Risk Assessment of Chemicals A Central European Perspective

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Introduction

During the last four decades in the Czech and Slovak federal Republic (CSFR) and Hungary, similar to the previous Soviet Union and all the Central and East European countries the prevention of the adverse health effects of chemicals in occupational and environmental settings, drinking water and food of population was intended to be achieved by determination and compulsory observance of hygienic limit values (MAC, TLV, ADI). From recent political developments it can be expected that due to the decay of the former Warsaw Pact and the related Council for Mutual Economic Assistance (CMEA) the next development of risk assessment will reflect that new situation. The OECD principles of toxicity testing and risk assessment of exposure to chemicals will be sooner or later accepted in principle in the framework of a general economic integration of Central and Eastern European countries with EEC. During the 80s there was a growing feeling of the necessity to harmonize the activities of OECD and CMEA countries in the field of toxicological methodology and approaches to risk assessment of chemicals because of the growing production and mutual trade including transport of industrial and agricultural chemicals. As a contributory factor supporting this effort there was growing cross boundary air and river pollution in Europe.

The former Council for Mutual Economic Assistance was an intergovernmental organization of 10 countries with a number of other countries and agencies cooperating with it in its work. CMEA was, and OECD still is concerned primarily with economic development but both had stated commitments to protecting human health and the environment. To help to mutual understanding and to promote harmonization of above mentioned obligations and commitments of the both organizations United Nations Environment Programme's International Registry of Potentially Toxic Chemicals and The International Programme on Chemical Safety (UNEP/IRPTC/(IPCS) convened an International Consultation on Toxicometric Methodology held in Moscow in November 1985 and IPCS organized a Technical Review Meeting to compare CMEA and OECD Approaches to Toxicity Testing and Risk Assessment in Geneva, May 1987 (UNEP/IRPTS/IPCS 1985; UNEP/ILO/WHO/IPCS 1987). A part of this effort was the publication of a Collection of Training Materials in Preventive Toxicology in the USSR within the UNEP/IRPTC project, Control of Hazards Posed by Chemicals to Human Health and the Environment (UNEP/IRPTC 1984).

Calculation of hygienic standard values

The methodological pattern of this approach in our countries has been based partially on the results yielded by animal experiments and partially on epidemiological data gathered in industry (Sanotsky, 1974; Ulanova, 1984; CMEA, 1986). As to the animal experiments the spectrum of parameters examined was wider, or at least more differentiated compared with the original the OECD set due to the inclusion of such parameters as e.g. conditioned reflexes and

immunological parameters. This is against the background of previous substantial differences between some of MACs or TWAs values in CMEA and OECD countries. This difference was not of a constant nature and there are some examples of opposing situations e.g. occupational MAC for vinyl chloride (VC) which is from four to ten times lower in OECD countries – 1 mg per m^3 or 1 ppm (which equals 2.6 mg per m^3) compared with the standard of 10 mg VC per m^3 in a work room air valid in CSFR, Hungary and Poland.

The "limit value" of vinyl chloride was calculated on the basis of the following principles (Ungváry, 1981), taking into account the results of the studies documenting its carcinogenic effect (Maltoni et al, 1974; Janysheva and Balenko, 1966; Shabad, 1979), as well as some physiological parameters.

Table 1: Tumour frequency in Sprague-Dawley rats exposed to VC (exposure: 4 hours/day, 5 days/week, for 52 weeks)

VC concentration	Initial No. of animals	No. of animals surviving	Tumours of zymbal-gland	Nephro-blastomas	Hepatic angio-sarcomas	Other angio-sarcomas	Brain neuro-blastomas	Other tumours	All
Control (air)	68	58	0	0	0	0	0	10	10
50	64	59	0	1	1	1	0	10	13
250	67	59	0	6	4	2	0	7	19
500	67	59	4	4	7	2	0	8	25
2 500	74	59	2	6	13	3	5	7	36
6 000	72	60	7	4	13	3	7	10	44
10 000	69	61	16	5	9	3	7	11	51

Maltoni et al (1974) – observation up to the 120 week.

Based on the data shown in Table 1 we have established, that the malignant tumour frequently induced by VC redoubles with the increase of the dose ($y = 10.7$ times $X^{0.3}$). Frequencies of VC and spontaneous tumours occurring in the control group (0/58, 10/59, respectively) do not differ significantly from the frequencies of VC and spontaneous tumours in Sprague-Dawley rats exposed to 50 ppm VC concentration (3/59, 10/59, respectively); 1 ppm = 2.6 mg m^3 VC.

The Sprague-Dawley rats weighed 600-900 g at the age of 1 year. Taking into account the 52 weeks of exposure, the mean body weight can be taken as 600 g. On this basis, the respiratory volume of the animals is: $2.1 \times 600 \times 0.75$ ml/min = 945 ml/min $\approx$ 1 l/min. The total volume of the air inhaled by one animal during the whole exposure time equals: $1 \times 60 \times 4 \times 5 \times 52 = 62.400$ litres = 62.4 m^3 in the case of 50 ppm VC concentration this volume contains 8110 mg of VC; in case of complete absorption 8.112 g of VC gets into each rat weighing 600 g, which is not carcinogenic. (Only 40% of VC is absorbed, the rest is exhaled – Bolt, 1980.)

Considering a man weighing 70 kg:

$\frac{70}{0.6} \times 8.110$ g VC = 946.4 g VC (which is not considered carcinogenic for Sprague-Dawley rats)

If the respiratory volume of a worker during light physical work is 15 litre/min, during 40 years of employment with 50 weeks of 40 working hours each, the total volume of inhaled air will be: $15 \times 60 \times 40 \times 50 \times 40$ litres = 72 000 000 litres = 72 000 m^3.

946.4 g VC divided by 72 000 m^3 gives the concentration which is not carcinogenic. This is the following:

$$\frac{946\,400\ mg}{72\,000\ m^3} = 13.14\ mg/m^3$$

Considering that
1. Sprague-Dawley rats are more sensitive to the tumourigenic effect of VC than the other kinds of rats, as well as hamsters and rabbits;
2. According to human epidemiological data, VC hepatic angiosarcoma had occurred in places where several hundred ppm of VC exposure lasting for decades was proven, the value of 10 mg/m^3 seems to be well founded, as it contains a safety factor of at least 30-100%.

Based on these, the workplace limit value (MAC) of VC recommended by us is 10 mg/m^3. This means that the concentration of VC in the work area must not exceed 10 mg/m^3.

The MAC value of the vinyl chloride monomer is determined by the concentrations, doses which do not cause tumours, mutations, and immune defects on the basis of the data presently available (Bencko et al. 1988). The other harmful effects appear only at significantly higher exposure values.

In the CSFR, Hungarian and Polish workplaces the maximal allowable concentration (MAC value) of vinyl chloride determined as a standard is 10 mg/m^3; the MAC value is marked by the small letter k, which indicates the carcinogenic property of the substance and at the same time that the substance has no threshold value which could guarantee the protection against tumourous diseases ("carcinogens have no threshold value"). Thus, this, MAC value represents an acceptable risk.

The Hungarian ambient air hygienic standard for VC immission gives 5 $\mu g/m^3$ limit value for the priority protection areas both for 24 hours and 30 minutes, and 100 $\mu g/m^3$ limit value for areas of II category protection both for 24 hours and 30 minutes. In Hungary there is no VC monitoring either in the residential areas or in the natural environment. A limit value is used for emission calculations when planning and operating factories and sanctions against factories are based on calculation of emissions. In the CSFR the regional ambient air standard for VC MAC day mean 30 $\mu g/m^3$, and 80 $\mu g/m^3$ that cannot be exceeded during 30 minutes sampling period has been accepted. In contradistinction to Hungary, in the CSFR the concentration of VC is regularly monitored in the vicinity of chemical plant polluting the environment with VC emissions in Upper Nitra Valley, Middle Slovakia region.

In the majority of our countries, all chemicals listed in the standard ("Air purity requirements in the workplace") are controlled (measured and registered) by environmental monitoring. Most significant air contaminants such as SO_x, NO_x and particulate matter are also controlled by continuous environmental monitoring in residential, ambient air of industrial agglomerations.

Chemical contamination of drinking water is controlled systematically, while the chemicals in food (in vegetables, fruits) are controlled only randomly. Unfortunately – possibly with the exception of drinking water – the environmental monitoring is not yet satisfactory.

In contrast with environmental monitoring activity one of the most important accomplishments of occupational hygiene and health in some Central and East-European countries is that, for about 20 chemicals, biological exposure indices are being regularly monitored, and if their levels exceed the biological limit values, they must be reported. A report is followed by the workplace physician and/or the hygienist of the locally responsible control body to identify the source responsible for the increased exposure and to control it. For example, in Hungary, between 1982 and 1991, 20 chemicals were responsible for about 2000-4000 cases of reported increased exposure annually, all detected by this monitoring. This represents at least 1.5%-2.0% of those occupationally exposed to the monitored chemicals. Just for illustration the total number of chemicals used in Hungarian industry is estimated to be between 20,000 and 40,000 (Ungváry, 1990, 1991).

Generally special attention is paid to both environmental and biological monitoring of mutagenic and carcinogenic chemicals.

The maximum allowable concentration (MAC) of nickel valid in the workplaces is 0.0005 mg/m^3. The letter "k" with the MAC value in the standard indicates that the substance is carcinogenic. (All chemicals listed in 1, 2A or 2B category by the International Agency for Research on Cancer (IARC) are marked by letter "k" in the standard: "Air purity requirements in the workplace"). Limit values guaranteeing safety for carcinogens generally are not recognized today. This principle, however, cannot be observed in case of chemicals, which are at the same time essential elements. Nickel is well known to play an important role in the regulation of the cardiovascular system (Anke et al., 1984; Mancinella, 1991). Thus it can be included in the list of substances having two limit values – one minimal and one maximal. Above the maximal limit value the substance increases the frequency of tumours, while below the minimal limit value it causes deficiency. Based on this principle, nickel has a real biological and environmental limit value (excluding the risk of tumours). The biological limit value of nickel is 100 μg Ni/l blood (1.70 μmol/dm^3). The number of workers with nickel exposure in Hungary can be estimated as 500-600. Biological monitoring of nickel has been compulsory since 1986. The number of cases of increased nickel exposure reported varied between 5 and 20 in the years 1986-1991. Due to the small number of cases of increased exposure reported, changes of the risk of tumours caused by nickel could be hardly determined even if the time since the first year of reporting – 1986 – was longer than 10 years which is necessary to the manifestation of tumours (Ungváry, 1992).

In the hair of workers exposed to nickel the concentrations of nickel increased (up to a mean value of 216.75 μg/g). At the same time immunological parameters (IgG, IgA, IgM) were elevated. A significant rise in the concentration was also recorded in the case of A1AT, A2M, CPL and LYS (Bencko, et al., 1986). It can be concluded that biological monitoring and immunological parameters increase the validity of risk assessment of adverse health effects of nickel.

Biological monitoring of environmental pollution by toxic metals

The data provided by biological monitoring can constitute a basis for identifying areas excessively contaminated with industrial emissions, including their geographical delimitation. This aspect is of growing importance from the point of view of public health authorities. Against the background of growing interest is the simple fact that the total extent of environmental pollution is often difficult to assess, both qualitatively and quantitatively. Analyses of non-systematically collected air and surface water samples yield virtually worthless data in this respect, for the actual degree of environmental contamination may vary across a relatively wide range.

Ideally from the technical point of view, a continuous measurement of the environmental pollution can be effected through the use of a network of automated monitoring systems preferably those capable of automatic sampling, analysis, registration and evaluation of data. These automated monitoring systems are not easily accessible at present, both technically and economically, and their use in the near future is in Central Europe expected to remain limited to localities having the greatest degree of environmental pollution (Bencko, 1991).

As an alternative to the technical approach to this problem, biological indicators could be used to monitor pollution of the environment. What we understand by the term biological indicators could be used to monitor pollution of the environment. What we understand by the term biological monitoring is a systematic collecting of human material or other biological specimens with a consequent determination of the substance concentration, its metabolites or biotransformation products in these specimens (IAEA, 1976). This approach appears to be particularly well suited to demonstrating environmental pollution by potentially toxic trace elements, including toxic metals.

Already in the first half of the thirties Teisinger (1936) used biological methods for monitoring exposure in persons occupationally exposed to lead. With respect to the use of this approach for monitoring of environmental pollution mention should be made of the pioneer work of Svoboda (1936) who described approximately at the same time the so called Tesín's disease in honey bees caused by arsenic contamination of the environment. Both these examples demonstrate that at least half a century old Czechoslovak tradition of using biological methods to monitor the environmental pollution and the exposure of man to toxic trace elements, including toxic metals.

It is now common knowledge that e.g. peat moss plants, due to the special anatomic structure of their respiratory system, have the ability to accumulate toxic metals which are present in the air in the form of aerosols. As an example, impacts on animal kingdom species such as the above mentioned count losses or even extinction of honey bee populations may serve to indicate environmental pollution in areas affected by emissions containing arsenic.

Of animal species, game animals such as hares have repeatedly proved to be useful as indicators of environmental pollution (Nováková and Paukert, 1973). Considering the depression which affected the hare population in Central Europe and also the fact that the use of hare is limited to a relatively short time period of the hunts in the autumn, some authors decided to try the use of a murid rodent, the common vole. The advantage of the common vole lies in the fact that it can be caught all the year round and that its radius of activity amounts to about 10 m only, so that this species may provide more detailed information (Paukert and Obrusník, 1986). In our field studies we preferred to test biological material from domestic rabbits (Bencko et al., 1981).

The examination of plant and animal samples is able to complete the information obtained by the examination of humans. It may be even assumed that the changes of body burdens of toxic metals in animals start earlier than those in man, because the animals are exposed to the impact of contamination more directly, by all routes, including the local food chain. Thus, the free-living animals might signal in advance the danger threatening the human inhabitants. Interestingly, hematological changes found in hares living in an area polluted from a known source of industrial emissions were comparable with those encountered in local children. Similarly, we found virtually identical concentrations of arsenic in the hair of children and hair of rabbits living in the same locality (Bencko, 1990).

The health risk assessment of environmental pollution is becoming increasingly a major public health concern. In this context a primary concern is the assessment of human exposure. For this the examination of a suitable human tissue appears to be more appropriate than the analysis of plant or animal materials currently used in ecological studies to demonstrate environmental pollution. The human biological materials that are accessible for sampling include blood and urine, but also hair and nails. Successful attempts have also been made to measure e.g. lead, and of non metal elements fluorine accumulation in deciduous teeth to demonstrate over exposure to these elements in children (Cikrt, Bencko, 1990).

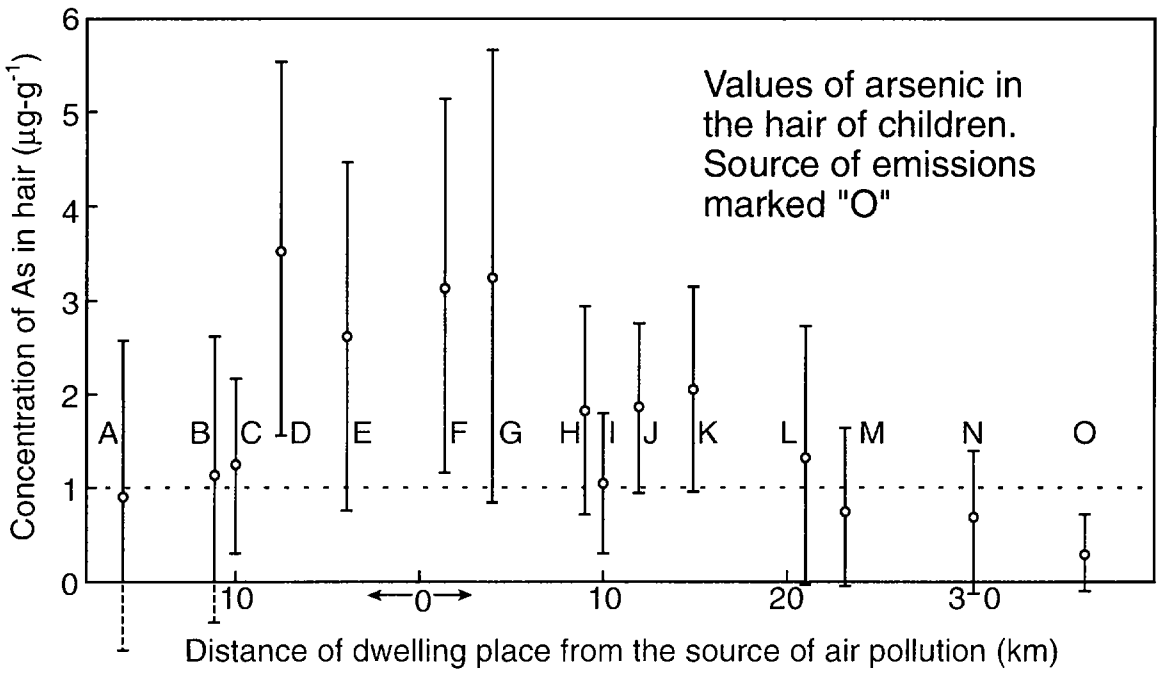

Figure 1

Our study conducted in the mid-60s demonstrated that determination of arsenic in human hair has potential utility as an indicator of the environmental contamination with this noxious agent (Bencko, 1966). Later studies Figure 1 revealed that a correlation can be established between arsenic content of hair and the expected degree of arsenic contamination of air (Bencko and Symon, 1977). These studies show that the tests for arsenic content of hair, used for years to demonstrate the existence of arsenic exposure for the purpose of forensic or industrial toxicology, are equally applicable to environmental pollution monitoring if the method of group examination is applied. Today, extensive data are available in the literature, including monographs which document the advantages of this approach. The usefulness of hair analysis for the demonstration of exposure to toxic metals in man has also been repeatedly confirmed in a series of our studies concerned with toxic trace elements e.g. manganese, lead, nickel, cobalt, antimony and mercury (Bencko et al., 1986).

Sampling, transport and storage of hair samples is incomparably easier than sampling, transportation and processing requirements of blood or urine samples, the most common specimens used today to demonstrate human exposure to a variety of noxious environmental agents. Human hair samples are also very easy to preserve for later control re-analyses.

In contrast to blood and urine specimens, hair should first be cleansed of external contaminants prior to element analysis. Despite the fact that there is no general concensus on how the washing procedure should be done the procedure recommended by IAEA (1977) should be preferred to other techniques that are not standardized. In this context it should be noted, however, that excessive external contamination of hair may reflect massive exposure to a given environmental pollution, which is actually what is to be demonstrated by these tests in most instances (Bencko, 1990).

Naturally, the use of human hair analysis technique is far from being the universal tool for monitoring exposure to environmental pollutants and considering the broad spectrum of pollutants encountered in the general environment one can hardly expect that such a screening tool would ever exist. However, for a great majority of toxic trace metals this technique has proved well suited for the monitoring of over exposure of man originating either from man-made or natural sources.

Conclusion

On basis of the examples given we have tried to demonstrate some specific features of risk assessment of exposure to chemicals in environmental and occupational settings. The objective of our presentation is not an exhaustive description of existing differences between previous CMEA and present OECD approaches to risk assessment and management. Although the approach to risk assessment and management was similar in many respects in the CMEA countries, implementation and hygienic practice was different in the individual countries in terms of many details and effectiveness. Due to long lasting experience with environmental pollution including health impact on humans e.g. in the "Dirty Triangle of Europe" and other heavily contaminated areas a considerable knowledge has been gained. In some instances there are quite unique examples of exposure of humans to specific pollutants in environmental and occupational settings.

Bearing in mind that in our part of the world:

- workplaces are frequently in poor condition from both technical and technological point of view; therefore the workplace contamination, and the risk of adverse effect of "workplace-chemicals" (among them carcinogenic and mutagenic ones) is relatively high

- emissions arising from industry are not adequately controlled, the environment in industrialized areas is highly contaminated

- the residential air in those areas and capitals of our countries is frequently extremely contaminated by industry, local heating and traffic – SO_x, CO_x, NO_x, O_3, PAH, Pb and particulates

- rivers draining industrial areas are heavily contaminated and some areas have severe problems with drinking water quality

- the food basket of our population is contaminated by some agrochemicals due to their local over use e.g. by Cd, nitrates, PCBs

- a decisive part of industrial as well as municipal waste is not properly treated and disposed
- at least part of the gathered knowledge has been published in local languages only, another part has been "confidential" and not allowed to be published.

For that we would like to propose:

- to collect existing knowledge concerning both methodology and local epidemiological studies including those in Central and East European countries
- to analyse critically and evaluate the knowledge and experience and present it to the international scientific community and international institutions and organizations such as UNEP, ILO, IPCS, IRPTC and last but not least OECD
- these institutions/organizations could take part in harmonizing further activities.

To achieve this we would recommend the organization of

- post graduate education or seminars for experts from Central and East Europe dealing with risk assessment and management to harmonize approaches to the problem
- to introduce regular interlaboratory quality control practice procedures for environmental and biological monitoring
- to establish an international system of regular exchange of information concerning environmental quality control and management.

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