; the recommended