List of Alternative Test Methods and Strategies (or New Approach Methodologies [NAMs]) First Update: December 5<sup>th</sup>, 2019<sup>1</sup>:

## **INTRODUCTION**

The Toxic Substances Control Act (TSCA) Section 4(h)(2)(C) requires EPA to develop "a list, which the Administrator shall update on a regular basis, of particular alternative test methods or strategies the Administrator has identified that do not require new vertebrate animal testing and are scientifically reliable, relevant, and capable of providing information of equivalent or better scientific reliability and quality to that which would be obtained from vertebrate animal testing."

The New Approach Methodologies (NAMs) presented in this List are not meant to be an exhaustive list of NAMs that could be used for TSCA decisions<sup>2</sup>. Rather, they are representative lists for consideration by EPA. Many of the NAMs have been reviewed and were established by different organizations<sup>3</sup> (i.e., OECD, EURL-ECVAM and ICCVAM) and meet the section 4(h)(2)(C) criteria for scientific reliability, and relevancy. The extensive test method evaluation process, developed by EURL-ECVAM and ICCVAM, is accepted internationally, as described in the OECD Guidance Document 34, and was designed to identify NAMs for regulatory acceptance. In addition, there are some NAMs on the list that represent existing practices or policies within EPA.

#### **CONTENTS OF LIST/TSCA DECISION CONTEXT**

Appendix A consists of tables of different methods and approaches that do not use vertebrate animals to develop new data/information. Two tables are based on accepted OECD (and other) test guidelines/methods. The other tables represent EPA-specific NAMs. One includes EPA-specific policies adopted by one or more of the three offices within the Office of Chemical Safety and Pollution Prevention (OCSPP) (i.e., the Office of Pesticide Programs [OPP], the Office of Science Coordination and Policy [OSCP], and the Office of Pollution Prevention and Toxics [OPPT]). The other includes NAMs that have been historically used for the New Chemicals Program in OPPT.

<sup>&</sup>lt;sup>1</sup> This list replaces the Original List published on June 22, 2018.

<sup>&</sup>lt;sup>2</sup> Consistent with Sections 4 (testing), 5 (new chemicals) and 6 (existing chemicals), EPA expects to consider NAMs for the following TSCA decision contexts, among others where testing issues may arise: screening candidates for prioritization, prioritization, risk evaluations and other risk-based decisions. These contexts follow the concept of "fit-for-purpose" which is interpreted to mean that a particular NAM may be suitable for one regulatory use and not others

<sup>&</sup>lt;sup>3</sup> OECD = Organization for Economic Cooperation and Development; EURL-ECVAM = European Union Reference Laboratory for Alternatives to Animal Testing; ICCVAM = Interagency Coordinating Committee for the Validation of Alternative Methods.

<sup>&</sup>lt;sup>4</sup> EPA has played a key role for many years in the review and validation/vetting process for the OECD test guidelines program, including the new performance-based and defined approach methods identified in Chapter 5 of the Strategic Plan. ICCVAM has been a recognized, official partner in these OECD deliberations since 2018. The collaboration of NICEATM, ICCVAM and EPA is an important and strong presence in the international arena as new NAMs are being identified, developed and implemented for EPA's regulatory use.

<sup>&</sup>lt;sup>5</sup> https://ec.europa.eu/jrc/en/eurl/ecvam/alternative-methods-toxicity-testing/validation

 $<sup>^{6}\ \</sup>underline{\text{https://ntp.niehs.nih.gov/pubhealth/evalatm/resources-for-test-method-developers/submissions/index.html}$ 

<sup>&</sup>lt;sup>7</sup> http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2005)14&doclanguage=en

Appendix B is a table labeled "Other Useful Information" which contains tools and approaches which may enhance the use of NAMs for regulatory use under TSCA.

Importantly, EPA will review any potential NAM that it receives, and determine the merits/relevance of the information based on whether it meets both the information needs and the objective of TSCA Section 4(h). To this end, EPA encourages all stakeholders to consult with the Agency on the development and/or use of NAMs.

EPA understands that as science progresses and as stakeholders develop new methods/approaches, OCSPP is in a unique position to inform the development of NAMs since they are submitted to the Agency in various stages of development to support pre-manufacture notice applications for new industrial chemical substances under TSCA. Thus, OCSPP may have early knowledge of possible future NAMs that could go on this list. OCSPP views this as important in building confidence in the understanding and use of NAMs for regulatory purposes.

Finally, EPA expects to consider NAMs for a number of TSCA decision contexts, including the prioritization of existing chemicals and hazard identification and characterization for both new and existing chemicals. These methods/approaches will need to be considered in a "fit-for-purpose" approach, because a particular NAM may be suitable for one regulatory decision (e.g., prioritization) context but not others (e.g., quantification of hazard or risk).

At this time, it is understood that the value of most of the NAMs on this list is to provide important information that may be used as weight-of-evidence in characterizing a mechanism of action or hazard to develop a risk profile for a chemical substance. As such, each NAM alone may not be used for a specific TSCA decision context. However, some may be combined for a specific purpose. For example, there are several defined approaches available for evaluating skin sensitization that use 2-3 separate OECD Test Guideline protocols which, taken together, will result in a decision on whether a chemical substance is a skin sensitizer (OCSPP Skin Sensitization Policy).

### NAM CRITERIA FOR RELEVANCE AND RELIABILITY

The methods and approaches on the list meet the eight criteria for NAMs to be listed under TSCA as described in Chapter 5 of the *Strategic Plan*, which are reproduced here:

- 1. The decision context should be clearly defined.
- 2. Where possible, the NAMs should be mechanistically and/or biologically relevant to the hazard being assessed. The chemical domain of applicability of the NAMs should also be defined to determine relevance to the TSCA chemical landscape.
- 3. The criteria for selecting reference or training chemicals should be defined and supporting information should be adequately referenced.
- 4. The reliability of the NAM should be considered within the context of intended use and accepted best practices within the given field and the variability of the existing animal model.
- 5. The NAMs should be transparently described and information made available to the public (e.g., any datasets are publicly available, and its known limitations are clearly

- described). Information claimed as CBI may not allow public accessibility of all information in some cases.
- 6. Uncertainty should be described to the fullest extent possible, both independently and compared to the existing animal model (if possible).
- 7. The NAMs should undergo an independent review in order to raise confidence in the approach.
- 8. Access and use by third parties should be possible (i.e., the alternative approach must be readily accessible commercially and/or the relevant protocols should be available).

#### **THE LIST**

Below is a brief description for each table in Appendix A.

Test Guidelines – Human Health Effects. The NAMs in this table identify Test Guidelines that have gone through the OECD Test Guidelines Program, the ICCVAM process or the ECVAM process, and thus, meet the criteria in section 4(h)(2)(C). These NAMs are all experimental methods designed to identify/evaluate an adverse effect or endpoint relevant to human health concerns and would not use vertebrate animals. Importantly, in the new section "Other Useful Information", there is a table with links for how some of these experimental methods may be combined with an Integrated Approaches to Testing and Assessment (IATA) framework or with Defined Approaches (DAs) for specific regulatory use scenarios.

Test Guidelines – Effects on Biotic Systems. Like the Health Effects table above, the NAMs in this table identify Test Guidelines that have gone through the OECD Test Guidelines Program, and thus, meet the criteria in section 4(h)(2)(C). These NAMs are all experimental methods designed to identify/evaluate an adverse effect or endpoint relevant to evaluating toxicity to environmental organisms. Although many of the methods in this table use plants or invertebrate species, these data are valuable in helping to determine possible species sensitivities/distribution, and thus, could potentially obviate the need to perform testing in environmental vertebrate species.

EPA NAM-Related Policies Which May Be Relevant to TSCA. This table includes EPA-specific NAM policies adopted by EPA's OCSPP; four are more relevant to OPP but may be used/relevant to OPPT (i.e., acute dermal toxicity waiver guidance, acute toxicity waiver for birds, acute toxicity waiver/bridging guidance and the eye irritation alternative testing framework; links provided in the table); and one is the use of NAMs in screening for endocrine activity by OSCP for the endocrine disruptor program. The OCSPP Skin Sensitization Policy is currently in use by OPPT and explains OCSPP's general approach to replace vertebrate animal tests for skin sensitization with non-animal tests. Each of the tests incorporated under the policy are existing OECD Test Guidelines (i.e., 442C, D & E). The policy uses two DAs in review by the OECD (see Other Useful Information below) for use in a regulatory context.

Other NAMs Used for TSCA. This table provides NAMs (e.g., computational toxicology tools, chemical category and tiered testing approaches, screening methods) that have been used by OPPT in the New Chemicals Program. EPA has been using (and plans to use) other models/approaches developed outside of OPPT or even the Agency as they become available. For example, OPPT has been using the OECD QSAR Toolbox – which contains several EPA models and has been vetted through the OECD. Other examples include tools that are available through EPA's Center for Computational Toxicology and Exposure (CCTE), some of which are in the early stages of deployment in the New Chemicals Program. For example, the EPA CompTox Chemicals Dashboard is presented in the "Other Useful Information" section.

# Appendix A – The List

Test Guidelines – Health Effects <sup>1</sup>		
Test Guideline No.	Title	Information Gathered
OECD TG NO. 428	Skin Absorption: in vitro Method	Provides information on absorption of a test substance (can be from human or animal source)
OECD TG NO. 430	in vitro Skin Corrosion: Transcutaneous Electrical Resistance Test (TER)	Evaluates corrosivity (rat skin as source)
OECD TG NO. 431	in vitro Skin Corrosion: Reconstructed Human Epidermis (RHE) Test	Evaluates corrosivity (human skin as source)
OECD TG NO. 432	in vitro 3T3 NRU Phototoxicity Test	Evaluates Phototoxicity to mouse cells in culture
OECD TG NO. 435	in vitro Membrane Barrier Test Method for Skin Corrosion	Evaluates corrosion using a synthetic membrane
OECD TG NO. 437	Bovine Corneal Opacity and Permeability Test Method for Identifying Ocular Corrosives and Severe Irritants	Evaluates eye irritation/corrosivity in bovine eyes
OECD TG NO. 438	Isolated Chicken Eye Test Method for Identifying Ocular Corrosives and Severe Irritants	Evaluates eye irritation/corrosivity in chick eyes
OECD TG NO. 439	in vitro Skin Irritation: Reconstructed Human Epidermis Test Method	Evaluates irritation (human skin as source)
OECD TG NO. 442C	In chemico Skin Sensitisation	No animal or human cells used, evaluates simple binding of a chemical to a receptor
OECD TG NO. 442D	In vitro Skin Sensitisation: ARE-Nrf2 Luciferase Test Method	Evaluates skin sensitization using human cells
OECD TG NO. 442E	In vitro Skin Sensitisation: (h-CLAT)	Evaluates skin sensitization using human cells
OECD TG NO. 455	Performance-based Test Guideline for Stably Transfected Transactivation <i>in vitro</i> Assays to Detect Estrogen Receptor Agonists and Antagonists	Evaluates estrogenic effects using human cells
OECD TG No. 456	H295R Steroidogenesis Assay	Evaluates possible endocrine effects using human cells

Test Guidelines – Health Effects <sup>1</sup>		
Test Guideline No.	Title	Information Gathered
OECD TG No. 458	Stably Transfected Human Androgen Receptor Transcriptional Activation Assay for Detection of Androgenic Agonist and Antagonist Activity of Chemicals	Evaluates androgenic effects using chinese hamster ovary cells
OECD TG No. 460	Fluorescein Leakage Test Method for Identifying Ocular Corrosives and Severe Irritants	Evaluates eye corrosivity/severe irritation with canine kidney cells
OECD TG No. 471	Bacterial Reverse Mutation Test	Evaluates mutagenicity in bacterial cells
OECD TG No. 473	in vitro Mammalian Chromosome Aberration Test	Evaluates chromosomal effects in either human or rodent cells
OECD TG No. 476	in vitro Mammalian Cell Gene Mutation Tests using the Hprt and xprt genes	Evaluates gene mutations in either human or rodent cells
OECD TG No. 487	in vitro Mammalian Cell Micronucleus Test	Evaluates chromosomal effects in either human or rodent cells
OECD TG No. 490	In vitro Thymidine Kinase Mutation Test	Evaluates gene mutations in either human or rodent cells
OECD TG No. 491	Short-time Exposure for the Detection of Chemicals Causing Serious Eye Damage, and Chemicals Not Requiring Classification for Serious Eye Damage or Eye Irritation	Evaluates eye corrosivity/severe irritation with rabbit cornea cells
OECD TG No. 492	Reconstructed Human Cornea-like Epithelium for the Detection of Chemicals Not Requiring Classification and Labelling for Eye Irritation or Serious Eye Damage	Evaluates eye irritation with reconstructed human cells (either eye or skin)
OECD TG No. 493	Performance-Based Test Guideline for Human Recombinant Estrogen Receptor (hrER) in vitro Assays	Evaluates estrogenicity in human cells
OECD TG No. 494 <sup>2</sup>	Vitrigel-Eye Irritancy Test Method for Identifying Chemicals not requiring Classification and Labelling for Eye Irritation or Serious Eye Damage	Recommended to identify chemicals not requiring classification for serious eye damage or eye irritation.
OECD TG No. 495 <sup>2</sup>	Reactive Oxygen Species (ROS) Assay for Photoreactivity	Evaluates photoreactivity in chemico

Test Guidelines – Health Effects <sup>1</sup>		
Test Guideline No.	Title	Information Gathered
OECD TG No. 496 <sup>2</sup>	In Vitro Macromolecular Test Method for Identifying Chemicals Inducing Serious Eye Damage and Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage	Recommended as initial step of a testing strategy (see OECD Guidance Document 263 in Potentially Useful Information table) to identify chemicals that induce serious eye damage.
TM2016-08 (US) <sup>2,3</sup>	The ToxCast Estrogen Receptor Agonist Pathway Model	Mathematical model that combines results from 18 assays to predict estrogen receptor agonism
TM2004-07 (EU) <sup>2,3</sup>	In vitro BALB/c 3T3 Cell Transformation Assay	Assay to measure carcinogenicity potential
TM2009-01 (EU) <sup>2,3</sup>	Ocular Irritection®	Assay to predict potential eye irritation for classification/labelling purposes
TM2008-14 (EU) <sup>2,3</sup>	3T3 Neutral Red Uptake cytotoxicity assay	Assay to specifically identify non-classified chemicals (for classification/labelling purposes) with a cutoff value of 2000 mg/kg-bw (oral)
Eye Irritation Test 4	Cytosensor Michrophysiometer <sup>TM</sup> in vitro test method for eye safety	In vitro test to evaluate eye irritation

<sup>&</sup>lt;sup>1</sup> OECD Test Guidelines (Health), ICCVAM (Alternative Methods Accepted by US Agencies; excludes methods used for specific purposes by other agencies (e.g., vaccines by FDA), and ECVAM source (filtered by "regulatory acceptance/Standards" by Step and "finalized" by Step Status.

<sup>&</sup>lt;sup>2</sup> Added to list in First Update (December 2019)

<sup>&</sup>lt;sup>3</sup> From ECVAM (see footnote 1)

<sup>&</sup>lt;sup>4</sup> From ICCVAM (see footnote 1)

Test Guidelines – Effects on Biotic Systems <sup>1</sup>		
Test Guideline No.	Title	Information Gathered
OECD TG NO. 201	Freshwater Alga and Cyanobacteria Test	Evaluates toxicity to algae
OECD TG NO. 202	Daphnia Species Acute Immobilization test	Evaluates toxicity to freshwater invertebrates
OECD TG NO. 207	Earthworm Acute Toxicity test	Evaluates toxicity to soil invertebrates
OECD TG NO. 211	Daphnia magna Reproduction Test	Evaluates reproductive effects in freshwater invertebrates
OECD TG NO. 212 <sup>2</sup>	Fish Short-term Toxicity Test on Embryo and Sac-Fry Stages	Evaluates toxicity to fish development.
OECD TG NO. 218 <sup>2</sup>	Sediment-Water Chironomid Toxicity Using Spiked Sediment	Evaluates toxicity to sediment-dwelling invertebrates
OECD TG NO. 219 <sup>2</sup>	Sediment-Water Chironomid Toxicity	Evaluates toxicity to sediment-dwelling invertebrates
OECD TG NO. 221	Lemna species Growth Inhibition Test	Evaluates toxicity to freshwater aquatic plants of the genus Lemna (duckweed).
<u>OECD TG</u> <u>NO. 222</u>	Earthworm Reproduction Toxicity Test	Evaluates reproductive effects in soil invertebrates
OECD TG NO. 225 <sup>2</sup>	Sediment-Water Lumbriculus Toxicity	Evaluates toxicity of sediment-associated chemicals endobenthic living organisms
OECD TG NO. 233 <sup>2</sup>	Sediment-Water Chironomid Life-Cycle Toxicity	Evaluates chronic toxicity to the life-cycle of sediment-dwelling freshwater dipteran Chironomus species.
OECD TG NO. 235 <sup>2</sup>	Chironomus sp. Acute Immobilisation test	Evaluates acute toxicity (immobilisation) to chironomid species.
OECD TG NO. 236	Fish Embryo Acute Toxicity (FET)	Evaluates toxicity to fish using zebrafish embryos
OECD TG NO. 238 <sup>2</sup>	Sediment-free Myriophyllum spicatum Toxicity Test	Evaluates toxicity to a submerged, rooted macrophyte species (water milfoil)

Test Guidelines – Effects on Biotic Systems <sup>1</sup>		
Test Guideline No.	Title	Information Gathered
OECD TG NO. 239 <sup>2</sup>	Water-Sediment Myriophyllum spicatum Toxicity Test	Evaluates toxicity to a submerged, rooted macrophyte species (water milfoil)
OECD TG NO. 242 <sup>2</sup>	Potamopyrgus antipodarum Reproduction Test	Evaluates reproductive toxicity to a mudsnail
OECD TG NO. 243 <sup>2</sup>	Lymnaea stagnalis Reproduction Test	Evaluates reproductive toxicity to a freshwater snail
OECD TG NO. 319A <sup>2,3</sup>	Determination of in vitro intrinsic clearance using rainbow trout hepatocytes (OECD TG NO. 319A)	Evaluates the capacity for fish (rainbow trout) to metabolically clear chemical via the liver.  This in vitro clearance measurement can be
OECD TG NO. 319B <sup>2,3</sup>	Determination of in vitro intrinsic clearance using rainbow trout liver S9 sub-cellular fraction (RT-S9) (OECD TG NO. 319B)	applied to models to predict chemical bioconcentration in fish (BCF). The application is described in the guidance document (see No. 280, Other Useful Information table)

<sup>&</sup>lt;sup>1</sup> Does not include tests in terrestrial plant species.

<sup>2</sup> Added to list on First Update (December 2019)

<sup>3</sup> These Test Guidelines are classified by the OECD as evaluating *Environmental Fate and Behavior*.

EPA NAM-Related Policies Which May Be Relevant to TSCA		
Link to Policy	Type of NAM	Information Gathered
OCSPP Skin Sensitization	Choice of Two Defined	Combination of NAMs to predict
Policy (To be updated when	Approaches (DAs)	skin sensitization in humans
finalized)		
Waiver Guidance – Dermal	Process for waiving dermal	Acute dermal toxicity
Toxicity 1	toxicity testing for pesticides; but	
	may be applicable to industries	
	considering performing these	
	studies for TSCA purposes.	2 11
Waiver Guidance - Birds <sup>1</sup>	Waiving	Draft policy open for public comment
Waiver Guidance - Acute	Waiving or the use of Bridging	Acute toxicity for pesticides (by route
Toxicity <sup>1</sup>	(read-across)	and including irritation/sensitization)
Alternative Testing	Decision tree for <i>in vitro</i> testing	Eye irritation
<u>Framework - Eye Irritation</u> <sup>1</sup>	for labeling	
Process to Evaluate and	Alternative approaches to	Documents a process to be followed
<u>Implement Alternative</u>	evaluating acute toxicity in lieu of	to submit to EPA (Office of Pesticide
Approaches to In Vivo Acute	an in vivo study	Programs)
Toxicity Studies <sup>1</sup>		
Use of NAMs for Endocrine	Use of high throughput assays and	Screening for tiered testing for
Disruptor Screening <sup>1</sup>	computational tools in the	endocrine activity
	endocrine disruptor screening	
	program	
<sup>1</sup> Added to list on First Update (Decen	mber 2019)	

Other NAMs Used for TSCA <sup>1</sup>		
NAM	Parameter/ Information Gathered	
The OECD QSAR Toolbox <sup>2</sup>	Compilation of models and information to predict physical- chemical properties and hazards of chemicals. EPA has contributed models to this tool and it is used by scientists at EPA to understand and evaluate new and existing chemicals under TSCA	
Ecological Structure-Activity Relationships Program (ECOSAR)	Hazard <sup>3</sup> – In silico tool to predict aquatic hazard	
OncoLogic	Hazard <sup>3</sup> – In silico tool to predict potential to cause cancer in humans	
Analog Identification Methodology (AIM)	Hazard <sup>3</sup> – Database tool to facilitate identification of analogs for read-across	
Chemical Assessment Clustering Engine (ChemACE)	Hazard <sup>3</sup> – Database tool to facilitate structural clustering	
New Chemicals Program Chemical Categories Document	Hazard <sup>3</sup> – Documentation of TSCA chemical categories	
Estimation Programs Interface (EPISuite <sup>TM</sup> )	Physical/chemical properties and environmental fate <sup>3</sup> – e.g., bioconcentration/bioaccumulation	
Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER)	Exposure <sup>4</sup> – tools and models to estimate environmental releases and worker exposures	
Exposure and Fate Assessment Screening Tool (E-FAST)	Exposure <sup>4</sup> - tools and models to estimate consumer, general public and environmental exposures to chemicals.	
Approaches to Estimate Consumer Exposure	Exposure <sup>4</sup> – a variety of tools and models to estimate exposure to various consumer products and materials	

<sup>&</sup>lt;sup>1</sup> General Guidance on all approaches - <a href="https://www.epa.gov/tsca-screening-tools">https://www.epa.gov/tsca-screening-tools</a>
<sup>2</sup> Added to list on First Update (December 2019)

<sup>&</sup>lt;sup>3</sup> Hazard - <a href="https://www.epa.gov/tsca-screening-tools/using-predictive-methods-assess-hazard-under-tsca#models">https://www.epa.gov/tsca-screening-tools/using-predictive-methods-assess-hazard-under-tsca#models</a>;

<sup>4</sup> Physical/Chemical Properties, Environmental Fate and Exposure - <a href="https://www.epa.gov/tsca-screening-tools/using-predictive-methods-assess-hazard-under-tsca#models">https://www.epa.gov/tsca-screening-tools/using-predictive-methods-assess-hazard-under-tsca#models</a>; methods-assess-exposure-and-fate-under-tsca#fate

# **Appendix B – Other Information or Strategies**

Appendix B - which is a new addition to the list - includes non-specific tests/experimental methods that are different from the information presented in Appendix A. This section includes tools developed by entities outside of OPPT, important Federal Advisory Committee Act (FACA) committee findings for OCSPP evaluations/work products that use NAMs, and guidance documents considered national or international consensus documents.

As with the TSCA Section 4(h)(2)(C) list above, the information in the table below is not meant to be exhaustive. It includes information/tools that OPPT has knowledge of and experience with under TSCA. The table below provides links and a brief description of the source of information identified. General information on the publications from the OECD can be found under <u>Series on Testing and Assessment/Adopted Guidance and Review Documents</u>.

Other Useful Information <sup>1</sup>		
Source	Content	
EPA CompTox	Compilation of publicly available information on over 850,000 chemicals.	
Chemicals		
<u>Dashboard</u>		
FIFRA SAP	Prioritizing the Universe of Endocrine Disruptor Screening Program (EDSP)	
January 2013 <sup>2</sup>	Chemicals Using Computational Toxicology Tools	
FIFRA SAP	Continuing Development of Alternative High-Throughput Screens to Determine	
November, 2017	Endocrine Disruption, Focusing on Androgen Receptor, Steroidogenesis, and	
	Thyroid Pathways	
FIFRA SAP	Evaluation of a Proposed Approach to Refine the Inhalation Risk Assessment for	
December, 2018	Point of Contact Toxicity: A Case Study Using a New Approach Methodology	
	(NAM)	
OECD No. 34	Guidance Document on the Validation and International Acceptance of New or	
	Updated Test Methods for Hazard Assessment	
OECD No. 69	Guidance documents on the validation of (Quantitative) structure-activity	
	relationship [(Q)SAR] models	
OECD No. 102	Guidance document for using the OECD (Q)SAR application toolbox to develop	
	chemical categories according to the OECD guidance on grouping chemicals	
OECD No. 184	Guidance document on developing/assessing adverse outcome pathways	
OECD No. 194	Guidance on grouping of chemicals, second edition	
OECD No. 203	Guidance document on an integrated approach on testing and assessment (IATA) for skin corrosion and irritation	
OECD No. 211	Guidance Document for Describing Non-Guideline In Vitro Test Methods	

Other Useful Information <sup>1</sup>	
Source	Content
OECD No. 214	Guidance Document on the <i>In Vitro</i> Syrian Hamster Embryo (SHE) Cell Transformation Assay
OECD No. 231	Guidance Document on the In Vitro Bhas 42 Cell Transformation Assay (BHAS 42 CTA)
OECD No. 237	Guidance Document on Considerations for Waiving or Bridging of Mammalian Acute Toxicity Tests
OECD No. 255	Guidance Document on the Reporting of Defined Approaches to be Used Within Integrated Approaches to Testing and Assessment
OECD No. 256	Guidance Document on the Reporting of Defined Approaches and Individual Information Sources to be Used Within Integrated Approaches to Testing and Assessment (IATA) for Skin Sensitisation, Annex 1, Annex 2
OECD No. 260	Guidance Document for the Use of Adverse Outcome Pathways in Developing Integrated Approaches to Testing and Assessment (IATA)
OECD No. 263	Guidance Document on an Integrated Approach on Testing and Assessment (IATA) for Serious Eye Damage and Eye Irritation
OECD No. 280	Guidance Document on the Determination of In Vitro Intrinsic Clearance Using Cryopreserved Hepatocytes (RT-HEP) or Liver S9 Sub-Cellular Fractions (RT-S9) from Rainbow Trout and Extrapolation to In Vivo Intrinsic Clearance

<sup>&</sup>lt;sup>1</sup> Added at First Update (December 2019)

<sup>&</sup>lt;sup>2</sup> FIFRA SAP = Federal Insecticide, Fungicide and Rodenticide Act, Scientific Advisory Panel. Although several meetings/evaluations are presented in this table, interested parties are encouraged to review the SAP link for other meetings related to NAMs