THE TOXICOLOGY FORUM

Chlorinated Organic Chemicals:

Their Effect on Human Health and the Environment

Berlin, 19-21 September 1994.

A summary report prepared for Eurochlor by JPC Consulting.

General Comment.

It was repeatedly stated that chlorinated organic compounds cannot be treated as one category or even as several categories in terms of evaluating health and environmental effects.
However Greenpeace and Danish EPA pressed for such grouping. (Relevant to approaches at North Sea Conference?)

Only at one point during the 3 days was there an outburst of spontaneous applause, and that was during the final panel discussion when Dr. Detlev Kayser, a respected "elder statesman" from the BgVV, said that "Chlorchemie" is an artificial expression; that there is a very large body of data on organochlorine chemicals. The main problem is not so much the toxicity as the persistence, bioaccumulation and environmental pathways of substances. In the whole meeting we haven't discussed chlorine chemistry, but instead persistent chemicals. The topic should be "all persistent substances"! (Applause).

Political Aspects.

Clemens Stroetmann, Staatssekretär, BMU, gave the keynote speech in place of Prof. Töpfer. He emphasised that the German Govt. and its Parties do not support a withdrawal from chlorine chemistry. They see a need to differentiate between benefits and disadvantages. Also closing of the chlorine cycle is needed and where closing is not possible, the Govt. has not hesitated to impose restrictions. He mentioned a demonstration project in Buna AG for 40.8 MM DM which is aimed at closing the cycle, including HCl recovery, pyrolysis and monitoring of the PVC plant.

On the Enquête Kommission, he said that while there were calls at the start for a ban on chlorine chemistry, the majority is in favour of a conversion, and clearly some parts of chlorine chemistry will disappear. The work of the EK is not completed and he hopes Parliament will allow the EK to continue its work in 1995.

Prof. Dr. J. Starnick (Tech. Univ. Berlin), a member of EK, said that the EK considered that the German chlorine chemistry industry has 100 MMM DM turnover and 500,000 employees. Also that the ecological problems have been considerably reduced in recent years, which has not generally been recognised. A partial conversion is already underway in industry. The needs are to promote internal cycling within industry and to pay attention to emissions to the environment especially when damage is suspected or demonstrated.

The proposed new EK will look into sustainable development and how chlorine chemistry and other chemistries fit in (there was a brief mention of Dr. Schlegel of SRI !).

Bernd Heins (Envt.[1] Programme of IG-Chemie-Papier-Keramik) said that we need sustainable use of resources and environmental protection, but by acting we should not increase social problems. We need a real ecological policy. Parliament's Office of Technology recently highlighted some deficiencies here, e.g. relating to substitution [needs follow-up?].

"Green Organisations"

Consisted of 3 from Greenpeace (Dr. Paul Johnston, Greenpeace Exeter Research Labs.), Mats Knapp (Greenpeace Sweden), Manfred Krautter (Greenpeace Germany), as well as Dr. Andy Meharg (Inst. of Terrestrial Ecology) who seemed to be a close follower of Greenpeace,and Dr. Rainer Griesshammer, Oeko-Institut.

The main themes were:

- they have adopted the "conversion" terminology though not the prefix "partial"
- the problems are far from solved, and have not been solved by regulation
- most of the problems arise from "bulk production"
- there is "cynical exploitation" of fixed emission controls
- regulation on a substance-by-substance approach is not appropriate since discharges
  are complex in nature; particularly in the case of dioxins the need is to regulate the processes that give rise to them and not just to regulate the group of dioxins
- large-scale production of natural AOX is no excuse for large-scale emissions by industry
- need to follow the precautionary principle, i.e. no excuse to continue discharges until the questions are answered
- a strong emphasis on the need to run risk assessments for species other than humans
- hints that another class of chemicals (PAHs) is on the "hit-list".

There was considerable emphasis on the persistent, toxic, bioaccumulating substances, especially on PCBs, dioxins, chlorophenols.

In his speech, Johnston queried how the North Sea Ministerial Conference will monitor the 1990 Declaration's target of 70% reduction of dioxins since these are not even on the list of substances to be determined.

He queried lime-kilns (organochlorine wastes), steel works (PVC-contaminated scrap) and non-ferrous metal works as sources of dioxins.

Production and incineration of PVC were quoted as sources of numerous contaminants and so as an argument against regulation on a substance-by-substance basis.

In the panel discussion, Prof. Nader was challenged strongly on two points:

1) evaluation of chemicals one-by-one ("do we assess all the chemicals in seals one-by-one?")
2) dioxins.

On chemicals evaluation, Nader responded with the requirements of the Existing Chemicals Programme and of required data-bases for new products as providing a sound basis for setting priorities in the case-by-case approach.

With dioxins he had a harder time and did not have good, snappy answers available on challenges such as

- "dioxins are formed in all stages of industrial chlorine chemistry, i.e.
  production (including membrane process, oxychlorination),
  use,
  disposal (PVC incineration on balance of evidence)".

There seemed to be a fairly general assumption among the audience that the chlorine source for dioxins formed in combustion processes (incineration, etc.) has to be organic in nature.

Knapp (Greenpeace Sweden) raised the question of tris-chlorophenylmethanol which has been appearing at "high levels" in the environment, is probably toxic and "no one knows where it comes from". It was first recorded in the literature ~2 years ago (*Ambio*) and has been found in the Baltic Sea, Australia, USA, Antarctica.

Regulators.

There was an interesting contrast between Eva Lise Bendixen, EPA of Denmark, and Anders Johnson, National Chemicals Inspectorate of Sweden. Ms. Bendixen fretted about how to advise her Govt. on how to regulate "11,000 chlorinated organic chemicals", whereas Mr. Johnson described how the Swedish Govt. sets priorities and controls/eliminates the "bad actors", with his emphasis being in the field of agricultural chemicals.

Technical and Scientific Aspects.

Toxicological Implications of Chlorine Chemistry.

Prof. Dr. Helmut Greim, Institute for Toxicology, GSF-Forschungszentrum für Umwelt und Gesundheit GmbH, Germany.

His conclusion was that chlorine chemicals are not uniformly dangerous toxicants. Toxic potentials and potencies vary widely and each compound has to be evaluated specifically. There are different rates and routes of metabolisms, different cytotoxic mechanisms and different mechanisms of carcinogenesis.

Within the MAK commission, the cancer classification of 2,3,7,8-TCDD is not yet decided, but from the trend of the discussion it is likely that substances contaminated by TCDD will be classified.

Natural Sources of Organochlorines.

Prof. Anders Grimvall, Dept. of Water and Environmental Studies, Linköping University, Sweden.

Mentioned unconfirmed claims of natural sources of tric. and other chlorinated solvents. Kindler et al. (1993) compared observed and calculated concentration ratios between the northern and southern hemispheres for methylene chloride, tric. and perc. There was some evidence for natural sources of tric. This needs to be confirmed.

Mono-, di- and trichloroacetic acids are widespread in Nature. They have been cited as man-made, deriving from atmospheric degradation of certain chlorinated solvents, and causing forest damage. Prof. Grimvall described his recent work in which he has found DCA and TCA in ancient lake deposits in N. Sweden. He concludes that AOX and these chloroacetic acids could have a common natural source.

For PCBs, analysis of archaic samples clearly shows them to be anthropogenic.

Ms. Bendixen asked "where do all the natural organochlorines come from and what can regulators do about them?" Grimvall replied that there are similarities in mechanisms of formation of natural and industrial organochlorines, but the most harmful organochlorines originate from human activities so there is a good reason for regulators to regulate.

Johnston said that chlorine was used industrially before 1840 so this could have influenced data on "pre-industrial" PCDDs. Grimvall said no - pre-1840 use was very small and there is other evidence.

Occurrence in Food, Human Tissues and Human Milk.

Dr. Hans Beck, BgVV, Germany.

Concerned about chloroparaffins which are increasingly used as replacements for PCBs, are difficult to analyse and for which there is insufficient data.

Gave figures for reductions of hexachlorobenzene and organochlorine pesticides in human milk fat since 1970s, and of dioxins since 1989.

Atmospheric transport of organochlorines - the Arctic case as an example. Dr. Roland Kallenborn, Norwegian Inst. for Air Research (NILU).

Only 48-72 hours needed for transport of air masses to Arctic from Europe.
In 3-5 years, ~1% of North Sea water is carried to Greenland by ocean currents.
In ~8 years, ~0.1% of North Sea water is carried to Baffin Bay.

A combination of the two is involved in the transport of contaminants to the Arctic, with small quantities being carried quickly by air and large quantities slowly by water. Little is known about the long-term consequences of harmful substances in the highly sensitive Arctic Ocean area.

Neurotoxicity.

Prof. Marcello Lotti, Istituto di Medicina del Lavoro, University of Padua, Italy.

Dealt with selective rather than general neurotoxic effects of organochlorines. They generally target both the central and peripheral nervous systems.

Tric. is unusual in that it targets the trigeminal nerve. The metabolite dichloroacetaldehyde has been suggested as the reason, with the selectivity being due to the activation of a latent herpes virus.

Immunotoxicity.

Prof. Dr. Joseph Vos, National Institute of Public Health and Environmental Protection, Netherlands.

The mere presence of chlorine in a molecule does not necessarily mean involvement in immunotoxicity.

Dinitrochlorobenzene was quoted as a powerful autoimmunotoxic material.

VCM, trichloroethylene, perchloroethylene and hexachlorobenzene were mentioned as immunotoxicants. Some evidence was presented in the case of hexachlorobenzene.

The 1988 "seal kill" in Europe was discussed. Caused by phocid distemper virus (PDV), with laboratory evidence for immunosuppressive action of organochlorines /PCBs, PCDDs, etc.). He described an experiment (first part published in *Ambio*, March 1994) whereby seals were fed for 1 year with either

- Atlantic herring or
- Baltic herring.

The "Baltic" group showed

- decrease of NK cell activity (NK = natural killer cells),
- decrease of T cell activity,
- lower antibody titre,
- depression of delayed type hypersensitivity (DTH).

Since the Baltic herring has 10x the levels of contaminants compared to the Atlantic herring, this was regarded as evidence that these contaminants made the seals of the Baltic region more susceptible to disease.

Epidemiological Principles in Assessing the neurodevelopmental Effects of Fetal Exposure to Organochlorines.

Dr. Nigel Paneth, Michigan State Univ.

Stressed the need for scientific objectivity and gave, as example of the opposite, a "report" on sperm density studies which he described as a "hodgepodge" with "dubious conclusions".

He presented evidence that PCBs may not be the only factors involved in the Michigan and N. Carolina studies.

In the discussion, he and Prof. Joseph Jacobson, Wayne State Univ., commented that evidence relating to PCBs, etc. cannot be used to suggest that all chlorinated organics have such effects.

Nephrocarcinogenicity of Trichloroethylene.

Prof. Dr. Dietrich Henschler, Institut für Toxikologie, University of Würzburg, Germany.

"Strong evidence that warrants further investigation".
Adequately covered by ECSA.

Organochlorines and Breast Cancer: Lessons from the Past.

Dr. John Baron, Dartmouth Medical School.

Gave examples:

- soft tissue sarcoma and phenoxyherbicides,
- breast cancer and DDT,

where initially high relative risks later proved to be low or none at all.

Problems have been

- unknown real exposure
- difficult exposure assessment
- co-variates
- chance, sample size.

Recent work on breast cancer and DDE, PCBs (Wolff et al. 1993, Krieger 1994?) has aroused media interest with indications of racial differences. Baron felt that insufficient attention had been paid to covariants, and that the racial differences were due to chance, since net effect in the Krieger cohort was none.

His conclusions were:

PCBs - no overall effect,
DDE - very slight positive effect,
TCDD - no overall effect.

Ms. Bendixen, Danish EPA, said that the conference seems designed to prove that organochlorines are not responsible for breast cancer, but we know that lipophilic organochlorines are increasing along with breast cancer. So what tests/experiments are needed? Baron said that it is dangerous to draw such simple conclusions; studies need to be conducted with larger samples, etc., and that these studies are being conducted outside the arena of political preconceptions!

Occupational Aspects.

Dr. John Doull, Univ. of Kansas.

Described how ACGIH operates, giving priority to data on humans, with recent re-classification of trichloroethylene as example.

In the discussion, Johnston asked whether he had any example of a chemical identified as environmentally harmful before being put into production. Doull responded that most candidates for setting TLVs come from the New Product Registration procedures and that many companies use gene-tox. data as an early screening tool. D. Farrar (ICI) said that the pre-manufacturing notification scheme has resulted in some chemicals not reaching the market-place.

Ms. Bendixen asked whether it was dangerous to have a preference for epidemiological data, i.e. to allow product to circulate first for 20-30 years? Doull said that usually ACGIH gets clinical data first.

Can Toxic Equivalency Factors be Justified? Prof. Dr. Christian Schlatter, ETH Zürich.

The principle of weighing and adding effects induced by same or similar mechanisms is basically sound and can be applied to

dioxins,
PCBs,
estrogen mimics.

Commented that choosing the wrong end-point will give false results, e.g. LD_{50} in rats and mice. Also that organ distribution is important ("man is not a big rat").

Proposed the Nordic TCDD equivalency factors (TEF) for certain dioxin-like effects of PCBs. Non-dioxin-like effects must be separately evaluated.

Use of TEFs in situations other than food (e.g. stack emissions) is not scientifically justified unless environmental transfer factors of individual congeners into human food are taken into account, and these are not yet available. Example - 40x difference from same starting level between transfer of OCDD and TCDD from grasses to cow to human. However measurements are improving so they are acceptable for regulatory purposes. This was challenged by Prof. Schubik but supported by Prof. Dr. Somogyi, Director of BgVV ("regulators operate on best available science").

Knapp (Greenpeace Sweden) raised the point that limits should be set to protect species that are more sensitive than man, and was advised that this is a political and not a scientific question (Dr. J. Schuster, BgVV).

Toxic Effects of Organochlorines on Terrestrial Species/Wildlife.
Dr. Donald Tillitt, U.S. National Biological Survey.

First order decay of PCBs, DDE, HCB in fish and birds over past 20 years, but first order means that the lower levels are likely to persist for a long time. The question is where do these lower levels sit with respect to the threshold levels for mortality, etc.?

In his experience, adding an atom of chlorine to a molecule does not cause it to become toxic or persistent, and it does not make sense to group all chlorinated organics for wildlife risk/hazard assessment (except for TCDDs and similar compounds where he said that the best correlation between chlorinated organics and effects on wildlife occurs with dioxin-like equivalence).

Acute, Long-term and Reproductive Effects of Organochlorines on Aquatic Species.
Prof. Dr. John Giesy, Michigan State Univ.

Described work with albatross. Critical contaminants that are at or near a threshold level are PCBs, DDT and DDE. Of these, DDE is the lesser problem (lower levels).

Aerobic and Anaerobic Biodegradation of Organochlorines.
Dr. Jan Dolfing, Research Institute for Agrobiology and Soil Fertility, Ministry of Agriculture, Netherlands.

Concentrated on microbial degradation.

Higher chlorinated compounds are better degraded under anoxic conditions, lower chlorinated compounds are better degraded under oxic conditions.

Combined anoxic/oxic treatments look promising.

Drugs.

Prof. Dr. Gerhard Schlüter, Bayer AG.

"Introduction of chlorine into a molecule generally increases the chemical reactivity and hence the biological activity of an organic molecule".

Classes of drugs with adequate data to compare activity with and without chlorine are

- benzodiazepines
- dihydropyridines
- imidazoles, triazoles

"There were no hints for chlorine-related drug toxicity pointing towards estrogen mimics (probably because the types of compounds that are likely to be estrogen mimics would be avoided in the new drug search and screening process).

Pulp and Paper.

Dr. Keith Solomon, University of Guelph.

Looked at differences between chlorine and chlorine dioxide in bleaching of pulp and paper. In going stepwise from 100% chlorine to 100% chlorine dioxide, reduced quantities of chlorinated organics produced and reduced degree of chlorine substitution, so that

"mills bleaching with chlorine dioxide and employing secondary treatment present insignificant risk".

Estrogens.

Of particular scientific interest was his recent finding that sitosterol causes similar estrogen-mimicking effects to pulp mill effluents, and is found in pulp mill effluents. He is trying to define the NOEL. Another active component is present that is causing "MFOs" and he is trying to identify this also.

Abbreviations:

BgVV = Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin
BMU = Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit
EK = Enquête Kommission

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