toxicology and regulatory news

november 2022

Health risk assessment of endocrine disruptors

Congratulations to bibra toxicologist Helen Gregory, who recently completed an intensive course (and passed the subsequent examination) on the health risk assessment of endocrine disruptors (EDs), an online module of the Advanced International Training Programme in Health Risk Assessment from the Institute of Environmental Medicine (IMM) of the Karolinska Institute in Sweden.

The course covered mechanisms of action, from molecular initiating events to adverse outcomes, as well as methodologies for identification and analysis of EDs. The EU scientific criteria were examined and future challenges in the health risk assessment of EDs were discussed.

So please come to Helen if you would like her input on any ED issues of concern to you or your company.

Toxicology and Regulatory News

Contents

Toxicology and Regulatory News

Here at TRN, our aim is to keep the **bibra** toxicologists – and our wider readership – fully up to date on:

- Pertinent pronouncements on **toxicology** from national and international authorities, government departments and other expert groups
- Major health-related findings (including key legislative developments) that may affect **product safety** and **regulatory acceptability**

In this publication you will find brief commentaries written by **bibra** toxicologists that aim to bring to the attention of their peers important news relating to chemical toxicology and its associated regulatory application. The documents they highlight are identified by diligent and intelligent screening of a large number of key websites and publications from official bodies, national/international authorities, government departments and expert groups.

All documents – and others of a less-newsworthy but nonetheless important nature – are indexed with key terms and details are added to our searchable chemical toxicity database (TRACE).

If you are interested in:

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We'd love to hear from you!

International

OECD…

…releases supporting documents for *in vitro* eye irritation tests

The OECD has released a supporting document to the draft Test Guideline (TG 467) on Defined Approaches (DAs) for serious eye damage/eye irritation. This document describes two rule-based DAs for eye hazard identification based on physico-chemical properties and/or *in vitro* data for neat or diluted non-surfactant liquids. Both DAs employ validated i*n vitro* OECD test methods, including the Bovine Corneal Opacity and Permeability (BCOP), Reconstructed human Cornea-like Epithelium (RhCE) and Short Time Exposure (STE) assays.

In addition, a peer review report on the *in vitro* SkinEthic™ Human Corneal Epithelium (HCE) Time-to-Toxicity Test (TTT) has been released. It demonstrated that this test method is able to reliably distinguish the eye hazard classification category (1: serious eye damage, 2: eye irritation, or not classified, according to GHS criteria) for substances and mixtures, liquids and solids. The peer-review panel therefore considers it to be scientifically valid for regulatory use as a full replacement for the *in vivo* acute eye irritation test, although it cannot distinguish between eye irritants and mild eye irritants (GHS categories 2A and 2B).

Organisation for Economic Cooperation and Development (2022). Supporting document for evaluation and review of test guideline 467 on defined approaches (DAs) for serious eye damage / eye irritation. Series on Testing and Assessment No. 354. ENV/CBC/MONO(2022)10.

Peer review report - SkinEthic™ human corneal epithelium time-to-toxicity test for eye irritation. Series on Testing and Assessment No. 355. ENV/CBC/MONO(2022)11.

…finalises review of the miniaturised Ames test

The bacterial reverse gene mutation (Ames) test outlined in OECD TG 471 is the most widely used mutagenicity screening assay across a range of sectors and (despite an update of the guideline in 2020) has remained mostly unchanged since 1997. In recent years, several miniaturised versions of the assay have been developed and are primarily used in the pharmaceutical industry for early screening of new products during research and development, and to test impurities at later stages. They are characterised by a reduction in vessel size and/or format for treatment and scoring, and therefore use fewer bacteria. Some employ non-standard strains of bacteria as well as high throughput detection methods. The OECD has finalised a detailed review paper evaluating the performance of several types of these miniaturised assays and has provided recommendations regarding their future use. A validation study must be

conducted in the future to assess whether these miniaturised assays could be used as an alternative to the standard Ames test, as they are currently not widely accepted by regulatory authorities.

Organisation for Economic Cooperation and Development (2022). Detailed review paper on the miniaturised versions of the bacterial reverse gene mutation test. Series on Testing and Assessment No. 358. ENV/CBC/MONO(2022)14.

…releases supporting document for the GARD™ skin sensitisation test

A supporting document on the Genomic Allergen Rapid Detection (GARD) test method for skin sensitisation (GARD™skin) has been released by the OECD. This document describes the origin and biological relevance of the GARDskin Genomic Prediction Signature (GPS), and a detailed description of the analytical workflow.

Organisation for Economic Cooperation and Development (2022). Supporting document to the genomic allergen rapid detection test method for skin sensitisation (GARD™skin), described in test guideline 442E. Series on Testing and Assessment No. 357. ENV/CBC/MONO(2022)13.

…investigates an *in vitro* skin sensitisation test method for nanomaterials

The OECD has released a Swiss report demonstrating the applicability of OECD TG 442D for *in vitro* skin sensitisation testing of nanomaterials The report concludes that the KeratinoSens™ test method can be applied for the testing of manufactured nanomaterials. The report should provide a good basis for future adaptations of this or related test methods.

Swiss Confederation (2022). Study Report: Applicability of the key event based TG 442D for *in vitro* skin sensitisation testing of nanomaterials.

…explores the applicability of the *in vitro* micronucleus test for nanomaterials

The OECD has released a report on the *in vitro* micronucleus assay (OECD TG 487) for testing engineered nanomaterials (ENM). As there is no harmonised version of the test protocol for ENM, the EU Joint Research Centre (JRC) conducted an investigation into any necessary adaptations of TG 487 for this purpose. This report summarises their findings, covering the main technical issues related to ENM, interlaboratory comparisons, and preliminary guidance.

Organisation for Economic Cooperation and Development (2022). Study report and preliminary guidance on the adaptation of the *in vitro* micronucleus assay (OECD TG 487) for testing of manufactured nanomaterials. Series on Testing and Assessment No. 359. ENV/CBC/MONO(2022)15.

…develops Performance Standards on *in vitro* phototoxicity testing

An OECD "Performance Standards" document has been released, which relates to the validation of similar or modified reconstructed human epidermis methods for *in vitro* phototoxicity testing of dermally applied substances. Guidance is provided on evaluating the reliability and relevance of these test methods which, if successfully validated, may be added to TG 498 (*In vitro* Phototoxicity - Reconstructed Human Epidermis Phototoxicity test method).

Organisation for Economic Cooperation and Development (2022). Performance standards for the assessment of proposed similar or modified in vitro phototoxicity: reconstructed human epidermis (RhE) test methods for testing of topically applied substances, as described in test guideline 498. Series on Testing and Assessment No. 356. ENV/CBC/MONO(2022)12.

…reviews *in vitro* immunotoxicity test methods

Exposure to immunotoxic compounds can have detrimental effects on the response to both communicable and non-communicable diseases. It is therefore important to understand the immunotoxic potential of chemicals and the risk they pose to humans. Current practices in immunotoxicity assessment involve animal testing, and while a number of non-animal-based testing methods have been developed, not many have been validated or accepted by regulatory authorities. The OECD has released a detailed review paper discussing the use of *in vitro* immunotoxicity assays, with a focus on immunosuppression.

Organisation for Economic Cooperation and Development (2022). Detailed review paper on in vitro test addressing immunotoxicity with a focus on immunosuppression. Series on Testing and Assessment No. 360. ENV/CBC/MONO(2022)16.

JECFA…

…technical report on certain contaminants in food

JECFA's 90th meeting (held in October-November 2020) assessed the acceptability of previous cargo chemical substances present in fats and oils, and the technical report of the meeting has now been released. A substance is considered acceptable if it meets certain criteria including: 1) any resultant residues do not give rise to adverse health effects in humans, 2) the Acceptable Daily Intake (ADI) or Tolerable Daily Intake (TDI) is greater than or equal to 0.1 mg/kg bw, and 3) it does not contain a known food allergen. The Committee concluded that the following substances met these criteria:

- 1,3-propanediol
- 1,4-butanediol
- calcium ammonium nitrate
- calcium nitrate
- ethyl tertiary butyl ether
- isodecyl alcohol
- isononyl alcohol
- isooctyl alcohol
- methyl tertiary butyl ether
- mineral oil (medium and low viscosity, class II and class III)
- myristyl alcohol
- propylene tetramer
- soybean oil epoxidized (ESBO)
- tridecyl alcohol
- unfractionated fatty alcohols

The following substances did not meet these criteria:

- mineral oil saturated hydrocarbons (as they may contain mutagenic and carcinogenic substances)
- montan wax (due to insufficient data to characterise its risk)
- calcium lignosulfonate (due to a lack of relevant toxicological data).

Joint FAO/WHO Expert Committee on Food Additives (2022). Evaluation of certain contaminants in food. Ninetieth report. WHO Technical Report Series 1032.

...technical report on residues of veterinary drugs in food

The technical report from JECFA's 94th meeting (held in May 2022) has been released. The following decisions on certain residues of veterinary drugs in human food are of particular interest:

- Imidacloprid: an oral Acceptable Daily Intake (ADI) of 0.05 mg/kg bw was set, based on a No-Observed-Adverse-Effect Level (NOAEL) of 5.25 mg/kg bw/day from an extended one-generation reproductive toxicity study. In addition, an Acute Reference Dose (ARfD) of 0.09 mg/kg bw was established, based on a benchmark dose level of 9 mg/kg bw from an acute neurotoxicity study in rats.
- Ivermectin: the ADI of 10 μg/kg bw and ARfD of 200 μg/kg bw remained unchanged.
- Nicarbazin: an ADI of 0.9 mg/kg bw was set, based on a NOAEL of 42.5 mg/kg bw/day from a developmental toxicity study in rabbits. The setting of an ARfD was not considered necessary.
- Selamectin: a revised ADI of 0.05 mg/kg bw was established, based on a NOAEL of 5 mg/kg bw/day from a 1-year rat study. The existing ARfD of 0.4 mg/kg bw was retained.

Joint FAO/WHO Expert Committee on Food Additives (2022). Evaluation of certain veterinary drug residues in food. Ninety-fourth report. WHO Technical Report Series 1041.

WHO Expert Committee on Drug Dependence 45th meeting

At its October meeting, the WHO Expert Committee on Drug Dependence (ECDD) reviewed the chemistry, pharmacology, toxicology, therapeutic use, epidemiology and drug dependence of several novel drug substances, including a synthetic cannabinoid receptor agonist, two benzodiazepines, four novel synthetic opioids, two cathinones/stimulants and Zopiclone (a medicinal drug). The corresponding critical review and pre-review documents are now available.

World Health Organization (2022). Forty-fifth meeting of the Expert Committee on Drug Dependence (ECDD). 10-14 October 2022. Pre-reviews and critical reviews available.

Europe

ECHA...

...health risks resulting from occupational exposure to 1,2,3-TCP and 1,2-DCP

In recent evaluations of 1,2,3-trichloropropane (1,2,3-TCP) and 1,2-dichloropropane (1,2-DCP), the non-threshold carcinogenic nature of these substances prevented the establishment of an Occupational Exposure Limit (OEL). An Exposure-Risk Relationship (ERR) was instead derived in each case, the critical effect being cancer of the oral cavity and of the lung, respectively.

European Chemicals Agency (2022). ECHA Scientific reports for evaluation of limit values at the workplace. 1,2,3-Trichloropropane and 1,2-dichloropropane. 19 October. And also here.

...call for evidence on MOCA

ECHA has issued a call for evidence (by 16th November) on 4,4'-methylenebis[2-chloroaniline] (MOCA), in order to validate or refute the Agency's proposed need for the preparation and submission of an Annex XV restriction dossier.

European Chemicals Agency (2022). Current calls for comments and evidence.
See also: Annex XV report. An assessment of whether the use of MOCA in articles should be restricted in accordance with article 69(2) of REACH.

Classification and labelling…

…proposal for harmonised classification and labelling on clopyralid

Under the EU Classification, Labelling and Packaging (CLP) regulation, there is a legal obligation for suppliers to evaluate the hazards of chemicals (substances and mixtures) that are to be placed on the market, and to classify and label them appropriately. An option also exists for Member State Competent Authorities or industry to propose harmonised classification and labelling of a substance across Europe. Following the submission of a Harmonised Classification and Labelling (CLH) proposal, ECHA organises a public consultation period of 60 days. Under this scheme a CLH report has been submitted by the Finnish authority to standardise the classification and labelling of clopyralid for reproductive toxicity, specific target organ toxicity following repeated exposure, and skin corrosion/irritation, as well as aquatic toxicity.

European Chemicals Agency (2022). CLH report. Proposal for harmonised classification and labelling based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2. Clopyralid (ISO); 3,6-dichloropyridine-2-carboxylic acid.

Biocidal Products Regulation

…BPC opinions on four active substances

In October 2022, ECHA's Biocidal Products Committee (BPC) adopted opinions on the approval (or non-approval) of the following active substances:

- mecetronium ethyl sulphate in product-type (PT) 1 (human hygiene)
- ozone generated from oxygen in PTs 2 (disinfectants and algaecides not intended for direct application to humans or animals), 4 (food and feed area), 5 (drinking water) and 11 (preservatives for liquid-cooling and processing systems)
- sulphur dioxide generated from sulphur by combustion in PT 4
- sulphur dioxide released from sodium metabisulphite in PT 9 (fibre, leather, rubber and polymerised materials preservatives)

Conclusions were also made available on applications for Union authorisation of a biocidal product family based on the following active substances:

- active chlorine released from sodium hypochlorite in PTs 2, 3 (veterinary hygiene), 4 and 5
- hydrogen peroxide in PTs 2, 3 and 4
- peracetic acid in PTs 2 and 4.

European Chemicals Agency (2022). Annex to news: Highlights from September BPC meeting.

EFSA…

…opinions on β-hydroxybutyrate salts and iron milk proteinate as novel foods

The EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) has delivered an opinion on calcium, magnesium and sodium salts of β-hydroxybutyrate as a Novel Food (NF). Due to inconsistencies in the reporting of the identity, production process and composition of the test material used in the submitted toxicity studies (including human studies), it was concluded that the safety of these salts as a NF could not be established. In a separate opinion, the NDA Panel considered that the consumption of iron milk proteinate was "not nutritionally disadvantageous".

European Food Safety Authority (2022). NDA Panel. Safety of iron milk proteinate as a novel food pursuant to Regulation (EU) 2015/2283 and bioavailability of iron from this source in the context of Directive 2002/46/EC. Novel Foods and Food Allergens (NDA). EFSA Journal 2022;20(9):7549.

Safety of β-hydroxybutyrate salts as a novel food pursuant to Regulation (EU) 2015/2283. EFSA Journal 2022;20(10):7449.

…releases reports on various plant protection products

A Member State draft assessment report has been released on bensulfuron-methyl, and further data have been made available on amidosulfuron, pyrimethanil and triclopyr in relation to their potential for endocrine disruption (ED). Conclusions on the pesticide peer reviews of benfluralin, flutianil (again in light of potential ED effects), rimsulfuron and quartz sand have also been published, identifying areas of concern and data gaps.

Available at European Food Safety Authority (2022) or under Public Consultations.

…safety evaluation of β-galactosidase

In three separate assessments, the EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) concluded that the food enzyme β-galactosidase (produced from the non-genetically modified (non-GM) *Neobacillus* strain AE-LT, the non-GM fungal strain *Aspergillus oryzae* AE-LA, and the GM *Aspergillus niger* strain TOL) does not give rise to safety concerns under the intended conditions of use. All three assessments considered the potential risk of sensitisation in consumers which, although not entirely excluded, was considered to be low.

European Food Safety Authority (2022). CEP Panel. Safety evaluation of the food enzyme β-galactosidase from: Non-genetically modified Neobacillus sp. strain AE-LT. EFSA Journal 2022;20(10):7573.

Non-genetically modified Aspergillus oryzae strain AE-LA. EFSA Journal 2022;20(10):7569.

Genetically modified Aspergillus niger strain TOL. EFSA Journal 2022;20(10):7570.

…assessment of T-2 and HT-2 toxins for ruminants

Based on new evidence, reference points (RPs) for adverse health effects resulting from the presence of the fusarium derived toxins T-2 and HT-2 in feed were derived by the EFSA Panel on Contaminants in the Food Chain (CONTAM). RPs of 0.01 mg/kg feed were established for sheep (with a concern for lactating sheep at this level) and 0.2 mg/kg feed for cows and goats.

European Food Safety Authority (2022). Panel on Contaminants in the Food Chain (CONTAM). Assessment of information as regards the toxicity of T-2 and HT-2 toxin for ruminants. EFSA Journal 2022;20(9):7564.

…cumulative risk assessments of pesticides with regard to craniofacial alterations

EFSA established Cumulative Assessment Groups (CAGs) for several pesticides and then conducted Cumulative Risk Assessments (CRAs) for two types of craniofacial alterations (alterations due to abnormal skeletal development, and head soft tissue alterations / brain neural tube defects) in 14 European populations of women of childbearing age. To this end, cumulative dietary exposure was estimated using monitoring data collected by Member States (MS) between 2017-2019 on the consumption of 36 raw primary commodities, two processed commodities (olive oil and wine), and drinking water. Probabilistic data monitoring allowed a conclusion, with varying degrees of certainty, that the Total Margins of Exposure (MOET) resulting from cumulative dietary exposure exceeded 100 for all MS and for both CAGs [where a MOET of 100 is considered a general threshold for safety]. For head soft tissue alterations and brain neural tube defects, the MOET was found to exceed 500.

European Food Safety Authority (2022). Retrospective cumulative dietary risk assessment of craniofacial alterations by residues of pesticides. EFSA Journal 2022;20(10):7550.

…publishes roadmap for action on risk assessment of mixtures

There is a growing concern in society about exposure to mixtures of chemicals via food and the environment. EFSA's aim is that, by 2030, EFSA and its partners will be equipped for the routine implementation of human health risk assessment to multiple chemicals. It has therefore developed a

roadmap for achieving this aim, including the mapping of available mixtures risk assessment methodology in applicable areas (i.e., pesticides, food additives, food-contact materials), identifying current scientific gaps and challenges, and defining short-, medium-, and long-term research projects aimed to fill the identified gaps / remove any challenges or blocks.

European Food Safety Authority (2022). Roadmap for action on Risk Assessment of Combined Exposure to Multiple Chemicals (RACEMiC). EFSA supporting publication 2022:EN-7555.

…draft opinion on N-nitrosamines in food

N-Nitrosamines (N-NAs) are known genotoxins and carcinogens. As such, their presence in food constitutes a potential concern for human health. This comprehensive draft opinion, issued by the EFSA CONTAM Panel, reviews the available toxicological data on ten carcinogenic N-NAs found in food. The incidence of rat liver tumours induced by N-nitrosodiethylamine (NDEA, considered the most potent N-NA) was selected to derive a benchmark dose lower confidence limit for a 10% response ($BMDL_{10}$) of 10 μg/kg bw/day to be used in a margin of exposure (MoE) approach to the risk assessment of the ten N-NAs in meat and meat products. Dietary exposures ranged from 0-209 ng/kg bw/day, resulting in estimated MoEs of less than 10,000 for all age groups. Citing previous EFSA guidance that, for substances that are both genotoxic and carcinogenic, an MoE "of 10,000 or higher, if based on the $BMDL_{10}$ from an animal carcinogenicity study, would be of low concern from a public health point of view", the CONTAM Panel concluded that dietary exposure to these ten N-NAs may indicate a health concern.

European Food Safety Authority (2022). Panel on Contaminants in the Food Chain (CONTAM). Draft scientific opinion on the human health risks related to the presence of N-nitrosamines (N_NAs) in food. Opinion and supporting information available.

EMA releases herbal monographs and assessment reports

EMA's Committee on Herbal Medicinal Products (HMPC) has released a final EU herbal monograph on Indian pennywort (*Centella asiatica*) and couch grass (*Agropyron repens*) rhizome, along with the related assessment reports that summarise the available toxicity data. In addition, HMPC has released an addendum to its assessment report on green tea (*Camellia sinensis*), describing new data made available since the original assessment report and herbal monograph, which were not considered sufficient to justify a full revision.

European Medicines Agency (2022). EU herbal monographs and public statements, and associated assessment reports, references and addenda, available.

SCCS opinion on genistein and daidzein

A final opinion has been released on the safety of two common isoflavone phytoestrogens, genistein and daidzein, in cosmetic products. Considering the potential endocrine-disrupting properties of phytoestrogens, as well as other critical toxicity endpoints, SCCS concluded that genistein and daidzein can be safely used in cosmetic products up to maximum concentrations of 0.007% and 0.02%, respectively.

Scientific Committee on Consumer Safety (2022). Opinion on genistein and daidzein. SCCS/1641/2022. Final version. Corrigendum October 2022.

United Kingdom

COC guidance on carcinogenicity assessment

The COC has issued a guidance statement which provides an overview of the risk characterisation methods used to assess exposures to chemicals with carcinogenic properties. This statement discusses:

- the estimation of cancer risk by extrapolation from human and laboratory animal studies
- the assessment of threshold and non-threshold carcinogens (with the lower 95% confidence limit of the benchmark dose (BMDL) being preferred as the point of departure)
- the derivation of margins of exposure and minimal risk levels
- approaches used by other authorities (but not recommended by the COC), including low dose extrapolation of animal data, linear extrapolation to identify a Derived-Minimal-Effect Level, and the use of the T25.

Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (2022). Cancer risk characterisation methods. Guidance. 25 August 2022.

COM October meeting

At its most recent meeting the COM discussed and drafted guidance on the use of biomarkers in genotoxicity risk assessment, as well as a strategy for the genotoxicity testing of chemicals.

Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment (2022). COT meeting: 13 October 2022. Reports available.

COT statement on perfluoroalkyl substances (PFASs)

The COT has reviewed the European Food Safety Authority (EFSA) opinion on the risks to human health related to the presence of PFASs in food, and assessed the potential risks to the UK population from this group of compounds. Exposure estimates (for each sub-population) exceeded the Tolerably Weekly Intake (TWI) set by EFSA, indicating a potential health concern. However, it was noted that there is "considerable uncertainty as to the appropriateness of the derivation of the TWI and of the biological significance of the response on which it is based, which complicates interpretation of the possible toxicological significance of exceedances".

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (2022). Statement on the EFSA opinion on the risks to human health related to the presence of perfluoroalkyl substances in food. September 2022.

United States

NTP technical reports on the subchronic and genotoxicity of (+)- and (+/-)-usnic acid in rodents

Following 90-day dietary exposure to (+)-usnic acid, male rats showed liver toxicity at ≥360 ppm, while effects on clinical chemistry were seen at ≥60 ppm in male mice. Based on these results, the No-Observed-Adverse-Effect Levels (NOAELs) were concluded to be 120 and 30 ppm for rats and mice, respectively.

For (+/-)-usnic acid, liver toxicity was observed in male rats at ≥120 ppm and ovarian atrophy was seen at ≥180 ppm in female mice. Based on these results, the NOAELs were considered to be 60 ppm for both rats and mice.

In a separate 2-week dietary study, an increased incidence of micronuclei was reported in the erythrocytes of mice exposed to either form of usnic acid at 600 ppm.

National Toxicology Program (2022). NTP technical reports on the toxicity studies of: (+)-Usnic acid (CASRN 7562-61-0) administered in feed to F344/N Nctr rats and B6C3F1/Nctr mice. NTP TOX 104. October.

Usnea lichens containing (+/-)-usnic acid (CASRN 125-46-2) administered in feed to F344/N Nctr rats and B6C3F1/Nctr mice. NTP TOX 105. October.

TCEQ issues draft Development Support Document (DSD) on *tert*-butyl alcohol

TCEQ has released a draft DSD on *tert*-butyl alcohol. An acute 1-hour reference value (ReV) of 5000 ppb (15,000 μg/m^3) was derived, based on observations of ataxia, hyperactivity and hypoactivity in a 12-day inhalation study in rats. A chronic ReV was set at 2700 ppb (8200 μg/m^3), based on increased absolute kidney weights in female rats exposed, again by inhalation, for 13 weeks.

Texas Commission on Environmental Quality (2022). tert-Butyl alcohol. CAS Registry Number: 75-65-0. Development Support Document. Draft.

Outcome of the 162nd meeting of the CIR Expert Panel

Following its September meeting, the CIR Expert Panel has released six final safety assessments covering several cosmetic ingredients (see below). These reports summarise chemical properties, manufacturing/usage and toxicological data addressing a range of human health endpoints.

- diatomaceous earth
- fatty ester end-capped alkoxylates
- glycolactones
- hydroxyacetophenone
- *Portulaca oleracea*-derived ingredients
- starch phosphates

In addition, the following four tentative safety assessments were also released:

- clays
- polyhydroxystearic acid
- *Rosa centifolia*-derived ingredients
- trisodium ethylenediamine disuccinate

Cosmetic Ingredient Review Expert Panel (2022). Findings of 162nd meeting held on 26-27 September 2022.

CIR reports are searchable via: https://www.cir-safety.org/ingredients

Rest of the World

Health Canada…

…residential indoor air quality guideline for xylenes

Health Canada has finalised its residential indoor air quality guideline on the three isomers of xylene (p-, m- and o-). The recommended airborne exposure limit for short-term (1-hour) exposure is 7200 µg/m^3, based on neurological symptoms, respiratory effects, and irritation of the eyes, nose and throat. The recommended long-term (24-hour average) exposure limit is 150 µg/m^3, the critical effect being impaired motor coordination.

Health Canada (2022). Residential Indoor Air Quality Guidelines. Xylenes. October.

…guideline technical documents for dimethoate and omethoate in drinking water

Health Canada has released a drinking water quality guideline on dimethoate and its metabolite omethoate. An acceptable daily intake (ADI) of 0.002 mg/kg bw is proposed for dimethoate, based on cholinesterase inhibition; the resultant maximum acceptable concentration (MAC) is 0.02 mg/L (covering both compounds).

Health Canada (2022). Guidelines for Canadian Drinking Water Quality. Dimethoate and Omethoate. September.

…screening assessments on nine substances (including several aldehydes)

Health Canada and Environment and Climate Change Canada have recently drafted a screening assessment discussing the human health and environmental effects of benzaldehyde, methylbenzylaldehyde, nonanal, octanal and vanilla oil, identified for action under the Chemicals Management Plan (CMP).

In addition, the screening assessment for the protein derivatives (protein hydrolyzates, collagen hydrolyzates and isostearoyl hydrolyzed collagen) and yeast extract group was finalised.

It was concluded that none of the chemicals met section 64 criteria of the Canadian Environmental Protection Act (CEPA), which defines a compound as "toxic" in terms of its risk to human health or the environment.

Health Canada/Environment and Climate Change Canada (2022). Draft Screening Assessment. Aldehydes Group. October.
Final Screening Assessment. Protein Derivatives and Yeast Extract. October.

AICIS draft evaluation statements on industrial chemicals

Under the AICIS Rolling Action Plan, draft evaluation statements have been released for the following chemicals or groups of chemicals:

- 1-(1,1-dimethylethyl)-3,4,5-trimethyl-2,6-dinitrobenzene and 3-(1,1-dimethylethyl)-1,5-dimethyl-2,4-dinitrobenzene
- 1-bromo-3-chloropropane and 1,3-dibromopropane
- 3-iodo-propynyl butylcarbamate
- aluminium
- cadmium sulfide pigments
- carbendazim
- estragole
- glyoxylic acid
- hydroquinone and p-benzoquinone
- lauryl sulfates
- long chain (C≥10) alkyl benzene sulfonates
- methacrylamide
- octanohydroxamic acid
- pentachlorobenzene (PeCB) and hexachlorobenzene (HCB)
- polymers incorporating glycidyl methacrylate

These statements summarise the human health and/or environmental hazards, and propose means of managing risks, for each chemical.

Australian Industrial Chemicals Introduction Scheme (2022). Draft evaluation statements. October.

APVMA public release summary on isocycloseram in an insecticide

A new public release summary evaluates the toxicological effects of isocycloseram, an active constituent in an insecticide. The APVMA established an acceptable daily intake (ADI) of 0.02 mg/kg bw based on blood plasma effects in an 80-week dietary study in mice. An acute reference dose (ARfD) was set at 0.08 mg/kg bw for women of child-bearing age, with the critical effect being developmental toxicity (observed in rats). There were no objections on human health grounds to the approval of isocycloseram.

Australian Pesticides and Veterinary Medicines Authority (2022). Public Release Summary on the evaluation of isocycloseram in the product Simodis Plinazolin Technology Insecticide. APVMA product number 89460. October.

Cover image: A cup of green tea.

See also: Our article on page 10 relating to the herbal monograph for green tea published by the European Medicines Agency (EMA).

Further information: The toxicologists at bibra are experts in hazard and risk assessment of natural extracts.

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