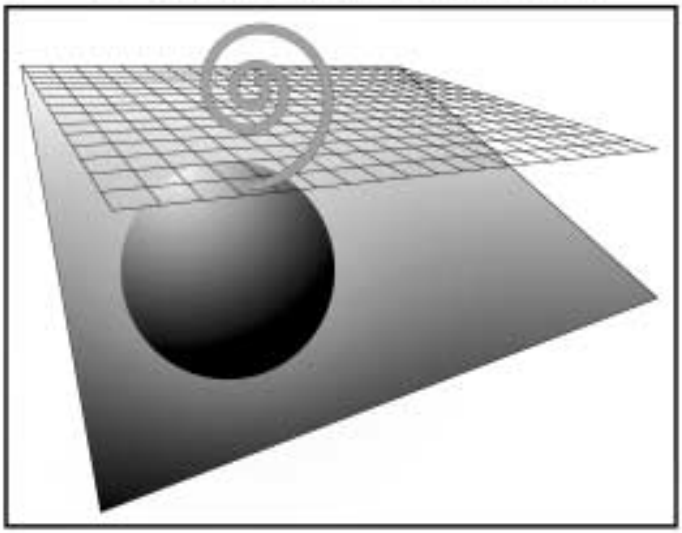
WHO MEETING, LODZ, POLAND, 10-12 APRIL 2000



METHODS OF ASSESSING RISK TO HEALTH FROM EXPOSURE TO HAZARDS RELEASED FROM WASTE LANDFILLS

EUR/00/5026441
ORIGINAL: ENGLISH
EUROPEAN HEALTH21 TARGET 10
E71393

EUROPEAN HEALTH21 TARGET 10

A HEALTHY AND SAFE PHYSICAL ENVIRONMENT

By the year 2015, people in the Region should live in a safer physical environment, with exposure to contaminants hazardous to health at levels not exceeding internationally agreed standards

(Adopted by the WHO Regional Committee for Europe at its forty-eighth session, Copenhagen, September 1998)

ABSTRACT

The Working Group was convened to produce practical guidelines for assessing exposure to hazardous materials that can be released from waste landfills. Exposure assessment studies near a waste site may be required to ensure regulatory compliance, to address community concerns or for epidemiological research. Exposure assessment includes both the measurement of actual exposure to contaminants and the calculation, estimation and modelling of exposures based on existing data. The Working Group recommended a stepwise approach with an increasing level of complexity. A multidisciplinary team should be involved in the assessment, using standardized methods and communicating with stakeholders at all stages. The method emphasizes the need to identify complete exposure pathways. The report specifies conditions for any epidemiological studies to be conducted. Standardized methods are recommended in order to facilitate comparisons of different studies and areas.

Keywords

ENVIRONMENTAL EXPOSURE
ENVIRONMENTAL MONITORING
HAZARDOUS SUBSTANCES
PUBLIC HEALTH
REFUSE DISPOSAL
RISK ASSESSMENT

This document was text processed in Health Documentation Services
WHO Regional Office for Europe, Copenhagen

CONTENTS

Page

1. Introduction

Potential risk to health from waste disposal, both hazardous and non-hazardous, in landfills is an issue of continuing public concern. This concern is based on equivocal evidence. A WHO meeting, convened in Bilthoven in 1998 to review the available research information, concluded that present data do add to a suspicion that population exposure to emissions from waste landfills may pose a risk to populations in the vicinity *(1)*. However, the available data are insufficient for reliable risk assessment. A major problem is the paucity of quantitative exposure information and the weakness of the exposure assessment methods used. There was a consensus in the meeting that more, and better focused, scientific data are needed to assist governments and the waste management industry regarding the optimization of practices, prevention of an impact on health and improvement in risk communication. In addition, European countries needed to combine their efforts and expertise in order to provide a more solid basis for decisions.

In continuation of the Bilthoven meeting, a WHO working group was convened by the Bilthoven and Rome Divisions of the WHO European Centre for Environment and Health, in cooperation with and hosted by the Nofer Institute of Occupational Medicine, to meet in Lodz, Poland from 10 to 12 April 2000. Dr Robert Spengler chaired the meeting, Dr Stanislaw Tarkowski was elected vice-chairperson and Dr Lesley Rushton rapporteur. The support of the meeting by the Nofer Institute of Occupational Medicine is gratefully acknowledged.

2. Scope and purpose

The aim of the meeting was to recommend methods of assessing exposure to hazards released from waste landfills, and to produce practical guidelines, with relevant exposure indicators and methods for their design, for future exposure assessment in local situations. The focus of the Working Group discussion was on risks to human health; risks to the environment, not affecting health, were not considered. Potential occupational exposure of waste workers was not a subject of specific discussion.

It is postulated that the use of standardized exposure assessment methods would allow (i) comparability between sites included in one study, and (ii) comparison of exposures assessed by different site investigations. It would also facilitate combined analysis of results from epidemiological studies, and aid the identification of specific characteristics of landfills which might be associated with increased adverse health outcomes. This should contribute to improved design and operation of landfills, increasing their safety and the protection of public health, and facilitate future monitoring and risk assessment.

The working group consisted of invited experts from nine European countries and the United States working in relevant research disciplines, including environmental chemistry, environmental engineering, risk assessment, environmental exposure measurement and analysis, toxicology, epidemiology, geology and public health. A list of participants is given in Annex 1.

In advance of the meeting, invited experts prepared four background papers reviewing the available information on various aspects of the characteristics of waste landfills and on studies relevant to the assessment of their health impacts. These background papers were distributed to the participants and constituted the background to the discussions at the meeting. The summaries

of the background papers, prepared by their authors, are presented in Annex 2. The discussion was held in three groups focusing on:

- characterization of a site, determination of the potential exposures emanating from a site using available data, identification of exposure pathways and potential contact media;
- characterization of the population at risk and evaluating the need for exposure measurement;
- evaluating the need for and the design of a health study, and the information requirements.

The results of the discussions were reviewed and coordinated by plenary sessions at various stages during the meeting. The main points of the discussion are in section 3 of this report. Section 4 presents the main product: the guidelines for the assessment of exposure to hazards emanating from waste sites. In addition to the guidelines, the meeting formulated conclusions and recommendations (section 5).

3. Summary of discussion

The group agreed that the assessment of exposure near a waste landfill site could be needed for a variety of reasons, such as for ensuring regulatory compliance, addressing community concerns or epidemiological research. Participants also considered the communication of potential risks to the general public an important trigger of an exposure assessment study, in view of the fact that in many situations there may not actually be exposure or any risk to human health. Although substances may pose a toxic threat, the participants felt it was important to point out that this threat will not necessarily be realized.

It was agreed that the following would form a basic framework for the purposes of formulating the guidelines.

- The different purposes for carrying out exposure assessment need to be clarified before any investigation.
- A *landfill site* would be defined as "a localized waste site, which incorporates placement or burial of waste in the ground" (referred to as a waste site). This would include sites with both controlled and uncontrolled placement, underground storage and injection. The meeting would include old sites, sites currently in use and consideration of future sites or changes in the use of sites.
- The *population at risk* could include workers on the site, a resident population on or in close proximity, or some future population if the site were to be used for a different purpose. The heterogeneity of affected populations and the issue of susceptible and vulnerable groups were also discussed.
- "Exposure assessment" is a general term used to cover both the measurement of actual exposures or concentrations of contaminants and the calculation, estimation and modelling of exposures based on existing data. For the purposes of this document, the terms "exposure measurement" and "exposure estimation" are used for clarity.
- A standard or common set of criteria and indicators for carrying out exposure measurement and estimation should be developed for use in any situation. This would facilitate comparison between sites and between studies using different sites. It should enable essential information to be collected and avoid unnecessary expense in obtaining information which might not be useful in interpreting a local situation.

4. Guidelines for assessing exposure to hazards released from waste sites

4.1 A framework for assessing exposure

A checklist approach has been adopted in these guidelines, which focus on the essential issues of concern in assessing exposure to potential hazards from waste sites. Advice should be sought from appropriate experts such as engineers, geologists, biologists, environmental scientists, epidemiologists and health professionals at various stages of this process. It is important to be aware that the presence of a contaminant source is not sufficient to cause a risk to health. As pointed out in the presentations, there has to be a complete exposure pathway i.e. a source, environmental media and transport mechanisms, a point and route of exposure and a receptor population.

Need for the assessment of exposure

An important first step is to define reasons why assessment of exposure might be needed. These include:

- population demand or community health concerns
- to comply with legislation
- litigation
- a proposed change in land use
- research.

Each "assessment trigger" mechanism leads to a specific set of questions and information requirements, and the assessment process must be adapted appropriately to maximize resources and satisfaction with the end result. The need for clear communication of risk and early involvement of the population are also essential elements in the assessment process.

Steps towards an assessment of exposure

Before any special data collection is undertaken, the available information should be explored to support further investigation and determine its scope. This initial assessment process can be divided into five essential steps:

1. Using all currently available information carry out a **site characterization** – description of the nature of the site and its surroundings, review of potential contaminants of concern and identification of migration or transport pathways up to the point of release. The essential questions to be asked at this stage include:
    - What is the current use of the site?
    - Is there any information on the nature of the waste in the landfill?
    - Is the site engineered or non-engineered?
    - Is the site accessible or non-accessible to the general public?
    - Are substances of concern emanating from the site?
    - Are other exposure sources present near the site?

2. Carry out a **receptor characterization,** describing the surrounding population at potential risk of exposure. The following essential questions should be answered:
    - What is the size and composition of the population at risk?
    - What are the characteristics of the most highly exposed population?

3. Identify potential **exposure pathways** which create a route of exposure to a human population. In particular, the essential questions relate to existence of the water resources (surface water or groundwater) which are used in the vicinity of the landfill. Dispersion of the hazards through the air should be also considered.

4. Using available data or by carrying out sampling, **determine the concentrations of contaminants** in the environmental compartments with which humans might be in direct contact, such as soil, indoor- and outdoor air, food and water for domestic or recreational purposes at the site boundary or at the point of exposure. The essential questions are:
   - What are the maximum concentrations?
   - Do the levels exceed the applicable limit or standard?

5. Carry out **exposure estimation** using available data on concentrations, intakes and the population at risk. If this analysis indicates that there is a potential for population exposure which might result in a health concern, the need for further studies or actions should be considered. If a special survey to assess exposure is required, the most appropriate methods should be chosen. This may depend on the reason for the assessment ("assessment trigger"). Detailed site-specific assessment of exposure would most often be implemented if it is triggered by a research need. An assessment triggered by a suggested change in land use might require extrapolation from environmental impact assessment studies and should lead to a health impact assessment.

If the assessment gives clearly negative answers at steps 1, 2 and 3, there is unlikely to be any risk to health related to exposures from the landfill site of concern, and the assessment procedure can be halted. Fig. 1 presents a flow diagram of the assessment process.

4.2 Site characterization and determination of concentration of contaminants

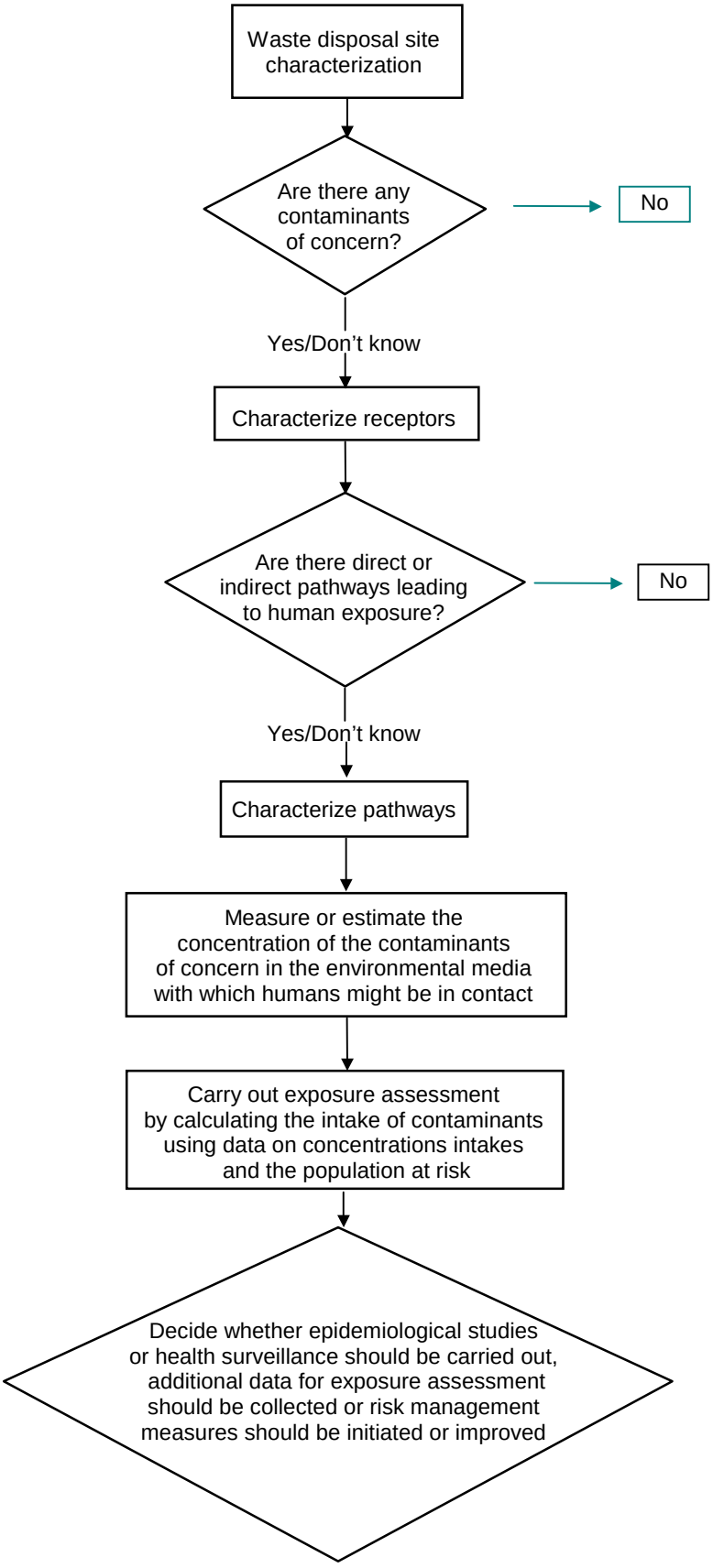
This section gives guidelines on the collection of information that characterizes the site of concern and determines the levels of contamination of relevant environmental media by potential hazardous substances emanating from the sites. Useful categories of data on the technical aspects of a waste disposal site are listed, as are a number of key contaminants.

Key areas of information required for characterizing a site

Important categories of data include:

1. The waste disposal site:
   - nature and quality of the wastes deposited (e.g. hazardous or biodegradable) and the time over which deposition occurred;
   - the construction of the site;
   - natural and engineered controls, including seals, surface cover, gas collection system;
   - monitoring data in and around the site;
   - presence and depth of leachate.

Fig. 1. Steps in the assessment of exposures at waste disposal sites



2. Human activities on and within 1 km[1] of the site, marked on a map:

   - on-site workers
   - residential properties with/without gardens (note if they have basements)
   - schools/kindergartens
   - children's play areas
   - homes for elderly people
   - hospitals
   - open spaces for public use
   - commercial areas
   - industrial areas (note types and possible emissions).

3. Agricultural activities on and within 1 km of the site:

   - areas where crops are grown or animals raised for personal consumption;
   - areas where crops are grown for commercial purposes;
   - areas where farm animals may ingest vegetation (e.g. grass) or soil which may be exposed to contamination (e.g. dust).

4. Groundwater abstraction points within a radius of 2 km of the site. If the direction of the groundwater flow is known, identify the abstraction points which are down hydraulic gradient. For each abstraction point, note:

   - the stratum from which water is abstracted;
   - the rate of abstraction (high or low);
   - use of the water, e.g. public supply, private supply, irrigation, industrial use/cooling water, food manufacture;
   - any information on groundwater quality.

5. The geology, hydrogeology, and hydrology of the site including:

   - the nature of the surrounding geology, particularly method of flow (intergranular or fissure flow) and permeability (high or low);
   - depth of groundwater;
   - direction of groundwater;
   - surface watercourse continuity with groundwater.

6. Surface watercourses and abstraction points up to 2 km downstream of the site:

   - rate of abstraction;
   - use of the surface water (e.g. fishing, bathing, swimming, fish farming);
   - use of the abstracted water, e.g. public supply, personal supply, irrigation, industrial use/cooling water, food manufacture;
   - surface water quality.

[1] Most studies use at least 1–2 km as a plausible area of impact, although this distance might be greater according to site and emissions characterization.

The minimum requirements for a site characterization report are information on natural and engineered controls, types of waste or emissions and potential pathways to a local human population. Available data sources include geological and hydrogeological reports, air, water and soil monitoring data, site history reports, community organizations, and local and regional authority departments.

In compiling a report it is important to review the possible exposure pathways. For example, if methane is produced at the site, it is important to consider the dispersion of the gas via air (inhalation) or through lateral motion below ground (resulting in potentially explosive situations in houses or other structures). Direction and flow of both water and air from the site should be documented.

Contaminants of concern

The following groups of substances should be considered in waste site investigations:

- metals
- total petroleum hydrocarbons
- polycyclic aromatic hydrocarbons
- other aromatic hydrocarbons
- chlorinated hydrocarbons
- polychlorinated biphenyls
- pesticides
- methane
- dioxins
- asbestos
- pharmaceuticals
- pathogens.

These substances are defined as priority pollutants on the basis of toxicity, environmental persistence and mobility, bioaccumulation and other hazards such as explosivity, and, as indicated, may be present in one or more media. This list should be regarded as indicative only and wherever possible a site-specific list of contaminants of concern should be derived.

When reviewing the surrounding area for potential receptors, a radius of 1–2 km should be applied in general, as mentioned above. However, it is important to be aware that some environmental media can provide an indirect exposure route to human populations over longer distances. For example, if drinking wells or water supply systems are contaminated, even if the human population lives outside this radius, a pathways report should still be conducted.

Estimation of concentration of the contaminants

It was not the purpose of this workshop to discuss in detail the methods of determining concentration of substances which might potentially emanate from waste sites. This is an essential part of investigating potential problems, however, and advice should be sought from appropriate experts.

It is suggested that:

- data from readily available sources should be used where possible;
- if limited information is available or the information is out of date, new measurements should be taken;

- it may often be necessary to drill boreholes to:
  - investigate the geological structure
  - investigate the depth of the saturated and unsaturated zone
  - investigate the depth, gradient and flow direction of the groundwater
  - obtain groundwater samples
  - obtain waste or leachate samples;
- depending on the physico-chemical properties of the contaminants, gas sampling should be considered at locations within and outside the site, taking into account the prevailing wind direction and including inside buildings and enclosed spaces in the vicinity;
- groundwater should be measured for contamination with leachate from the site, taking account of the use of groundwater resources locally and regionally.

4.3 Characterizing the population

The following data on population are necessary inputs to exposure assessment investigation:

- identification of the geographical locations of the population and the distances from the site;
- basic demographic data such as numbers of males and females in different age groups;
- patterns of work of the local population, including industrial areas and heavily used commuting routes;
- location of schools and other educational establishments, hospitals and other buildings with high numbers of residents/users;
- location of local leisure facilities and patterns of usage;
- presence and proximity of potentially sensitive groups such as children and elderly, long-term sick and disabled people;
- population behaviour with regard to consumption of local produce.

4.4 Establishment of a completed exposure pathway

Screening for potential exposure pathways and contact media should be carried out using checklists, which include the following:

- inhalation pathway:
  - ambient air
  - indoor air
  - sedimented dust;
- ingestion pathway:
  - drinking-water
  - soil
  - food (vegetables, animal feed)
  - surface water and sediments (with reference to recreational use);
- dermal pathway:
  - direct contact with waste
  - contact with contaminated soil
  - contact with contaminated water.

Full characteristics of the exposed population, collected according to the checklist in section 4.3, should be completed for each of these contact media, where appropriate.

4.5 Estimating the exposure

The screening process summarized above should facilitate the construction of a matrix of pathways and media, together with population characterization data. For those completed exposure pathways, exposure data should be obtained either from readily available sources or from additional sampling. An example of such a procedure is presented in Box 1.

Standard values of intakes are available for air inhalation and soil ingestion. Intakes of food and water and dermal contact will require more detailed information (perhaps obtained by questionnaire or interview) such as consumption of locally obtained food, sources of drinking-water etc. and activity patterns. The concentrations of substances identified in the relevant contact media can then be combined with the intake information to provide an overall estimation of exposure.

The estimated exposures for specified pathways should be compared with available guidelines or standards. Appropriate expert advice should be sought to evaluate the potential impact on the population of the estimated exposures. If the impacts are considered unacceptable but too uncertain for immediate remedial action, the collection of additional data or information to facilitate a more robust exposure assessment may be necessary. Such investigation, using approaches summarized in Annex 3, may require an expert involvement. If an increase in risk is indicated by the collected data, risk management measures at the site must be improved or initiated. Repeated exposure assessment and health surveillance may follow this action.

Box 1. Estimating exposure from polluted groundwater

There may be a suspicion, or available data, that indicate the potential for pollution of groundwater by substances emanating from a waste site. To assess the potential risk to health due to the pollution, the following exposure pathways and contact media should be considered:

(a) ingestion:

- sources of drinking-water, particularly locally obtained drinking-water;
- food – local vegetable and animal produce;
- surface water and sediments;

(b) inhalation:

- indoor air, if the pollutant is volatile;

(c) dermal contact:

- domestic water
- swimming in surface water.

Information should be collected on the characteristics of the populations potentially exposed via these pathways, together with available data on concentrations of the contaminants of concern, and the environmental conditions of the site.

5. Epidemiological investigations

This section provides guidelines (i) for deciding when an epidemiological study should be carried out, (ii) on how to choose an appropriate design, and (iii) deciding what information should be collected.

5.1 When epidemiological investigations should be carried out

Reviews of epidemiological studies have indicated that there is potential for adverse human health effects in populations living near certain waste disposal sites *(2–5)*. Exposure is generally poorly characterized in past epidemiological studies, which constitutes a major limitation in establishing causal relationships.

Future epidemiological investigations are recommended only when characterization of sites and populations, characterization of exposure pathways, environmental monitoring and/or exposure estimations have indicated that a completed exposure pathway is likely to exist (source – pathway – receptor).

When a completed exposure pathway has been established at a particular site of concern, there are various ways of following up these concerns. An epidemiological investigation is only one of the options. Other options are to conduct a health risk/impact assessment or to set up health surveillance. Health surveillance is a routine system of reporting cases within existing health systems. The analysis of the data should indicate whether there has been a significant increase in the reported number of the outcome of interest. A sentinel health network near the waste site can keep a watchful eye on the target population and warn when some other investigation or action should take place. Health risk assessment aims to characterize qualitatively and/or quantitatively health risks related to a specific site based on concentrations of released contaminants, their exposure pathways, and their toxicological profile. Health impact assessment follows similar procedures to health risk assessment in providing information on possible health impacts, and is increasingly required as part of environmental impact assessments of projects such as the opening of new waste sites.

The method chosen to follow up concerns depends on the purpose of the health study, e.g.:

- to advance scientific knowledge regarding causality: *epidemiological study*;
- to address priority public health concern: *health surveillance*;
- to assist in the decision-making process, for example with regard to site remediation, when quick answers are needed: *health risk assessment*;
- for regulatory purposes: *health impact assessments* are increasingly required as part of environmental impact assessments during or after the execution of large infrastructure projects.

5.2 The type of epidemiological study to be carried out

There are a number of well-developed epidemiological study designs, including:

- cross-sectional surveys
- geographical comparison (“ecological”) studies
- cohort studies
- case-control studies.

These types of study are described in Annex 4, together with a description of possible sources of bias. Issues specific to studies of the health impacts of waste sites are choice of health outcome, single- or multi-site studies and specific types of investigation.

Choice of health outcome

The choice of which health outcomes to study should depend on the toxicological profile of the substances to which the population is exposed (as established from site characterization, environmental monitoring and exposure measurement). Considerations should include concentrations of these substances, timing of exposure, latency periods and routes of exposure. Priority can be given to the seven main groups of health outcomes listed by the Agency for Toxic Substances and Disease Registry *(2)* on the basis of a review of toxicological and epidemiological literature:

- birth defects and reproductive disorders
- cancer at selected anatomic sites
- immune function disorders
- kidney dysfunction
- liver dysfunction
- lung and respiratory diseases
- neurotoxic disorders.

Public concerns and the quality of available data should always be taken into account in the choice of health outcome for study. However, in general, public or political pressures alone should not determine the choice of health outcomes or whether a study should be conducted. Hypotheses starting from information about toxicological profiles will improve the scientific value of a study.

Single- or multi-site studies

Epidemiological studies of waste disposal sites can be divided into those studying health outcomes near one single waste disposal site and those studying health outcomes near many waste disposal sites. Single-site studies are generally useful only for relatively common health outcomes, for example respiratory effects, or in situations where the site is located in a densely populated area. Multi-site studies are recommended for the study of rare health outcomes, for example cancers and reproductive outcomes. It is generally more difficult and requires more resources to collect detailed information on site and population characteristics and exposure when many sites are included in a study. Multiple site studies have the advantage of allowing the investigation of exposure gradients (comparing high, medium and low exposure between sites with similar contaminants). The establishment of an exposure–response gradient is particularly valuable in assessing causality.

Specific types of investigation which may prove particularly valuable

When planning an epidemiological study of waste landfill sites, the following designs should be considered as potentially the most powerful:

- before and after comparisons: these have been extremely useful in interpretation of past studies, for example including a period before the start of the waste disposal site as well as after, or investigation before and after remediation of a site;

- studies of vulnerable populations: groups of the population likely to develop adverse effects at lower exposure levels than the general population, for example foetuses, infants, children, elderly people;
- studies of high exposure populations: for example children (because of contact with contaminated soil), workers, people who eat food produced locally, etc.

5.3 Minimum data requirements for good quality epidemiological studies

Assessment of exposure

In all the study designs discussed above, valid assessment of exposure is essential. Various approaches are available for assessing exposure of human populations to substances from waste sites. The US National Research Council *(3)* has shown a hierarchy of data quality for different exposure assessments (see below). Many past studies have used approaches shown at the bottom of this hierarchy such as residential proximity to a site or residence in a geographic area containing a site. In order to advance scientific knowledge we strongly recommend that approaches from the top of the list (points 1–3) are used in future epidemiological investigations.

1. quantified individual measurements/estimates (personal or biological monitoring);
2. quantified area or ambient measurements/estimates (environmental monitoring and/or modelling) in the vicinity of the residence or other sites of activity;
3. quantified surrogates of exposure (e.g. estimates of drinking-water use);
4. distance from the site and duration of residence;
5. residence or employment in a geographical area in reasonable proximity to site where exposure can be assumed;
6. residence or employment in a defined geographical area (e.g. a county) containing the site.

Definition of health outcome

In any epidemiological investigation, it is essential to have a detailed definition of the health outcome(s) to be studied. Diagnosis and classification of the health outcome should be given important consideration.

Confounding factors

Confounding occurs when the exposure of interest is associated with some other characteristic which is also a risk factor for the disease of interest. For example, the incidence of lung cancer may be increased in people living near an incinerator just because they smoke more than the average population. Analytical techniques are available which can take into account or adjust for the effects of potential confounding factors. Where available, information on confounding factors should be collected at individual level to allow for as detailed adjustment as possible. The following list shows confounding factors which should be taken into account when studying exposures to waste disposal sites:

- other sources of environmental exposure (e.g. nearby industries);
- occupational exposure;
- residential history;
- socioeconomic status;

- lifestyle risk factors (e.g. tobacco smoking);
- demographic characteristics (age, gender);
- risk factors specific to health outcome (e.g. reproductive history when studying reproductive outcomes).

5.4 The use of biomarkers of health effects

The use of biomarkers for assessing health risks linked to exposure to substances from waste disposal sites may be a valuable tool in epidemiological studies. Biomarkers of health effects can be used as indicators of: (a) an alteration in tissue or organ; (b) an early event in a biological process that is predictive of development of a health impairment; (c) a health impairment or clinically recognized disease; (d) a response peripheral or parallel to a disease process but correlated with it *(6)*. Annex 5 gives more detail of the use of biomonitoring in the investigation of waste sites.

In studies of the health effects of waste disposal sites, the priority in selecting biomarkers of effects should be given to those that are available for detecting early signs of health effects, most frequently found in association with exposures from waste disposal sites.

Before initiating field studies in which biomarkers are to be used, it is cost–effective to make a critical evaluation of the suitability of selected biomarkers for the study. Such an evaluation should be based on the statistical sensitivities of the specific tissue or function biomarkers and health endpoints for detecting changes. Effective biological monitoring depends on the availability of sensitive, precise and accurate analytical techniques for measuring biological markers. In addition, specimen collection should be strictly standardized in order to minimize sampling variation. Biomarkers must be validated before application in the risk assessment process by establishing the relationship between the biomarker, the exposure and the health outcome.

6. Recommendations

The participants made the following recommendations.

1. Exposure assessment should be carried out by a multidisciplinary team with appropriate expertise.
2. Accessible and transparent methods of communicating all stages of any investigation should be used.
3. The assessment of exposure should be carried out in five steps:
    a. using all currently available information, carry out a **site characterization** describing the nature of the site and its surroundings and the present use of the land, reviewing potential contaminants of concern and identifying migration or transport pathways up to the point of release;
    b. carry out a **receptor characterization** describing the surrounding population at potential risk of exposure;
    c. identify potential **completed exposure pathways** which create a route of exposure to a human population;
    d. using available data or by carrying out sampling, determine the **concentrations of contaminants** in the environmental compartments with which humans are in direct

contact such as soil, indoor and outdoor air, and food and water at the site boundary or at the point of exposure;

e. carry out **exposure assessment** using data on the intakes of concentrations and the population at risk.

4. A two-stage approach for the collection of exposure and site information should be used:
   a. using data from readily accessible sources
   b. carrying out further measurements of air, water, soil and food.
5. If a closed site is to be reused or a change in use of the site is proposed, a risk assessment should be used.
6. Care must be taken when an investigation is carried out at the site to avoid further contamination of environmental media.
7. Documents indicating the use of the land for a waste disposal site must be kept with the documents relating to the ownership of the land by the local administration to ensure that the site is not used in an inappropriate way.
8. Standardized methods of assessment and analysis should be used to facilitate comparison with other sites.
9. Epidemiological investigations should only be considered if completed exposure pathways have been clearly established.
10. The use of health surveillance, health risk assessment and health impact assessment could be considered as alternative options to an epidemiological investigation.
11. An appropriate health outcome for study should be chosen after consideration of the toxicological profile of the substances of concern.
12. The design of an epidemiological study should reflect the main purpose of the study.
13. Levels and timing of exposures, latent period, population structure (including potential vulnerable groups) and quality of data on exposure and confounding factors should be considered when choosing an appropriate design for an epidemiological study.
14. If biomonitoring is considered, biomarkers of both exposure and effects should be carefully selected for detecting exposure and early signs of health disorders.

7. References

1. *Health effects from landfills – impact of the latest research:* report on a WHO meeting. Copenhagen, WHO Regional Office for Europe, 1998 (E62017).
2. JOHNSON, B.L. *Impact of hazardous waste on human health.* CRC Press Inc., New York, 1999.
3. NATIONAL RESEARCH COUNCIL. *Environmental epidemiology. Vol. 1: Public health and hazardous wastes*. Washington, DC, National Academy Press, 1991.
4. UPTON, A.C. Public health aspects of toxic chemical disposal sites. *Annual review of public health,* **10**: 1–25 (1989).
5. VRIJHEID, M. Health effects of residence near hazardous waste landfill site – A review of epidemiological literature. *Environmental health perspectives,* **108** (Suppl. 1): 101–112 (2000).
6. NATIONAL RESEARCH COUNCIL. Biological markers in environmental health research. *Environmental health perspectives,* **74**: 3–7 (1987).

8. Additional useful reading and websites

Evaluation and use of epidemiological evidence for environmental health-risk assessment: Guideline document. Copenhagen, WHO Regional Office for Europe, 2000 (EUR/00/5020369).

Biomarkers and risk assessment: concepts and principles. Geneva, World Health Organization, 1993 (Environmental Health Criteria 155).

Risk assessment for contaminated sites in Europe. Vol. 1. Scientific basis. LQM Press, 1998.

Risk assessment for contaminated sites in Europe. Vol. 2. Policy Frameworks. LQM Press, 1998.

Websites

www.clarinet.at
(The Contaminated Land Rehabilitation Network for Environment Technologies in Europe)

www.atsdr.cdc.gov
(Agency for Toxic Substances and Disease Registry, USA)
Extensive source materials including information on toxic chemicals, hazardous waste sites, and recent research findings.

www.epa.gov/epaoswer/hazwaste/id/hwirwste/risk.htm (accessed on 15 October 2000)
www.epa.gov/ada/ (accessed on 15 October 2000)
(US Environmental Protection Agency – some exposure software models can be downloaded)

9. Glossary of key terms

Bioaccumulation – or bioconcentration: the uptake and retention of substances by organisms via any mechanism or pathway.

Biomagnification: the process by which the concentration of contaminants gets higher and higher in organisms along the hierarchy levels (bottom to top) of the food chain.

Contaminants of concern: the site-specific substances selected for the evaluation of potential health effects owing to their physico-chemical and toxic properties.

Environmental media: groundwater, surface water, air, surface and subsurface soil, sediment, edible biota (e.g. crops, cattle, fish).

Pathway: potential or existing physical links between sources and receptors. They may be direct when the source is in contact with the receptor or indirect when emissions from the source are transported through environmental media and reach the receptor.

Point of exposure: location of potential or actual human contact with a contaminated environmental media.

Receptors: organisms or environmental medium that are exposed to the contamination. For the purpose of health effects assessment, the final receptor is the human population.

Source: contaminants in the waste or, if the nature of waste is unknown, in the contaminated media (soil, leachate and gas, for example).

Waste disposal site: a site which contains contaminated material from disposal activities; this can include closed or open landfills and controlled or uncontrolled (by natural or engineered methods) locations.

Annex 1

PARTICIPANTS

Temporary advisers

David S. Brown
Environmental Protection Agency, Athens, Georgia, USA

Alina Buczyńska
The Nofer Institute of Occupational Medicine, Lodz, Poland

Magdalena Chiriac
National Research Institute for Environment, Bucharest, Romania

Gyula Dura
National Institute of Environmental Health, Budapest, Hungary

Anne Fabricius
Medical Officer, Stadslægen, Copenhagen N, Denmark

Pierre Geuzens
Environmental Diagnostics, Mol, Belgium

Andrea Hancová
Department of Preventive Occupational Medicine, SUHE, Banska Bystrica, Slovak Republic

Leslie Heasman
M.J. Carter Associates, Warwickshire, United Kingdom

Lars Jarup
School of Medicine, Imperial College, London, United Kingdom

Torben Jørgensen
COWI Consulting Engineers & Planners, Odense S, Denmark

Christian Laurent
Université de Liège, Laboratoire ORME, Liège, Belgium

Francesca Quercia
National Agency for the Protection of the Environment, Rome, Italy

Ryszard Rolecki
The Nofer Institute of Occupational Medicine, Lodz, Poland

Lesley Rushton *(Rapporteur)*
MRC Institute for Environment and Health, University of Leicester, United Kingdom

Luciana Sinisi
National Agency for the Protection of the Environment, Rome, Italy

Robert Spengler *(Chairperson)*
Agency for Toxic Substances and Disease Registry, Atlanta, Georgia, USA

Stanislaw Tarkowski *(Vice-Chairperson)*
The Nofer Institute of Occupational Medicine, Lodz, Poland

Martine Vrijheid
London School of Hygiene & Tropical Medicine, London, United Kingdom

Joop van Wijnen
Department of Environmental Medicine, Municipal Health Service, Amsterdam, Netherlands

WHO Regional Office for Europe

WHO European Centre for Environment and Health, Bilthoven Division
Michal Krzyzanowski *(Scientific Secretary)*
Debbie Romaniuk
Agnes Soares da Silva

WHO European Centre for Environment and Health, Rome Division
Candace Chandra

Annex 2

SUMMARY OF PRESENTATIONS

Potential release of hazardous substances from landfills of various technical/engineering characteristics and methods of operation *(L. Heasman)*

Waste disposal sites comprise a whole spectrum of sites ranging from uncontrolled dumps to planned, engineered, managed and regulated controlled landfills. The sites can contain wastes which range from inert wastes only to hazardous waste only. Some waste disposal sites are located in sensitive natural environments such as close to residential properties and in highly permeable geological strata with groundwater that is used for public water supply. Other waste disposal sites are located in a non-sensitive natural environment some distance from residential properties and in low permeability geological strata with no usable groundwater.

The potential for exposure of sensitive receptors (such as people and groundwater) to contaminants migrating from a waste disposal site depends on the existence of a source (the contamination in the waste disposal site), a receptor (e.g. people or groundwater) and a pathway connecting them. Where any one of these components is absent there is no exposure pathway.

An assessment of the exposure of any receptor to contaminants from a waste disposal site should consider:

- the nature of the waste and the mobile contaminants present in the site;
- the proximity and sensitivity of receptors;
- the likelihood of the presence of a pathway connecting the source of contamination and the receptor, taking into account:
  - engineered protection measures
  - natural protection (e.g. low permeability geological strata)
  - monitoring data to demonstrate whether emissions are present;
- the duration and concentration of any exposure.

Toxicological characteristics of contaminants potentially released from waste landfills *(R. Rolecki, S. Tarkowski)*

Each waste disposal site can be considered unique in its composition and effluent. Surveys have shown that, although up to 2000 different chemicals may be present, certain classes of contaminant are more frequently detected. At about 70% of sites volatile organic compounds (VOCs) and inorganic compounds have been found, with about a third having halogenated pesticides and polyaromatic hydrocarbons (PAHs) and just under a quarter with phenols or phenoxy acids and phtalates *(1)*.

As a result of studies performed in the early 1990s in the United States, 56 substances have been identified at 10% or more of sites with completed or potentially completed exposure pathways *(2)*. Thirty of these contaminants, called completed exposure pathway priority substances (CEPPS), have been found in completed exposure pathways identified for 6% or more of these sites. It should be noted that besides 18 carcinogens listed as CEPPS, there are 12 systemic toxicants which have been shown to cause a variety of serious toxic effects (depending on exposure level and duration) on the central nervous system, liver, kidneys, heart, lungs, immune system, skin, and reproduction and child development *(3)*.

These appear to pose a considerable toxic threat. However, in practice this threat may not be realized. For this, it is necessary to have a complete exposure pathway, i.e. a pathway which proceeds from the source

of contamination via environmental media and transport mechanisms to the point of exposure and by some route of exposure to an exposed population. Typical hazardous substances with completed exposure pathways include, for example, trichloroethylene, lead, tetrachloroethylene, arsenic and benzene *(4)*. Monitoring data in air, groundwater and soil around waste sites have shown a clear diminution of concentrations with increasing distance from the site, with, for example, the levels of many airborne contaminants greatly reduced beyond 1 km from the site *(5)*.

There have been a considerable number of studies of the potential adverse health effects of exposure to substances emanating from waste disposal sites. Priority health outcomes are considered to be birth defects and reproductive disorders, certain cancers, immune function disorders, kidney and liver dysfunction, respiratory diseases and neurotoxic disorders *(2)*. Almost all of the studies to date have, however, used some measure of proximity to the sites to assess exposure, i.e. a very unreliable exposure indicator. Confirmation of the adverse health effect(s) may also be lacking in these studies. An inherent limitation of studying this issue is that exposure will be to multiple substances and hence attribution to any one specific substance may prove difficult. In addition, concentrations have been shown to be generally low so that consideration of chronic health effects, rather than acute effects, may be more appropriate, introducing other important issues such as duration and frequency of exposure and latency. Little attention has been paid in previous studies to the issue of the heterogeneity of the exposed populations and it may be necessary in the future to collect data on several confounding variables to address this issue.

References

1. AGENCY FOR TOXIC SUBSTANCES AND DISEASE. *Public health assessment guidance manual*. Chelsea, Lewis Publishers, 1992.

2. Report to Congress 1993, 1994, 1995. Atlanta, Agency for Toxic Substances and Disease, 1995.

3. JOHNSON, B.L. & DEROSA, C.T. The toxicological hazards of superfund hazardous waste sites. *Reviews on environmental health* **12**(4): 235–251 (1997).

4. JOHNSON, B.L. *Impact of hazardous waste on human health*. CRC Press Inc., New York, 1999.

5. ZMIROU, D. ET AL. Short-term health effects of an industrial toxic waste landfill: a retrospective follow-up study in Montchanin, France. *Archives of environmental health*, **49**(4): 228–238 (1994).

v

Transport of the hazards from landfills through various environmental pathways and media *(C. Laurent)*

The existence of hazardous waste sites presents an important environmental issue due to the uncertainties concerning their impact on the environment and their potential effects on the health of humans and on wildlife. Each site may be characterized by its geological, soil and hydrogeological properties and its ecological, industrial and human environment. The situation may be considered as a whole problem and includes the **transport** of potential contaminants from the **source**, by various pathways to a **receptor** where exposure may occur. The source can be characterized by the nature, origin and physical state of the wastes together with the size and annual filling state of the landfill. Transport pathways will depend on the properties of the pollutant released but include surface and underground water and gaseous migration both via the atmosphere and also through saturated or unsaturated soils. Receptors may be human or wildlife. Exposure to humans may occur through inhalation, dermal contact or ingestion of food and drinking-water.

A landfill may be described as a system of incoming and outgoing flows behaving in a similar way as a bioreactor due to micro-organism activity. The incoming flow comprises water from different origins and the different types of waste, added progressively to the landfill. Outgoing flows are produced by physico-chemical reactions leading to the production of leachates, biogas and odours.

The high number of the micro-components of biogas, their low relative concentrations, and their half-life associated with the high number of possible mixtures generated both at the emission or immission sites makes monitoring landfill gas emissions a very complex problem. Concentrations in the air depend on many factors such as emission levels, dispersion and transformation during transport, adsorption to particles, physico-chemical properties, and local atmospheric and geographical parameters. Leachates are aqueous mixtures of bacteria and chemical compounds of both organic and mineral origin. Their composition will depend on the nature of the wastes, the age of the landfills, the pH of the microenvironment and the volume of rainfall. If pollution by biogas is diluted by atmospheric flows, leachate may be a potent concentrated source of pollution for groundwater if not properly treated by adequate waste management. Determination of groundwater flow may be complex if there are completely saturated zones adjacent to partially or totally unsaturated ones.

Despite the large number of studies performed and the evidence of potent toxic properties displayed by compounds detected in several waste landfills, no consensus has been reached regarding the potential health effects in human populations living in the vicinity of waste landfills. The reasons for this include the wide diversity and multiplicity of sites and surrounding populations, a lack of precision and bias in the characterization of exposure, uncertainties in the data on health outcomes and other important confounding variables.

The use of cytogenetic and molecular biomarkers complements environmental monitoring. In addition to validated assays such as chromosome aberrations, sister-chromatid exchanges and micronucleus, new techniques include detection of gene mutation, unscheduled DNA synthesis, HPRT mutants in T-lymphocytes (hypoxanthine guanine phosphoribosyltransferase gene) and determination of adducted nucleic acids or proteins. The high sensitivity of these methods facilitates the detection of adducts formed due to low-level environmental exposures, improves quantitative estimation of target doses, and allows different patterns of exposures over time to be explored.

The danger of using increasingly complex and sophisticated methods is that the results may only be understood by scientific experts. It is essential that accessible and transparent methods of communication are developed, to ensure that residents of areas around landfill sites are kept fully informed of the outcome of any study, including the complexities and uncertainties, and the implications for any ensuing decisions.

Methods of exposure assessment applicable in landfill studies *(L. Jarup)*

The vast majority of studies on the health effects of waste disposal sites have used an ecological design. They therefore suffer from the limitation of having no individual information on either exposure to potential hazards or major potential confounders. Given the limitation of ecological studies, particularly their inability to draw from conclusions concerning causality, a key question should be: how much effort should be spent trying to identify potential harmful exposures emanating from waste disposal sites? An alternative approach might be to prioritize the performance of etiological studies.

The presence of a potentially hazardous substance is not enough to conclude that exposure has occurred. For this to happen there has to be contact between the substances and the human. Concentrations obtained from monitoring data may be a poor proxy for human exposure. For example, contaminated water may give rise to direct exposure through the use of wells or indirect exposure from the consumption of home-grown produce. However, drinking-water is equally likely to be provided from a distant uncontaminated source. Concentrations of substances emanating from sites measured in the air have been found to be rapidly diluted with increasing distance from the sites. There are many highly toxic chemicals potentially emanating from waste disposal sites, but concentrations on site will be very low and decrease with increasing distance from the site. Other potentially hazardous substances for which there is little literature on either transport or effects include micro-organisms and endotoxins. Dispersion by animals or birds is also often not considered when assessing exposure.

In assessing exposure the choice of an appropriate exposure metric, such as cumulative or intermittent exposure, is important. Duration, intensity and frequency of exposure all contribute to the calculation of cumulative exposure. However, mechanistically, evaluation of intermittent or peak exposure also may be important. The period of exposure and the latency time must also be considered, depending on the particular health outcome. Each waste disposal site needs to have well defined and validated location data (including a grid reference), together with prevailing meteorological and geological conditions and information on other nearby sources of exposure, such as other industry. Information on the management of the site, engineering controls, substances received at the site, and how these have changed over time would facilitate the interpretation of any monitoring data.

For effective analytical epidemiological studies, exposure assessment at an individual level is required. This can include estimates of exposure for each individual location (for example, using exposure models), microenvironmental data, time-activity information, and individual information on lifestyle factors, occupational exposures and medical history. Biomarkers may also be useful, particularly if an integrated dose from all sources is required.

Annex 3

METHODS OF ASSESSMENT OF EXPOSURE

This annex provides a brief outline of basic approaches and terminology used in the assessment of exposure. It is based on the monograph *Human exposure assessment* published in the WHO/IPCS Environmental Health Criteria Series.[2]

Exposure measurement

Exposure is defined as a contact over space and time between a person and one or more biological, chemical or physical agents. Exposure assessment identifies and defines the exposures that occur, or are anticipated to occur, in human populations. Exposure is described by the concentration of an environmental agent in the carrier medium at the point of contact with the body together with the duration of the contact. For short exposures, this is usually the estimated sum of instantaneous concentrations over time; for longer duration of exposure (months, years), exposure is usually represented by an exposure concentration averaged over the exposure period.

Quantitative exposure assessment approaches can be categorized as *direct* (measured) and *indirect* (estimated) *assessment* methods. These two approaches are independent and complementary. Each relies on different kinds of data and has different strengths and weaknesses. It is potentially useful, therefore, to employ multiple approaches as a way of checking the robustness of results.

Direct approach

Direct methods include measurements of the concentration of the agent at the interface between the exposure medium and the human body. Data collection from personal monitoring or using biological markers of exposures is carried out for all individuals participating in a study.

Personal monitoring can be carried out, in principle, for all potential exposure media (air, water, soil, food). However, there are several limitations to this approach. Sample collection methods that are sensitive, easy to operate, able to provide sufficient time resolution, free from interference and cost–effective are not always readily available. Consideration should also be given to the possibility that the inconvenience of complying with a personal monitoring protocol may alter the normal behaviour of study participants. Methods of personal monitoring include the following.

- For exposures by inhalation, the use of personal air pollution monitors. The sampling devices may be passive (e.g. diffusion tube for sampling of gases, such as VOCs) or active, with air pumped through a filter to collect aerosols and their components. They can collect the air over a specified time period and are then returned to a laboratory for analysis (integrated samplers) or can contain an analytical system to measure and record the pollutant concentration immediately (continuous samplers).
- For dietary exposures, the contamination in food may be measured through the collection of meals prepared for consumption by members of the study population (duplicate portion samples). The samples will also include any drinks consumed (e.g. tap water if it is consumed without boiling).

[2] *Human exposure assessment*. Geneva, World Health Organization. International Programme on Chemical Safety, 2000 (Environmental Health Criteria 214).

- For dermal exposures, dermal patches and skin wipes should be used to assess the transfer of pollutants deposited on the skin (e.g. pesticide residues from soil). For assessment of dermal exposure during bathing, the concentration of pollutants in bathing water is measured, together with the duration of the contact with the contaminated water.

A biomarker of exposure is defined as a xenobiotic substance, or its metabolite(s), or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism. Annex 5 gives more details of biomarkers. They can represent past exposures (e.g. the presence of lead in shed teeth), recent exposure to an external source (e.g. VOCs in the exhaled breath) or even future internal exposure sources (e.g. pesticides in adipose tissue). However, to date, very few biomarkers have been effectively used for quantitative evaluation of environmental exposure to contaminants. In most cases, they provide qualitative or semi-quantitative indicators for the monitoring of such exposures. A disadvantage of biological markers of exposure is the difficulty in characterizing the different sources of exposure which contribute to the subject's total exposure.

Indirect approaches to exposure estimation

Indirect methods include environmental monitoring of pollution in (micro)locations where exposure occurs, development of models of individual or population exposure, and the collection of information using qualitative methods such as the use of survey questionnaires.

Environmental monitoring. Estimates of exposure based on the indirect approach are made by combining measurements of pollutant concentrations at fixed sites with information on their rates of contact with these media recorded in data logs and diaries or from time-activity surveys. Examples:

- air pollution data in specific locations with time activity records
- food contamination data with information on dietary habits
- pollutant concentration on the skin with data on the frequency and duration of hand-to-mouth contact.

Although the collection of environmental, time-activity and questionnaire data needed for this approach is simpler than for personal monitoring, it is still invasive and laborious and may be subject to bias.

Models are useful tools for a quantitative description of the relationship between exposure and important explanatory variables. They are also useful for the extrapolation of exposure information to estimation for new populations, or to future exposure situations based on certain scenarios. In addition to the deterministic exposure models, probabilistic and statistical models are used. Validated exposure models reduce the need for expensive measurement programmes. However, the challenge is to develop exposure databases and models that allow maximum extrapolation from minimum measurements and costs.

Questionnaires provide qualitative, often retrospective, information on potential exposures and have been a primary tool for exposure assessment in many epidemiological studies. They are also useful for the interpretation of results from personal or environmental monitoring. Prior knowledge of determinants and conditions influencing exposure is needed for the design of questionnaires, which are often used to collect the data on proxy indicators of exposure. Data on time-activity patterns of individuals and populations, used as an input to models and for combination with micro-environmental monitoring data, may also be obtained in this way.

Annex 4

EPIDEMIOLOGICAL STUDY DESIGNS

Study designs

The following study designs have been used in the past to study health effects near waste disposal sites.

Cross-sectional health surveys assess the status of an individual with respect to the presence or absence of both exposure and disease at the same point in time *(1)*. Since exposure and disease are assessed at the same point in time, cross-sectional surveys cannot distinguish whether the exposure preceded the disease and are therefore not suitable for testing a hypothesis. Cross-sectional study designs are not recommended for establishing whether a causal relationship exists between exposure to waste disposal sites and adverse health effects. Cross-sectional studies may be of use when there is a need for quick prevalence data or for establishing degrees of exposure within a population.

Geographical comparison studies (ecological studies) correlate disease rates with exposure to hazards on a geographical basis. These studies require relatively few resources because they make use of routinely available data. An example of a geographical comparison is the comparison of mortality rates for municipalities containing a landfill site with the average rates for an entire country. A major limitation of this approach is that it does not take account of individual differences in exposure or of confounding factors. Geographical comparison studies are useful in generating hypotheses which would subsequently need confirmation from studies based on individual data.

In a *cohort study*, individuals who have been exposed to suspected hazards are followed over time, and their disease incidence is compared to that of an unexposed group. In cohort studies information on disease incidence or health problems can be collected prospectively or historically. In relation to landfill sites, cohort studies have been mostly historical: an exposed population (e.g. residents close to the site) and unexposed population (residents elsewhere) are defined at an earlier time period and information on disease incidence or health problems is collected from the time of exposure to the present. For the purpose of establishing causality the use of prospective cohort study designs is recommended whenever possible. Prospective studies are useful for the study of health outcomes with relatively short latency periods such as pregnancy outcomes or childhood leukaemia. Other health outcomes, such as some cancers, would require a lengthy follow-up period. Accurate definition of exposure groups is essential to the design of prospective follow-up studies (see below). Retrospective cohort studies can be useful for studying long latency health outcomes such as most types of cancer and should be done only when good exposure information or estimates are available.

A *case-control study* starts with the identification of a group of *cases* – individuals who have developed the disease of interest – and a group of *controls* – individuals who do not have the disease. Past exposure to suspected hazards is then compared between the two groups. Waste-site studies, for example, have compared the distance of residence to a waste site or self-reported exposure for cases of a certain disease and healthy controls. The difficulties in case-control studies are the selection of appropriate controls and the unbiased ascertainment of past exposures, particularly when exposure is established from personal recall. Case-control studies are extremely useful for the study of rare health outcomes. In past case-control studies, assessment of exposure has often been based on proxy exposure measures and it is recommended that future studies use more accurate exposure measurement where possible, to avoid misclassification of exposure.

Possible sources of bias

The following possible sources of bias specifically related to the study of waste disposal sites should be considered at the design stage of the study. If they are not eliminated at this point, biases cannot be adjusted for in the analysis stage of a study.

Misclassification of exposure bias

Exposure misclassification bias occurs if exposed populations are classified as unexposed and vice versa. This is often due to uncertainties in the information used. When such misclassification is random, i.e. when it affects diseased and non-diseased populations to the same extent, it will usually decrease the power of a study to find a true effect and bias the true relative risk towards null. Non-random misclassification of exposure may lead to either over- or underestimation of the relative risk. For example, a type of exposure misclassification bias is migration bias. When exposure is measured at the time of diagnosis of a disease, people may have migrated into or out of the exposed areas between the time of exposure and the time of diagnosis, which would lead to misclassification of the exposure.

Reporting or recall bias

Studies which rely on self-reported information may suffer from reporting or recall bias. This bias may also differ between subgroups of individuals. For example, people living next to waste sites may remember health problems better than other people and therefore report a higher incidence of disease. In a case-control study, people who have become ill may be more motivated to remember past exposure than controls.

Selection bias

Selection bias occurs when the relationship between exposure and disease is different for those who participate and those who are theoretically eligible for study *(2)*. Selection factors for participation should be the same as far as possible for cases and controls.

References

1. HENNEKENS, C.H. & BURING, J.E. *Epidemiology in medicine*. Boston, Little, Brown & Co., 1987.
2. ROTHMAN, K.J. & GREENLAND, S. *Modern epidemiology*. Philadelphia, Lippincott-Raven, 1998.

Annex 5

BIOLOGICAL MONITORING IN STUDIES OF WASTE SITES

L. Jarup, C. Laurent, S. Tarkowski

Biomarkers of exposure

Exposure assessment may be carried out using several approaches, all of which have their advantages and disadvantages (Annex 1). Environmental monitoring (the measurement of exposures either directly or indirectly in environmental media) may not reflect the dose actually received by a given individual.

An alternative approach is the use of biological monitoring, which refers to measurements of concentrations of biological markers (biomarkers) in human indicator media such as blood, urine, faeces, hair or maternal milk (1). The aim of biological monitoring is to provide a measurement of the internal dose of exposure, effect or susceptibility of an individual to a substance. Markers have been developed which allow the identification of components of a complex mixture, confirm that exposure has occurred, or provide an integrated measure of a biologically effective dose from a multiple source (2). A major advantage of using biomarkers is that the measurement of internal exposure is more likely to be directly related to adverse health effects than the measurement of external exposure. The concepts and principles of application of biomarkers to health risk assessment and criteria for selection and validation were reviewed by a WHO Task Group on Biomarkers and Risk Assessment in 1992 (3).

Measurements of concentrations of potentially harmful agents in a critical organ or site of action (the most sensitive organ or site, where adverse effects are seen at the lowest concentrations) such as the brain, liver, kidneys or skeleton is rarely possible unless an autopsy or surgery is carried out. Instead, a biomarker that mirrors the result of the exposure may be measured in human indicator media. Ideally, biological monitoring mirrors the concentration of the hazardous agent in the critical organ. Biological monitoring has proved to be particularly useful for assessing exposure to metals (4) as well as for more than 50 organic substances (5).

It has been suggested that biomarkers (of exposure, but also of early health effects and individual susceptibility) may be useful tools in studies assessing health effects in populations living in the vicinity of waste dump sites (6). They have the advantage that they take into account inter-individual differences in absorption, metabolism, bioavailability, excretion and distribution (7). Although it also has limitations, biological monitoring is complementary to environmental monitoring because it takes into consideration the biokinetics or toxicokinetic factors of a compound. In addition, biological monitoring may reflect different patterns of exposures over time that might not have be detected in sporadic environmental measurements, and integrates exposure occurring shortly before the sampling (some hours) with exposure occurring some days previously. However, a measured internal dose may reflect the accumulation of repeated exposures. A prerequisite for biological monitoring is knowledge of the physico-chemical properties, kinetics and stability of the compound and the sensitivity and specificity of the monitoring methods.

Examples of substances which may be of concern related to waste sites and for which biomarkers have been developed to assess exposure include:

Substances	*Biomarker*
Lead	Blood lead
Cadmium	Urinary cadmium
Chromium	DNA-protein cross-links
Mercury	Urine mercury
Polychlorinated biphenyls (PCB)	Serum PCB
Volatile organic compounds (VOC)	Blood VOC
Chlorinated pesticides	Breastmilk chlorinated pesticide
Polycyclic aromatic hydrocarbons	DNA adducts

Biomarkers of exposure (dose) may be used in a similar way as personal monitoring. Appropriate biomarkers are only available for a limited number of substances, and should only be used when there are clear indications of exposure (e.g. from stationary monitors in houses).

Biomarkers of health effects

Biological markers of health effect have been defined by the US National Research Council as "indicators of an endogenous component of the biological system, or an altered state of the system that is recognised as impairment or disease" *(8)*. They can be used in three main ways: (i) to screen for preclinical signs of a disease, (ii) to facilitate conventional epidemiological studies of disease etiology, and (iii) to monitor variations in health risk *(2)*.

In terms of measurable health effects, biological markers may be used as indicators of (i) an alteration in a tissue or organ; (ii) an early event in a biological process that is predictive of a development of a health impairment; (iii) a health impairment or clinically recognized disease; (iv) a response peripheral or parallel to a disease process but correlated with it and thus usable in predicting the development of a health impairment *(9)*.

The application of well established biomarkers for a specific endpoint or health outcome linked to exposure and toxic mechanism has the potential to enhance the reliability of predictions of risk. However, there are large inter-individual variations in responses to equivalent doses of chemicals and such biomarkers may not be specific for a single toxic chemical as a causative agent.

Many biomarkers of effect have been established and used in occupational and environmental epidemiology as tools for detecting early and reversible clinical effects in target tissues and organs. In studies on health effects of effluents from waste landfills, the priority in selecting biomarkers of effects should be given to those which are available for detecting early signs of health effects most frequently found in association with exposures from waste landfills *(6)*.

Examples of health effects for which biomarkers have been developed

Health effect	*Select biomarker examples*
Hepatotoxicity	Serum aspartate and alanine transaminases Enzymes
Nephrotoxicity	Functional markers – serum creatinine, albumin, α_2-microglobulin Cytotoxicity markers – tubular antigens, urine enzymes Biochemical markers – sialic acid, glycosaminoglycans Tubular proteinuria – beta-2-microglobulin, NAG, RBP
Immunotoxicity	Lymphocyte changes – T cells, IgE antibodies
Pulmonary toxicity	Neutrophils, cytokines
Neurotoxicity	Plasma and erythrocyte acetylcholine esterase inhibition
Genotoxic carcinogenesis	Chromosome aberrations, micronuclei, sister chromatid exchanges.

Biomarkers of health effects related to environmental exposure are generally not specific. However, it may be possible to eliminate various other factors affecting the estimations of biomarkers and thus improve specificity. Biomarkers must be validated before application in the risk assessment process by establishing the relationship between the biomarker, the exposure and the health outcome. Using biomarkers for assessing health risks related to exposure to toxic effluents from landfills may provide an alternative to the use of traditional health outcome measures. However, a clear understanding is needed of the significance and methodological pitfalls of the biomarkers applied in the study. The use of biological markers in epidemiological research should be a means, not an end *(10)*. Before initiating field studies in which biomarkers are to be used, it is cost–effective to make a critical evaluation of the suitability of the

biomarkers selected for the study. Such an evaluation should be based on the statistical sensitivities of the specific tissue or function biomarkers and health endpoints for detecting changes.

References

1. *Human exposure assessment*. Geneva, World Health Organization. International Programme on Chemical Safety, 2000 (Environmental Health Criteria 214).

2. VAINIO, H. Promise of molecular epidemiology – epidemiologic reasoning, biological rationale and risk assessment. *Scandinavian journal of work, environment and health*, **25**: 498–504 (1999).

3. *Biomarkers and risk assessment: concepts and principles*. Geneva, World Health Organization, 1993 (Environmental Health Criteria No. 155).

4. ELINDER, C-G. ET AL. *Biological monitoring of metals*. Geneva, World Health Organization, International Programme on Chemical Safety, 1994 (Chemical Safety Monographs. WHO/EHG/94.2).

5. LAUWERYS, R. & HOET, P. *Industrial chemical exposure. Guidelines for biological monitoring*, 2nd ed. Boca Raton, Lewis Publishers, 1993.

6. INDULSKI, J.A. & LUTZ, W. Biomarkers used for the assessment of health hazards in populations living in the vicinity of communal and industrial waste dump sites. (Review). *International journal of occupational medicine and environmental health,* **8**: 11–16 (1995).

7. BOND, J. ET AL. Assessment of exposure to pulmonary toxicants. *Fundations of applied toxicology,* **18**: 161–174 (1992).

8. NATIONAL RESEARCH COUNCIL. *Environmental epidemiology: Vol. 1. Public health and hazardous wastes*. Washington, DC, National Academy Press, 1991, pp. 20–21, 114.

9. COMMITTEE ON BIOLOGICAL MARKERS OF THE NATIONAL RESEARCH COUNCIL. Biological markers in environmental health research. *Environmental health perspectives*, **74**: 3–7 (1987).

10. MCMICHAEL, A.J. Invited commentary "molecular epidemiology": new pathways or new travelling companion? *American journal of epidemiology*, **140**: 1–11 (1994).