Chemicals in Food, Water and Consumer Products

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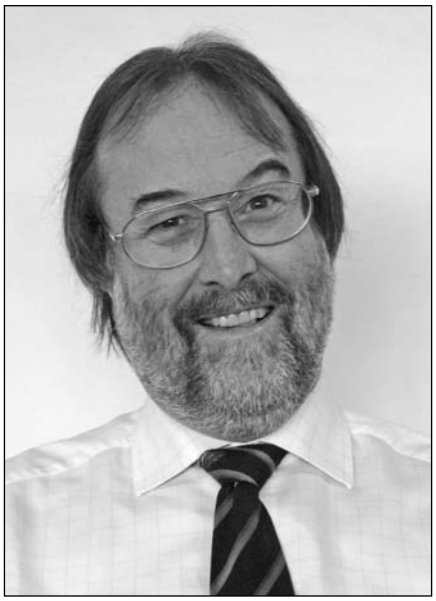

Over the past 50 years, life expectancy in the UK has increased substantially, and we now enjoy longer and healthier lives than ever before. This benefit has been achieved principally through advances in science and technology, including the discovery and wide-ranging exploitation of large numbers of new chemicals. However, while the net effect of technological progress has been positive, there are notable examples of harm to human health and wildlife from chemicals that have been introduced into our food or environment, either deliberately (eg asbestos, organochlorine insecticides) or inadvertently as by-products of new technology (eg motor vehicle exhaust). In looking to the future, therefore, our challenge is to maximise the benefits from technological advances while minimising adverse effects. This objective is pursued through appropriate risk management.

The starting point when managing risks from chemicals is a scientific assessment of risk, which entails three main steps:

- Hazard identification – what are the potential adverse effects of the chemical?
- Hazard characterisation – how does the probability and severity of these hazards relate to the circumstances and level of exposure to the chemical?
- Characterisation of risk – given the expected circumstances and levels of exposures to the chemical, what harm can be expected?

It should be noted that the risks from chemicals depend importantly on the circumstances and extent of exposure. Handling an intact lump of asbestos poses no material risk to health, whereas inhalation of microscopic asbestos fibres can cause serious lung disease, the probability of disease varying according to the cumulative amount of asbestos inhaled over time. Exposure to uranium provides another example. We are all exposed daily to tiny quantities of uranium in the water that we drink, but this is not of concern because the risks from such low levels of exposure are negligible.

Various sources of information may contribute to risk assessment for chemicals, including:

- Knowledge of chemical structures – for example, some molecular features make it more likely that a substance will bind to the DNA in cells, possibly causing cancer
- Experiments in vitro – for example, tests for mutagenicity (ability to damage DNA) in bacteria
- Experiments in laboratory animals
- Case reports and epidemiological studies of exposed humans and wildlife
- Experimental studies in humans (where these are judged ethically acceptable)
- Studies to assess levels of chemicals in food, water, air, soil and other environmental media
- Studies to assess the extent to which people or wildlife are exposed to chemicals from different sources and by different pathways

However, even where extensive scientific data are available, there will always be an element of uncertainty in the assessment of risk. Uncertainty can arise because few relevant studies have been conducted; because available studies are imperfect in their design or execution, and liable to statistical error because of their limited size; and in the extrapolation from findings in vitro and in laboratory animals to human exposures. As would be expected, such uncertainty tends to be greater for new chemicals than for those that have been present in the food or environment for many years.

Risk assessment therefore requires not only an estimate of the possible risks from a chemical, but also consideration of the uncertainty in risk estimates. In the communication of risk assessments it helps to distinguish between risk and uncertainty. The

presence of a risk implies that a proportion of exposed people (or animals) will suffer harm as consequence of their exposure. However, uncertainty often extends to a scenario in which there is no elevation of risk whatsoever. For example, currently available evidence does not indicate a risk of hip fracture from fluoridation of drinking water, but there is some uncertainty. While our best estimate is that there is no risk, we cannot exclude the possibility that a small risk has been missed by the research conducted to date.

Risk management builds on risk assessment by comparing estimates of the risks, benefits and costs, and of the attendant uncertainties, for each of several options (eg whether or not to permit the use of a chemical in a particular way), and choosing the one that is considered preferable. This entails the application of value judgements. For example, some people worry more about the uncertain risks of fluoridation than others. Thus, while risk assessment is a scientific activity, risk management is not. Where the choices under consideration affect only one person, risk management is ideally devolved to the individual concerned, who can then apply his or her own values in deciding what to do. However, where multiple stakeholders are affected by a decision, the weighing of risks, benefits, costs and uncertainties becomes a political activity.

The Committee on Toxicity

The Committee on Toxicity provides independent scientific advice to Government and to the public on the assessment of risks from chemicals in food, consumer products and the environment. It currently comprises a chairman and 14 scientific members, mostly from academia, who are appointed on merit (according to the rules of the Commissioner for Public Appointments) on the basis of their expertise in relevant areas of science and medicine. In addition, two 'lay members' bring a broader perspective to its deliberations and communications. The secretariat is provided jointly by the Food Standards Agency (FSA) and the Health Protection Agency. Its work is co-ordinated with that of two sister committees – the Committee on Carcinogenicity and the Committee on Mutagenicity.

The Committee considers questions, most of which are referred to it by its two sponsoring departments, FSA and DH, or (less frequently) by other Government departments and advisory committees. In addition, the Committee carries out its own horizon-scanning, and may identify other topics which it feels should be addressed. Its main outputs are published statements in which it draws conclusions and makes recommendations on the questions that it has considered. Additionally, the chairman (with or without other members) may attend meetings with departmental bodies (eg the FSA Board) to discuss findings, and the publication of statements may be accompanied by press releases or press conferences. The Committee endeavours to be as open as possible in its business, making its meetings open to the public and publishing minutes on its website. Exceptions may occur (eg because a scientific paper under discussion is still under consideration for publication in a scientific journal), but in these circumstances, full minutes are published once the original obstacle has been removed.

Examples of topics on which the Committee has recently issued statements, or which currently are under consideration, include:

- Effects of mixtures of food colours and a preservative on behaviour in children
- Ill-health in commercial air crew and the cabin air environment
- Use of PAVA as an incapacitant spray
- Reproductive effects of caffeine
- Reproductive outcomes in people living near landfill sites
- The Lowermoor water pollution incident
- Possible risks from plant toxins in honey
- Air fresheners
- Chlorination disinfection by-products in drinking water
- Safety of milk and meat from animals that have eaten bracken

It should be noted that the work of the Committee is not restricted to man-made chemicals, and that several of the investigations listed above concern naturally occurring substances. This underlines the important message that natural does not imply safe. Many of the most toxic chemicals (eg ricin, aflatoxin) occur naturally, while many synthetic chemicals have very low toxicity.

Future needs

One of the threats to the future of chemical risk assessment in the UK is a possible shortage of scientists with the relevant expertise in areas such as toxicology, epidemiology and exposure assessment. Applied sciences of this type have tended to fare less well in university research assessment exercises, in part because their output is seen as less innovative and exciting. And perhaps for the same reason, it has become more difficult to attract high quality graduates into these fields. The Medical Research Council has recently embarked on an initiative to expand training in toxicology, but other diciplines also need to be re-invigorated.

Meanwhile, resources for risk assessment must be managed with care. Substantial input is needed for chemicals that intrinsically are more hazardous (eg pesticides and medicines), and for new products to which exposure will be extensive. For others, a lighter touch is more appropriate.

The role of the Pesticides Safety Directorate in regulating Pesticides and Detergents

Dr Kerr Wilson
Chief Executive, Pesticides Safety Directorate

The Pesticides Safety Directorate (PSD) is the UK Regulatory Authority for pesticides and detergents. On 1 April 2008 PSD transferred to the Health and Safety Executive (HSE). Prior to the move to HSE, PSD was an Executive Agency of Department for Environment Food and Rural Affairs (Defra). PSD reports on operational matters to HSE and to Defra Ministers and to four other Departments on pesticide and detergents policy issues. Pesticides and detergents are regulated at both European and national level.

Detergents

Detergents legislation is primarily set to protect the environment. Companies wishing to manufacture and sell detergents must be able to demonstrate that the active ingredient (surfactant) meets the required standard of biodegradation. Companies are not required to submit their test results to PSD but must provide the data if asked to do so. In exceptional circumstances, where the surfactant does not meet the required standard, companies can apply to the regulatory authority for a derogation.

Pesticides

In contrast to the detergent regime, pesticides are heavily regulated and this relies on a scientific assessment of the risk. The scientific data required to get an approval to supply and use a pesticide is extensive and thorough and undergoes intensive scrutiny by PSD and other bodies. Pesticides, in common with other chemicals, are used to benefit society but because of their toxic properties and the way they are used they have to be carefully assessed and regulated to minimise harm to both people and the environment.

The active ingredients in pesticide products are regulated at European level. Getting an active compound on the approved European list involves submitting a detailed scientific dossier. The dossier is evaluated by a selected national regulator and further scrutinised by other Member State regulators. The European Food Safety Authority's independent experts advise the European Commission before Member States vote on whether to list the active ingredient.

Products (containing the listed actives) are approved at national level. Companies wishing to sell products in the UK submit a data package to PSD. No pesticide can be supplied or used without approval. For approval to be granted a company must be able to demonstrate that the product is efficacious and that risk to human health, the environment and wildlife is minimal. Post approval monitoring is in place to ensure the controls are working and to identify any emerging adverse effects.

Pesticides in food

The protection of the public is a key consideration for PSD and other regulators such as the Food Standards Agency, particularly in relation to residues in food. The PSD consumer risk assessments follow internationally agreed scientific protocols for toxicological studies and crop residue studies. When assessing the consumer risk both chronic and acute exposures are applied to a range of ten different people categories. The results from residue trials identify the highest residues from proper use and these data are used to calculate the potential consumer intake. Approvals are granted only if the predicted exposure is less than the health-based reference dose. Taking an example pesticide, the Acceptable Daily Intake for Kresoxim Methyl is 0.4mg/kg whereas the calculated consumer exposure is 0.0012mg/kg.

Residues on produce are controlled using the concept of the Maximum Residue Level (MRL). This is a limit based on the residues likely to be found on produce following good agricultural practice. It is a trading standard and not a health-based standard. Produce which has residues above the MRL must not be sold. The limits set for MRLs are often significantly lower than would give rise to intakes near to health based reference doses. From September 2008 the default MRL for all residues will be 0.01mg/kg (effectively zero in analytical terms) unless specific data are provided to support higher values.

As part of our post-approval monitoring we sample food for pesticide residues at a cost of about £2m pa. About 98% of samples are generally found to have residues below the MRL. Produce that repeatedly shows up with MRL exceedences is subject to special attention by PSD. For example, some years ago testing revealed residue levels in lettuce. PSD's advice to growers and other interventions has effectively driven down residue levels.

The Committee on Toxicity published a report on the risk assessment of

mixtures of pesticides and suggested that a methodology should be developed for cumulative risk assessment. PSD is supporting the European Food Safety Authority in developing an approach for assessing cumulative risk.

Pesticides in water

Protection of water courses from pesticides is an important aspect of PSD's work. The standard we are working to is to ensure any pesticide residue in drinking water is less than 0.1µg/litre. Pesticides which are sprayed on crops may drift into water courses or leach through the soil into ground water. Point sources of contamination can be major contributors to pollution. PSD has been active in commissioning R&D into possible sources of contamination, particularly field drains and point sources. Research has shown that contamination to water from sprayers at the end of an operation is significant and the use of bio-beds can reduce contamination significantly. Even the washings from a single pair of gloves can contaminate a water ditch 100m x1m x 1m to a level in excess of the 0.1µg/litre limit. PSD validated models are used to predict the likelihood of concentrations exceeding 0.1 limit in a range of vulnerable soil and climate scenarios.

PSD works closely with the Environment Agency who has an extensive surface and groundwater monitoring programme throughout England and Wales. Out of nine commonly detected pesticides, two have been withdrawn and two will be phased out by 2009. The remainder will be reviewed when they appear for re-registration.

Current issues

The availability (or non-availability) of pesticides is moving up the political agenda because of concerns over food supply and food security. The issue of pesticide availability has come about largely as a result of the European Review of pesticides. A large number of pesticides have been taken off the market some for safety and some for commercial reasons. Approximately 60% of pesticides have been removed from the approved list. Existing legislation and proposed new European legislation will inevitably have further implications for pesticide availability.

The UK is an active participant in the European negotiations on proposed new pesticide legislation and a Sustainable Use Directive and we are well ahead in having developed our own national strategy. The UK strategy covers five areas – human health, water, biodiversity, amenity use and availability. Working groups drawn from a wide group of stakeholders are taking these workstreams forward.

Finally, the move of PSD into HSE will put chemical regulation into one single body. Over the next year PSD will be working with colleagues engaged on biocides and chemicals (REACH) regulation to share best practice and to explore how we can make best use of our combined expertise. Maintaining our internationally respected UK regulatory science expertise will be essential if we are to play our part protecting people and the environment whilst recognising the benefits that modern technology can bring to society and the economy.

CHEMICALS IN FOOD, WATER AND CONSUMER PRODUCTS

Why should we be concerned about our exposure to chemicals?

Gwynne Lyons
CHEM Trust [1]

There is insufficient information available on the toxicity of many industrial chemicals on the market today to undertake even a basic assessment of the risks they pose to human health and the environment. Therefore, to some extent, protection of the public is based on wishful thinking rather than good science. Yet the stakes are high, because there is ubiquitous exposure to many of these chemicals from their extensive use in consumer products, and from air, water or food contamination.

Of course, not all chemicals are bad, but there are mounting concerns about those which have endocrine disrupting properties. Such chemicals can mimic or de-rail the normal functioning of hormones, which are the body's own chemical messengers.

Over the last decade, in response to the mounting worry about possible widespread effects, the European Commission has spent a total of €161m (around £125m) on research into endocrine disruption. Many excellent UK scientists are contributing to world class research in this area.

The main concerns that have been identified include reproductive

1 CHEM (Chemicals, Health and Environment Monitoring) Trust is a new charity set up with initial funding from WWF-UK, with a mission to protect wildlife and humans from harmful chemicals.

disorders in men (including declining sperm quality and quantity, and defects in baby boys' genitalia), and increases in breast and testis cancer. The rate of increase in cancers of the breast and testis is such that it cannot solely be due to genetic factors. Some environmental factor(s) (which could include life-style) are also at play, because genes in a population just don't change that quickly.

Hormonal action is key to the origin or progression of these disorders, and so it is likely that hormone disrupting chemicals are involved. The suspicion that certain chemicals play a role is underpinned by information from in-vitro studies and animal experiments. Indeed, some scientists point out that the 'phthalate syndrome' which is a group of symptoms (including un-descended testes, shortened ano-genital distance, and reduced sperm counts) caused by de-masculinization of laboratory animals by phthalates, is remarkably similar to many of the problems which now seem to be increasing in men. Phthalates have many uses, particularly in plastics, and some have well known anti-androgenic properties. However, proving which chemicals are causing effects in humans is problematic. Many interacting influences may play a part, and it is generally only possible to uncover the role of a particular chemical when it exerts, by itself, a very strong impact on the disease process. Some epidemiological studies are, however, adding to the weight of evidence. For example, a US study found baby boys with shorter ano-genital distance and impaired testicular descent (both markers of de-masculinization) were born to mothers with higher exposure to certain phthalates during pregnancy.

Similarly, with regard to breast cancer, it is suspected that oestrogen mimicking chemicals may be involved, as it is well established that factors which increase a woman's lifetime oestrogen exposure, increase her risk of breast cancer. Now, studies in women exposed to oestrogenic pesticides are backing up that concern. For example, a study in Spain has found an increased breast cancer risk in some women with higher total exposure to several oestrogen mimicking pesticides measured as the total effective man-made oestrogenic burden.

Hormone disrupting chemicals found in consumer products

People can be simultaneously exposed to large numbers of hormone disrupting chemicals. Chemicals with endocrine or hormone disrupting properties are found in a vast array of consumer products. A few notable ones include:

some phthalates used to make plastics flexible;

certain parabens, such as butyl paraben, an antioxidant used in some cosmetics;

benzophenone and 4-methyl-benzylidene camphor, UV filters used in sun-screens;

bisphenol A, which can leach from polycarbonate and from the epoxy resin lining used on the inside of food tins.

some brominated compounds used as flame retardants.

Pesticides with hormone disrupting properties

Moreover, many endocrine disrupting pesticides, even those long since banned in the EU, can still be found as food contaminants, either because of illegal usage, or due to their environmental persistence, or because they are still used on imported products grown outside of the EU.

There is much more information on the toxic properties of pesticides as compared to many other chemicals, and the active ingredients used in the EU have been subject to review. Thus, some pesticides with hormone disrupting properties, such as the vinclozolin and atrazine (where the concern was groundwater pollution) are now no longer permitted. Others such as procymidone (used, for example, on plums and cucumbers) and fenarimol (used on tomatoes, peppers, melons, aubergines etc) are still allowed, although due to be removed from the authorised list after June 2008. Nevertheless, vinclozolin, procymidone and fenarimol, all of which have anti-androgenic properties, can still be used outside the EU and can be found as residues in imported produce.

Currently, the EU plant protection products legislation is being updated and negotiations are ongoing. The proposed text of this new legislation could lead to EU usage of other endocrine disrupting pesticides being prohibited unless human exposure is negligible. However, the final wording of the legislation, and how it will be implemented has yet to be seen.

Need for better test methods and improved methods of assessment

Many pollutants now recognised as hormone disruptors, such as TBT and certain phthalates, were only identified through scientific studies, not by routine safety testing. There is therefore a need to develop novel, regulatory test methods, and to implement the best available test methods in legislative frameworks, and to subject the test methods used to regular review.

Few chemicals have been adequately investigated using even the test methods available now, which are sufficient to identify at least some chemicals with endocrine disrupting properties.

Furthermore, even when some information is available, the current methods of assessing a chemical's safety may not be suitable for assessing hormone disrupting chemicals. In particular the assumption of a threshold may not be tenable because these chemicals act together with natural hormones already present. Even small amounts of hormone disrupting chemicals may therefore add to the overall effects, and moreover, it is likely that due to the limited sensitivity of established test methods, such effects are overlooked.

In addition, at the nub of much of the concern is the knowledge that we are now exposed to many hormone disrupting chemicals, which are known to be able to act additively. Experiments have shown that several oestrogen mimicking chemicals can cause effects, even when each is below its individual threshold for effect. Anti-androgenic chemicals and thyroid disrupting chemicals have also been shown to have additive effects. There have been some attempts to get to grips with concurrent exposures and the cocktail effect, and notable is the UK Committee on Toxicity's Working Group on Risk Assessment of Mixtures of Pesticides. Unfortunately, this has not led to adequate policy reform to address the issue, which needs to be dealt with in EU-wide guidance. For example, an oestrogen mimicking chemical, such as bisphenol A, is

assessed by itself, with no due regard to the knowledge that many other chemicals have similar mechanisms of action.

Expert interpretation of the science highlights the need for action

Networks of excellence, international conferences, and years of painstaking research have enabled many scientists in this field to develop a broad understanding of endocrine disruption and the effects of chemicals with such properties. Concerned about what the science was telling them, in 2005, hundreds of scientists working at the cutting edge of research into endocrine disruption signed the Prague Declaration. In this Declaration, scientists outlined what they had found, gave their interpretation of the science, and made some recommendations. They noted that while causality was well established for detrimental effects in wildlife, there were inherent difficulties in establishing causal links in humans. Furthermore, they concluded:

"In view of the magnitude of the potential risks associated with endocrine disrupters, we strongly believe that scientific uncertainty should not delay precautionary action on reducing the exposures to and the risks from endocrine disrupters."

Anyone concerned about public health might like to read the full seven-page Prague Declaration, which is available at the following web site: http://www.ehponline.org/docs/2007/10517/suppl.pdf

The Declaration went beyond the concerns about male reproductive health and hormone related cancers, and highlighted the in-utero susceptibility of the immune system to certain pollutants. It also flagged potential effects on brain development and brain ageing, as scientists conjectured that problems could be expected based on their knowledge of thyroid hormone physiology. The need for further investigation of the role of hormone disrupting chemicals in obesity and stress related disorders were similarly noted.

There is an important role for politicians

Expert judgement is therefore that there is a need to reduce exposures to hormone disrupting chemicals where possible, but it will take political will in many EU countries to take that forward on all fronts. To this end, CHEM Trust has written to selected Member States, including UK representatives, urging them to draft dossiers to put some chemicals with hormone disrupting properties onto the candidate list for prior authorisation under REACH (the new EU Chemicals Regulation concerning the Evaluation, Authorisation and Restriction of Chemicals). This would subject these non-pesticide hormone disrupting chemicals to much stricter controls, and would stimulate the use of safer alternatives.

It is sometimes difficult to gain consensus amongst the EU's 27 Member States, and controls over chemicals can be thwarted by a powerful industry lobby. However, with some political leadership from the UK, and with policies based on good science and expert interpretation of that science, there may be just a chance of preventing much future suffering.

The following points were raised during discussion:

Testicular cancer is certainly on the increase. However mortality statistics have been increasing since the 1930s. Hence causative factors must have been established as early as 1910. The later appearance of endocrine disruptors does not appear to account fully for the overall increase in this disease. Regarding breast cancer the role of increased oestrogen exposure is certainly correct. Regarding trends for breast cancer, other factors also need to be taken into account such as the effect of a delay in the timing of the first pregnancy, and the effect of screening which increases incidence.

Mixtures or combined exposures to chemicals are widely raised and a report is in preparation by COT. Interactions or the joint effects of two chemicals may generate a combined exposure effect which may amount to more than an additive effect.

What was the level of maternal smoking in 1910? Was this an important factor in testicular cancer in 1910? Why is multiple sclerosis in Orkney and Shetland twice as high as it is in the south of England? Is it related to latitude? Is the falling sperm count in men and gynaecomastia (breast development) in young boys, which is now a major problem, related to oral contraceptive in the water supply? Are organo-phosphate pesticides responsible for neurological damage now totally off the market?

Chemicals certainly do not account for all the evidence as with multifactorial disease it is difficult to evaluate the full weight of evidence. One can only speculate that polyaromatic hydrocarbons (PAHs) were around in the early part of the 20th century and they are endocrine disruptors. The data from epidemiological studies and those on animals need to be combined to understand the processes involved. The roles of asbestos and tobacco can be difficult to identify and the problems become much more difficult when many chemicals are involved. Hence the importance of the Prague Declaration calling for reduction in exposure to chemicals which come from a multiplicity of sources often from objects in everyday use. The possible relationship between low levels of oestrogen in water and men with mammary tissue is a hypothesis requiring further work.

The impression has been created that the REACH programme is not doing what it was intended to do or it is not stringent enough and that regulation is not working. Implementation of REACH is now under the control of the 27 member states. Regulation should be based on the full range of evidence and on risk, not on hazard and there are uncertainties in the science. The highest risk generation of men at risk from smoking and lung cancer were born in 1905 and for women those born in 1925 so smoking does not relate to testicular cancer rates. Multiple sclerosis is latitude related and is an effect in early life, possibly due to infection by epstein barr virus. Risk analysis on multiple chemicals is difficult to estimate due to the additive effect. Hence hazard may sometimes be the only useful guide to risk. If we regulate on hazard we need to find out if there is a benefit to be gained which outweighs disadvantages and balances risk. The Precautionary Principle is a general rule relating to uncertainty in risk and politicians wish to make sure they have set up institutional arrangements which provide a mechanism for managing risk in a well informed manner.