
Methods and tools for assessing chemical exposure in humans: protocol for a systematic scoping review

Summary

The project 'Ontology-driven and artificial intelligence-based repeated dose toxicity testing of chemicals for next generation risk assessment' (ONTOX) under the EU programme Horizon 2020 is running from 01.05.21 to 30.04.26 and is coordinated by Vrije Universiteit, Brussel, Belgium (project website, URL: <https://ontox-project.eu/project/>). The vision of ONTOX is to provide a functional and sustainable solution for advancing human risk assessment of chemicals without the use of animals in line with the principles of 21st century toxicity testing and next generation risk assessment. ONTOX will perform exposure assessment on selected chemicals. Preferably existing dietary, dermal and inhalation exposure methods and/or tools will be used. In order to have the best selection of tools available, we will conduct this scoping review to get an overview over publicly available exposure methods/tools. We will assess the advantages and disadvantages of the different methods that we identify.

Title:

Methods and tools for assessing chemical exposure in humans: protocol for a systematic scoping review

Protocol for systematic scoping review

Commissioner:
WP6 ONTOX

Commissioned date:
01.10.2021

Due date:
30.06.2023

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Approved by:

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Commission

This scoping review is a part of the EU project “Ontology-driven and artificial intelligence-based repeated dose toxicity testing of chemicals for next generation risk assessment’ (ONTOX)” under the EU programme Horizon 2020

Introduction, aim and research question

The project 'Ontology-driven and artificial intelligence-based repeated dose toxicity testing of chemicals for next generation risk assessment' (ONTOX) under the EU programme Horizon 2020 is running from 01.05.21 to 30.04.26 and is coordinated by Vrije Universiteit, Brussel, Belgium (project website, URL: <https://ontox-project.eu/project/>). The vision of ONTOX is to provide a functional and sustainable solution for advancing human risk assessment of chemicals without the use of animals in line with the principles of 21st century toxicity testing and next generation risk assessment. Specifically, ONTOX will deliver a generic strategy to create innovative new approach methodologies (NAMs) in order to predict systemic repeated dose toxicity effects that, upon combination with tailored exposure assessment, will enable human risk assessment.

Task 6.1 in ONTOX will perform exposure assessment on selected chemicals. Initially data-rich chemicals will be studied but in the second phase chemicals will be studied for which ONTOX will generate new hazard and exposure data. Preferably existing dietary, dermal and inhalation exposure methods and/or tools will be used. A systematic approach will be used to get an overview over publicly available exposure methods/tools, and the advantages and disadvantages with the different methods will be explored and described.

The aim of the systematic scoping review will be to get an overview over existing exposure methods/tools for assessment of chemical exposure through oral, dermal and inhalation routes in humans. Data (output) from the exposure methods/tools will be included to validate the methods. This will serve as a basis for decision making regarding exposure methods/tools to be used in the ONTOX project.

Table 1. These research questions to be addressed in the systematic review.

	No	Research questions
Exposure methods/tools	1	What exposure methods/tools exist for oral exposure of chemicals?
	2	What exposure methods/tools exist for dermal exposure of chemicals?
	3	What exposure methods/tools exist for inhalation exposure of chemicals?
	4	Are the exposure methods/tools publicly available for use in ONTOX?

Method

Primary literature describing exposure assessment methods for chemical exposure in humans through oral, dermal and inhalation route will be included in the systematic scoping review.

Eligibility criteria

The eligibility criteria are described below and summarised in Table 2.

Study design:

Papers describing in full exposure assessment methods/tools will be included. The methods should provide data from applying the method on chemicals relevant for the ONTOX project. Only methods/tools with full description/code, such as algorithm, methodology, software, tool or toolbox, will be further considered in the ONTOX project.

Route of exposure:

Chemical exposure can occur from different sources such as food and drink, consumer products and indoor and outdoor air, which will include oral, dermal and inhalation exposure routes. Humans will be exposed to chemicals via all these routes simultaneously, and therefore all these exposure routes will be included in this systematic review on exposure assessment methods.

Outcome of interest:

All methods with full description of methods/tools (see above) for assessing exposure to chemicals for the general population will be included. Methods that estimate exposure for a variety of environmental chemicals, food additives and cosmetic ingredients will be included. Such methods can often be applied to different chemical groups, sometimes with small modifications. ONTOX aim at exploring and using existing methods before new methods are developed. Methods addressing mixtures and particles will not be included.

Population:

Only exposure methods for the general population will be considered, as methods for occupational exposure are not relevant for the ONTOX project. Children below 1 year of age will be excluded since exposure through breast feeding will not be included.

Language:

Only papers written in English will be included, as the scientists involved in the work will not be able to read other languages.

Publication data:

The publications included will be restricted to a publication date of 2000 or newer. It is assumed that methods older than 2000 will be outdated, as the field has been moving forward with new methods since 2000.

Table 2. Eligibility criteria for exposure assessment methods/tools.

Study design	Original papers describing methods for exposure assessment. Papers should include full description/code for the method and data (output) from applied methods for validation (not including mixtures and particles).
Route of exposure	Oral, dermal or inhalation exposure.
Outcome of interest	General exposure methods for any environmental chemical, e.g. food additive, cosmetics ingredients, biocides, pesticide or pharmaceutical
Population	The general population only (excluding occupational exposure), age limits 1-60 years.
Language	Only papers in English will be included
Publication date	Only papers after 2000

Literature search

The search strategy was developed in cooperation with an experienced information specialist, and the literature searches was conducted 19.10.2021 We aim to search the following electronic databases:

- MEDLINE (Ovid),
- Embase (Ovid),
- Web of Science
- Scopus

The electronic database searches will be supplemented by searching Google and web pages of relevant public bodies such European Food Safety Authority, U.S. Food and Drug Administration and U.S. Environmental Protection Agency for publicly available tools and/or exposure assessment methods.

The search strategy for MEDLINE (Ovid), Embase (Ovid), Web of Science and Scopus is available in Appendix 1. The evidence retrieved from each bibliographic database will be imported and combined into the bibliographic reference management software Sys-Rev (<https://sysrev.com/>). Duplicates will be removed.

Selection of studies

Screening titles and abstracts

Pairs of reviewers will screen titles and abstracts independently. The identified references will be screened according to the predefined eligibility criteria (Table 2). A publication should be included when there is doubt whether the publication meets the eligibility criteria.

Screening full text

For the papers included after screening of abstract and titles, pairs of reviewers will screen the full text of publications independently. In case of disagreement, the two reviewers will discuss the paper to reach consensus. If the disagreement persists, a third reviewer will be consulted.

Data extraction

The project group will jointly develop a data extraction form. We will extract information on papers and methods from each included paper according to the description below:

Data extraction

- Authors
- Title
- Journal
- The full reference
- Year of publication
- Route of exposure
- Chemical/additive or pharmaceutical assessed
- Method of exposure
 - Purpose of method
 - Description/code of the method
 - Population characteristics
 - Input parameters
 - Public availability
 - Validation
 - General view on the pros and cons with the use of the method/tool as discussed in the paper

One scientist will perform the data extraction from the included papers, while another scientist will go through the data extraction and ensure that the data extraction is performed correct. Discrepancies will be resolved through discussions. The data extraction form will be pilot tested before implemented. If needed, the data-charting form will be modified, and the reasoning for modification will be noted.

Presentation of results

The data will be summarised in a narrative way to provide information on existing methods/tools for exposure assessment of chemicals from oral, dermal and inhalation route. The different exposure methods will be presented and grouped according to their characteristics, such as deterministic or probabilistic approaches, chemical and regulatory applicability, route of exposure and availability. The data synthesis will also include a short evaluation of the pros and cons using the methods for exposure assessment for the general population in Europe.

How to use the results from this systematic scoping review

The systematic scoping review will be used for decision making regarding exposure methods to be used in the EU project ONTOX. Methods that have regulatory applications and has been explored by several groups will also be preferred, but the selection will for the ONTOX project will not be included in the scoping review.

Per review of the project plan

The project plan was reviewed by Inger-Lise Steffensen, Senior Scientist at NIPH.

Time plan

Commissioned date: 01.10.2021

Due date: 30.06.2023

Appendix 1. Search strategy

ONTOX exposure methods

Contact person: Trine Husøy
Search: Marita Heintz
Per review: Ragnhild A. Tornes
Duplicate check in End- Before duplicate control: 12096
Note: After duplicate control: 5774

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946 to October 15, 2021>

Dato: 19.10.2021

Antall treff: 2894

1	(assess* adj2 exposure adj9 (method? or methodolog* or model? or software or tool? or toolbox* or data toolbox*)).tw,kf.	2834
2	"modelling of exposure".tw,kf.	90
3	(exposure adj (algorithm? or estimation? or method? or methodolog* or model? or software or tool? or toolbox*)).tw,kf.	2932
4	(assess* adj1 risk? adj9 (method? or methodolog* or model? or software or tool? or toolbox* or data toolbox*)).tw,kf.	17688
5	1 or 2 or 3 or 4	22995
6	hazardous substances/ or pesticides/	31541
7	(chemical? or pesticide? or hazardous substance?).tw,kf	745972
8	6 or 7	754763
9	5 and 8	3455
10	limit 9 to yr="2000 -Current"	3078
11	limit 10 to english language	2942
12	11 not (comment or editorial or letter).pt.	2928

Database: Embase 1974 to 2021 October 18

Dato: 19.10.2021

Antall treff: 2588

1	(assess* adj2 exposure adj9 (method? or methodolog* or model? or software or tool? or toolbox* or data toolbox*)).tw,kf.	3541
2	"modelling of exposure".tw,kf.	110
3	(exposure adj (algorithm? or estimation? or method? or methodolog* or model? or software or tool? or toolbox*)).tw,kf.	8134
4	(assess* adj1 risk? adj9 (method? or methodolog* or model? or software or tool? or toolbox* or data toolbox*)).tw,kf.	25181
5	1 or 2 or 3 or 4	36232
6	hazardous substances/ or pesticides/	42299
7	(chemical? or pesticide? or hazardous substance?).tw,kf.	999429
8	6 or 7	1011098
9	5 and 8	4534
10	limit 9 to yr="2000 -Current"	3980
11	limit 10 to english language	3806
12	limit 11 to embase	2600
13	12 not (Conference Abstract or Letter or Editorial).pt.	2588

Database: Web of Science Core Collection: Science Citation Index Expanded (SCI-EXPANDED) --1987-present, Social Sciences Citation Index (SSCI) --1987-present, Arts & Humanities Citation Index (A&HCI) --1987-present, Emerging Sources Citation Index (ESCI) --2015-present

Dato: 19.10.2021

Antall treff: 4078

1	TS=(assess* NEAR/1 "exposure" NEAR/8 (method\$ or methodolog* or model\$ or "software" or tool\$ or toolbox* or "data toolbox*"))	3242
2	TS=("modelling of exposure")	16
3	TS=("exposure" NEAR/0 (algorithm\$ or estimation\$ or method\$ or methodolog* or model\$ or "software" or tool\$ or toolbox*))	6533
4	TS=(assess* NEAR/0 risk\$ NEAR/8 (method\$ or methodolog* or model\$ or "software" or tool\$ or toolbox* or "data toolbox*"))	25502
5	#1 or #2 or #3 or #4	34418
6	TS=(chemical\$ or pesticide\$ or "hazardous substance\$")	1902024

7	#5 and #6	5022
8	#5 and #6 Timespan: 2000-01-01 to 2021-12-31 (Publication Date)	4519
9	#5 and #6 and English (Languages) Timespan: 2010-01-01 to 2021-12-31 (Publication Date)	4430
10	#5 and #6 and English (Languages) and Letters or Editorial Materials or Meeting Abstracts or Proceedings Papers (Exclude – Document Types) Timespan: 2010-01-01 to 2021-12-31 (Publication Date)	4078

Database: Scopus

Dato: 19.10.2021

Antall treff: 2502

1	TITLE-ABS-KEY (assess* W/1 exposure W/8 (method or method? or methodolog* or model or model? or software or tool or tool? or toolbox* or "data toolbox**"))	1588
2	TITLE-ABS-KEY "modelling of exposure"	75
3	TITLE-ABS-KEY (exposure PRE/0 (algorithm* or estimation* or method or method? or methodolog* or model or model? or software or tool or tool? or toolbox*))	10536
4	TITLE-ABS-KEY (assess* W/0 (risk or risk?) W/8 (method or method? or methodolog* or model or model? or software or tool or tool? or toolbox* or "data toolbox**"))	16329
5	#1 or #2 or #3 or #4	28204
6	TITLE-ABS-KEY (chemical or chemical? or pesticide or pesticide? or "hazardous substance**")	4904535
7	#5 and #6	3517
8	#5 and #6 AND PUBYEAR > 1999	3098
9	#5 and #6 AND PUBYEAR > 1999 AND (LIMIT-TO (LANGUAGE, "English"))	2873
10	#5 and #6 AND PUBYEAR > 1999 AND (LIMIT-TO (LANGUAGE, "English")) AND (EXCLUDE (DOCTYPE, "cp") OR EXCLUDE (DOCTYPE, "cr") OR EXCLUDE (DOCTYPE, "ed"))	2502