Health research over 50 years

Understanding the health issues behind environmental concerns and regulatory initiatives

CONCAWE has been working on health issues since its formation in 1963. In the early years, the focus of this work was on occupational health hazards and risks in the refining industry. Over the years, especially in the past decade, broader human health issues have been at the centre of environmental and regulatory debate, with 'health effects' increasingly being the driver behind environmental improvement and occupational health initiatives. Against this background, CONCAWE's health research has expanded to deal with these new and emerging issues.

Health issues are complex and need to be addressed by experts in several different areas. Through its member companies, CONCAWE has been able to maintain, as its 'Health Management Group', a strong team of occupational physicians, toxicologists, industrial hygienists, exposure and risk assessors, and product stewards with particular expertise in oil industry-related issues. Academic researchers are also called upon to undertake specialised research, as appropriate.

In the 40th anniversary *Review* (October 2003), we reviewed CONCAWE's involvement in three initiatives: (1) the Clean Air for Europe Programme (CAFE), an EU strategy for air quality management; (2) chemicals legislation and the increasing demand to inform the public about health and environmental hazards of chemicals; and (3) a global environment and health strategy with a special focus on children (EU SCALE initiative). Interestingly, these initiatives from 10 years ago continue to influence CONCAWE's work on health research, its objectives being to identify key health-related issues and gaps, develop cost-effective, leveraged research programmes to address these gaps, and provide CONCAWE members with advice, guidance and support on the significance of these issues based on scientific and professional evaluations.

In this 50th anniversary article, we summarise CONCAWE's involvement in three new or expanded areas: chemicals legislation and its requirements under REACH; the health effects of air pollution; and benzene product stewardship.

Chemicals legislation

Ten years ago, in 2003, the precise requirements of REACH were still under discussion. In anticipation and preparation for what the REACH requirements would be, CONCAWE initiated an ambitious programme to acquire information on human exposures, in the form of both descriptions of use and measured data. It was clear that these types of data would be necessary for the risk assessment of petroleum products. As a consequence, between 2000 and 2005, exposure data reviews and measuring campaigns were implemented to obtain current exposure information on gasoline, gas oils, kerosenes and other petroleum substances. Methodologies for monitoring airborne levels of LPG and bitumen fumes were also updated.

In the past 10 years, in addition to maintaining and evaluating the toxicology database for 22 petroleum substance categories, and submitting the dossiers to the European Chemicals Agency (ECHA) in 2010, CONCAWE has prepared for REACH by initiating several health research activities to anticipate potential data needs. Three key health science contributions that established the industry standard and provided valuable insights towards the REACH effort were:

- Development of the exposure assessment tools for both workers and consumers: CONCAWE developed the approach for characterising the health risks for workers and consumers from identified uses in different categories of petroleum substances. During the development of its exposure estimates, CONCAWE identified the need to include additional risk management measures in its estimates based on commonly applied controls during the manufacture and use of petroleum substances. This approach has become accepted as the standard industry methodology.
- Derivation of the 'Derived No Effect Level' (DNEL) for petroleum substances categories: CONCAWE reviewed the toxicology database on petroleum substances and calculated the REACH required DNELs. This involved extensive review of the available data and the approach developed by CONCAWE was published in a peer-reviewed journal.
- Justification to support the industry assessment of the cancer hazard classification of residual aromatic extracts (RAEs): CONCAWE developed a round

robin research programme which showed that, by using a well-established modified mutagenicity test, the carcinogenic hazard of an RAE could be predicted. The results of this programme provided the underpinning for the industry's technical justification of the cancer classification for RAEs.

To further support the assumptions on the exposure assessments for REACH, CONCAWE prepared a compendium of the assumptions related to REACH chemical safety assessments for petroleum substances. In addition, dermal exposure studies were commissioned to provide further technical justification for the assumptions used in the exposure assessments. And as part of the REACH requirement, interim risk management measures for use of petroleum substances with testing proposals were prepared and communicated. (See also the 'Petroleum Products' article in this *Review*.)

Health impacts of air quality

Ten years ago, the EU strategy for air quality management was based on the Clean Air For Europe (CAFE) programme. The main driver for the regulatory measures proposed by the European Commission was, and still is, the protection of human health from air pollution, especially particulate matter (PM), nitrogen oxides and ozone.

Recently, the World Health Organization (WHO) Task Force on Health coordinated an international project called REVIHAAP (Review of the Evidence on Health Aspects of Air Pollution) and HRAPIE (Health Risk of Air Pollution In Europe). These initiatives provide the scientific assessment to the European Commission and its stakeholders on the evidence for human health impacts from air pollution. This assessment is based on a review of the latest scientific evidence of those air pollutants regulated in recent Directives (2008/50/EC and 2004/107/EC). Pollutants have been expanded to include nitrogen dioxide, sulphur dioxide, some heavy metals, and polycyclic aromatic hydrocarbons, as well as a growing concern about indoor exposure to air pollutants.

To date, the evaluation of the health effects of airborne pollutants relies mostly on observational epidemiology investigations rather than on data from controlled clinical and toxicological studies. Not surprisingly, CONCAWE voiced concerns within the CAFE programme about the reliability of many study findings, and continues to emphasise the need for sound science in regulatory decision making. Scientific issues that have been routinely raised include: adequacy of the science to determine limit values, uncertainty in the dose-response functions, accuracy with which personal exposures are estimated, the ability to quantify life expectancy effects of air pollution changes, and possible double-counting of air pollutant effects.

Anticipating 2013 as the 'Year of Air', CONCAWE implemented several projects focused on addressing health data gaps in air pollution studies. These included:

- VE3SPA study (Validation of ESCAPE Exposure EstimateS using Personal exposure Assessment), a project that monitored personal exposure to key pollutants, and where the data have been used to evaluate whether the commonly used Land Regression models (area monitoring) can be reliably used to predict personal exposures at the street level.
- Critical review of the epidemiology data on key pollutants (PM, ozone, NO_x and SO_x) which provided an understanding of the current science and the basis for CONCAWE's contributions to the regulatory discussions on these pollutants.
- Human Exposure to Ozone in a Controlled Environment Study which was conducted at the University of Rochester in New York and evaluated ozone exposure under controlled conditions, measuring various cardio-respiratory parameters.

The health impacts of air pollution are also of interest at other international organisations such as the International Agency for Research on Cancer (IARC). IARC is part of the WHO and reviews and categorises chemicals as to their carcinogenic hazard potential. IARC recently designated diesel engine exhaust as a 'proven' human carcinogen, gasoline engine exhaust as 'possibly' carcinogenic to humans, and occupational exposure to bitumen and their emissions as either 'possibly' or 'probably' carcinogenic to humans depending on the type of bitumen and its occupational sector of use. IARC has undertaken a series of reviews of agents and these reviews may contribute to an assessment of ambient air pollution later in 2013.

CONCAWE has also responded to the regulatory focus on air pollution by organising two technical workshops in 2007 and 2009, which brought together the researchers and stakeholders to discuss key issues in the field of air quality science. These workshops helped confirm CONCAWE's position as a valued and respected contributor to the debate. CONCAWE will continue to engage in health-related discussions on air pollution to promote the use of sound science in policy decision making.

Benzene research programme

For many years, the effects of benzene on human health have been of concern to health experts and air quality regulators. Because of these concerns, regulatory limits and technological developments have resulted in the reduction in benzene concentrations in transport fuels and in ambient air. The basis for today's worker and environmental benzene regulations in Europe and more globally was an epidemiological study completed in the 1980s. This study, called the 'pliofilm study', evaluated benzene-induced leukaemia in workers exposed to benzene vapour through the manufacturing of pliofilm polymers, mainly in the 1950s and 1960s. To fill some of the knowledge gaps from the pliofilm study, the petroleum industry sponsored three independent epidemiological studies of occupational exposure to benzene in the 1990s. While these studies did not find any relationship between benzene exposures and some types of leukaemia (e.g. chronic myeloid leukaemia and acute lymphatic leukaemia), higher incidences of other forms of leukaemia, including acute myeloid leukaemia and chronic lymphoid leukaemia, were observed in some of the studies.

To better understand the importance of these findings, a 'pooled analysis' of these epidemiology studies was initiated in 2006 to combine ('pool') and update the entire worker population. With support from API and other trade associations, CONCAWE coordinated this major research programme which integrated data from the three studies into a single dataset. This enabled the 'pooled' results to be analysed with a statistical confidence that could not be achieved from the individual studies.

The study did not find a clear relationship between various blood leukaemias and today's typical benzene exposure levels. This conclusion suggests that existing regulatory standards for benzene, such as occupational exposure limits, are already sufficient to protect worker health for benzene-related leukaemias. The study did identify a relationship between myelodysplastic syndrome and certain types of exposures but this new finding requires more investigation to determine whether it is of relevance for today's benzene exposure control strategies.

CONCAWE will continue to investigate and initiate, as needed, research programmes that provide insight on the benzene science.

Outlook

In addition to the regulatory requirements of REACH, in 2013 and beyond, various advisory and regulatory bodies will continue to formally assess the hazards/risks of petroleum substances and their constituents.

The three initiatives described above emphasise the need for a thorough scientific understanding and analysis of the cost-effective management of health risk. CONCAWE remains committed to this principle in its health science activities, as in all the other areas covered by its remit.