# MEDICHEM CONGRESS – LIVING TOGETHER: THE CHEMICAL INDUSTRY AND THE COMMUNITY (Melbourne, Australia, 18–21 October, 1994)

The Congress was attended by 148 persons. Out of this number 100 participants represented Australia and 48 a number of other countries. During the Congress 40 papers and finidings were presented in 15 sections.

*D.M. Ferguson* (USA) presented a general approach to the risk assessmnet of chemicals. The author stressed that assessing risk one should take into account both risk of exposure among workers of a given plant and hazard to the environment in which the plant is located. Risk can be defined simply as the product of exposure time and magnitude of hazard posed by individual chemicals. In the United States methods for estimating industrial risk have been developed and approved by the US National Research Council (NRC). The Council released its publication known colloquially as the "Red Book". The NRC identifies four steps in risk assessment: 1. Hazard identification – determining what adverse effects the chemical in question causes in the human and/or animal; 2. Dose response – understanding the relationship between exposure (or dose) and severity of adverse effect; 3. Exposure assessment – defining the intensity, frequency and route of exposure, and 4. Risk characterizaton – combining the assessments of exposure and response. It also includes the degree of uncertainty associated with the estimate expressed in quantitative terms.

Since 1983 the US Environmental Protection Agency (EPA) has produced guidance on exposure assessments and risk assessments for different endopoints. The author stated that in practice risk assessment is difficult because one must rely on incomplete data. Hazard identification is the first step of a multi stage process. It can be based on case reports and individual findings. In the absence of human data, a more common starting point for risk assessment is toxicological studies in animals. The design and conduct of an animal study, determination of toxic effect, selection of animals, etc. affect the final assessment of experiment. The purpose of such studies is to find out that dose or level of exposure does not cause adverse effects. By definition, this is the "No Observed Adverse Effect Level" (NOAEL).

The author stressed, however, that there are significant differences in toxicity between animals and humans and also between individual animal species. These differences may apply to metabolism and they can even occur among different strains or between sexes of the same species. Interpolaton between high and low doses is usually necessary to find out whether there is a relationship between risk and the size of dose.

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In most countries, two forms of extrapolation are used, depending on the nature of the toxic endpoint – one for cancer, the other for non-cancer endpoints.

Taking into account aforesaid factors as well as time factor such terms as an "Acceptable Daily Intake" (ADI), a "Permissible Exposure Level" (PEL) and so on, are used.

Permissible levels differ greatly in individual countries because of the nature of the exposed population usually composed of healthy and strong people. Considering the environment, possible toxic effects on children and the elderly should be taken into account.

Assessment of cancer risk and mutagenicity is a quite different issue. Over the last years an idea has developed that no threshold of risk is permissible. This view is derived from experience with radiation.

According to this hypothesis, even a single molecule of a chemical carcinogen is capable of triggering the complex biological process that lead to tumor formation. In practice it is accepted, on the basis of mortality data, that risks in the range of $10^{-5} - 10^{-8}$ are regarded as of limited significane relative to other risks.

Assessment of cancer risk is complicated by the fact that symptoms can occur after a long period of exposure and even many years after cessation of exposure. Risk assessment is based on the relationship between lifetime daily doses and tumor incidence according to so-called Linearized Multi Stage (LMS) model.

In summary the author said that exposure related risk assessment should contain an evaluation of "strength" of toxic effect based on observations in humans and on animal studies, route of exposure, dose duration and if possible an analysis of the uncertainties associated with the risk estimates. It is obvious that a risk assessment and NOAEL dose should be revised when better exposure data become available.

*LA. Wallace*, Representative of the US Environmental Protection Agency, presented an interesting comparison of outdoor and indoor sources of exposure to toxic chemicals.

The author pointed out that only in the 1980s it became possible for the first time to measure outdoor and indoor exposure to a large number of chemicals. The US Environmental Protection Agency (EPA) studied exposure to organic chemicals of more than 1 000 persons representing more than one million residents of ten US cities. The study measured 24-hour personal exposures in air and drinking water to 20–25 target volatile organic compounds. Subjects were selected according to a stratified survey design. A total of about 800 subjects representing more than 800 000 residents of the various cities collected two 12-hour air samples and one or two tap water samples during a 24-hour period. Air samples were collected from outdoor and about 350 of the subject's home. The applied method was capable of detecting more than 100 volatile chemicals. In addition, breath measurements were taken by means of spirometer to identify the composition of air. It was indicated that seven volatile chemicals and four pesticides exceeded the minimum risk level of $10^{-6}$ by a factor of 10 or more. They were: benzene, vinylidene chloride, p-dichlorobenzene, chloroform, ethylene dibromide, methylene chloride and carbon tetrachloride and four pesticides: chlordane, heptachloaldrin and dieldrin.

Risk in families smoking cigarettes was particularly stressed (two studies showed that children of smokers die of leukemia at two or more times the rate of children of nonsmokers.

Among other interesting observations, exposure to benzene in attached garages is worth metioning. In the author's opinion chloroform found in water, particularly in hot water (showers), and chloroform used for disinfection of water in swimming pools proved to be other important sources of exposure.

Seven volatile organic chemicals have upper-bound risks ranging from $10^{-6}$ to $10^{-4}$ in the air at homes. In conclusion, the author pointed out that indoor air pollution is greater threat to public health than outdoor air pollution. He also turned attention to the indoor presence of such compounds as tetrachloroethylene from dry-cleaned clothes and DDT which may enter the home by being tracked in on people's shoes covered with sand and soil. Beverages produced with chloroform disinfected water, e.g. cola soft drinks (50 μg/L) are additional source of chloroform found in indoor air.

*P.A. Illing* (United Kingdom) discussed extrapolation from toxicity data to occupational limits.

Occupational exposure limits (OELs) were set among others by the Royal Society Study Group in 1983. They are based on the following elements: 1. Hazard – the situation that could lead to harm; 2. Harm – the loss to a human being or a group of persons consequent on damage; 3. Damage – the loss of inherent physical or biological quality; 4. Risk – the probability that a particular adverse factor occurs during a stated period of time.

The main point of the presentation was how far OEL could be useful in protecting workers from diseases and occupational damage in the form of ill-health. The author believes that exposure effects can be described as either stochastic – carcinogenic and mutagenic compounds – or non-stochastic – where the severity varies with the exposure level and for which there may be a threshold. Stochastic compounds exist for individual workers while non-stochastic ones apply to a whole group of persons exposed. For compounds of dose related toxicity the author introduced an expression "No Observable Adverse Effect Level" (NOAEL) and he stressed that there is no threshold for carcino- and genotoxic compounds that could be assumed as NOAEL.

Occupational sensitation represents a peculiar problem and a NOAEL can be difficult to determine in this case. Extrapolation from a study in one group of people or animals to another group is limited by a number of factors. Determining a NOAEL on animals one or several genetically inbred strains are usually used what may become a significant source of an error. In practice, it would be more advisable to use animals of various strains and, at least, of several species. Scaling of toxic substance concentrations based on mg/kg body weight or surface area is also a far reaching extrapolation. As far as the length of the study on animals is concerned, the author presumed that it should not be prolonged beyond 6 months. Routes of administration of toxic substances (inhalation, alimentary tract, skin) should also be considered.

Occupational exposure limit (OEL) is set through a relevant scaling of NOAEL doses, however, it needs to be constantly verified for each substance when better data based on human and animal observations become available. According to the author's opinion expressed after Hart and Jensen, the final assessment of an OEL is not feasible.

*A.I. Terr* (USA) dealt with multiple chemical sensitivities (MCS). This is a very complex issue because of unclear clinical symptoms. Primarily "multiple chemical

sensitivities" was described as neurasthenia and now it is known as the chronic fatigue syndrome. Patients with the diagnosis of MCS are almost exclusively adults and 60–80% of them are women. Most common complaints are poor concentration, a feeling of lightheadedness, short-term memory, fatigue or sleep disturbance. Among somatic symptoms muscular pains, headache, paresthesias, mucosal irritation, etc. are most frequently reported. The author presented a table of most common substances causing multiple sensitivities. Physical examinations reveal no objective findings of abnormalities. Neither anatomopathological changes nor microscopic pathology have been reported. The prevelance of the condition is also unknown. Various ways of desensitization and different treatment modalities have not yield thusfar positive effects. A number of theories of disease causation exist such as adaptation theory, allergic theory, auto-immune theory and immunotoxic theory. None of those theories, however, have been proven by detecting relevant antibodies or other immunological changes. The author stressed that the clinical features of MCS bear no resemblance to allergy, auto-immunity or immune deficiency. A neurotoxic theory is based on an irritating effect of toxic substances on the olfactory nerve and its connections to the limbic system and hypothalamus.

The author stated that a theory, popular among a certain group of physicians, according to which exposure to low levels of numerous chemicals can cause an immune system disease has not been proven to date. In his opinion none of proposed hypotheses on MCS pathogenesis has been scientifically proven.

*G. de Jong* (The Netherlands) dealt with the performance of health management in preventing occupational diseases. The European Chemical Industry Council (CEFIC) – the Brussels-based organization representing National Chemical Federations and Chemical Companies of Europe issued Guideliness on Occupational Health Management in 1991. The author is of the opinion that a key element, namely monitoring of performance is missing among numerous parameters of the health management system in industry. Development of better management systems should prevent from major ecological accidents such as those which took place in the late eighties (the Sandoz fire, the Exxon Valdez oil spill, etc.).

On the basis of experience gained as a result of those major accidents and developed safety systems, an integrated management system for health, safety and environment is now being introduced in Shell companies world-wide. The system is based on the Plan-Do-Check-Feedback/Improve "Quality Loop".

The hazard management process embraces the following steps: hazard identification, hazard assessment, hazard control, hazard recovery, health risk assessment and others.

The author discussed then types of performance monitoring system in occupational disease prevention. He distinguished two types of monitoring systems – active comparing achievements against pre-determined performance criteria and – reactive monitoring incidents, illnesses, absence and damage.

Among performance indicators the author pointed to incidence of occupational diseases classified to 10 categories and time lost due to illnesses including the proportion of occupational diseases.

Among occupational diseases listed by the author there are, among others, infectious and parasitic diseases, disorders due to mental stress and other illnesses generally approved as occupational ones.

Measuring health performance is considered as a key requirement for successful management of occupational health. It is, however, complex and difficult because of reluctance to report on occupational diseases. The comparison of incidence of occupational illnesses is the only method for performance monitoring.

*G. Adams and J. Bisby* (Australia) presented the results from the epidemiological program in the Australian petroleum industry. The program covered a twelve-year study of cancer and leukemia incidence because of benzene exposure. The authors stressed that smoking doubles the risk of developing cancer and exposure to benzene increases about twice incidence of leukemia.

*M. MacKellar* (Australia) presented his paper entitled "Community views – their impact on Australia's chemical industry". The author reviewed results of a study run in November 1992 which covered 800 persons in five Australian cities living near or remote from chemical plants. About 90% of people knew nothing about the industry, 75% were concerned about the industry, 42% believed that the risks of the products and operations outweighted the benefit and 49% of people thought that the industry had improved its HSE performance but only because it was forced to do so. In addition to the National Community Advisory Panel twenty Local Community Panels have been set up around major Australian chemical manufacturing centres (there were only two in 1988). The Local Community Panels involved in activities of a given plant deal with such issues as reduction in noise, odour and volatile toxic substance emissions as well as tree plantings in streets and buffer zones around the facilities, etc. The Advisory Panel was also involved in placement of waste substances. Recently, community work groups have involved both industry and community representatives. Several companies present to their neighbours data on their emissions harmful to the environment. Some of those companies organise "Open Door Days" to host local community visits to their facilities. Fifty open sites were visited by 30 000 persons.

Community involvement, in the authors' opinion proved to be very beneficial in the regulation of the health, safety and environmental performance of the chemical industry. Due to such involvement it was possible to consider factors which are most strenous for people and areas located in the vicinity of industrial plants. The communitty factor complemented limited, as is natural, Government inspection capabilities. It also contributed to reducing substantial costs to companies of accidents, emissions and so on.

*D. Douglas*, Consultant in Occupational and Environmental Health (Australia) presented a paper on exposures of workers to organic compounds in bitumen fumes. Workers exposed to bitumen fumes for many years reported headaches, irritation and dryness of the eyes and upper respiratory tract, coughing and nausea. The frequency of these health effect have increased with the use of polymer modified bitumens. New methods for measuring both inspirable particulates and fumes released during bituminization, including a quantitative measurement of polycyclic aromatic hydrocarbon concentrations, have been applied. The results showed that the measurement of inspirable particulates were not appropriate for assessing exposure while the measurement and analysis of organic compounds in the vapour phase of the fume, including naphthalene, methylated naphthalenes, polycyclic aromatic hydrocarbon, revealed that naphthalene and its derivatives pose the greatest hazard to workers. In vapours under study benzanthracene, benzopyrene, chrysene and pyrene were not detected. It was also indicated that the temperature

of the bitumen, whether conventional or polymer modified is the most important factor in fume generation.

*D.M. Heydanek* (USA) presented the role of community advisory panels at the Dow Chemical Company in preventing from environmental hazards.

*J.M.M. Meijers, G.M.H. Swaen and LJ.N. Bloemen* (The Netherlands) dealt with a comparison between animal and human data in cancer risk assessment. The study was based on the rich literature data. The authors analysed 37 substances generally considered as carcinogenic. They conclude that a quantitative risk assessment based on experimental studies departs considerably from the outcomes of epidemiological studies. Therefore, one has to be very careful when extrapolating experimental outcomes from animals to human working conditions.

*C. Mitchell* (Australia) discussed occupational asthma. Describing pathogenesis of the disease, the author turned attention to the fact that most agents causing asthma are high molecular weight organic compounds capable of producing specific IgE antibodies, while the mechanism by which the majority of low molecular weight compounds cause asthma is uncertain. It is quite possible that potent irritants damage the airway epithelial cells and produce inflammation which, if severe or recurrent, may lead to the development of sthma. The author also pointed that development of asthma is very often caused not by one but by two or even more factors. In his opinion a worker should be early removed from occupational exposure when the first symptoms of asthma are manifested since working in the offending environment with treatment suppressing symptoms of asthma may lead to a persistent condition of bronchospasm.

*H. Lagast et al.* (Belgium) presented findings which deny that there are links between polypropylene production and colorectal cancer.

*P. Hope et al.* (Germany) discussed their study aimed at answering the question: "Are there clearly characterizable risk groups towards moderately elevated concentrations of environmental ozone?" The study covered three age groups: 41 senior citizens, 43 juvenile asthmatics and 41 forestry male workers. The concentrations of ozone, the subjects were exposed to, were determined. The lung function measurements were carried out. The comparison of changes showed that while the senior citizens seemed to benefit from the exposure to ozone, the two other groups of subjects manifested decrement of the lung function.

*I. Nakamura et al.* (Japan) focused on the effects of beryllium on porphyrin metabolism. The study involved experiments on mice and measurement of enzymes related with porphyrin metabolism in erythrocytes and liver. A significant effect of beryllium on the activity of porphobilinogen deaminase (PBG-D) in the liver and erythrocytes was indicated.

*J.M. Davis, D.J. Svendsgaard and E.J. Calabrese* (USA) discussed U-shaped dose-response relationships in toxicology. The authors oppose this kind of response against classical linear responses with directly dose-related toxic effect. Various designs of U-shaped dose-response relationships were described on the basis of a broad literature review. The authors estimated the incidence of U-shaped relationships at a 12 to 24% rate. That suggests the need to consider such a response when assessing the effect of toxic doses or permissible concentrations of given substances.

*A.J. Woolcock* (Australia) dealt with effects of chemicals on lungs. High concentrations of chemicals may result in toxic effects such as oedema (chlorine,

carbon disulfide, etc.). Sensitisation is evoked mostly by exposure to isocyanates, wood dust, plicatic acid (cedarwood) and platinum salts.

*A. Zober and H.G. Ott* (Germany and USA) delivered a paper on "Epidemiological analysis of health data currently available in industry". The authors used the BASF Medical Information System. The Occupational Medical and Health Protection Department of BASF Company employs at two clinics 20 occupational health physicians who are responsible for about 50 000 employees.

The authors presented various applications of health data collected by the occupational health service such as targeting of wellness programs covering among others workers with hypercholesterolemia, low back pain, etc.; prevention of work-related injuries, attention was turned to exposure to UV-radiaton among workers who were not welders but happened to be in the same work areas and were not wearing proper eye protection.

Finaly, at the request of the Ministry of Labour they examined the health condition of workers exposed to N,N dimethyl forman (DMF). There were no significant differences in incidence between those exposed to DMF and other grups of workers. The authors also investigated possible etiologic factors among them N-vinylpyrrolidone (NVP) and 2,3,7,8, tetrachlorodibenzo-p-did. They utilized referent data from liver enzymes tests but in their opinion analyses of lymphocyte subsets should be performed in regard to these substances.

The authors stress that computerization of all data collected by the occupational health service is essential.

*F. Schuckman* (Germany) devoted his paper to the effects of accidental release of mixture of organic chemicals in a production plant of a big chemical company in Frankfurt. The major part of the mixture consisted of o-nitro anisole classified as "weakly carcinogen". The author did not present final conclusions. He only mentioned that irritation of mucous membrane observed in persons exposed had been rather caused by the presence of the mixture of caustic soda and formic acid.

*V. Fiserova-Bergerova* (USA) discussed the development of biological exposure indices indicating the degree of occupation exposure to harmful factors. The indexes named BEI (Biological exposure indices) in the United States and BAT (Biologische Arbeitsstofftoleranzwerte) in Germany should encompass data resulting from the following observations: animal studies and case reports, laboratory studies in volunteers, field studies comparing results of air monitoring in the workplace and levels of determinants in specimens collected from workers. In addition, epidemiological data on unexposed population as well as pharmaco kinetic models should be considered.

The following variables should be taken into consideration in determining the indices: degree and duration of exposure (usually BEI values are determined for chronic exposure — 8 hours per day, 5 days per week while performing work with a moderate energy expenditure — 50 W); timing and duration of sampling essential for determination should be given in each BEI value. In addition, biological and physiological parameters of people living in the vicinity of plants — nonexposed to other chemical hazards, should also be considered.

The author concluded that BEI values should be compared with TVs (Threshold Limit Values) and whenever BEI exceeds the no-effect level or a change of the TLV is proposed, revision of the BEI and the TLV is needed.

*P.R. Adams* (Australia) presented the significance of polychlorinated biphenyls (PCBs) to health of workers and persons non-occupationally exposed to them. PCBs

consist of two benzene rings and two or more chlorine atoms. They are non-flammable compounds of excellent dialectric qualities which make them attractive to industry and therefore they are widely used. The first incidence of PCB poisoning applied to rice contaminated with PCB containing oil. Chloracne was one of the leading signs in those who became ill. A similar incident occurred in Taiwan. PCB mixtures may contain several types of chlorinated compounds such as polychlorinated naphthalenes and dibenzofurans. All those compounds are very stable in the environment. PCBs have not been manufactured in Australia, however, they are still found in transformers and capacitors used throughout Australia. Removal of PCB waste is a separate question. Animal studies indicate considerable differences in toxicity in different species. In humans, lower levels of PCBs may produce such effect as headaches, abnormal fatigue and joint soreness. Higher level may result in dermatological effects.

Following the studies on possible carcinogenic effect of PCBs, they are currently classified as Category 2 carcinogens, the so-called probable carcinogens. It was stated that a daily dietary intake of PCBs is 0.2 μg/kg of body weight that is much below a dose considered as a toxic one (200 μg/kg of body weight per day). Exposure to PCB through food intake is usually through the consumption of fish.

The author concluded that the tendency towards reducing exposure of the whole population to PCBs should be maintained, however, a balanced approach is required since findings on their toxicity has not been proven to date.

*K. Kotseva* (Bulgaria) focused on prevalence of arterial hypertension and coronary heart disease in xylene production workers. A total of 160 xylene production workers and 152 controls properly matched were investigated. A significantly higher prevalence of arterial hypertension was observed in workers exposed to xylene and especially in those with long employment.

Good organization of the Congress deserves a special mention as well as availability of sets of submitted papers and abstracts highly appreciated by participants.

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