## Development of a database to derive inhalation TTC values for airborne compounds

F. Boisleve<sup>7</sup>, M. Singal<sup>8</sup>, N. Sadekar<sup>2</sup> and S. E. Escher<sup>1</sup>

<sup>1</sup>Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany; <sup>2</sup>Research Institute for Fragrance Materials, Woodcliff Lake, New Jersey, USA; <sup>3</sup>Cosmetics Europe, Brussels, Belgium / International Collaboration on Cosmetics Safet (ICCS), New York, USA; <sup>4</sup>Procter & Gamble, Cincinnati, Ohio, USA; <sup>5</sup>U.S. Environmental Assurance Centre, Unilever, Sharnbrook, UK; <sup>7</sup>Chanel S.A.S., Neuilly-sur-Seine, France; <sup>8</sup>L'Oréal, Clark, New Jersey, USA

#### Introduction

Threshold of Toxicological Concern (TTC) are generic human exposure threshold values for groups of compounds below which a risk for human health is negligible.

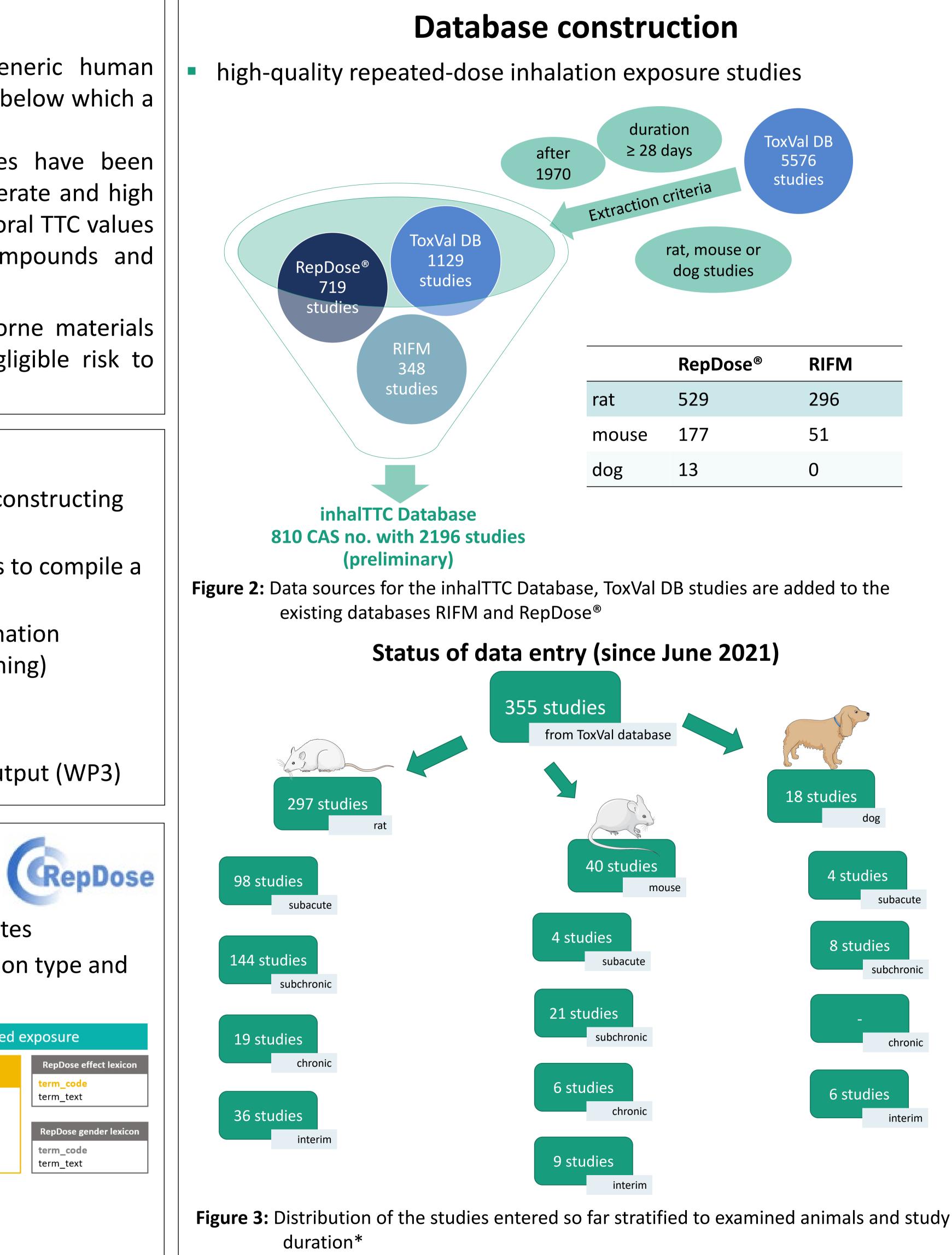
Developed for oral exposure, yet oral TTC values have been determined on three structural classes of low, moderate and high toxicity (Cramer class 1 to 3). This classification and oral TTC values cannot be directly extrapolated for inhalable compounds and inhalation risk assessment.

**AIM:** Define appropriate threshold values for airborne materials below which inhalation exposure is of low to negligible risk to human health

### **Objectives**

- **Obj. 1:** Identify possible toxicity data sources and constructing the combined inhalation TTC database (WP1)
- **Obj. 2:** Define criteria for local and systemic effects to compile a database with NOAEC and LOAEC values (WP1)
- **Obj. 3:** Develop the appropriate chemical discrimination approach based on toxicity potency (machine learning)
- **Obj. 4:** Define the 5<sup>th</sup> percentile thresholds (WP2)
- **Obj. 5:** Build the prediction tool (WP2)
- **Obj. 6:** Publication and dissemination of project output (WP3)

#### Data model



- Oriented to Fraunhofer database: RepDose<sup>®</sup>
- Terminology mapped to OECD Harmonized Templates
- Database includes: basic study details with inhalation type and exposure form, detailed effect data

		High qu	ality	in vivo inhalation	studi	es with repeated	exposu
tab_chemical		tab_study		tab_organ		tab_effect	RepDo
chemical_regnumber — cas chemical name SMILES	<u>1:n</u>	chemical_regnumber study_regnumber species, strain, gender inhalation type	1:n	study_regnumber organ_regnumber organ/target 	1:n	organ_regnumber effect_regnumber effect affected gender	term_t
p/c parameters p/c = physicochemical		study duration exposure data 		RepDose species lexicon		effect LOEL 	term_c term_t
				term_text	]		

**Figure 1:** Data model, adapted from RepDose<sup>®</sup>

#### Acknowledgement

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**Disclaimer**: This poster does not reflect US EPA policy.

# M. Schwarz-Zocher<sup>1</sup>, A. M. Api<sup>2</sup>, K. Joshi<sup>2</sup>, A. Giusti<sup>3</sup>, J. Rose<sup>4</sup>, S. Collins<sup>4</sup>, G. Patlewicz<sup>5</sup>, A. M. Bowden<sup>6</sup>,

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Study effect profiles reviewed to distinguish local and systemic lowest observed adverse effect concentrations (LOAEC) Transparent set of criteria under development to set the LOAEC. Excluded

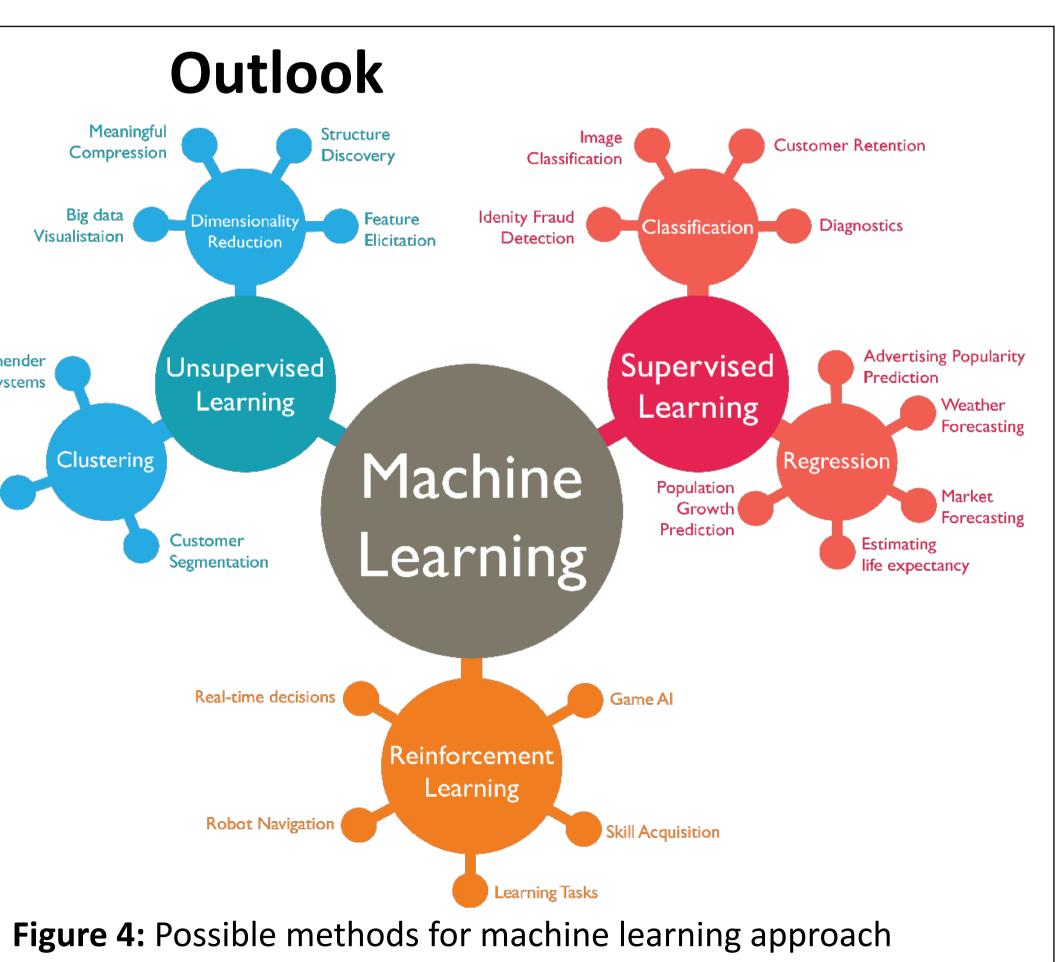
are:

Organ	Effoct	Pational	Docision
Organ	Effect	Rational	Decision
Kidney	alpha2u nephropathy	typical age related effect in male rats; not human relevant	not human relevant
Spleen	Hemosiderosis	typically seen in aged rats; not considered to be adverse if seen in isolation e.g. without hematological findings or disturbed hematopoiesis in bone.	Not adverse
Body weight	Weight change	Weight change < 10%	Not adverse
Organ weight	Weight change	in relation to bw. change; brain and testes do not decrease with decreasing bw here we consider abs. wt. changes as finding. For liver and other proliferating organs rel. wt. changes are indicative.	Case by case
Clinical chemistry	Enzyme change	without additional effects such as histopathology or wt. changes, the effect is considered potentially adaptive	potentially adaptive
Lymph node		local lymph node data is an indicator of local effects but only if sufficient details are available; otherwise considered a systemic effect	Systemic vs. local
Body weight	Body weight gain	with food consumption alone as only systemic effects	Not adverse
FOB		all effects considered to be systemic	Systemic
Eye/nose	Encrustation/ exudate	without matching effect in histopathology	Not adverse
•••			

Clustering substances Compression according to their Big data Visualistaion toxic potency using machine learning Potential parameters to include: Targetted Marketing structure, physicochemical properties, fraction unbound, inhalation type, MMAD



### **Deriving LOAEC/NOAEC values**



#### References

https://repdose.item.fraunhofer.de/ Toxicity Values Database (ToxVal DB) accessible from https://comptox.epa.gov/