

REVIEW

HUMAN EXPOSURE ASSESSMENT LOCATION (HEAL) – HISTORICAL REVIEW

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The first part of the review describes events and newly acquired knowledge that anticipated the making of the HEAL project and its preparatory phase. The pilot study relied on the belief that the total exposure assessment should take into account different pollutants and their relative contribution in the human intake from different environmental media such as air, drinking water, food chain, and soil. The pilot study included exposure assessment to lead and cadmium, nitrogen dioxide, hexachlorobenzene, and DDT-complex. Concurrently, another study on indoor air quality in Kenya and Gambia took place.

In its second phase, the project evaluated the actual trends and outlined potential future directions. It was decided that the project should focus on the promotion of exposure studies, particularly in developing countries, and that it should establish a closer relation with health risk assessment and environmental epidemiology.

The last part of the review describes the participation of the Institute for Medical Research and Occupational Health in Zagreb, Croatia in the project and in related research activities performed after the pilot phase.

Key words:

asbestos, heavy metals, nitrogen dioxide, organochlorine pesticides, pilot studies, preparatory phase, quality control, radionuclides

PROJECT BACKGROUND AND THE PREPARATORY PHASE

Following the UN Conference on the Human Environment in Stockholm in 1972, World Health Organization (WHO), supported by UNEP's Environment Fund, initiated global monitoring networks for the air, water and food. These networks have been a part of the Global Environmental Monitoring System (GEMS) for the air since 1974, and for the water and food since 1976.

Based on several research findings (1), the awareness has gradually emerged that data based on environmental surveillance may not be representative for human exposure. The fixed monitoring or sampling stations of the GEMS-Air programme are situated in residential, commercial and/or industrial parts of the cities. Urban population, however, moves around and spends most of the time indoors. Samples of food are most often taken from types which are thought to be suspect or contaminated. People's diet varies, however, and is dominated by cooked or preserved food. The quality of drinking water is monitored for the piped distribution system, but the actually consumed water may not be identical to that of the water supply. Therefore, a government-designated expert group which met in 1977 (CEP/77.6, see Table) recommended that the WHO/GEMS environmental monitoring programme be expanded to include pilot projects on biological monitoring and on detailed studies of human exposures to air pollutants.

Following these recommendations WHO in cooperation with UNEP and a team of experts developed a second air monitoring project which also forms a part of GEMS, but which consisted of a number of pilot projects on exposure monitoring in different parts of the world. The purpose of these studies was twofold: to test various techniques for determination of the exposure to air pollutants and to gather data on exposure conditions in different cities around the world. By 1982, two of the studies were completed: measurement of human exposure to carbon monoxide and suspended particulate matter (SPM) in Zagreb (2) and to sulphur dioxide, nitrogen dioxide and SPM in Toronto (3), followed in 1984 by the study of human exposure to SPM and sulphate in Bombay (4), and in 1985 to carbon monoxide and SPM in Beijing (5). WHO/UNEP pilot project on the assessment of human exposure through biological monitoring has been launched with the aim to identify the most reliable biological indicators of exposure. The project was divided in two parts: Assessment of Human Exposure to Lead and Cadmium through Biological Monitoring and Assessment of Human Exposure to Selected Organochlorine Compounds through Biological Monitoring.

The following countries participated in the first project: Belgium, Iran (only in the initial phase), Israel, Japan, Mexico, People's Republic of China (from May 1981), Peru, USA, and former Yugoslavia (Croatia). The coordinating institution was the National Institute of Environmental Medicine and the Department of Environmental Hygiene of the Karolinska Institute of Stockholm, Sweden. Lead and cadmium were measured in samples of venous blood in about 200 teachers in each of the participating country to obtain an indication of recent exposure. Cadmium was measured in samples of kidney cortex (about 50 cases of sudden death) to provide a measure of lifetime accumulation (6).

Following countries participated in the second project: Belgium, Germany (Federal Republic), India, Israel, Japan, Mexico, People's Republic of China, Sweden, USA and former Yugoslavia (Croatia). The coordinating institution was the National Food Administration of Uppsala, Sweden. Selected organochlorine compounds (mainly p,p'-DDT, p,p'-DDE, and β -HCH) and polychlorinated biphenyls (PCBs) were determined in samples of human milk. Samples were collected mostly during 1981–82 from at least 50 mothers in each country (7).

A proposal for further development of the WHO health related environmental monitoring programme of GEMS was made in March and June 1982 (see Table 1). It was suggested to establish 10–15 Human Exposure Assessment Locations (HEALs)

enabling a comprehensive exposure monitoring for a number of environmental pollutants of global concern and the project was named HEAL. In order to assist the implementation of the project (WHO/UNEP HEAL) several documents were prepared. (EFP/HEAL/84.1–84.9, see Table 1).

The document edited by H.W. de Koning in 1986 on “Guidelines for integrated air, water, food and biological exposure monitoring” summarized all topics relevant to the planned HEAL project (8). The document included sections on pollutant selection criteria, sampling and data evaluation, human exposure monitoring and epidemiology, quality assurance in environmental pollution exposure monitoring, human exposure to pollutants in drinking water, food, and air, biological specimen collection in environmental exposure monitoring, and relevant sources of environmental pollution other than those monitored routinely.

As stated in the introduction of the HEAL document, total or integrated human exposure assessment requires the measurement of the intake of a pollutant by all routes from all media. Those of greatest importance are generally inhalation and ingestion, which require measurement of the toxic agent in the air, water, food and occasionally in soil. Exposure can be best assessed through personal monitoring of the breathing zone air and through sampling of all water and food consumed by an individual. Generalization to a target population requires, for such studies, the statistical selection of representative individuals from the population. To facilitate establishing of the link between environmental measurements and the related adverse effects on health, exposures must be verified by body burden measurements. The best measures of body burden for assessment studies are those that require the least restriction on potential respondents such as exhaled breath, urine, hair, and mothers’ milk. Blood and fat samples are more invasive and reduce response rates. While the concept of exposure assessment is simple, the process to be followed in the sampling, measurement and data analysis programme presents a significant challenge. Assumptions made to simplify the process most often produce spurious or at least questionable results. There are many difficult choices to be made in the design of a successful programme the goal of which is to obtain accurate exposure data bases for selected target populations (8).

International cooperation in the field of exposure monitoring was started as a response to the difficulties mentioned above. The cooperation resulted in the development of the Human Exposure Assessment Location (HEAL) project.

The objectives of the HEAL project were defined as follows (8):

- to provide the framework required to develop an international consensus on techniques and procedures for measuring and assessing human exposure to environmental pollution and to demonstrate their applicability in locations with different lifestyles and pollution profiles;
- to provide a standing arrangement for making detailed human exposure assessment for pollutants considered to be of priority importance by countries/institutions participating on the project and provide better support and data for epidemiological studies on health effects of environmental pollution;
- to provide means to promote research/development of new procedures and approaches for the assessment of human exposure to environmental pollution.

It was agreed that simultaneous water, air, food and biological monitoring should be carried out for a number of priority pollutants in about 12–15 locations, each in

a different country (PEP/HEAL/86.1, see Table 1). The project phased in four HEALs at the start, succeeded by others.

It was decided that the first phase of the HEAL project would be performed at four locations: Yokohama (Japan), Stockholm (Sweden), Zagreb (Croatia – at that time part of Yugoslavia) and one location in the USA. Gradually, other countries would be included (China, India and Brazil showed the interest to participate).

The project was meant to include environmental monitoring and exposure monitoring. The environmental monitoring related to selected pollutants, with preference to those already included in the GEMS network. Namely, one of the goals was to assess the suitability of the present GEMS programme. Exposure monitoring was intended to measure real exposure of selected population groups to given pollutants by all routes of intake, as well as to measure biological indices of exposure with the aim to estimate total body burden and to provide a framework for international consensus on techniques and procedures for measuring and assessing human exposure to environmental pollutants.

Priority was given to pollutants for which personal exposure measurements were feasible, where existed some previous experience, it was possible to carry out biological monitoring, the costs were reasonable, and other prerequisites for practical application were present.

It was agreed that priority should be given to lead (Pb) and cadmium (Cd) in the group of metals, to chlorinated hydrocarbons hexachlorobenzene (HCB), DDT, and optionally benzo(a)pyrene (BaP) in the group of organic compounds, and to SO₂ (NO₂) in the group of pollutants to which people are exposed by inhalation only. Environmental and exposure monitoring were to be combined for each pollutant. Each part of the project was intended to have a Technical Coordinating Centre (TCC).

A TCC was intended to have a complete technical responsibility for a pollutant or a group of related pollutants. The responsibility of a TCC was to prepare a protocol (specifying sampling procedures, analytical methods, quality assurance, and data handling procedures), to assist in the implementation of the programme, to analyse data, and to prepare reports.

It was decided that no more than three pilot projects were to run simultaneously. The first run included (a) Pb/Cd – TCC: Sweden, (b) DDT/HCB – TCC: USA and (c) SO₂/NO₂ (BaP) – TCC: Japan.

At a meeting organized in Chattanooga, USA (July 1986), the participants in the HEAL pilot study presented information about relevant locations chosen for the study in their countries with the description of study programmes. There was also a discussion on protocols for measuring HCB/DDT, and on draft protocols for Pb/Cd, and NO₂.

IMPLEMENTATION OF THE HEAL PROJECT – PILOT STUDY

Exposure monitoring for Pb and Cd

People can be exposed to Pb and Cd in the working environment, in the ambient air, through food, drinking water, and through tobacco smoke. Biological monitoring is the best means to estimate total exposure and risk. The earliest effect of a long-term

low-level exposure to Pb is related to heme synthesis indicated by inhibition of δ -aminolevulinic acid dehydratase and elevation of protoporphyrine in erythrocytes. The early effect of a long-term low-level exposure to Cd is the kidney tubular dysfunction indicated by β -2-microglobuline in urine.

The exposure monitoring should assess the participation of different routes of exposure through the measurement of Pb and Cd in samples of indoor and outdoor air, consumed food, drinking water and beverages, as well as in blood and feces.

Sweden, as a TCC for the Pb and Cd pilot phase of the HEAL project, prepared the Protocol which was discussed and agreed upon at the WHO consultation on HEAL project in Stockholm in October 1986.

The sampling programme for exposure monitoring included:

- sampling of airborne particles on membrane filters using personal samplers
- collection of duplicate portions of all food and beverages (including drinking water) consumed over the study period
- collection of blood samples
- collection of feces samples

Environmental monitoring was to be performed:

- in outdoor air at two sites; one with high and the other with low levels of air pollution. Samples were to be collected around the clock during the whole study period.
- representative samples of food and beverages (including drinking water) were to be collected throughout the study period and to include the minimum of 10 locally obtained foodstuffs.

The Protocol described analytical methods which were to be used as an alternative.

In order to obtain reliable data, the recommendations as to the subject selection in the pilot phase regarded a small motivated group of people who could be trusted to perform the sampling correctly, e.g. 10–15 subjects from the institutes participating in the HEAL project. The subjects were to be healthy, occupationally non-exposed, non-smoking women aged between 25 and 50 years. Each subject was to be surveyed for one week over the winter. At least three subjects were to be covered each week in order to complete the sampling in 5 weeks.

Personal samples of airborne particles and samples of duplicate diets were to be collected daily over 7 consecutive days.

Blood samples were to be collected at the end of the test period and so were the four 24 h feces samples corresponding to the food intake over the first 4 days of the test period. The sampling of feces was to start on the third day of collecting food and it was recommended to use a coloured marker to prevent errors.

The Protocol Annex gave examples of questionnaires for the subjects: activity record, food record questionnaire, food record follow up questionnaire, general questionnaire (personal data, working conditions), questionnaires on analytical procedure and equipment, and forms for preanalytical and analytical quality control.

Four countries participated in the Pb/Cd pilot project: China, Japan, Sweden and former Yugoslavia (Croatia), while Brazil, India, and the USA participated only in a part of the training programme. The project was realized in two phases: 1) analytical training phase and 2) pilot exposure monitoring study with extensive quality control

programme. The subjects were non-smoking women aged between 23 and 53 years. Twelve were in Beijing, 3 in Yokohama, 15 in Stockholm, and 17 in Zagreb. The second phase was carried out in the first quarter of 1988. The final report on the accomplishment of the pilot phase was issued in 1990 (9).

The experience from the study led to the following conclusions: A pilot study of the present design and with a small number of selected subjects may identify the main problems in the collection and analysis of different types of samples for exposure monitoring, as well as the major routes of exposure to lead and cadmium. Such information is important for the design of a full-scale study on a representative sample of the general population. Furthermore, the experience shows that comparable measurements on an international scale is possible, however costly and complicated. The experience from the analytical quality control (QC) programme of the project shows that it is important that QC samples have a matrix similar to that of the monitoring samples, that the QC samples should cover the range of concentrations expected to be found, and that one or a few reference samples are not sufficient for the evaluation of the analytical performance.

Exposure monitoring for NO₂

The first phase of pollutant monitoring coordinated by TCC Japan was intended for the exposure study to SO₂. However, as it was assessed that the development of a suitable passive sampler for very low concentrations of SO₂ encountered indoors would take some time while passive sampler for NO₂ was available and verified, priority was given to NO₂.

The Japan TCC prepared a Protocol for NO₂, which was discussed and agreed upon at the Tokyo meeting in March 1987. The Protocol determined that the environmental monitoring was to be performed continuously throughout the project period at two sites: a/ with high pollution and b/ with low pollution. Sampling was either to be automatic or manual and the results were to be integrated over 24 hours.

Exposure monitoring consisted of direct monitoring by personal samplers and of indirect estimation by calculating exposure from the data of activity records and concentrations measured in various indoor and outdoor environments.

The sampling programme for exposure monitoring was as follows:

- Subjects were to be 10–15 healthy non-smoking women, exposed to various levels of NO₂.
- Sampling period was to last one week in winter.
- Exposure was to be monitored by badge samplers provided by TCC.

The Protocol issued instructions on the sampling procedure, sampling storage, analytical procedure, and internal quality control, as well as instructions as to the identification of HEAL sites, description of procedures and equipment for sampling and analysis, quality control, reporting data, general information on subjects, home and workplace, and activity record.

After the training phase, in which the reliability of analysis of each participating institution was confirmed through the analysis of quality control samples, implementation of the pilot phase of the study started in the first quarter of 1988. The NO₂ project consisted of three pilot phase studies. The first study was located in Beijing

(China), Stockholm (Sweden), Zagreb (Croatia, former Yugoslavia at the time), and Yokohama (Japan). The second pilot phase study took place in Bombay (India) the following year. The third pilot phase study took place in Los Angeles and Orange County (USA) as a part of a larger survey and therefore deviated a little from the WHO Protocol. Therefore, the results of the three studies were presented separately in the final report prepared by TCC issued in 1991 (10).

The following conclusions were suggested from the results of the study:

- The personal NO₂ badge method was useful for the measurement of personal exposure level.
- A predominant factor affecting personal NO₂ exposure level was indoor pollution. The indoor pollution load on the personal exposure level would increase over the heating season at each site as the air ventilation in a home decreased and the influence of indoor emission sources increased with regard to the non-heating season.
- There was a significant correlation between the observed and estimated personal exposure values calculated from NO₂ concentrations/time spent indoors. The estimated personal exposure values could prove useful for the first-level estimation of NO₂ exposure of a general population.
- Improvements of methodology were required to accurately estimate personal exposure level from NO₂ concentrations/time spent in various microenvironments. The improvement would include development of more sensitive NO₂ analysis/sampling methodology by which NO₂ concentrations could be measured only for the time a subject spent indoors.
- The first-level estimation of personal exposure level of a general population could be performed with the methodologies at hand when the outdoor pollutant was the most important factor in the indoor pollution of homes of the target population.

Exposure monitoring for organochlorine pesticides (HCB, DDT)

Organochlorine pesticides have been widely used and, although many are banned in some countries, can still be detected in the environment. Their levels in foodstuffs such as cereals, pulse, fruit, and vegetables, are generally low (often below detection limits). Organochlorine pesticides are lipophilic and accumulate in fatty tissues. Hence, the levels in dairy milk are often high and the concentrations in human milk are often well above those in cow milk. The levels vary from country to country and reflect the current use, legislation on use, and food importation patterns.

People can be exposed to organochlorine pesticides through inhalation, ingestion or skin absorption. Occupational contact or accidental spraying on food or persons can result in high exposure. A more widespread environmental contamination occurs through the food-chain when persistent pesticides accumulate in fatty tissues and are transmitted unchanged from prey to predator, which leads to biomagnification.

The organochlorine compounds selected for the HEAL pilot study were HCB, 4,4'-DDT, 4,4'-DDD, and 4,4'-DDE (11). The list was proposed to extend to β-HCH and PCBs. The choice was based on the logistics of monitoring lipophilic compounds in the human body and on the occurrence frequency of organochlorine pesticides in

many countries. The TCC for organochlorine pesticides, US Environmental Protection Agency (US EPA) prepared a draft protocol which was discussed and finalized during a meeting held in Chattanooga in July 1986. The Protocol provided detailed information on the procedure to be followed. The pilot study was proposed to last 30 days and to involve both environmental and exposure monitoring. Monitoring was to involve seven lactating women in each of the three strata (rural, suburban, central urban), totalling 21 women. Environmental monitoring was to include ambient air, drinking water, food and exposure monitoring food (duplicate diet), mothers' milk, indoor air, and, optionally, blood and adipose tissue. At the meeting held in Geneva in October 1987, the TCC proposed a revision of the protocol to provide better approach to exposure monitoring for pesticides and to allow incorporation of other total human exposure monitoring studies being conducted in the United States. The participating countries agreed that the original protocol be modified for the exposure monitoring component to eliminate the stratification of the sampling schedule and that the environmental monitoring component be made optional. The pilot study was intended to last seven days for each subject and was to involve both biological and exposure monitoring. The monitoring involved seven nursing women and began at the 4th week of nursing. Pilot phase monitoring scheme included the analyses of food (duplicate diet, one-week diary, three-day composite/subject), mothers' milk, and blood (one sample/subject). Personal air monitoring, breath sampling, indoor air monitoring, and dermal monitoring were recommended.

As the programme started, it was realized that a minimum level of QC would be necessary to allow valid data comparisons due to the international diversity in human exposure concerns, instrument capabilities, funding, and other factors in the participating countries. The pilot study concentrated on the methodological protocol, training and quality assurance aspects of assessment to see if internationally comparable data were feasible to obtain. Limited human exposure data were also obtained.

Quality assurance started in October 1986. The TCC prepared a document entitled *Plan for International Analytical Performance Evaluation Programme*. Six types of samples spiked with HCB, 4,4'-DDT, 4,4'-DDD, 4,4'-DDE, and β -HCH, each in two concentrations, were provided to the participating countries. Sweden's National Food Administration provided soybean oil (surrogate for human milk) and butter fat (fatty food surrogate). The US EPA provided the soil samples, water spiking solutions, plasma spiking solutions, and porcine adipose (human adipose tissue surrogate) samples. US EPA Pesticide Repository and Quality Assurance Materials Bank also provided gas chromatographic column packings, florisil and analytical standards. Another set of QC samples was prepared and sent to the participating laboratories in September 1987 (blood spikes, water spikes, and a spiked soil, each in four concentration levels) and in March 1988 (butterfat and soybean oil, each in two concentration levels). Standard analytical methods of solvent extraction and fractionation, followed by gas chromatographic analysis using column packings supplied by the TCC, were strongly recommended to ensure comparability of the results obtained in different laboratories.

Six countries – USA, Sweden, former Yugoslavia (Croatia), Brazil, Japan, and China – participated in the QC and training programme for pesticides. Because of the complexity of pesticide analysis, the QC exercises presented problems, for both TCC and the participating countries (11). Most of the laboratories deviated either partially or completely from the proposed methods. There was some variation in processing

QC samples for analysis and in reporting data. The TCC evaluated the results using a number of techniques for data analysis including the MAD (Maximum Allowable Deviations) test and a “laboratory score” that compared the percentage extraction of pesticides with the total present in the sample. Few laboratories met the criteria for the MAD test as insufficient reference samples of different concentrations were provided for a thorough MAD assessment of laboratory performance. “Laboratory scores” provided a useful performance indicator of the participating laboratories. The laboratories showed considerable variation in the scores. It was concluded that pesticide analysis was too problematical for immediate incorporation into a full-scale programme. The recommendations concerned changes in the protocol, improvement of instructions, and the use of a wider range of reference concentrations in the QC tests.

Despite difficulties with regard to quality assurance in the pilot study, some preliminary data on levels of exposure to selected organochlorine pesticides were gathered at the participating HEAL sites. The countries that provided exposure data were Japan, USA, and former Yugoslavia (Croatia). In the USA, a study of pesticide exposure levels in households – the Non-Occupational Pesticide Exposure Study (NOPES) – adopted the EPA’s Total Exposure Assessment Methodology (TEAM) programme in order to estimate exposure to air, food, water and dermal contact. Thus, the data for HCB and DDT were gathered according to the NOPES programme in the USA and according to the HEAL programme in other countries with USA providing TCC (11).

The Croatian study revealed that the levels of γ -HCH and HCB in drinking water were at, or close to, the detection limits, while DDT-complex and α - and β -HCH could not be detected. The USA study revealed no presence of HCB in the air or water, but DDT was detected in several indoor air samples. In the Japanese study, HCB and DDT were below the detection limits in blood samples. These generally low levels agree with the published data and reflect the low solubility of HCB and DDT in aqueous media.

Higher levels of pesticides were detected in the dietary samples, particularly in butter and cow milk, reflecting the high solubility of these substances in fats. The Croatian data showed that cow milk contained the highest levels of DDT-complex, HCB, and γ -HCH, but the reported levels were below the recommended FAO limits for foodstuffs and were similar to those found in developed countries in and outside Europe. In the USA, the dietary exposure to HCB and DDT was estimated at 110 ng/day. In Japan, DDT was detected in only one dietary study and HCB not was found at all. HCB and DDE were detected in human milk in the Japanese study, but DDT was detected in a single sample of human milk. The Croatian study revealed the HCB, γ - and β -HCH, 4,4'-DDE and 4,4'-DDT presence in a pooled sample of human milk. Although all pesticide levels proved very low, they showed that personal monitoring could provide valuable data for exposure assessment.

The differences in the adopted methods and samples between the countries as well as the small sample size make direct comparison of the results difficult. However, it was concluded that the total exposure assessment methodology used in the USA study could easily adapt to different cultural, socioeconomic, and geographical conditions in monitoring of many pollutants and could provide useful basis for the operational phase of the HEAL programme.

Indoor air quality studies in Kenya and Gambia

In 1986/87 special studies of biomass smoke exposure were performed in Kenya (12) and the Gambia (13) and published under HEAL. The indoor air pollution study was incorporated into the organizational setting of ARI (acute respiratory infections) studies by the WHO and the National Academy of Sciences (NAS), USA. The objectives of the study in Kenya were to measure carbon monoxide, carbon dioxide, nitrogen dioxide, and respirable suspended particulate matter with their associated polycyclic aromatic hydrocarbons (PAH's) as an indicator of air pollution in a representative number of households in the Maragua area. Further objectives were to evaluate the main factors contributing to the high indoor air pollution and the exposure of children aged below five years in the study population and to explore the feasibility of assessment of the relationship between the level of indoor air pollution and the incidence of acute respiratory infections. Thirty six households were randomly selected from 250 in the area. The air pollution survey consisted of a questionnaire, 24-hour average measurements, and daily pollution pattern measurements.

In the Gambia, repeated 24-hour measurements of suspended particulate matter and nitrogen dioxide were carried out in 18 randomly selected kitchens. Occasional hourly measurements were performed in a few cases.

SECOND PHASE – REVIEWING PROGRESS

Within the frame of the International Symposium on Total Human Exposure Assessment, an informal one day meeting of the HEAL coordinators took place in Las Vegas in December 1989.

At the Zagreb meeting held at the Institute for Medical Research and Occupational Health from 10 to 14 September 1990, Brazil, China, Hungary, India, Japan, Sweden, USA, and former Yugoslavia (Croatia) presented information as to the current status of activities and discussed future action. The countries agreed that it would be highly desirable, if not necessary, to continue the studies on exposure to the three groups of pollutants from the pilot phase of the HEAL project. It was considered particularly important in view of the fact that new countries were joining the HEAL programme. The countries agreed that TCCs for the three groups of pollutants should continue to operate. Concerning the choice of other pollutants for the future HEAL project, priority was to be given to exposure assessment to mercury in certain areas. Fluorides were also suggested to enter the programme. A number of countries expressed interest in establishing a volatile organic chemicals project, although the cost of analysis were relatively high. An emphasis was also put on the issue of respirable particulate matter.

A part of the Meeting schedule was dedicated to supporting activities. Several workshops had been and were to be conducted to support the HEAL project including the training seminar on "Household air pollution survey in developing countries" at the East-West Center, Environment and Policy Institute, Honolulu, USA, which was supported by the HEAL project.

In the second round of the Zagreb HEAL coordinators meeting, Mel Kollander and David Mage of the US EPA prepared a two-day seminar “Survey design methodology for human exposure field studies” on the concept of total human exposure and the indirect and direct methods of exposure estimation.

In 1992, Bad Elster, Germany hosted a WHO/UNEP GEMS/HEAL workshop on statistical survey design and human exposure assessment monitoring.

Followed the November 1992 meeting of the HEAL coordinators in Bangkok, Thailand, hosted by the Thai Ministry of Public Health. The HEAL programme meeting reviewed the health effects of human exposure to lead and the lead related component of the WHO/UNEP HEAL project. In addition to the background information on the field application of human exposure assessment and environmental epidemiology, quality control in the HEAL programme and the US EPA integrated exposure uptake biokinetics model for lead in children, the meeting report describes various country studies in the health effects of lead (14). Quality assurance/quality control (QA/QC) was the most important and contentious subject discussed at the meeting. The suggestion that participating countries obtain their QC samples from a common commercial source was rejected. The countries were unanimous that the TCC's role in overseeing QA/QC was crucial. The Bangkok meeting concluded with a list of pollutants of interest for HEAL programme in participating countries.

EVALUATING PRESENT STATUS AND POTENTIAL FUTURE DIRECTIONS

After the pilot phase of the HEAL project, the number of participating countries increased from the initial 7 to 27, which, apart from confirming the importance of international activities in human exposure assessment, brought new difficulties. The most experienced participants were overwhelmed by the workload consisting of providing assistance and QA/QC to the new participants. In addition, most studies were conducted on a relatively limited scale, which did not make them a useful instrument for making decision. Having seen the advantages and disadvantages of the first two phases of the HEAL project, some countries proposed in 1994 that the HEAL change the course of activities. Future activities should focus on training and promotion materials to ensure that all countries get access to appropriate methods and technologies for environmental health management. The HEAL project and its activities are intended to link human exposure assessment more directly to environmental epidemiology investigations and decision making relevant to environmental health. Training and technical support activities are intended to fully integrate exposure assessment with other aspects of environmental health management.

The Progress Report of WHO/UNEP GEMS/HEAL for 1993 summarises the problems as follows: initially, WHO provided direct HEAL support to national exposure monitoring programmes through funding and/or assistance on individual study designs. As the number of participants increased to 27 countries in 1992/93, it became impractical to continue having a single TCC supporting all who wish to carry out HEAL studies for the relevant pollutant. With the growth in the number of participating

countries coupled with a shortage of experienced personnel, the Japanese and Swedish TCC's have been unable to provide the full range of assistance required for NO₂ and Pb studies that are normally called for under the HEAL project. This has resulted in short-term subcontracting for services in the case of the Japanese TCC and in a limit to the number of Pb standards for environmental media that can be prepared by the Swedish TCC, which continues to prepare blood Pb standards for a portion of the countries. John Spengler as assigned consultant prepared a review of the HEAL project stressing its advantages and disadvantages. The advantages of the HEAL programme lie in TCC training in scientific sampling methods and in the fact that the collaborating organizations can conduct limited studies and produce reliable data. The disadvantages are that the studies have a limited scope and a small sample size, the number of participating institutions and countries is still relatively small, the list of pollutants is limited, and that the studies are designed as pilot or demonstration studies. Furthermore, it has not been acknowledged in the HEAL documents that exposure through the air and water might dominate in situations when the concentrations are quite high. In that case, the exposure framework fix location in monitoring can be of great value in determining the primary contributions.

PROGRAMME RE-ORIENTATION AND DECISIONS TAKEN

After consulting the HEAL coordinators and the participating institutions in different countries on the present situation of the HEAL project and potential future activities, HEAL coordinator organised a meeting in Sosnowiec, Poland, on 21 November 1996. The meeting was held in conjunction with "The Joint WHO/IOMEH Workshop on Human Exposure Assessment in Environmental Health Decision-Making" that took place between 19 and 23 November 1996 and was hosted by the Institute of Occupational Medicine and Environmental Health (IOMEH) in Sosnowiec, Poland.

The HEAL coordinators meeting included a short discussion about the achievements, limitations, organization of HEAL, and future activities. A "Discussion paper" on the issues had been circulated in advance. A new concept was introduced that integrated the HEAL project into the WHO – Information for Decision-making in Environment and Health (IDEAH).

The key conclusions of the Meeting were as follows (15):

1. HEAL had been successful in the development of human exposure monitoring and quality control methodologies for the determination of heavy metals, air pollution and pesticide exposure.
2. HEAL had been successful in globally promoting human exposure studies and providing quality control schemes. Laboratories had improved their analytical performance considerably due to training and their participation in the external quality control scheme provided by the HEAL project.
3. For the last years, the HEAL project had received financial support from Japan and US EPA but UNEP was not able to continue with its financial contribution.

The reduced funding made it impossible to continue with the provision of quality control samples and with the sponsorship of specific HEAL studies, but the work on methodology and training materials continued.

4. HEAL had been useful in promoting exposure studies in developing countries. It was felt that the HEAL expertise was still needed, especially with regard to external quality control.
5. It was agreed that the HEAL project needed change in direction. The initial HEAL concept and its extension to additional pollutants and media (discussed at the Bangkok meeting in 1992) could not be afforded.
6. It was agreed that the HEAL project keep its name. The L could now stand for the “linkage” between the participating institutes and the “leadership” in human exposure assessment that they provide. The exact word behind the L is still to be decided.
7. It was important that the HEAL project establish closer links with health risk assessment and environmental epidemiology.

Those key conclusions were followed by a number of specific recommendations:

- a/ To reorient HEAL towards human resources development, distribution of information, and networking. There were several ways to do it:
 - by networking of institutions involved in exposure studies and QA/QC
 - by making use of WHO distribution systems such as the WHO Global Environmental Epidemiology Network (GEENET) and the WHO Global Health and Environmental Library Network (GELNET)
 - by developing an infrastructure to decentralize the access to information material
 - by preparation of teaching material
 - by networking of institutions offering teaching courses
 - by teaching courses
 - by establishing a network and document distribution using the INTERNET.
- b/ To publish a summary report on the HEAL project containing the achievements of the programme.
- c/ To expand HEAL by including additional institutions interested in human exposure assessment.
- d/ To develop a procedure which would allow laboratories, especially those in developing countries, to participate in existing commercial and non-commercial external quality control schemes and/or to get access to provide analytical standards.
- e/ To prepare a HEAL workshop for the annual meeting of the International Society of Environmental Epidemiology (ISEE) in Boston, 1998. The workshop was intended to heighten the profile of HEAL in the international scientific community.

Table 1 shows the list of meetings related to preparation and implementation of the HEAL project. Presented data are based on the table included in the HEAL Final Report prepared by Gutschmidt and Kjellstrom, Office of Global and Integrated Environmental Health (Geneva, Switzerland) in 1995.

Table *List of the meetings connected with preparation and implementation of the HEAL project*

Meeting	Doc./No.	Recommendations/Results (since 87*)
Meeting of government expert group on health-related Monitoring; Geneva, Switzerland 28 March – 1 April 1977	CEP/77.6	Develop greater orientation toward exposure assessment of the general population as well as specific groups considered at high risk.
Consultation on health-related environmental monitoring; Geneva, Switzerland 22 – 24 April, 1981	EFPP/81.12	Review of results of pilot projects and recommendation to include a number of multi-media exposure assessment studies in the health-related monitoring programme either as a fixed component or, alternatively, as a less symptomatic approach.
Consultation on health-related monitoring; Geneva, Switzerland, 9 – 13 November, 1981		Preparation and review of background paper for next Government designated expert meeting.
Meeting of government designated experts on health-related monitoring; Geneva, Switzerland, 8 – 12 March, 1982		The group endorsed the concept of establishing Human Exposure Locations (HEAL) as a possible framework for internationally co-ordinated assessments of a human exposure to environmental pollutants.
Meeting on health-related environmental monitoring; Geneva, Switzerland 14 – 18 June, 1982		Planning implementation of HEAL project.
Review of documentation for Human Exposure Assessment Location (HEAL) project; Geneva, Switzerland, 12 – 23 March, 1984		Final review of a set of 9 HEAL technical documents**
Consultation on the Human Exposure Assessment Location (HEAL) project; Geneva, Switzerland, 29 April – 3 May, 1985	EFPP/HEAL/ 85.6	Meeting of HEAL co-ordinators: – pollutant selection – role of TCCs.
Consultation on the food component of Human Exposure Assessment Location (HEAL) project; Washington, DC, USA 20 – 30 August, 1985		Discuss technical and operational aspects of the HEAL food monitoring component.
Consultation on the Human Exposure Assessment Location (HEAL) project; Geneva, Switzerland, 20 – 21 May, 1986	PEP/HEAL/ 86.1	Meeting of the HEAL co-ordinators; – review of project activities; increased responsibility for TCCs to implement assigned tasks.
Consultation on the Human Exposure Assessment Location (HEAL) project; Chattanooga, TN, USA, 14 – 18 July, 1986		Review of protocol*** for measurement of HCB/DDT and draft protocols*** for Pb/Cd and NO ₂

<p>Consultation on the Human Exposure Assessment Location (HEAL) project; Stockholm, Sweden 13 – 17 October, 1986</p>	<p>Review of protocol*** for Pb and Cd and draft protocol*** for NO₂. Initiation of QA for HCB/DDT.</p>
<p>Consultation on the Human Exposure Assessment Location (HEAL) project; Tokyo, Japan 23 – 27 March, 1987</p>	<p>Review of NO₂ protocol*** and review of initial QA results for HCB/DDT and Pb/Cd.</p>
<p>Consultation on the Human Exposure Assessment Location (HEAL) project; Geneva, Switzerland, 5 – 9 October, 1987</p>	<p>PEP/HEAL/ 87.9 Discussion on background document PEP/HEAL/87.8: general review of HEAL; further project development; co-ordination and management; action items for TCCs</p>
<p>Human Exposure Assessment Location (HEAL) co-ordinators meeting; Geneva, Switzerland 28 February – 3 March, 1989</p>	<p>PEP/HEAL/ 89.19 Discussion on work papers: 1) proposals for change; 2) modification of monitoring component; 3) proposal for additional components; 4) management, co-ordination and financial aspects; 5) workplan and budget for 1989 and 1990.</p>
<p>Informal Meeting of HEAL Participants; Las Vegas, NV, USA 1 December, 1989</p>	<p>Annex 3; PEP/HEAL/ 90.15 Current status; draft sampling and QA documents; collaborative studies; technical support; new directions</p>
<p>Co-ordinators meeting on the Human Exposures Assessment Locations (HEAL) programme; Zagreb, Croatia 10 – 14 September, 1990</p>	<p>PEP/HEAL/ 90.15 Review of current status; country activities; future activities; seminar on survey design methodology for human exposure field studies.</p>
<p>HEAL workshop on statistical survey design and human exposure assessment monitoring; Bad Elster, Germany October/ November, 1991</p>	<p>Workshop, 1992</p>
<p>HEAL meeting; specialised on lead; Bangkok, Thailand 16 – 19 November, 1992</p>	<p>WHO/EHG/ 95.15 US EPA lead exposure distribution model</p>
<p>Co-ordinators meeting on the HEAL programme; Sosnowiec, Poland 21 November, 1996</p>	<p>Review of HEAL activities; new directions; discussion on proposals.</p>

* see report PEP/HEAL/87.9

** pollutant selection; sampling and data collection; monitoring and epidemiology; quality assurance; drinking water monitoring; food monitoring; air monitoring; biological specimen collection; other sources of pollutants

*** selection of sampling strategy; sample preparation; analytical techniques; quality assurance; selection of study population; collection of ancillary information through questionnaires; data handling; etc.

OUR OWN EXPERIENCE WITH THE PROJECT AND RELATED ACTIVITIES

The Institute for Medical Research and Occupational Health in Zagreb, Croatia has been involved in various environmental exposure studies for a long time. It was one of the first to promote the approach of multimedia exposure assessment and direct measuring of human exposure as an essential element in accurate risk assessment.

The Institute joined the HEAL project from the beginning and took part in the pilot phase related to the total human exposure assessment to heavy metals (lead and cadmium), organic chemicals (DDT, HCB), and nitrogen dioxide. After the completion of the HEAL pilot phase in 1990, the Institute continued the study in 1991.

The HEAL project pilot phase gave the Institute an opportunity to verify the reliability of methods used for sampling and analysis through interlaboratory quality control and comparison of results. In addition to the quality control exercise organized by TCCs, we took the opportunity of the joint study to distribute equal parts of real samples of airborne dust for Pb and Cd analysis. The results were obtained from the Yokohama City Institute of Health (Japan), Air Research Laboratory in Nyköping (Sweden), and the Institute for Medical Research and Occupational Health in Zagreb. A very good agreement in the measured values was obtained between the compared laboratories (16).

The same approach as in the Pb/Cd pilot phase of the HEAL project was used in a study on a lead smeltery in Slovenia (17). The environmental contamination and exposure of population to Pb and Cd in the region has been studied since 1967 (18). With the introduction of an efficient emission control system in 1978, the concentrations of lead in the air dropped drastically, but the biological indicators of lead exposure, though showing a trend towards normalization, still remained slightly above the normal levels. The analysis of Pb and Cd intake through food and drink showed that the Pb and Cd content in drinking water and in most foodstuffs purchased in shops was below the permissible levels. However, home produced foodstuffs from orchards, gardens, and poultry as well as homemade beverages contained Pb and Cd above the permissible levels. The fact may be attributed to the persistent contamination of soil. Namely, Pb converts to heavily soluble compounds in soil as confirmed by laboratory experiments (19). Soil contamination was also the reason that Pb and Cd concentrations in settled dust and particularly in household dust were less reduced than in air.

The NO₂ pilot phase of the project gave the Institute an excellent opportunity to verify passive samplers developed at the Institute and compare them with the Japanese. Passive samplers proved suitable not only for personal sampling, but also for measuring spatial distribution of NO₂ in the indoor and the outdoor air. Our passive samplers were later compared with the samplers developed in the US Atmospheric Research and Exposure Assessment Laboratory within a joint project with EPA (20).

The Institute also studied exposure to persistent organochlorine compounds, volatile organic compounds, formaldehyde, ammonia, and long live radionuclides.

The results related to these studies were summarized in a number of papers published in *Environmental Management and Health* (21) under the common title, *Total Exposure to Environmental Pollutants and Risk Assessment* (guest editor: M. Šarić).

The studies on persistent organochlorine compounds in water and soil in Croatia showed that the presence of these compounds in water was comparable to the widely distributed organochlorine (OC) pesticides in other European countries. Recent measurements indicated that their levels were generally within acceptable limits characteristic of global environmental pollution (22). The levels of organochlorine compounds in population groups from Croatia and most European countries were found to be comparable. Despite the presence of OC pesticides in human milk, Croatia as other European countries have continued to favour breast-feeding (23).

The assessment of environmental exposure to trichloroethylene (TRI) and tetrachloroethylene (PER) in the residents of Zagreb was the subject of one of the studies. It was designed to biologically monitor the general population exposure to TRI and PER under normal environmental conditions, and to reveal the possible influence of these compounds in drinking water on body burden (24).

The study on long-term household exposure to ammonia was an attempt to produce information about distribution of exposure for four different groups of inhabitants of Zagreb (high school students, university students, employed, and retired persons). All results were lower than the guideline values. The comparison of the results with the guideline limit for long-term exposure to ammonia shows that ammonia exposure does not present an environmental health problem in Zagreb (25).

One of the studies dealt with the relationship between summer and winter formaldehyde levels in kindergartens and primary schools in Zagreb (26).

In addition to the previously performed studies on lead and cadmium exposure, including the study conducted within the HEAL pilot phase, other studies comparing Zagreb as an urban area and a smeltery area showed that 61–64% of absorbed lead and 92–96% of absorbed cadmium originated from ingested food in both populations (27).

The study on ^{137}Cs and ^{90}Sr in human food chain in Croatia showed that the estimated doses were far below the limits for the general population. At the moment, the risk associated with ^{137}Cs and ^{90}Sr ingestion for the population of Croatia can be considered low (28).

In 1993, the Institute published an approach to the integrated life-time exposure assessment (29).

The results of a study on the assessment of human inhalation exposure to polycyclic aromatic hydrocarbons performed at the Institute were published recently (30).

The Institute also carried out epidemiological studies on asbestos exposure in an area with an asbestos processing plant (31) and in an area with an asbestos-cement plant (32,33). The focus was placed on the incidence of respiratory and gastrointestinal tumors. Another study followed the incidence of acute respiratory diseases as well as the ventilatory impairment among children living in the vicinity of a fertilizer plant (34).

The Institute recently issued a publication with a review of the studies performed in the Republic of Croatia in the field of environmental exposure assessment and epidemiology for the period 1980–1995 (35).

Supporting the accepted new directions of the HEAL project, the Institute wishes to contribute to future HEAL activities.

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Sažetak

Ocjena izloženosti ljudi onečišćenjima na različitim lokacijama – povijesni pregled međunarodnog projekta HEAL

Pregled je podijeljen u nekoliko dijelova. Prvo se govori o zbivanjima i saznanjima koja su dala podlogu za osmišljavanje programa te o pripremnim radovima koji su obavljani da bi se projekt počeo ostvarivati. Polazna pretpostavka za pokretanje projekta bila je ova: U ocjeni izloženosti različitim onečišćenjima treba uzeti u obzir sve medije okoliša u kojem ljudi borave i djeluju (zrak, voda za piće, hrana, tlo). Unos onečišćenja u čovjeka mora se mjeriti što je moguće direktnije, kako bi se dobila realna slika o unosu i opterećenju organizma određenim onečišćenjem. Pri tome je važan uvid u relativnu participaciju pojedinih medija u okolišu u ukupnom unosu. Realna ocjena izloženosti bitna je karika u procjeni rizika te u usmjeravanju mjera zaštite i upravljanju okolišem. Za ostvarenje zacrtanih ciljeva i unapređenje i racionalizaciju pristupa u realnoj ocjeni izloženosti nužna je usklađena međunarodna suradnja. Projekt je i zamišljen kao međunarodni s time da se započne u nekoliko zemalja te da se u kasnijem tijeku proširi.

U drugom dijelu pregleda prikazano je pokusno razdoblje projekta (pilot phase). Taj je dio uključio ocjenu izloženosti teškim metalima (olovo, kadmij), dušikovu dioksidu (NO₂) te organoklorovim pesticidima (heksaklorobenzen – HCB, DDT kompleks). Sudjelovale su ove zemlje: SAD, Švedska, Hrvatska (u sastavu tadašnje Jugoslavije), Brazil, Japan i Kina. Započelo se s kontrolom kvalitete laboratorijskih postupaka (analiza) da bi se nakon toga – slijedeći precizno dogovoreni program – pristupilo ocjeni izloženosti onečišćenjima zraka u zatvorenim prostorima (*indoor air*) povezano s uporabom otvorenih ognjišta u Keniji i Zambiji.

Sljedeći dio pregleda odnosi se na prikaz zbivanja do kojih je došlo nakon provedene prve, pokusne faze projekta. Razmatrale su se mogućnosti proširenja programa uključenjem drugih aktualnih onečišćenja. Posebno je razmatran problem organizacije učinkovite kontrole kvalitete laboratorijskih nalaza. Iskrsele su, naime, realne teškoće organizacijske i financijske prirode.

U nastavku se govori o evaluaciji postojećeg stanja projekta i njegovu daljem usmjerenju, odnosno određenoj preorijentaciji i odlukama koje su s tim u vezi donesene. Projekt je utro putove suvremenim shvaćanjima o postupcima koje treba poduzimati da bi se dobila realna ocjena izloženosti, što treba povezivati s ocjenom rizika i epidemiološkim ispitivanjima. U vezi s tim utvrđeni su i praktični zadaci, nabrojani u pregledu, na kojima bi u okviru međunarodne suradnje trebalo raditi u predstojećem razdoblju.

Završni dio pregleda prikazuje sudjelovanje Instituta za medicinska istraživanja i medicinu rada u projektu. Uz opis sudjelovanja Instituta u pokusnoj fazi, o čemu je prethodno bilo govora, izložena su ukratko i druga ispitivanja koja su u odnosu na ocjenu izloženosti u međuvremenu provedena. To se tiče dodatnih istraživanja o ocjeni izloženosti metalima, posebno olovu, zatim postojećim organoklorovim spojevima, razvoja pasivnih skupljača uzoraka zraka za ocjenu osobne izloženosti dušikovu dioksidu, ocjene izloženosti trikloretilenu i tetrakloretilenu te amonijaku u skupinama stanovništva u Zagrebu, pa formaldehidu u dječjim vrtićima i osnovnim školama također u Zagrebu. Istraživana je i izloženost radionuklidima ¹³⁷Cs i ⁹⁰Sr u prehrambenom lancu stanovnikâ Hrvatske. Radilo se i na ocjeni rizika u odnosu na pojavu raka dišnih i probavnih organa u vezi s izloženošću azbestu. Na kraju pregleda navodi se publikacija, koja je nedavno (1996.) objavljena u izdanju HAZU, u kojoj su sabrani rezultati provedenih ispitivanja u okolišu u Hrvatskoj (razdoblje 1980.–1995.) te o mogućim učincima tih onečišćenja na zdravlje ljudi.

Ključne riječi:

azbest, dušikov dioksid, kontrola kvalitete, organoklorovi pesticidi, pokusna faza, pripremni radovi, radionuklidi, teški metali

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