

Recent Changes in the Control of Toxic Substances

Len Levy

Emeritus Professor

Institute of Environment and Health

Cranfield Health

Cranfield University

UK

Changing Demography of Chemical Exposure in the UK

- **Loss of major traditional industries involving substance exposures (e.g. foundries, shipbuilding, rubber and plastics)**
- **Social dumping of manufacture of “difficult” chemical substances**
- **Better control technologies - COSHH Essentials**

Changes in UK Regulatory Approaches

- Major change in emphasis by HSE/HSC away from chemical exposures in the workplace
- Reliance upon EU for H & S Directives and technical guidance (e.g. Chemical Agents Directive)
- No domestic OEL-setting programme in the UK
- HSE has a targeted approach to chemicals (e.g. Disease Reduction Programme - DRP)
- Major current emphasis for chemical risk assessment and control is via REACH

Exposure Limits in the UK

- Workplace exposure limits (WELs) set via WATCH/ACTS process no longer exist
- Limits must now be adopted from DG Employment via the EU Scientific Committee on Exposure Limits (SCOEL)
- Two kinds of limits set – IOELVs and BLVs
- SCOEL consists of 23 expert nominees from Member States (MSs)

IOELVs and BLVs

- IOELVs ,when adopted by a tripartite committee, become part of a new Directive and must be adopted by MSs
- IOELVs are health-based limits and thus equivalent to WELs (socio-economic factors are not considered)
- Many recent IOELVs are lower than previous OELs in Europe and the US
- BLVs (lead and carcinogens) are problematical and a lengthier process

Some Problems with the EU OEL System

- The IOELV/BL system is severely under-resourced
- Documentation has to be produced by SCOEL members (busy people)
- Can be long process (nickel has taken over 10 years to produce draft for discussion)
- Danger of “laundering” of national limits by some members
- Possible conflict with REACH DNELs/DMELs

Problems with Setting Limits for Carcinogens in the EU

- IOELVs are health-based and thus cannot be used for genotoxic carcinogens or mutagens
- SCOEL has recommended limits for some “non-genotoxic” carcinogens (e.g. crystalline silica and formaldehyde)
- Process via the Carcinogens Directive is very laborious, requiring Regulatory Impact Assessment (in 27 MSs!)
- SCOEL has “parked” about 30 such substances

Possible Solution for Carcinogens

- Under Carcinogens Directive at present, the limit set must be a BLV (e.g. benzene and vinyl chloride)
- DG Employment is exploring simpler alternatives
- Research underway by a group led by IOM looking at a range of scientific and socioeconomic factors

„Dose-Effect Relations in the Low Dose Range and Risk Evaluation“
(Streffler et al. 2004; Europäische Akademie Bad

Chemical carcinogen,
causing tumours in humans and/or experimental animals

Genotoxic

Non-genotoxic

DNA reactive,
causing mutations

**Genotoxicity only on chromosome
level (e.g. spindle, topoisomerase)**

Clearly
DNA-reactive
& initiating

Borderline
cases

Weak genotoxin,
secondary mecha-
nisms important

A: No threshold,
LNT model to apply

B: Situation not clear
→ LNT as default

**C: Practical/apparent
threshold likely**

**D: Perfect/statistical
threshold likely**

Numerical risk assessment,
→ risk management procedures

NOAEL
→ health-based exposure limits

New Emphasis on Biological Monitoring by DG Employment

BM has in general not been very “fashionable” in the UK

- historical reluctance since late 1970s**
- WATCH/ACTS has produced a number of BMGVs over the years (see EH40/2008)**

Some countries use BM standards more commonly

- Germany has BATs**
- US (ACGIH) has BEIs**

SCOEL Activity on BM

- SCOEL is attempting to recommend BM values wherever possible
- These BGVs will be part of the final documentation, but not part of the Directive and thus not mandatory in MSs
- SCOEL is now working on extending BM to pragmatic “good practice” guidance values

UK Work on Updating Occupational Cancer Burden

- **As part of the DRP Programme HSE has commissioned research on an update of the Doll and Peto 4% estimate**
- **The team is led by Lesley Rushton at Imperial along with HSL, IOM and Cranfield**
- **They are tasked with looking at current and future trends**

Burden of Occupational Cancer

- The aim of the project was to estimate the burden of cancer due to occupation in GB
- All cancer sites for which IARC has classified Group 1 and 2A occupationally-related carcinogens
- Collaboration with Imperial College, IOM, HSE, HSL

Burden of Occupational Cancer

- Agents or occupations had either “strong” or “suggestive” evidence of carcinogenicity for the specific cancer site as defined by Siemiatycki (2004) and IARC
- 24 cancer sites
- 40+ occupational exposures considered
- Attributable fractions & numbers for mortality & incidence calculated

Burden of Occupational Cancer

- Burden:
 - Deaths – Men: 8.5% (6,599); Women: 2.3% (1,687)
 - Incidence – Men: 5.9% (10,370); Women: 2.2% (3,652)
- Cancer sites:
 - Mesothelioma (95%); Sinonasal (34.4%); Lung (15.2%); Nasopharynx (8.2%); Bladder (5.4%); Breast (4.6%); NMSC (4.6%); Larynx (4.6%); Oesophagus (2.5%); STS (2.3%)

Burden of Occupational Cancer

- **Agents/Occupations (registrations):**
 - Asbestos (4,216); Shift/night work (1,971); Mineral oils (1,690); Solar radiation (1,543); Silica (907); Diesel engine exhaust (802); PAHs (545); Occupation as a painter (437); Dioxins (334)

Occupational Mortality and Chemical Exposures

- HSE has also commissioned research to look at existing mortality amongst various occupational groups
- They have also asked for causes of mortality related to potential or possible chemical exposures
- The work involved Terry Brown of HSL and currently at Cranfield

Occupational Mortality 1991-2000

- Series of Registrar General's reports based on recently instituted registers of births, marriages & deaths began in 1837
- Early reports on occupational data restricted to studying relationship between occupation & violent death
- Decennial supplements dealing with occupational mortality appeared regularly dealing with routinely collected death registration data.

Occupational Mortality 1991-2000

- Current analysis based on all deaths in E&W during 1991-2000 at ages 16-74 years
- Underlying cause of death grouped into 226 categories
- Occupational codes aggregated into 181 job groups
- Associations characterised by PMRs, adjusted for age, sex & social class

Occupational Mortality 1991-2000

- **Key points:**
 - **Asbestos-related disease**
 - **Coal miners & other pneumoconiosis**
 - **Non-coal miners & quarry workers (silicosis)**
 - **Alcohol-related deaths in publican & bar staff**
 - **Sino-nasal cancer & wood dust/leather dust**

Occupational Mortality 1991-2000

- **Key points:**
 - Aircraft flight deck officers & melanoma
 - Shift work & work-related stress & IHD
 - Pneumococcal & unspecified lobar pneumonia in sheet metal workers & welders exposed to metal fume
 - Accidents in various occupations
 - Suicide among doctors, dentists, nurses & vets

Current Work of WATCH and ACTS

- There is no current UK OEL-setting function for WATCH/ACTS
- Much recent activity has been centred on asbestos-related cancers (lung and mesothelioma)
- New estimates are being produced at very low exposure levels
- Risk banding of various tasks is under active discussion
- There are ongoing discussions regarding the future of ACTS

The International Agency for Research on Cancer (IARC)

- Volume 100 of the Monograph series is updating all human carcinogens over several meetings
- They are trying to assess information on specific target organs and tissues (work for IARC?)
- They are including information on mechanistic evidence
- IARC website has just published an update on 31 Group 1 substances

Biomonitoring of the General Population

- More interest in exposure of the general population to industrial chemicals (REACH and NGOs)
- Some NGO activities to “promote” public concern in this area via sampling MEPs
- CEFIC has funded a study by Cranfield & HSL to look at background markers for some common substances to establish background ranges

Background Incidence of Key Biomarkers of Chemical Exposure within the General UK population by IEH and HSL*

- Biological Monitoring by post
- Approved by Ethics Committee
- Volunteers selected from electoral register (>18 years old)
- >5500 invitation letters sent
- Lifestyle questionnaire
- Urine samples from 358 (8.3%)

Chemical	Urinary biomarker
Benzene	S-Phenylmercapturic acid (S-PMA)
Cadmium	Cadmium
Caffeine	Caffeine
Chlorinated hydrocarbons	Trichloroacetic acid (TCAA)
Dithiocarbamates	Ethylene thiourea (ETU)
Mercury	Mercury
Naphthalene	1-Naphthol, 2-Naphthol
Nicotine	Cotinine
Di-(2-ethylhexyl) phthalate (DEHP)	Secondary phthalate metabolites – Mono (2-Ethyl-5-Hydroxyhexyl) Phthalate (5OH-MEHP), Mono-(2-Ethyl-5-Oxo-hexyl) Phthalate (5oxo-MEHP)
Pyrethroids, synthetic	Cis- and trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid (c/t-Cl ₂ CA) 3-Phenoxybenzoic acid (3-PBA)
Xylene	Methyl-hippuric acid (MHA)

*sponsored by the Cefic (European Chemical Industry Council) Long-range Research Initiative (LRI-D2.1-MRCI-0405)

Results (Provisional)

Biomarker	Reference Value*	
	Creatinine corrected ($\mu\text{g/g creatinine}$)	No correction applied (nmol/l)
Cadmium	0.9	7.9
Mercury	2.8	15.0
Pyrethroids		
3PBA	4.3	28.3
<i>cis</i> Cl ₂ CA	0.7	3.8
<i>trans</i> Cl ₂ CA	1.8	7.7
Br ₂ CA	1.3	5.3
Cl ₃ FCA	1.8	10.7
<i>cis</i> Cl ₂ CA & <i>trans</i> Cl ₂ CA	2.3	10.4
Cotinine	2963.0	3230.0 ($\mu\text{g/l}$)
ETU	5.2	48.0
MHA	94.7 (mg/g)	440.0 ($\mu\text{mol/l}$)
	11.9 (mg/g)	48.0 ($\mu\text{mol/l}$)
S-PMA	7.0	38.0
TCAA	8.7	49.6
Naphthalene		
1-Naphthol	15.2	108.0
2-Naphthol	9.6	81.0
DEHP		
5OH-MEHP	42.3	146.0
5oxo-MEHP	66.5	230.0

* derived from 95th percentile value for each biomarker.

Interdepartmental Group on Health Risks from Chemicals (IGHRC)

- **This UK platform was set up to harmonise chemical risk assessment across Departments and Agencies**
- **Its primary function is to promote and share good practice in human chemical risk assessment**
- **One major activity is producing authoritative guidance documents**
- **Another is to organise courses and workshops for government scientist and policy makers**

Previous guidance documents and reports

- **Assessment of Chemical Carcinogens: Background to General Principles of a Weight of Evidence Approach (2002)**
- **Uncertainty Factors: Their use in Human Health Risk Assessment by UK Government (2003)**
- **Guidelines for Good Exposure Assessment Practice for Human Health Effects of Chemicals (2004)**

(<http://ieh.cranfield.ac.uk/ighrc/ighrc.html>)

Recent IGHRC guidance documents

- **Route-to-route extrapolation of toxicity data when assessing health risks of chemicals (2007)**
- **Chemical mixtures: A framework for assessing risks (2009)**
- **Guidelines on exposure modelling in chemical risk assessment – current UK practice (Late 2009)**

Newer Concerns

- One major concern regards the potential hazards and risks from engineered nanomaterials
- These include nanotubes, nanoparticles and certain fibres
- There are many international and national initiatives addressing occupational environmental and consumer issues