toxicology & regulatory news

July 2014

Dates for your diary

Meet us at …

The EEMS (European Environmental Mutagen Society) 2014 conference

July 6-10

Lancaster University, LA1 4YT

Look for … Anne Edwards, Senior Toxicologist

bibra
toxicology advice
& consulting

Toxicology and Regulatory News

Here at TRN, our aim is to keep the **bibra** staff – and you – fully up to date on:

- Pertinent pronouncements on **toxicology and nutrition** 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, peer-reviewed toxicology and nutrition journals 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:

- An individual item or items herein
- Receiving *Toxicology and Regulatory News* on a regular basis
- Commenting on this publication
- The TRACE database on chemical toxicity and related information
- **bibra** membership
- Alerts relating to specific chemicals
- The safety-in-use of a specific substance, product or mixture

…then please do not hesitate to contact us via our website (www.bibratoxadvice.co.uk), by e-mail (info@bibratoxadvice.co.uk) or by telephone (+44 (0)20 8619 0770).

We'd love to hear from you!

Europe

REACH

…ECHA newsletter – guest column by bibra scientists

ECHA's June 2014 newsletter includes a guest column written by expert toxicologists at bibra. The column concerns the use of existing information to support high quality REACH registrations.

European Chemicals Agency. ECHA Newsletter: Through the deadlines towards safer chemicals. ECHA/NI/14/08. June 2014.
http://echa.europa.eu/view-article/-/journal_content/title/echa-newsletter-through-the-deadlines-towards-safer-chemicals
Also see http://www.bibra-information.co.uk/news_story-696.html

…ECHA reports on progress in the use of alternative methods

An ECHA report describes the progress made by registrants in using non-animal test methods including read-across and *in vitro* testing.

European Chemicals Agency. The use of alternatives to testing on animals for the REACH Regulation. Second report under Article 117(3) of the REACH Regulation. ECHA-14-A-07-EN. June 2014.
http://echa.europa.eu/documents/10162/13639/alternatives_test_animals_2014_en.pdf

…New version of Chesar (2.3) supports SCED-based consumer assessments

The latest update of ECHA's Chemical Safety Assessment and Reporting tool (Chesar) enables users to estimate consumer exposures using specific consumer exposure determinants (SCEDs) developed by associations from industry.

European Chemicals Agency (2014). Chesar 2.3 supports SCED-based consumer assessment. ECHA/NA/14/26. http://echa.europa.eu/view-article/-/journal_content/title/chesar-2-3-supports-sced-based-consumer-assessment

…Proposals for harmonised classification and labelling

Under EC Regulation No. 1272/2008 on Classification, Labelling and Packaging, there is a legal obligation for suppliers to evaluate the hazards of chemicals (substances and mixtures) 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 ask for the classification and labelling of a substance to be harmonised across Europe, whereupon ECHA organises a public consultation period of 45 days. Under this scheme, proposals have been submitted by the Polish and UK authorities to standardise the classification and labelling of chlorsulfuron and pirimicarb.

European Chemicals Agency. CLH reports. Proposals for harmonised classification and labelling based on Regulation (EC) No. 1272/2008 (CLP Regulation), Annex VI, Part 2.
Chlorsulfuron. Version 1. 14 February 2014. http://echa.europa.eu/documents/10162/ede24139-d666-456d-912a-0fb2afee5484
Pirimicarb. Version 1. September 2013. http://echa.europa.eu/documents/10162/9d910b70-d1df-4f98-90a0-87905da55311

…RAC opinions on the classification and labelling of seven substances

As announced in a June 2014 news alert, ECHA's Committee for Risk Assessment (RAC) has considered proposals (from the Czech, Dutch, Finnish and German authorities) to harmonise the classification and labelling of:

- bupirimate
- 1,2-dichloropropane
- flumioxazin
- glutaraldehyde
- 1-methyl-2-pyrrolidone
- propylene oxide
- Tinuvin 123

European Chemicals Agency (2014). RAC concludes on scientific opinions for CLH. ECHA/NA/14/27. http://echa.europa.eu/view-article/-/journal_content/title/rac-concludes-on-scientific-opinions-for-clh

…Four substances of very high concern (SVHCs) added to ECHA's "Candidate List"

As announced in a recent press release, ECHA has added the following SVHCs to its Candidate List for authorisation (which now contains 155 substances):

- 1,2-benzenedicarboxylic acid, dihexyl ester, branched and linear [diisohexyl phthalate]
- cadmium chloride
- sodium perborate
- sodium peroxometaborate

Each of these substances has been identified as carcinogenic, mutagenic, or toxic for reproduction (CMR). A decision will be made later on whether these chemicals will be subject to authorisation.

European Chemicals Agency (2014). Candidate List updated with four new SVHCs. ECHA/PR/14/11. http://echa.europa.eu/view-article/-/journal_content/title/candidate-list-updated-with-four-new-svhcs
Member State Committee documents in support of the inclusion of these substances in the Candidate List are available via http://echa.europa.eu/candidate-list-table

…Proposed restriction of inorganic ammonium salts and bisphenol A (BPA)

A recent Annex XV report submitted by the French authorities proposes a restriction on the placing on the market of inorganic ammonium salts in cellulose wadding insulation materials (unless these materials emit ammonia gas at less than 3 ppm). This aims to avoid eye and respiratory tract irritation due to the release of ammonia.

The French authorities have also proposed a restriction on the placing on the market of thermal paper containing BPA at 0.02% or higher (by weight). The restriction aims to reduce the risks of adverse health effects (including effects on the reproductive system, brain, mammary gland, and metabolism) arising in the children of workers and consumers exposed dermally to BPA during pregnancy.

European Chemicals Agency. Annex XV restriction reports. Proposals for a restriction.
Inorganic ammonium salts. Version number 2. May 2014. http://echa.europa.eu/documents/10162/999a106c-6baf-48c7-8764-0c55576a2517
4.4'-Isopropylidenediphenol (bisphenol A; BPA). Version number 2. May 2014. http://echa.europa.eu/documents/10162/c6a8003c-81f3-4df6-b7e8-15a3a36baf76

…ECHA committees agree on proposals for restriction and authorisation

ECHA's Committee for Risk Assessment (RAC) has adopted opinions on restriction proposals for nonylphenol/ nonylphenol ethoxylates in textiles, and the manufacture and use of 1-methyl-2-pyrrolidone (NMP). ECHA's Committee for Socio-Economic Analysis (SEAC) agreed on the restriction proposal for nonylphenol/nonylphenol ethoxylates.

Both committees agreed on draft opinions for applications for the authorisation of bis(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), lead chromate pigments and diarsenic trioxide.

European Chemicals Agency (2014). RAC and SEAC agree on restriction and authorisation proposals. ECHA/NA/14/28.
http://echa.europa.eu/view-article/-/journal_content/title/rac-and-seac-agree-on-restriction-and-authorisation-proposals

…Other items of interest

ECHA opens public consultation on alternatives to fuels/oils for decorative lamps and grill lighter fluids that are labelled as aspiration hazards (R65 or H304).
http://echa.europa.eu/addressing-chemicals-of-concern/restriction/call-for-evidence-consultation/-/substance/6121/search/+/term

Draft revised guidance on the preparation of dossiers for harmonised classification and labelling has been sent to Competent Authorities for REACH and CLP (CARACAL).
http://echa.europa.eu/support/guidance/consultation-procedure/ongoing-clp?panel=dossCnL2013#dossCnL2013

Testing proposals involving vertebrate animals: request for information from third parties on over 40 substances (deadline 17 or 21 July, or 1 August 2014).
http://echa.europa.eu/information-on-chemicals/testing-proposals/current

Biocidal Products Regulation

…Three transitional guidance documents published by ECHA

ECHA has recently published transitional guidance documents on efficacy assessments for antifouling products and preservatives, and the ecotoxicological assessment of mixtures of biocidal products.

European Chemicals Agency (2014). ECHA publishes three transitional guidance documents concerning biocides. ECHA/NA/14/24. http://echa.europa.eu/view-article/-/journal_content/title/echa-publishes-three-transitional-guidance-documents-concerning-biocides

…ECHA launches R4BP 3.1.2 for biocides submissions

The latest version of the Register for Biocidal Products includes:

- an improved user interface
- new search functionalities
- new processes to support applications for provisional authorisations
- new processes to support the renewal of national authorisations subject to mutual recognition

Most of the R4BP 3 submission manuals have also been updated.

European Chemicals Agency (2014). ECHA releases a new version of R4BP 3. ECHA/NA/14/29. http://echa.europa.eu/view-article/-/journal_content/title/echa-releases-a-new-version-of-r4bp-3
Submission manuals available at http://echa.europa.eu/support/dossier-submission-tools/r4bp/biocides-submission-manuals

…Public consultations on potential candidates for substitution

Public consultations have been launched on medetomidine and triclosan as potential candidates for substitution. The consultation periods run until 15 August 2014.

European Chemicals Agency (2014). Public consultation on potential candidates for substitution. http://echa.europa.eu/addressing-chemicals-of-concern/biocidal-products-regulation/public-consultation-on-potential-candidates-for-substitution

Toxtree updated

Toxtree, a standalone software application developed under a JRC contract, groups chemicals into structural categories, and predicts toxic effects by applying decision-tree approaches. The latest update (version 2.6.6) is now available.

European Commission. Joint Research Centre. Ideaconsult Ltd. Toxtree-2.6.6. Build date 15 June 2014.
http://toxtree.sourceforge.net/download.html

ANSES guidance on health risk assessment of reproductive toxins/endocrine disruptors…

A 105-page report by ANSES (in French) provides guidance on assessing the health risks associated with exposure to suspected reproductive toxins and/or endocrine disruptors in consumer products.

French National Agency for Food, Environmental and Occupational Health and Safety (ANSES). [Methodology for the evaluation of health risks associated with the presence of substances toxic to reproduction and/or endocrine disruptors in consumer products.] Ref n° 2009-SA-0331. Scientific edition, May 2014. http://www.anses.fr/sites/default/files/documents/CHIM2009sa0331Ra-00.pdf

…and toxicological profiles of five such candidate chemicals

Profiles have been issued on three substances currently classified as toxic to reproduction (category 2) in Europe:

- *cis*-1-(3-chloroallyl)-3,5,7-triaza-1-azonia adamantane chloride (*cis*-CTAC)
- n-hexane
- toluene

And on two potential endocrine-disrupting compounds:

- methyl-*tert*-butyl ether (MTBE)
- *o*-phenylphenol (OPP)

French National Agency for Food, Environmental and Occupational Health and Safety (ANSES). Links to the individual profiles (variously dated 2011-2013, although the cover page of each says 2014) are:
cis-CTAC: http://www.anses.fr/sites/default/files/documents/CHIM2009sa0331Ra-04-An02.pdf
n-Hexane: http://www.anses.fr/sites/default/files/documents/CHIM2009sa0331Ra-03-An02.pdf
MTBE: http://www.anses.fr/sites/default/files/documents/CHIM2009sa0331Ra-05-An02.pdf
OPP: http://www.anses.fr/sites/default/files/documents/CHIM2009sa0331Ra-01-An02.pdf
Toluene: http://www.anses.fr/sites/default/files/documents/CHIM2009sa0331Ra-02-An02.pdf

More flavouring group evaluations from EFSA

EFSA has released scientific opinions on flavouring group evaluations 74 revision 3 (FGE.74Rev3), FGE.82Rev1, FGE.91Rev2 and FGE.200.

Nine of the 19 simple aliphatic sulphides and thiols evaluated in FGE.74Rev3 were of "no safety concern at estimated levels of intake as flavouring substances". EFSA concluded that additional toxicity data were required for the remaining ten.

Similarly, four of the five epoxides assessed in FGE.82Rev1 were of no safety concern; additional toxicity data were requested for beta-ionone epoxide.

Meanwhile, EFSA was unable to evaluate seven of the 44 aliphatic and aromatic sulphides and thiols in FGE.91Rev2 due to the absence of suitable no-observed-adverse-effect levels (NOAELs). EFSA could not conclude that 3-(methylthio)-

heptenal is not of safety concern, as its commercially available form contains a possible genotoxin (2-(E)-heptenal). There were no safety concerns for the remaining 36 compounds.

In FGE.200, EFSA considered the genotoxic potential of 74 α,β-unsaturated aldehydes and precursors. The available data on the representative substance hex-2-(*trans*)-enal were not sufficient to rule out genotoxic concerns for any of the substances in this group, and EFSA recommended that further *in vivo* Comet and/or micronucleus assays should be performed on hex-2(*trans*)-enal and two other representative substances (nona-2(*trans*),6(*cis*)-dienal and oct-2-enal).

European Food Safety Authority. Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF). Scientific opinions on:
FGE.74Rev3: Consideration of simple aliphatic sulphides and thiols evaluated by the JECFA (53rd and 61st meeting) structurally related to aliphatic and alicyclic mono-, di-, tri-, and polysulphides with or without additional oxygenated functional groups from Chemical Group 20 evaluated by EFSA in FGE.08Rev5 (2012).
FGE.82Rev1: Consideration of epoxides evaluated by the JECFA (65th meeting).
FGE.91Rev2: Consideration of simple aliphatic and aromatic sulphides and thiols evaluated by the JECFA (53rd and 68th meetings) structurally related to aliphatic and alicyclic mono-, di-, tri-, and polysulphides with or without additional oxygenated functional groups evaluated by EFSA in FGE.08Rev5 (2012).
FGE.200: 74 α,β-unsaturated aldehydes and precursors from subgroup 1.1.1 of FGE.19.
EFSA Journal 2014, **12**(6), 3707-10.
http://www.efsa.europa.eu/en/publications.htm (search "FGE.74Rev3", "FGE.82Rev1", "FGE.91Rev2" or "FGE.200").

EFSA considers allergenic foods and food ingredients

EFSA has issued a draft report, updating its opinions relating to foods and food ingredients known to be allergenic. These include gluten-containing cereals, milk and dairy products, eggs, nuts, peanuts, soy, fish, crustaceans, molluscs, celery, lupin, sesame, mustard, and sulphites. The report includes information on the prevalence of food allergy, methods for the detection of allergens, and the doses reported to trigger adverse reactions.

European Food Safety Authority (2014). Panel on Dietetic Products, Nutrition and Allergies (NDA). Scientific opinion on the evaluation of allergenic foods and food ingredients for labelling purposes. http://www.efsa.europa.eu/en/consultations/call/140523.pdf

EFSA evaluates hexamethylene tetramine (HMT)

EFSA has evaluated the risks associated with the use of HMT as a food additive, considering the toxicological data made available since a previous assessment by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Although EFSA concluded that the existing toxicological database does not allow the establishment of an acceptable daily intake (ADI), it does not anticipate any adverse health effects for consumers of treated Provolone cheese, provided that the use of HMT does not result in residual formaldehyde (formed by HMT under acidic conditions) exceeding the maximum permitted level of 25 mg/kg.

European Food Safety Authority. Panel on Food Additives and Nutrient Sources added to Food (ANS). Scientific opinion on the re-evaluation of hexamethylene tetramine (E 239) as a food additive. *EFSA Journal* 2014, **12**(6), 3696.
http://www.efsa.europa.eu/en/efsajournal/doc/3696.pdf

EFSA assessments of substances used in food-contact materials

In recent evaluations, EFSA concluded that 5-norbornene-2,3-dicarboxylic anhydride and the ammonium salt of perfluoro{acetic acid, 2-[(5-methoxy-1,3-dioxolan-4-yl)oxy]} are not of concern with respect to human health when used in food-contact materials according to specified use conditions and restrictions.

European Food Safety Authority. Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF). Scientific opinions on the safety assessment of:
The substance, 5-norbornene-2,3-dicarboxylic anhydride, CAS No 826-62-0, for use in food contact materials.
The substance, perfluoro{acetic acid, 2-[(5-methoxy-1,3-dioxolan-4-yl)oxy]}, ammonium salt, CAS No 1190931-27-1, for use in food contact materials.
EFSA Journal 2014, **12**(6), 3714; 3718. http://www.efsa.europa.eu/en/publications.htm?entity=fip

EFSA dietary reference values (DRVs) – consideration of chromium(III)

EFSA has issued a draft opinion on DRVs for trivalent chromium, concluding that "there is no evidence of beneficial effects associated with chromium intake in healthy subjects". Thus, the derivation of an adequate intake (AI) value for chromium(III) was not considered appropriate.

European Food Safety Authority (2014). Panel on Dietetic Products, Nutrition and Allergies (NDA). Scientific opinion on dietary reference values for chromium. http://www.efsa.europa.eu/en/consultations/call/140606.pdf

EFSA assesses genetically modified oilseed rape

EFSA has released its opinion on genetically modified oilseed rape, variant MON 88302, for use in food and feed. The newly expressed CP4 EPSPS protein was not considered to be of toxicological concern, and MON 88302 is expected to be as safe as its conventional counterpart for humans and other animals.

European Food Safety Authority. Panel on Genetically Modified Organisms (GMO). Scientific opinion on application (EFSA-GMO-BE-2011-101) for the placing on the market of herbicide-tolerant genetically modified oilseed rape MON 88302 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 from Monsanto. *EFSA Journal* 2014, **12**(6), 3701.
http://www.efsa.europa.eu/en/efsajournal/doc/3701.pdf

EFSA assessments of animal feed additives

EFSA has released safety assessments on the following animal feed additives, drawing conclusions on the associated risks to human health (of consumers of relevant animal products, and of occupationally-exposed workers):

- astaxanthin
- diclazuril
- L-threonine

European Food Safety Authority. Panel on Additives and Products or Substances used in Animal Feed (FEEDAP). Scientific opinions on the safety and efficacy of:
Astaxanthin (CAROPHYLL® Pink 10% CWS) for salmonids and ornamental fish.
Synthetic astaxanthin as feed additive for salmon and trout, other fish, ornamental fish, crustaceans and ornamental birds.
Coxiril® (diclazuril) as a feed additive for chickens for fattening.
L-threonine produced by *Escherichia coli* for all animal species, based on a dossier submitted by HELM AG on behalf of Star Lake Bioscience Co.
EFSA Journal 2014, **12**(6), 3724-6; 3728.
Available via http://www.efsa.europa.eu/en/feedap/feedapscdocs.htm

EFSA concludes on two pesticides

PRAPeR, EFSA's Pesticide Risk Assessment Peer Review Unit, has published its conclusions on the pesticides flumioxazin and sulfoxaflor, covering human health and environmental aspects.

European Food Safety Authority.
Conclusion on the peer review of the pesticide risk assessment of the active substance flumioxazin. *EFSA Journal* 2014, **12**(6), 3736.
http://www.efsa.europa.eu/en/efsajournal/doc/3736.pdf
Conclusion on the peer review of the pesticide risk assessment of the active substance sulfoxaflor. *EFSA Journal* 2014, **12**(5), 3692.
http://www.efsa.europa.eu/en/efsajournal/doc/3692.pdf

EFSA opinions on 'basic substance' applications for sucrose and white willow bark

EFSA has assisted the European Commission in evaluating two applications for basic substances ("active substances, not predominantly used as plant protection products but which may be of value for plant protection"). Its views on white willow (*Salix alba*) bark and sucrose are now available.

European Food Safety Authority.
Outcome of the consultation with Member States and EFSA on the basic substance application for *Salix alba* bark and the conclusions drawn by EFSA on the specific points raised. EFSA Supporting Publication 2014:EN-609. http://www.efsa.europa.eu/en/supporting/doc/609e.pdf
Outcome of the consultation with Member States and EFSA on the basic substance application for sucrose/saccharose and the conclusions drawn by EFSA on the specific points raised. EFSA Supporting Publication 2014:EN-616.
http://www.efsa.europa.eu/en/supporting/doc/616e.pdf

Herbal product assessments from EMA

HMPC, the Committee on Herbal Medicinal Products, has finalised its Community herbal monographs on:

- anise oil and aniseed (*Pimpinella anisum*)
- ginseng (*Panax ginseng*) root
- passionflower (*Passiflora incarnata*)
- restharrow (*Ononis spinosa*) root
- thyme (*Thymus vulgaris* and *Thymus zygis*)

As described in a finalised public statement, a Community herbal monograph could not be established for Kalmegh (*Andrographis paniculata*), although an assessment report provides an outline of its medicinal use and resultant clinical experience/safety.

Meanwhile, draft monographs have been prepared on agrimony (*Agrimonia eupatoria*) herb and Iceland moss (*Cetraria islandica*).

European Medicines Agency. These reports, dated September 2013 to May 2014, can be accessed (together with accompanying background documents) by searching for the appropriate italicised Latin name at
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/herbal_search.jsp&mid=WC0b01ac058001fa1d

SCENIHR finalises its opinion on the safety of nanosilver

SCENIHR has finalised its opinion on the human health and environmental effects of nanosilver. This substance is commonly used in consumer and medical products because of its antimicrobial action, but a lack of information on its possible long-term effects led the Committee to conclude that a specific human health risk assessment was not feasible.

European Commission. Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Opinion on nanosilver: safety, health and environmental effects and role in antimicrobial resistance. SCENIHR approved this opinion at the 6th plenary of 10-11 June 2014.
http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_039.pdf

Copper and 1,4-dichlorobenzene reviewed by SCOEL

SCOEL, the EC Scientific Committee on Occupational Exposure Limits, has evaluated the relevant toxicity data on 1,4-dichlorobenzene and on copper (and inorganic copper compounds), with a view to establishing OELs.

For copper, an 8-hour time-weighted average (TWA) OEL of 0.01 mg/m^3 (respirable fraction) was derived, the critical effects being lung changes in rats exposed for 4 weeks via inhalation, and metal fume fever-like symptoms (including discomfort, chills and warmth, and stuffiness of the head) in exposed workers. A short-term exposure limit (STEL) could not be recommended due to uncertainties relating to the metal fume fever-like symptoms in workers.

SCOEL has also recommended an 8-hour TWA OEL of 12 mg/m^3 for 1,4-dichlorobenzene, based on a 52-week oral study in dogs in which effects were seen in the lung, liver and kidney. A STEL of 60 mg/m^3 was recommended based on nasal lesions in rats subject to long-term inhalation exposure.

European Commission.
Recommendation from the Scientific Committee on Occupational Exposure Limits for copper and its inorganic compounds. SCOEL/SUM/171. March 2014. http://ec.europa.eu/social/BlobServlet?docId=11815&langId=en
Recommendation from the Scientific Committee on Occupational Exposure Limits for 1,4-dichlorobenzene. SCOEL/SUM/65. March 2014. http://ec.europa.eu/social/BlobServlet?docId=11814&langId=en

United Kingdom

SACN draft report on carbohydrates and health

A draft report from SACN considers the evidence for a role of dietary carbohydrate on colorectal disease (including cancer, irritable bowel syndrome and constipation), cardiovascular disease (insulin resistance, glycaemic response and obesity), and oral health. Comments from the scientific community are sought, to be received by 1 September 2014.

UK Scientific Advisory Committee on Nutrition. Draft report. Carbohydrates and Health. Available on SACN website from 26 June 2014. http://www.sacn.gov.uk/news_press_releases/latest_news/publication_date_for_sacn_carbohydrates_and_health_public_consultation.html

ACNFP applications for extension of use

Applications have been submitted to the ACNFP to extend the use of three novel food ingredients. The dossiers provide toxicological, technical and anticipated exposure data on:

- dihydrocapsiate (synthetic) in food supplements
- isomalto-oligosaccharide in additional types of food (including beverages, desserts, crackers, nutritional food bars, snacks *etc*.)
- rooster comb extract (a source of sodium hyaluronate) in food supplements

UK Advisory Committee on Novel Foods and Processes.
Ajinomoto Co. Inc. Japan. Application for the extension of authorisation of dihydrocapsiate (DHC) for food supplement use. May 2014. http://multimedia.food.gov.uk/multimedia/pdfs/committee/acnfp/syntheticd.pdf
Bioiberica SA. Application for the authorization of the use of a rooster combs extract in food supplements. December 2013. http://multimedia.food.gov.uk/multimedia/pdfs/committee/acnfp/rooster.pdf
BioNeutra. Application for an extension of use and label correction of the novel ingredient isomalto-oligosaccharide (IMO), VitaSugar™/ VitaFiber™. May 2014. http://multimedia.food.gov.uk/multimedia/pdfs/committee/acnfp/imo.pdf

COT verdict on HCHs and PFOS in the infant diet

The COT has issued statements on the potential risks of perfluorooctane sulfonate (PFOS), and α-, β- and γ-hexachlorocyclohexane (HCHs) in the infant diet.

The COT and EFSA tolerable daily intakes (TDIs) for PFOS are 300 and 150 ng/kg bw/day, respectively (although EFSA is currently reviewing the issue). Limited data, particularly for the UK, suggest that maximum anticipated infant exposure from breast milk and infant formulae is roughly half the EFSA TDI. The COT concludes that, even allowing for additional exposure to PFOS precursors, the estimated exposures "do not indicate a need for formulation of dietary recommendations to protect the health of infants".

For γ-HCH (lindane), the Committee upheld the existing TDI of 40 ng/kg bw (derived by a Dutch expert committee), and concluded that infant exposures are generally below this level (although there is substantial uncertainty in the exposure estimates for infant formula and infant food). The COT was unable to endorse the existing TDIs and reference doses (RfDs) for α- and β-HCH, but a margin of exposure (MOE) approach did not raise any major concerns. (A potentially high intake of β-HCH from breast milk is based on old data and levels appear to have decreased more recently.) The Committee's evaluation "does not provide a basis for recommendations on the infant diet relating to HCHs…."

The COT comments are likely to form part of the Scientific Advisory Committee on Nutrition (SACN) review of complementary and young child feeding.

UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment.
COT statement on the potential risks from α-, β- and γ-hexachlorocyclohexanes in the infant diet. COT Statement 2014/03, April 2014.
http://cot.food.gov.uk/pdfs/cotstatmhchs.pdf
COT statement on the potential risks from perfluorooctane sulfonate (PFOS) in the infant diet. COT Statement 2014/02, April 2014.
http://cot.food.gov.uk/pdfs/cotstatmpfos.pdf

United States

New AEGLs for several airborne chemicals published by NRC (volume 17)

The NRC has recently announced the release of the seventeenth volume in its series covering acute exposure guideline levels (AEGLs) for selected airborne chemicals. AEGLs represent threshold exposure limits (levels above which certain adverse health effects may occur) and are applicable to emergency (*i.e.* very rare) exposures lasting from 10 minutes to 8 hours.

A three-tiered system is used to represent increasing toxic severity (ranging from AEGL-1 for non-disabling, transient effects, through the more serious AEGL-2 up to AEGL-3 for life-threatening effects). The appendices to this volume contain useful toxicity reviews and descriptions of the basis of the AEGLs for:

- acrylonitrile
- boron tribromide
- carbon tetrachloride

- cyanogen
- epichlorohydrin
- ethylene chlorohydrin
- hydrogen bromide
- toluene
- trimethylacetyl chloride

US National Research Council (2014). Acute exposure guideline levels for selected airborne chemicals: Volume 17. http://www.nap.edu/catalog.php?record_id=18796

One final and four proposed development support documents (DSDs) from TCEQ

TCEQ has released a finalised DSD on ammonia, and proposed DSDs on carbon disulfide, chromic acid, crotonaldehyde and pentene isomers. These documents are used to inform the derivation of inhalation effect screening levels (ESLs).

Texas Commission on Environmental Quality (TCEQ). Development support documents. http://www.tceq.texas.gov/toxicology/dsd/final.html

EPA finalises PPRTV documents on azodicarbonamide and guanidine compounds

In support of its Superfund Program, the EPA has made available two new provisional peer-reviewed toxicity value (PPRTV) reports on azodicarbonamide and on guanidine (and its chloride and nitrate salts).

For azodicarbonamide, a chronic provisional oral reference dose (p-RfD) of 1 mg/kg bw/day was proposed (based on reproductive effects in rats), together with a chronic provisional inhalation reference concentration (p-RfC) of 7×10^{-6} mg/m^3 (based on respiratory effects in exposed workers). RfDs and RfCs cover only non-cancer effects; no reference values based on cancer endpoints were determined.

For guanidine chloride, a chronic oral p-RfD of 0.02 mg/kg bw/day was proposed based on a number of case reports in humans (with effects including blood abnormalities, peripheral and central nervous system effects, and gastrointestinal pain). Based on the p-RfD for the chloride, screening p-RfDs were also determined for guanidine and guanidine nitrate. No inhalation p-RfCs or cancer-based values were determined.

US Environmental Protection Agency (EPA). Derivation support documents on:
Azodicarbonamide. 4 March 2014. http://hhpprtv.ornl.gov/issue_papers/Azodicarbonamide.pdf
Guanidine compounds. 19 March 2014. http://hhpprtv.ornl.gov/issue_papers/GuanidineChloride.pdf

Rest of the World

NICNAS updates Stage One chemicals list

In relation to its ongoing Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework, NICNAS has updated its list of Stage One chemicals. It has added nearly 250 chemicals that can be rapidly assessed for human health and/or environmental risks.

Australian National Industrial Chemicals Notification and Assessment Scheme. NICNAS Consultation. Assessment and prioritisation of existing chemicals on the Australian Inventory of Chemical Substances (AICS)–Stage One. Chemical Gazette No. C.06. 3 June 2014. http://www.nicnas.gov.au/communications/publications/chemical-gazette/chemical-gazette-June-2014/consultations/assessment-and-prioritisation-of-existing-chemicals-on-the-australian-inventory-of-chemical-substances-aicsstage-one [Follow link to "Stage One chemicals" list; then click on tab for "additional chemicals".]

NICNAS issues full public reports

Four recent reports provide details on the toxicological and environmental effects of the following five chemicals, and assess their risks to the public and to workers:

- aluminium molybdenum oxide (as a component of a catalyst for hydro-desulfurisation of heavy oils or fuels)
- bicyclo[2.2.1]hept-5-ene-2-carboxylic acid, ethyl ester (as a fragrance ingredient)
- dodecanoic acid, 1,1'-[1,6-hexanediylbis[nitrilo(2,2-dimethyl-1-propanyl-3-ylidene)]] ester (as a component of industrial sealants)
- dodecanoic acid, 3-[[3-[[[2,2-dimethyl-3-[(1-oxododecyl)oxy]propylidene]amino]methyl]-3,5,5-trimethylcyclohexyl]imino]-2,2-dimethylpropyl ester (as a component of industrial sealants)
- 1-propene, 1,3,3,3-tetrafluoro-, (1E)- (as an aerosol propellant)

Australian National Industrial Chemicals Notification and Assessment Scheme. Public reports, dated April and May 2014.
Aluminium molybdenum oxide. http://www.nicnas.gov.au/__data/assets/word_doc/0016/12382/STD1503-FR-Final.docx
Bicyclo[2.2.1]hept-5-ene-2-carboxylic acid, ethyl ester. http://www.nicnas.gov.au/__data/assets/word_doc/0004/12388/LTD-1731-FR-FINAL.docx
Dodecanoic acid, 1,1'-[1,6-hexanediylbis[nitrilo(2,2-dimethyl-1-propanyl-3-ylidene)]] ester and dodecanoic acid, 3-[[3-[[[2,2-dimethyl-3-[(1-oxododecyl)oxy]propylidene]amino]methyl]-3,5,5-trimethylcyclohexyl]imino]-2,2-dimethylpropyl ester.
http://www.nicnas.gov.au/__data/assets/word_doc/0018/12384/LTD-1711-FR.docx
1-Propene, 1,3,3,3-tetrafluoro-, (1E)-. http://www.nicnas.gov.au/__data/assets/word_doc/0016/12481/EX-187-STD1479-FR.docx

Derquantel registration is considered by APVMA

An application for the approval and registration of the veterinary active constituent, derquantel, is being considered. Based on a toxicological evaluation of the compound by the Australian Office of Chemical Safety, "the APVMA accepts

the findings and recommendations of its advisers", including a proposed acceptable daily intake (ADI) of 0.5 µg/kg bw and an acute reference dose (ARfD) of 10 µg/kg bw (based, respectively, on 90-day and acute toxicity studies in dogs).

Australian Pesticides and Veterinary Medicines Authority (2014). Notice – New veterinary active constituent – derquantel. Commonwealth of Australia Gazette. No. APVMA 11, 27-29. http://www.apvma.gov.au/publications/gazette/2014/11/gazette_20140603.pdf

APVMA report on occupational health and safety of fenthion

APVMA has issued a revised assessment report on this pesticide, which includes toxicity data, occupational exposure estimations, and associated risk assessments and recommendations.

Australian Pesticides and Veterinary Medicines Authority (2014). Chemical Review Program. Occupational health and safety assessment of fenthion. http://www.apvma.gov.au/products/review/docs/fenthion_ohs_assessment_april_2014.pdf

Health Canada approves diflufenzopyr-sodium

Health Canada's Pest Management Regulatory Agency (PMRA) has granted permission for the sale and use of sodium diflufenzopyr as a herbicide. The associated registration decision presents a very brief overview of the toxicology of this substance, along with consumer, occupational and environmental risk assessments.

Health Canada. Pest Management Regulatory Agency. Diflufenzopyr-sodium. Registration decision RD2014-12. 12 June 2014. http://www.hc-sc.gc.ca/cps-spc/alt_formats/pdf/pubs/pest/_decisions/rd2014-12/rd2014-12-eng.pdf

Cover image: Passionflower (Passiflora incarnata).

See also: Our article on page 10 relating to EMA's assessment of passionflower for use in herbal medicinal products.

Further information: bibra's team of scientists has extensive experience searching for and summarising health-related information on natural products.

bibra
toxicology advice
& consulting

Cantium House | Railway Approach | Wallington | Surrey | SM6 0DZ | UK
Tel +44 (0)20 8619 0770
info@bibratoxadvice.co.uk | www.bibratoxadvice.co.uk

Bibra toxicology advice & consulting Ltd, registered in England No. 4612011. Registered address, 8/10 South Street, Epsom, Surrey, KT18 7PF, UK