



A monthly update of key developments relevant to product safety across a wide range of industrial sectors

# Toxicology and Regulatory News

## 2010

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& consulting

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# Toxicology and Regulatory News

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This issue of *Toxicology and Regulatory News* is a compilation of expert commentaries written by **bibra** toxicologists on items added to our chemical toxicity database (TRACE), and associated databank, from 8 December 2009 to 13 January 2010. The items selected for inclusion cover key, health-related findings that may affect product safety and regulatory acceptability, as well as pertinent pronouncements from national and international authorities and other expert groups. Our TRACE database is maintained by screening a large number of peer-reviewed toxicology and nutrition journals, key websites, and official publications, in addition to many secondary sources. Members may obtain further information on the items appearing in this publication by contacting our helpdesk (e-mail [document@bibratoxadvice.co.uk](mailto:document@bibratoxadvice.co.uk)) and quoting the accession number contained in brackets at the end of each record.

### NEW YEAR – NEW LOCATION

Please note that as from 1 February 2010, our new address will be as follows:

**bibra**  
**toxicology advice & consulting**  
Citylink Centre  
Railway Approach  
Wallington  
Surrey SM6 0DZ  
UK

New contact numbers: +44 (0)20 8544 4150 (telephone); +44 (0)20 8544 4151 (fax)

Our website and general e-mail address remain unchanged:

Website: [www.bibratoxadvice.co.uk](http://www.bibratoxadvice.co.uk)

General e-mail: [info@bibratoxadvice.co.uk](mailto:info@bibratoxadvice.co.uk)

Until the end of January 2010 you can of course still contact us at:

Westmead House  
123 Westmead Road  
Sutton  
Surrey SM1 4JH  
UK

Telephone: +44 (0)20 8722 4675

## Coverage

*Toxicology and Regulatory News* covers important toxicological or nutritional pronouncements (including key legislative developments) from national and international authorities, government departments and other expert groups, as well as major health-related findings published in the primary literature. Relevant information is obtained by screening the official publications and pertinent websites of expert groups, and scanning a large number of peer-reviewed toxicology and nutrition journals, in addition to many secondary sources. The items are organised as follows: International, European Union, United Kingdom, United States and Rest of the World.

## International

### IARC verdicts on various chemical and occupational exposures

In October 2009, an IARC meeting was convened to reassess several chemicals and complex exposures (some occupationally related) that had been previously classified as carcinogenic to humans (Group 1). A brief summary appearing on the IARC website highlighted the decisions on three agents, dioxin (2,3,7,8-TCDD), formaldehyde and painting exposures, while a short report appearing in *Lancet Oncology* provided an overview of the meeting as a whole.

The Group 1 status for dioxin, previously based on animal data and strong mechanistic evidence, was confirmed in 2009 as sufficient evidence of carcinogenicity in humans had become available. Evidently this was the first time that an initial Group 1 classification had been subsequently confirmed by data showing increased cancer incidence in exposed individuals, and the IARC Working Group pointed out that this illustrated how preventive action based on mechanistic information could be appropriate in the absence of human cancer data. The same mechanistic events have also been established for defined dioxin-like compounds, and the IARC experts felt able to extend the Group 1 classification to 2,3,4,7,8-pentachlorodibenzofuran and 3,3',4,4',5-pentachlorobiphenyl, which are indicator chemicals for a large variety of chlorinated dibenzofurans and polychlorinated biphenyls. Formaldehyde, a nasopharyngeal carcinogen, had its Group 1 classification confirmed, and there was additionally now deemed to be sufficient evidence (from epidemiology and mechanistic studies) of it causing leukaemia in humans. The Working Group also concluded that occupational exposure as a painter can cause cancers of the lung, urinary bladder and pleural mesothelium, and although it was difficult to identify the causative agents or a causal mechanism, there was believed to be strong evidence that the exposures were genotoxic. Limited evidence was also reported for an association between maternal exposure to painting (before and during pregnancy) and an increased risk of childhood leukaemia in the offspring.

Other agents confirmed as Group 1 carcinogens (in most cases based on sufficient evidence in humans) included several aromatic amines and two related industrial processes, PAH (polycyclic aromatic hydrocarbon)-related exposures, and several chemicals: aflatoxins, benzene, 1,3-butadiene, sulphur mustard, vinyl chloride and ethylene oxide (epidemiological data were limited for ethylene oxide, but there was judged to be sufficient evidence for its carcinogenicity in rodents plus strong evidence of genotoxicity). Group 1 membership was also confirmed for various complex exposure scenarios (iron and steel founding, isopropyl alcohol manufacture using strong acids, mineral oils, the rubber manufacturing industry, shale oils and strong inorganic acid mists), although it was acknowledged that there was sometimes difficulty in identifying the causative agents in such situations.

[Baan R. *et al.*, *Lancet Oncology* 2009, **10**, 1143; [http://dx.doi.org/10.1016/S1470-2045\(09\)70358-4](http://dx.doi.org/10.1016/S1470-2045(09)70358-4) (click on TheLancet.com). A review of human carcinogens – Part F: chemical agents and related occupations. Preliminary report of the October 2009 meeting of the International Agency for Research on Cancer (this report is also destined for publication on the IARC website at <http://monographs.iarc.fr/ENG/Meetings/index1.php>). Brief highlights of the meeting are already given on the IARC website (at <http://monographs.iarc.fr/ENG/Meetings/100F-introduction.pdf>). The full meeting report will eventually be issued as part of Volume 100 in the IARC Monograph series.] {183920}

## **OECD – ‘draft final’ SIAR on alkyl sulfates/sulfonates**

Welcoming 2010 in style is a new ‘draft final’ SIDS Initial Assessment Report (SIAR) covering the (bumper) category of “alkyl sulfates, alkane sulfonates and  $\alpha$ -olefin sulfonates”. This review, which has recently appeared on the OECD website, provides a useful expert hazard evaluation of the critical toxicological data presented in the SIDS (Screening Information Data Sets) that it accompanies. Once processed for official publication, finalised SIARs will be accessible online (evidently via the UNEP site <http://www.chem.unep.ch/irptc/sids/OECD/SIDS/sidspub.html>).

[Organisation for Economic Co-operation and Development. Published OECD initial assessments of HPV chemicals: Drafts of SIAR from SIAM 25 available from the OECD website (via [http://www.oecd.org/document/63/0,3343,en\\_2649\\_34379\\_1897983\\_1\\_1\\_1\\_1,00.html](http://www.oecd.org/document/63/0,3343,en_2649_34379_1897983_1_1_1_1,00.html)).] {183921}

## **European Union**

### **No freeze on REACH activities**

Snowbound toxicologists should have little excuse for feeling bored as there are always developments to catch up with in relation to REACH (the European legislation on the Registration, Evaluation, Authorisation and Restriction of Chemicals). This is especially true as we greet the new decade, since REACH documents issued by ECHA (the European Chemicals Agency), have been landing thick and fast on its website in the last few weeks. If you need help in getting to grips with these winter flurries of activity (or just want to avoid sliding off the REACH path), e-mail **bibra** (at [info@bibratoxadvice.co.uk](mailto:info@bibratoxadvice.co.uk)) and we will contact you to discuss how our experienced toxicologists can help.

### **...More substances branded as SVHC**

ECHA has added 14 more substances (13 January 2010) to the “Candidate List” of substances of very high concern ([ECHA/PR/10/01](http://echa.europa.eu/doc/reach/pr10/01)). Decisions on whether these substances will be subject to authorisation will be taken at a later date.

### **...Updated manual for REACH registrations and PPORD notifications**

A revised version (Release 2.2, dated 15 December 2009) has been recently issued of Data Submission Manual 5: “How to complete a technical dossier for registrations and PPORD [Product and Process Orientated Research and Development] notifications”. The manual is available from ECHA (visit [http://echa.europa.eu/doc/reach/tech\\_dossier\\_manual.pdf](http://echa.europa.eu/doc/reach/tech_dossier_manual.pdf)). {177496}

### **...First agreement on the need for further animal tests under REACH**

The first decision by the Member State Committee on a chemical based on read-across data has not been favourable, suggesting that it may be difficult in some instances to reduce animal testing requirements for registration. After scrutiny of a registrant’s proposal to use read-across from another substance, the Committee deemed that there was not enough justification for this, and that studies for repeated dose toxicity and reproductive toxicity were required. Details concerning the substance (and registrant) have not been made public. More information is given in a news alert ([ECHA/NA/09/33](http://echa.europa.eu/doc/reach/na/09/33)) dated 7 December 2009, which reports that a final decision on testing requirements will be reached by ECHA.

### **...REACH Technical Completeness Check (TCC) plug-in**

To enable companies to check whether their registration dossiers are complete before submission, ECHA released (in December 2009) an IUCLID plug-in that can be accessed on the IUCLID website (via <http://iuclid.echa.europa.eu/>). Since the plug-in can also be used to check the technical completeness of Product and Process Orientated Research and Development (PPORD) dossiers, companies are advised to use it for this purpose, rather than the previous software made available, as the TCC rules have been updated.

### **...Database on registered substances**

On 18 December 2009, ECHA made available (under the REACH Regulation) information submitted by companies on the hazards and safe use of chemical substances that have already been registered, although the Agency pointed out that this data has not been verified. Some information is not disseminated because companies have claimed confidentiality. The database

can be accessed via <http://apps.echa.europa.eu/registered/registered-sub.aspx> on the ECHA website.

### **...Compliance checks on unfinished NONS dossiers**

Under previous legislation there was a requirement for the Notification Of New Substances (NONS), which were assessed by Member State competent authorities. Some of these assessments were not finalised before REACH came into force (revoking the preceding NONS Directive), and toxicity data may be missing from certain dossiers. As a consequence, ECHA is now undertaking a compliance check on unfinished NONS submissions. Further information is given in a news alert ([ECHA/NA/09/37](#)) dated 18 December 2009.

### **...Webinar presentations available online for registrants**

The second and third in a series of interactive webinars for Lead Registrants can be accessed (via [http://www.echa.europa.eu/news/webinars\\_en.asp](http://www.echa.europa.eu/news/webinars_en.asp)) on the ECHA website. These latest presentations on information requirements cover robust study summaries, weight of evidence approach, use of *in vitro* data, QSARs, waiving information requirements, read-across and categories.

### **...Forum check on how formulators comply with REACH**

The Forum for Exchange of Information on Enforcement has announced that its next joint REACH enforcement project will focus on formulators of mixtures who are the first level of downstream users in the supply chain. More details can be obtained in a news alert ([ECHA/NA/09/34](#)) issued on 14 December 2009.

### **ECB advises on applicability of REACH guidance documents to biocides**

A short publication available from the European Chemicals Bureau gives an indication of which REACH guidance documents are relevant to biocides. Particularly useful is the advice relating to different parts of the REACH guidance on "Information requirements and chemical safety assessment".

[The relevance of REACH Guidance Documents for dossier evaluation under the biocidal products Directive 98/8/EC. Endorsed at the 35th meeting of representatives of Member States competent authorities for the implementation of Directive 98/8/EC concerning the placing of biocidal products on the market (16-18 December 2009). This publication can be downloaded from [http://ecb.jrc.ec.europa.eu/documents/Biocides/TECHNICAL\\_NOTES\\_FOR\\_GUIDANCE/Relevance%20of%20REACH%20guidance%20for%20dossier%20evaluation%20under%20BPD.pdf](http://ecb.jrc.ec.europa.eu/documents/Biocides/TECHNICAL_NOTES_FOR_GUIDANCE/Relevance%20of%20REACH%20guidance%20for%20dossier%20evaluation%20under%20BPD.pdf) on the ECB website.] {183973}

### **Biocide evaluations available from EC Environment**

Final risk assessment reports of biocides recently included in Annex I of the biocides Directive 98/8/EC have been published on flocoumafen, which is used as a rodenticide, and tolylfluanid, which is used as a wood preservative. These documents, which cover both human health and environmental risks, were made available in December 2009 and may be accessed via [http://circa.europa.eu/Public/irc/env/bio\\_reports/library?l=/assessment\\_directive&vm=detailed&sb=Title](http://circa.europa.eu/Public/irc/env/bio_reports/library?l=/assessment_directive&vm=detailed&sb=Title) on the internet. {183967-8}

In addition, draft risk assessments prepared by rapporteur Member States are available on IR3535 (ethyl butylacetylaminopropionate) and *cis*-tricos-9-ene (muscalure), both for use as product-type 19 (repellents and attractants). The preliminary reports can be obtained by visiting [http://circa.europa.eu/Public/irc/env/bio\\_reports/library?l=/review\\_programme/ca\\_reports/pt\\_19\\_repellents&vm=detailed&sb=Title](http://circa.europa.eu/Public/irc/env/bio_reports/library?l=/review_programme/ca_reports/pt_19_repellents&vm=detailed&sb=Title) (where they were issued in December 2009). {183777-8}

### **EU risk assessment reports**

Further additions in December 2009 to the European Chemicals Bureau website include draft risk assessment reports on coco alkyl amines, 2-ethoxyethanol, high temperature coal tar pitch, hydrogenated tallow alkyl amines, (Z)-octadec-9-enylamine, octadecylamine, tallow alkyl amines, tris[2-chloro-1-(chloromethyl)ethyl] phosphate and tris(2-chloro-1-methylethyl) phosphate. All these documents, which cover human health and environmental aspects, can be accessed via <http://ecb.jrc.it/documentation/> (under "FileName", click on "existing-chemicals", then "risk assessment" and "report"). {173974; 182772-3; 182783-4; 182787-90}

### **Draft assessment reports on pesticides published by EFSA**

Preliminary risk assessment reports on 6-benzyladenine, bromadiolone and zinc phosphide, and revised (additional) reports covering these three pesticides, as well as asulam, bitertanol, carboxin, clethodim, fenbutatin oxide, fenoxycarb, flurochloridone, isoxaben, methyl bromide, pencycuron and tebufenozide were prepared by Member State authorities and issued in December 2009 or January 2010. These reports (plus background documents), which are available for comment, can be ordered by submitting an online request form via <http://dar.efsa.europa.eu/dar-web/consultation> on the European Food Safety Authority website. {170265; 171601; 172860; 183978-87; 183992}

### **HERA report on esterquats**

This draft human health risk assessment covers a range of esterified quaternary ammonium compounds that are used in fabric conditioners. The report (dated November 2009) is available at <http://www.heraproject.com/RiskAssessment.cfm> from HERA (the European Human and Environmental Risk Assessment on ingredients of household cleaning products). {183851}

### **Food-contact materials evaluated by EFSA**

Three more food-contact substances have come under EFSA scrutiny, two of which had not been previously assessed by EFSA's food-contact Panel or its predecessor, the Scientific Committee on Food (SCF). Basking in this recent expert attention were the cyclic oligomers of butylene terephthalate, 2,4-diamino-6-hydroxypyrimidine and the phenyl esters of alkyl (C10-C21) sulphonic acid. These compounds were all placed in SCF list 3 (substances for which an acceptable or tolerable daily intake could not be established but where the present level of use could be accepted), with various restrictions on their end-use.

[European Food Safety Authority's Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF). Scientific opinion on the safety evaluation of the substance cyclic oligomers of (butylene terephthalate), 2,4-diamino-6-hydroxypyrimidine and alkyl (C10-C21) sulphonic acid, esters with phenol for use in food contact materials. *EFSA Journal* 2009; 7(12):1397-9. Adopted on 26 November 2009. All three documents are available from EFSA (via <http://www.efsa.europa.eu/en/cef/cefscdocs.htm>).] {183798-800}

### **Mycotoxins and natural plant toxicants – an EFSA funded project**

Since no risk assessments have been carried out at the European level on morphine in poppy seeds or certain mycotoxins (*Alternaria* toxins, moniliformin, diacetoxyscirpenol, sterigmatocystin, phomopsins, ergot alkaloids and nivalenol), EFSA commissioned a background document on these food/feed contaminants to aid in possible future safety evaluations. Areas covered by the report include toxicity, occurrence data, methods of analysis and factors influencing levels of contamination.

[Scientific information on mycotoxins and natural plant toxicants. Awarded under Contract No. CFP/EFSA/CONTAM/2008/01 to Università Cattolica del Sacro Cuore, Agroinnova and the University of Parma. The background document, prepared by P. Battilani *et al.*, was accepted by the European Food Safety Authority on 23 November 2009 for publication on its website (at <http://www.efsa.europa.eu/en/scdocs/doc/024e.pdf>).] {183852}

### **EFSA reviews the palytoxin group of marine biotoxins**

As with other groups of marine biotoxins, an EFSA Panel considered there were insufficient data on chronic toxicity to derive a tolerable daily intake for the palytoxin (PITX) group of toxins, which are found in shellfish such as mussels. However, in view of their acute toxicity the Panel has established an oral acute reference dose (ARfD) of 0.2 µg/kg bw for the sum of PITX and its analogue, ostreocin-D. In order for an adult (weighing 60 kg) to avoid exceeding the ARfD, the Panel calculated that a large portion (400 g) of shellfish should contain no more than 12 µg of the sum of PITX and ostreocin-D (equivalent to 30 µg/kg shellfish meat). The Panel particularly noted that these biotoxins were toxic in laboratory animals after intratracheal administration, leading it to conclude that humans are likely to be at risk following inhalation exposure; poisoning has also been reported following contact with injured skin. In addition, the Panel recommended that further information was needed on the toxicity of other members of the PITX group, particularly of ovatoxin-A, to allow better characterization of their oral toxicity and relative potencies and thus lead to a more reliable estimation of risk.

[European Food Safety Authority's Panel on Contaminants in the Food Chain (CONTAM). Scientific opinion on marine biotoxins in shellfish – palytoxin group. *EFSA Journal* 2009, 7(12):1393. Adopted on 26 November 2009. Available to download from the EFSA website (at <http://www.efsa.europa.eu/en/scdocs/doc/1393.pdf>).] {183797}

### **Group flavouring evaluations from EFSA**

Using the group approach to the safety evaluation of flavourings, EFSA experts have issued two more assessments covering a number of flavouring ingredients. While many of the evaluated substances were judged to present “no safety concern” at the estimated levels of intake, others could not be assessed without further data (for example on geometric isomerism, composition or exposure levels).

[European Food Safety Authority's Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF). Scientific opinions on a request from the Commission related to Flavouring Group Evaluation (FGE) 16 Rev 2 on aromatic ketones from chemical group 21, and FGE 68 on cinnamyl alcohol and related flavouring agents evaluated by JECFA (55th meeting) structurally related to aryl-substituted saturated and unsaturated primary alcohol/aldehyde/acid/ester derivatives evaluated by EFSA in FGE.15Rev1 (2008). *The EFSA Journal* 2009, 7(11):1032; 7(12):1022. Adopted on 25 and 26 March 2009. Available from the EFSA website via [http://www.efsa.europa.eu/EFSA/ScientificPanels/efsa\\_locale-1178620753812\\_CEF.htm](http://www.efsa.europa.eu/EFSA/ScientificPanels/efsa_locale-1178620753812_CEF.htm) (type “flavouring group evaluation” in the “Search” box).] {183829-30}

### **EFSA Panel evaluates three more smoke flavourings...**

As announced in an EFSA [Press Release](#) of 8 January 2010, the first ever review of the safety of eleven smoke flavourings used in the European Union has been completed, which means that the European Commission can now establish a list of smoke flavouring products authorised for use in foods. The latest assessments to be issued were on AM 01, Scansmoke R909 and TRADISMOKE™ A MAX, all of which received the thumbs down from EFSA's flavourings Panel as the margins of safety were deemed insufficient for the intended uses. In addition, the Panel felt that for AM 01, an *in vivo* genotoxic potential could not be ruled out due to the limited data available.

[European Food Safety Authority's Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF). Scientific opinions on the safety of smoke flavour Primary Product – TRADISMOKE™ A MAX, Scansmoke R909 and AM 01. *EFSA Journal* 2010, 8(1):1394, 1395 and 1396. All three opinions were adopted on 26 November 2009 and can be accessed via <http://www.efsa.europa.eu/en/panels/cef.htm> (by typing “smoke flavourings” in the “Search” box).] {183964-6}

### **...and explains its Margin of Safety (MoS) approach**

Following an EFSA request for clarification on the MoS approach used in the safety evaluation of smoke flavourings, a statement has been issued by the flavourings Panel that explains how the complex nature of these ingredients, and the limited toxicity data available, makes it inappropriate to allocate an acceptable daily intake. Instead, the Panel calculates a MoS that is the ratio between the No-Observed-Adverse-Effect Level from a 90-day study and the anticipated dietary exposure for consumers (estimated from use levels provided by the applicant). Providing no potential *in vivo* genotoxicity is identified (three *in vitro* genotoxicity assays are stipulated as a minimum dataset requirement for these flavourings), an additional 3-fold safety factor is applied to supplement the default uncertainty factor of 100. While offering this general guidance, the Panel stresses that each safety assessment must be considered on a case-by-case basis, depending for example on chemical composition, and quality of the available toxicological data.

[European Food Safety Authority's Panel on Food Contact Material, Enzymes, Flavourings and Processing Aids (CEF). Statement on the safety evaluation of smoke flavourings Primary Products: Interpretation of the Margin of Safety. *EFSA Journal* 2010, 8(1):1325. Adopted on 26 November 2009. Available at <http://www.efsa.europa.eu/en/scdocs/doc/1325.pdf> on the internet.] {183963}

### **Polyglycitol syrup and natamycin assessed by EFSA for food additive use**

Although there were insufficient data on the toxicity of polyglycitol syrup or natamycin to establish acceptable daily intake levels, EFSA experts felt that neither food additive would pose a risk to consumer health at the proposed levels of use.

[European Food Safety Authority's Panel on Food Additives and Nutrient Sources added to Food (ANS). Scientific opinions on the use of polyglycitol syrup and natamycin (E 235) as food additives. *EFSA Journal* 2009; 7(12):1412 and 1413. Adopted on 24 or 26 November 2009. Both documents can be obtained from EFSA (via <http://www.efsa.europa.eu/en/ans/ansscdocs.htm>).] {183801-2}

## **United Kingdom**

### **COM Statement on genotoxicity of *para*-chloroaniline**

At the request of the UK Advisory Committee on Pesticides, COM has reviewed the genotoxicity of *para*-chloroaniline, a potential human metabolite of the pesticide difluzenuron. In its Statement, COM concludes that *para*-chloroaniline is an *in vitro* mutagen, but feels that there are insufficient data to determine the compound's *in vivo* mutagenicity. An *in vivo* genotoxicity testing strategy was proposed.

[UK Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment. Statement: Genotoxicity of *para*-chloroaniline, COM/09/S3, December 2009. Available at <http://www.iacom.org.uk/statements/documents/ParachloroanilineforcominternetsiteDec09.pdf> on the internet.] {183191}

### **COT December meeting**

During previous COT deliberations (in February 2009), Committee members questioned whether animal developmental neurotoxicity studies reliably identified potential human neurotoxicants. To assist in this ongoing debate, a discussion paper ([TOX/2009/41](#)) was prepared for the COT's December 2009 meeting that provided data on the developmental effects of four established neurotoxins, methyl mercury, valproic acid, perchlorate and chlorpyrifos {183773}. Also under consideration at the December meeting was an information paper ([TOX/2009/40](#)) outlining how the European Food Safety Authority reached its conclusion that the provisional tolerable weekly intake of 15 µg/kg bw for inorganic arsenic set by JECFA (the Joint FAO/WHO Expert Committee on Food Additives) was no longer appropriate {183774}. Other agenda items included a brief overview of the Waste and Resources Action Programme approach to the assessment of chemical risks to public, animal and environmental health associated with the agricultural use of compost ([TOX/2009/39](#)), and a discussion paper on the finalised report of the Government funded study of sheep dip exposure and "Dipper's flu" ([TOX/2009/36](#)) {183775-6}.

[UK Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment. Agenda and papers for the 15 December 2009 meeting can all be obtained from the COT website (via <http://cot.food.gov.uk/cotmtgs/cotmeets/cot2009/cotmeet15dec2009/cotagenda15dec2009>).]

### **Parliamentary report on nanotechnologies and food**

A report that examines issues relating to the introduction of nanotechnologies in food production has been published by the House of Lords Science and Technology Committee. The report considers the potential toxicity of ingested nanomaterials and identifies toxicological data gaps.

[UK House of Lords, Science and Technology Committee. 1st Report of Session 2009-10. Nanotechnologies and food. Volume I: Report and Volume 2: Evidence. HL Papers 22-I and 22-II. Available via <http://www.publications.parliament.uk/pa/ld/ldscitech.htm> on the internet.] {183962}

## **United States**

### **Provisional Advisory Levels for acrylonitrile, hydrogen sulphide and phosgene**

A special supplement (No. 3) to volume 21 of the journal *Inhalation Toxicology* includes an overview of the Provisional Advisory Level (PAL) programme and the methodology used in developing PALs (Young R.A. *et al.*, *Inhalation Toxicology* 2009, 21(S3), 1; Adeshina F. *et al.*, *ibid.*

2009, **21**(S3), 12). Three example technical support documents for acrylonitrile, hydrogen sulphide and phosgene (written by Goldhaber *et al.*, Marshall *et al.* and Glass *et al.*, respectively) are also included in the issue (on pages 17, 56 and 73). PALs provide guidance levels for exposure of the general public to priority chemicals (including toxic industrial chemicals, pesticides and chemical warfare agents), and are intended to assist in planning for, and responding to, emergency situations. Using a three-tiered system to represent increasing toxic severity (ranging from PAL 1 for mild transient effects, through the more serious PAL 2, up to PAL 3 for life threatening effects), levels are developed for exposure through drinking water and ambient air in relation to four exposure periods (1-, 30-, 90-day, and 2-year durations). About 800 PAL values have been developed so far covering more than 60 priority agents. Although the published supplement is not yet available on the relevant journal website (<http://www.informahealthcare.com/ihf>), early online versions of the papers can be accessed (via <http://informahealthcare.com/toc/ihf/0/0>). {183923-7}

The US Environmental Protection Agency is the lead agency in the PAL programme, and further information on the project can be found at <http://www.epa.gov/nhsrc/news/news121208.html> (the EPA's National Homeland Security Research Center website). Last updated in December 2009, this website lists other selected chemicals for which PALs have been determined: carbonyl difluoride, chloropicrin, diborane, fluoroacetate salts, hydrazine, hydrogen bromide, lewisite, malathion, methyl isocyanate, phosgene oxime, red phosphorous and tetrafluoroethylene.

### **113th meeting of Cosmetic Ingredient Review Expert Panel**

One of the items discussed at the CIR Expert Panel's most recent meeting was a tentative amended safety assessment covering polyethylene glycols (PEGs) – ingredients that were considered safe for use under the conditions described in the assessment. Other topics for discussion included three recently issued Scientific Literature Reviews (containing health effects data) on dimethiconol and its esters and reaction products, methyl acetate and related esters and alcohols, and triclosan.

[Cosmetic Ingredient Review. Results of the meeting held on 16 December 2009 are currently available from the CIR website (at [http://www.cir-safety.org/staff\\_files/results.pdf](http://www.cir-safety.org/staff_files/results.pdf)). All scientific reports can be purchased by non-CIR members (at prices ranging from \$80 to \$100 each plus international shipping fees of \$5 per report) from CIR, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702 (tel: +1 202 331 0651; fax: +1 202 331 0088; e-mail: [cirinfo@cir-safety.org](mailto:cirinfo@cir-safety.org)).] {183969-72}

### **Public health goal for bromate in drinking water finalised by OEHHA**

PHGs represent levels of drinking water contaminants that pose no significant health risk to individuals from a lifetime exposure and are judged to be protective of potentially sensitive subpopulations. For the drinking water disinfection by-product bromate, a final PHG of 0.1 µg/L was derived based on cancer effects (including mesothelioma, and kidney and thyroid tumours) reported in male rats given potassium bromate in the drinking water for up to two years.

[Office of Environmental Health Hazard Assessment of the California Environmental Protection Agency (Cal/EPA). Public health goal for bromate in drinking water. (Draft PHG announced in *Toxicology and Regulatory News* 2008, **47**(9), 157.) Final version, dated December 2009, is available from OEHHA (visit <http://www.oehha.ca.gov/water/phg/pdf/BromatePHG010110.pdf>).] {177966}

### **Tolerance petitions filed with EPA for several pesticides**

Brief summaries of the relevant toxicological data and accompanying exposure assessments are generally included in pesticide tolerance petitions submitted by industry to the US Environmental Protection Agency. Recent submissions providing new toxicity summaries relate to [fluopyram](#) (Docket ID: EPA-HQ-OPP-2009-0364), [indaziflam](#) (EPA-HQ-OPP-2009-0636), [pyroxasulphone](#) (EPA-HQ-OPP-2009-0717), [poly\(oxy-1,2-ethanediyl\), α-isotridecyl-ω-methoxy](#) (EPA-HQ-OPP-2009-0692) (*Federal Register* 2010, **75**, 864), and [tagetis oil](#) (EPA-HQ-OPP-2009-0821) (*ibid.* 2009, **74**, 66644). These petitions (proposing to amend 40 CFR Part 180) are accessible through FDMS, the Federal Document Management System, at <http://www.regulations.gov/> by typing the relevant Docket ID in the "Search" box, followed by "go". {183988-91; 183922}

### **EPA releases registration review documents for several pesticide ingredients**

Under the pesticide registration review programme, the US Environmental Protection Agency is periodically assessing each US registered pesticide to ensure that its intended function can still be performed without unreasonable adverse effects on human health or the environment. Further details of the status of pesticides in this programme are given on the EPA's pesticide registration review website (at [http://www.epa.gov/oppsrrd1/registration\\_review/reg\\_review\\_status.htm](http://www.epa.gov/oppsrrd1/registration_review/reg_review_status.htm)).

Summary documents and/or human health assessment scoping documents (summarising the toxicological literature) in support of registration reviews have now been issued on several more pesticides, notably [azoxystrobin](#) (Docket ID: EPA-HQ-OPP-2009-0835), [cyphenothrin](#) (EPA-HQ-OPP-2009-0842), [difenzoquat methyl sulphate](#) (EPA-HQ-OPP-2009-0787), [diquat dibromide](#) (EPA-HQ-OPP-2009-0846), [esfenvalerate](#) (EPA-HQ-OPP-2009-0301), [fenbutatin oxide](#) (EPA-HQ-OPP-2009-0841), [metalaxyl and mefenoxam](#) (EPA-HQ-OPP-2009-0863), [propoxur](#) (EPA-HQ-OPP-2009-0806), [thiodicarb](#) (EPA-HQ-OPP-2009-0432) (*Federal Register* 2009, **74**, 66645) {183787-95} and [ethylene](#) (EPA-HQ-OPP-2009-0877) (*ibid.* 2009, **74**, 68615) {183929}. Similar assessments have also been recently issued on several antimicrobials, including [2-bromo-4'-hydroxyacetophenone](#) (EPA-HQ-OPP-2009-0726), [disodium cyanodithioimidocarbamate](#) (EPA-HQ-OPP-2009-0723), [2,2-dibromo-3-nitrilopropionamide](#) (EPA-HQ-OPP-2009-0724), [sodium lauryl sulphate](#) (EPA-HQ-OPP-2009-0727) and [sodium 2-mercaptobenzothiazole](#) (EPA-HQ-OPP-2009-0725) (*ibid.* 2009, **74**, 66640). {183803-7}

All these registration review documents, together with related information, can be obtained through FDMS, the Federal Document Management System (at <http://www.regulations.gov>), by searching on the Docket ID provided in brackets above.

### **EPA BRADs for calcium acetate and 2-methyl-1-butanol**

Biopesticide Registration Action Documents (or BRADs) covering [calcium acetate](#) and [2-methyl-1-butanol](#) have recently been issued by the EPA. These fact sheets provide very brief human health and environmental risk assessments, as well as use profiles, regulatory history, dietary exposures and other information of relevance on these biopesticides.

[US Environmental Protection Agency (EPA) Office of Pesticide Programs (OPP). Biopesticide Registration Action Documents on calcium acetate and 2-methyl-1-butanol. An EPA press release (dated 16 December 2009; available via <http://cfpub.epa.gov/pesticides/recentadditions.cfm>) announced the issue of these BRADs. For a complete list of all biopesticide fact sheets, visit the EPA's website (at <http://www.epa.gov/opppppd1/biopesticides/ingredients/index.htm>).] {183976-7}

### **FDA GRAS status for L-arginine and crystalline lutein**

Letters recently issued by the FDA's Office of Food Additive Safety confirm that the Agency has no questions regarding company determinations of GRAS ("generally recognized as safe") status for [L-arginine](#) and [crystalline lutein](#) when used as ingredients in various foods and beverages. As always, the FDA has not made its own determination regarding the GRAS status of these ingredients.

[US Food and Drug Administration. Center for Food Safety and Applied Nutrition. Office of Food Additive Safety. Agency Response Letters GRAS Notice No. GRN 000290 and 000291 (dated 2 and 6 November 2009 respectively.) FDA GRAS Response Letters and industry-submitted GRAS notices can be obtained from the FDA website by visiting <http://www.fda.gov/Food/FoodIngredientsPackaging/GenerallyRecognizedasSafeGRAS/GRASListings/default.htm> (click on the GRAS notice inventory).] {183974-5}

## ***Rest of the World***

### **Dutch report on reproductive toxicity of ascorbic acid, and hydrogen- and sodium fluoride**

An expert Dutch Committee that evaluates the reproductive effects of substances used in the workplace has issued its final report on the reproductive toxicity of ascorbic acid (vitamin C). A lack of appropriate data prevented the Committee from making any recommendations regarding classification for effects on fertility, and labelling for effects during lactation. For developmental toxicity, human data were again lacking, but there were evidently sufficient data from animal

studies for the Committee to propose that “no classification for effects on development is indicated”.

The Committee has also issued a final report on hydrogen- and sodium fluoride. This concluded that there were sufficient data to support the view that classification is not indicated for effects on fertility or development, and that labelling is not required for effects during lactation.

[Health Council of the Netherlands. Subcommittee on the Classification of Reproduction Toxic Substances. Evaluation of the effects on reproduction, recommendation for classification. Ascorbic acid (2009/03OSH) and hydrogen fluoride and sodium fluoride (2009/04OSH). Both documents are dated 17 December 2009 and can be obtained from Gezondheidsraad (via <http://www.gezondheidsraad.nl/en/publications/healthy-working-conditions/results>).] {180579; 182622}

#### **NICNAS – Full Public Report on glyceryl glucoside**

This report, which is dated November 2009, summarises (unpublished) toxicology data provided by the sponsor and contains risk assessments for public health and occupational health and safety.

[Australian National Industrial Chemicals Notification and Assessment Scheme. Full Public Reports for new chemicals. The report on “D-glucose, ether with glycerol” is available via <http://www.nicnas.gov.au/Publications/CAR/New.asp> (under the letter “D”).] {183853}

#### **Potato glycoalkaloid poisoning**

Glycoalkaloids can be hazardous to human health at quite low levels (“a single intake of >1-3 mg/kg bw is considered a critical effect dose”), with poisoning typically involving gastrointestinal ailments and neurological symptoms. Rather worryingly, probabilistic modelling of potato consumption in three European countries (the Czech Republic, Sweden and the Netherlands) suggests that glycoalkaloid intake from this source, mainly in the form of  $\alpha$ -solanine and  $\alpha$ -chaconine, may exceed the critical dose for the most enthusiastic consumers (in the top 0.01% intake group). To ensure that the critical dose is not reached by the rest (99.99%) of the population, the investigators suggest a maximum level of 50 mg/kg for glycoalkaloids in raw unpeeled potatoes (Ruprich J. *et al.*, *Food and Chemical Toxicology* 2009, **47**, 2899; <http://dx.doi.org/10.1016/j.fct.2009.03.008>). {183779}

#### **FSANZ – risk assessments for $\beta$ -galactosidase and maltotetrahydrolase**

Two safety assessment reports recently released by FSANZ for public comment relate to food processing enzymes. Application A1032 refers to  $\beta$ -galactosidase prepared from *Bacillus circulans*, while Application A1033 covers maltotetrahydrolase derived from *Bacillus licheniformis* (genetically modified to contain a gene from *Pseudomonas stutzeri*). The reports, which are both dated 16 December 2009, can be accessed (together with supporting documentation) via <http://www.foodstandards.gov.au/standardsdevelopment/applications/> on the Food Standards Australia New Zealand website. {183883-4}

#### **Folic acid in late pregnancy and childhood asthma**

Advice given in the UK, the US and Australia, that a folic acid supplement of 400  $\mu$ g/day should be taken by pregnant women during the first trimester, is intended to protect against neural tube defects in babies. However, an Australian study involving over 400 mothers and their children suggests that taking the supplement late in pregnancy may increase the risk of childhood asthma (relative risk 1.26, 95% CI 1.09-1.47 for children aged 3.5 years). Persistent asthma (which was affirmed at age 5.5 years if the child had also had asthma when aged 3.5 years) was also found to be more prevalent among the offspring of mothers who took folate supplements during the later stages of pregnancy (Whitrow M.J. *et al.*, *American Journal of Epidemiology* 2009, **170**, 1486; <http://dx.doi.org/10.1093/aje/kwp315>). {183727}



**bibra**  
toxicology advice  
& consulting

Citylink Centre  
Railway Approach  
Wallington  
Surrey SM6 0DZ  
UK

Tel +44 (0)20 8544 4150

Fax +44 (0)20 8544 4151

[info@bibratoxadvice.co.uk](mailto:info@bibratoxadvice.co.uk)

[www.bibratoxadvice.co.uk](http://www.bibratoxadvice.co.uk)

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