MINISTRY OF HEALTH OF UKRAINE
O.O. BOGOMOLETS NATIONAL MEDICAL UNIVERSITY

"Approved"
at the methodological conference of hygiene and ecology department
Head of the department
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GUIDELINES
FOR STUDENTS

Subject	Hygiene and ecology
Module № 1	Assessment of the environment and its impact on the population health
Submodule №1	General questions of hygiene and ecology
Topic of the lesson	Hygienic assessment of the potential risk of the environmental factors impact on the human body and population health.
Course	6
Faculty	medical
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Kiev

1. Learning objective

Master theoretical knowledge and general scheme on the risk assessment for population health caused by the environment factors.

2. Basics

2.1. You should know:
2.1.1. Main definitions used in the risk assessment methodology.
2.1.2. Main stages of the risk assessment methodology.

2.2. You should have the following skills:
2.2.1. To calculate the relative and population health risk.
2.2.2. To operate with microcomputer or PC.
2.2.3. To identify the hazard factor and state the qualitative value of harmful effects for health.
2.2.4. To substantiate the scheme and content of main stages of the risk methodology.
2.2.5. To apply information and normative materials.

3. Self-training questions

3.1. Risk assessment methodology. Problem's characteristic and main definitions.
3.2. Main stages of the risk assessment methodology:
3.2.1. Identification of the hazard factor (factors).
3.2.2. Exposure assessment.
3.2.3. "Dose-response" relationship assessment.
3.2.3.1. "Dose-response" relationship assessment for non-carcinogens.
3.2.3.2. Biomarkers. Indicators of exposure, effect, susceptibility.
3.2.3.3. "Dose-response" relationship assessment for carcinogens.
3.2.4. Risk characterization.
3.3. Connection between the risk assessment and risk management. Risk management and hygienic regulation.
3.4. Problems of the risk assessment methodology application in Ukraine.

New scientific-practical approach – Evidence-Based Medicine was formed in medical science last years. General hygienic methods, connected with detection and assessment of the risk-factors' negative impact on development and further progress of the individual and population health, have improved. Definition of "risk" in medicine is caused by necessity to reflect the relative and probable interaction patterns of the organism vital activity and the environment. Probability means the measure which gives quantitative characteristic of possibility of phenomenon appearance or achievement of certain result. Probability ranges from 0, when the phenomenon never appears in the specific system, to 1, if the phenomenon appears inevitably. These extreme variants of the phenomenon development are determined inflexibly.

The term “risk” comes semantically from the following Greek words *risikon, ridsa* – rock, cliff. In Italian the word *risiko* means danger, threat; *risikare* – maneuver between rocks; in French *risdore* – threat, risk (expressis verbis: go around rock, cliff).

Method of risk assessment is used to compare different probabilities of any human state appearance (disease, etc.). It is based on the comparison of the possibility of the evidence development during certain period of time in certain conditions and the possibility of the evidence development during the same period of time in other conditions. Risk factor (or health risk) means any factor which increases the probability of the negative consequences appearance for health in some Ukrainian (Ye.G. Goncharuk, A.M. Serduk, Yu.V. Voronenko and others) and foreign (Gundarev I.A., Lisitsin V.Yu.) scientists’ opinion.

It is well known, that the human deals with many different potential risk-factors during everyday activity. The main task of hygiene is the determination and assessment of these risk-factors, and, based on the received results, scientific substantiation and working out of the most effective measures for elimination of these risk-factors if it is possible; minimization to acceptable level of risk-factors, if the community can manage them.

Classification of “risk” and “risk factors” (individual and population level) by G.I. Stegunov, 1975, Robbinsa, 1980, and C. Varkevisser, 1995 must be used for the risk classification in public health from social and hygienic point of view

The social and hygienic risk (hazard) classification must be continued and divided by two types – natural and artificial. Natural risks by types can be endogenic (age, gender, etc.) and exogenic (flora, fauna, etc.). Risks by localization are divided by connection with lithosphere, atmosphere, hydrosphere or Space. According to the official standard there are physical, chemical, biological and psycho-physiological risks (hazards) of the health disorders. Natural risks, by the sources of origin can be phenomenons, objects and processes; by consequences for health from the risk-factors impact – fatigue, disease, trauma or death.

From the position of risk during the human (population) health study there are the following types of risk: individual, social, relative.

There are the following types of risk: relative, attributive, attributive population and population fraction of attributive risk during assessment of the human health state deterioration.

Hierarchical classification of risk factors by peculiarities of their impact on the individual and population, duration, etc. are applied nowadays.

Generalized data of this research are represented on fig.1.

The following classification of risk (hazard) in the system of public health and medical care was composed for practical application and unification. The most important characteristics of the risk were the background of this classification: 1) origin, type *(type, origin, object)*; 2) realization place *(periodicity, medium, sphere and priority of appearance)*; 3) realization damage *(level of impaction human)*; 4) impact on the time risk-factor *(structure of appearance, type of impact, registration of the time factor, duration of impact, impact rate)*; 5) prediction *(level of prediction, range of effect, level of damage, removal, compensation, management)*; 6) type of management decision *(level, time and type of taking decisions).*

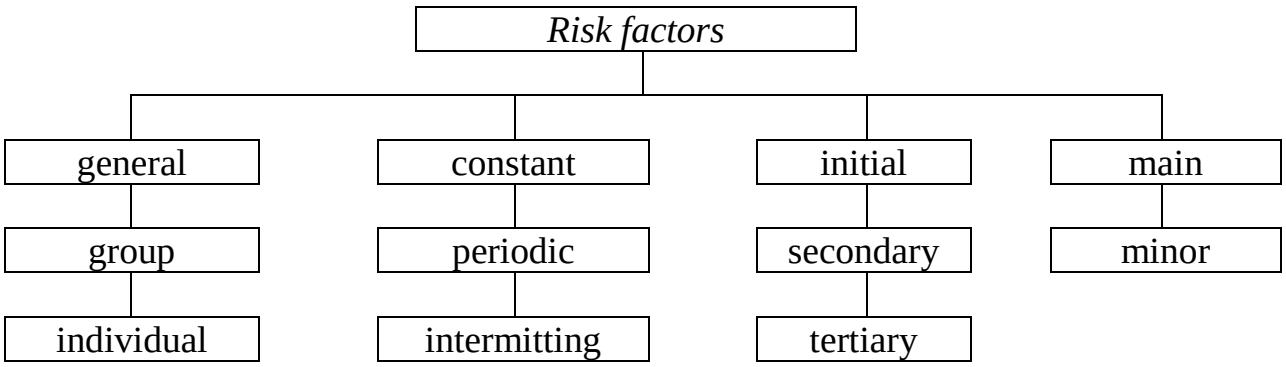


Fig. 66.1 Hierarchical classification of risk factors

Based on the definition of "risk" and "danger" listed above, experience of systemic classifications, the following generalized classification of risk and danger in the public health system can be proposed (table 1).

Table 1

Generalized classification of risk (danger) in public health

Signs of classification	*Factors*
By type	Natural, technogenic, mixed
By the hazard type	Physical, chemical, biological, information and semantic, complex
By origin	Space, abiogenic, biogenic, biological, biotic, natural and human caused, human caused, antropic
By object	individual, group (social, collective, etiological, social and economic, social and psychological), specific
By priority of appearance	Initial, secondary
By periodicity of appearance	Periodic, non-periodic
By the medium of origin	Atmospheric, water, geomorphological, edafitic, physiological, genetic, population, biocenotic, ecosystemical, biospheric
By place of appearance	External and internal (both types of risk have proper classification)
By the degree of impact on human	Lethal, extremal, limited, disturbing, carcinogenic, mutagenic, teratogenic
By degree of impact of the medical care organization	Acceptable, critical, catastrophic
By structure of appearance	Simple, derivate
By character of impact	Active, passive
By the time factor	Static and dynamic
By duration of impact	Short-term, medium-term and long-term
By frequency of impact	One-time, periodic, constant
By degree of prediction	Predicted, non-predicted
By spectrum of impact	Selective effect, general effect
By level of damage	Minimal, average, optimal, maximal, critical, catastrophic
By level of removal	Those removed totally, ... partly, ... are not removed at all
Be level of compensation	Compensated, partly compensated and non-compensated
By management	Controlled, non-controlled
By level of making the decision	Macroeconomic and microeconomic
By time of making the decision	Forward, opportune and late
By type of making the decision	Rational (substantiated), irrational (non-substantiated), adventurous (risky)
By probability of the situation origin	Stochastic (probability of appearance), uncertain (uncertainty of appearance) and competitive (in terms of conflict)
By objectivity	With objective probability, subjective probability and subjective-objective probability
By level of acceptance	Obligatory acceptable, acceptable, non-acceptable

Signs of classification	*Factors*
By level of propriety	Lawful, unlawful
By human perception	Voluntary, forced

Application of the risk assessment methodology significantly influences quality of epidemiological researches. The risk assessment in preventive medicine is multi-stage process directed on the probability determination or prediction of negative impact of harmful substances polluted residential or industrial environment on the population health. The risk assessment is based on the information about level of this pollution, toxic properties of the substance, its migration and transformation in the environment, ways of impact on human, peculiarities of human population, influenced this substance.

Specific methodology of "risk assessment" in special meaning was accepted by the governmental Environment Protection Agency of USA (US EPA) and recommended by different international organizations (WHO, UNEP).

The concept of risk for the environmental factors impact is not applied in practice in Ukraine. Researches are restricted to statements about the health state deterioration, i.e. indication of the hazard resulted from the harmful environment factors impact. If we try to identify the difference in methodology of the harmful factors standardization between our country and other states, the following conclusion can be drawn – the science's progress on the way to knowledge is restricted by some social conditions.

The legal statement for the risk assessment application in Russia is Resolution of the Principal state sanitary doctor of RF and Principal state inspector of RF on the environment protection from November 11, 1997 "On application of the risk assessment for the management of the environment and population health in Russian Federation". Application of the risk assessment for the control of the environment quality and population health is approved by this Resolution, but, at the same time, the necessity of its adaptation to the conditions in Russia were pointed and main directions of this adaptation were planned.

System of hygienic regulation, adopted nowadays, for provision of the effective prevention of hazardous impact and harmonization with international conceptions requires application of the risk assessment methods. Practices of the environment assessment and public health, which were widely used in our country in previous period of state ownership of industry and planned state economics, strict system of state sanitary inspection, has significant differences from foreign system of control over the legislative norms and rules compliance. This obligates to force the changeover into other form of properties with adequate caution, taking into account the future entering into the World Trade Organization.

The risk assessment plays significant role for the optimization in choosing of the prior monitoring factors, determination of the environment pollution sources, identification of points and means for the exposure control, substantiation of indicator criteria for the influenced environment and affected population.

Main definitions

Risk is defined as realized hazard of appearance of event with consequences, negative for the population health in space and time. Risk is the quantitative value. Risk is characterized either by values from zero (means assurance that the hazard affects

nobody) to one (means assurance that hazard affects everybody), or expected frequency of negative effects which affect the population from determined harmful impact. First type of the risk determination is treated sometimes as the individual, second one – as population risk.

Hazard (threat) is defined as natural, man-caused or social event with predicted, but unmanageable hazards of the adverse effects appearance in certain period of time and on the certain territory. These hazards can impact the population health and cause damage, including material, etc. Hazard is the qualitative value.

This form of the risk identification is universal because it allows to connect in one index different data about the object and subject of the hazard. This, in further, allows to receive the integral risk assessment from unlimited processes of any origin.

Source of hazard, or hazardous factor (in American and international documents – hazard), is defined as chemical substance, biological or social agent in the environment which forms the possibility of the risk for the population health and is realized only in certain conditions of exposure.

Exposure means either the simple statement of the hazardous factor impact or quantitative value of such impact on the individual organism, group or population taking into account its magnitude.

Dose means the main value of exposure which characterizes quantity of substance influencing the organism during inhalation of the air polluted by this substance, consumption of polluted water or food, contact of the skin with this matter. The following terms corresponds to this definition: "*potential dose*" in American documents, "*intake*" in some international documents, "*administered dose*" concerning toxicological experiments on animals.

Other definitions of dose accepted by the American methodology: "*applied dose*" (quantity of the substance on the free bounder of anatomical barrier between external and internal environment of the organism), "*internal dose*" (quantity of the substance which is adsorbed into the internal environment of the organism) and "*biologically effective dose*" (quantity of the substance which penetrates into the organ, and causes the development of main harmful effects of exposure) are scientifically interesting, but rarely applied due to excessive ambiguity of their calculations in real researches concerning the risk assessment.

Effaced dose ("*reference dose*" (RfD) in Americal documents and "*tolerable intake*" – TI in international one) is defined as a dose, influence of which on the human population, including the most sensitive subgroups, does not pose the risk of any harmful effects during the whole lifetime.

The reference concentration – RfC is established for the risk assessment from the harmful substance content only in the air and reference dose is not taken into account.

Hazard quotient is defined as a correlation of the affected dose (or concentration) to acceptable one.

Response is a portion of the human or laboratory animal population which expresses the determined harmful reaction on determined dose of hazardous factor.

Identification of the hazard source (sources) (hazard identification) is the stage of the risk assessment which means the qualitative characteristic of the negative effects of hazardous factors impact of the polluted environment in this zone, city (town), region on the

organism, and factors which can be potential hazardous sources for the health of population who live in this locality or any other its part.

Exposure assessment is the stage of the risk assessment and means the determination of routes (components of the environment, its quantitative level – expressed as a concentration in this component and/or as a dose) of the real or potential impact of the specific hazardous factor on the human population of its part taking into account its magnitude.

Assessment of the "dose (concentration) – response" is the risk assessment stage, which includes determination or prediction of the connection between the dose or concentration of the hazardous factor and algebraic number of people with defined intensity of the qualitative adverse effect expressed quantitatively.

Risk characterization is the final stage of the risk assessment, means synthesis of data from the three previous stages and ambiguities connected with them, substantiation of conclusions expressed in quantitative, semi-quantitative or descriptive form which must be submitted to the person or organization, which make decisions concerning the ecological policy and public health management, or subject of economical activity who ordered this risk assessment.

Ambiguity is oriented assessment of limits, where predicted true values of those quantitative parameters, which are used at different stages of the risk assessment, are positioned, and is its final characteristic. However, only reasons for ambiguity and expected signs of its impact on the final risk assessment are pointed frequently.

Risk management is defined as a system of political, technical, administrative, legislative and normative solutions, directed on liquidation or significant decreasing of the risk for the population health. This is set based on the results of the risk assessment taking into account range of its sources, comparative hazard (for individual and whole population) of possible negative effects, magnitude of population, exposed to this risk, and all those factors of politics, economics and social consciousness, which influence the making of decisions in certain place and time. The different risk management scenarios, which are worked out, allow to choose those, that can be the most effective in conditions when the expenditure is minimum and/or realization – maximum.

Information about risk (risk communication) means the responsibility of the expert or expert organization, who perform the risk assessment, for transition of the detailed results of this assessment to persons (authorities) which make a decision, adequate notification about these results to organizations and movements on environment protection, population (through mass-media) and different variants of the risk management are proposed for them at the same time.

The following concepts are used most frequently during epidemiological researches concerning the population health study and assessment – relative risk, attributive risk, attributive population risk and population fraction of attributive risk.

Relative risk is defined as a ratio between the risk of the disease or death appearance among those who were exposed to different factors and the risk among non-exposed population. The value of relative risk allows to measure the pathogenic power of conditions which associated with risk-factor. But this value does not give adduction concerning absolute value of the morbidity prevalence. The attributive risk is used for this purpose.

Attributive risk is defined as a level of disease or other pathological state, which can be resulted from the factor impact. It is established by subtraction of the pathological state level presented in the population not exposed to the factor impact (as usual this is morbidity or mortality) from level in the studied group. In contrast to relative risk, attributive risk measures its consequences. As opposite to the relative risk, which measures the power of the pathological impact, attributive risk measures its consequences, which can be expressed as quantity of people who became ill during certain period of time per magnitude of population.

Relative and attributive risks allow to compare the probability of morbidity in different population groups with presence or absence of risk-factors. But these risks do not give the conception on pathogenic significance of the factor to the whole population. The following index – *attributive population risk* – is used for this purpose. This type of risk is calculated according to the following equation $(I_1 - I_2) \times P$, where P is the number of people with specific risk-factor.

Population attributive risk (synonyms – *population fraction of attributive risk, attributive population fraction or etiological population fraction*) is defined as a morbidity (or other pathological state) associated with the risk-factor impact. Population fraction of attributive risk is used for assessment among the population of the portion of the morbidity caused by the risk-factor to morbidity of this disease in general. It is calculated as ratio of population attributive risk to total quantity of people who became ill on this disease in specific population per same period of time. It is expressed in percentage and calculated using the following formula:

$$P(\%) = \frac{N_e(M_e - M_n)}{N_t \times M_t},$$

where: P – risk;

N_e – number of exposed or those who were affected by the risk-factor impact;

N_t – number of people in the population;

M_e – morbidity among exposed people;

M_n – morbidity among non-exposed people;

M_t – general morbidity among the population.

General description of the risk assessment methodology

There are 4 stages of the risk assessment methodology:

- identification of the hazard(hazardous factor) source,
- exposure assessment,
- assessment of the „dose – response”,
- risk characterization.

Attempts to ignore some stages lead to many complications. That is why the methodological background of the risk assessment in medical and ecological researches is the first law of hygiene.

Connection between listed above stages can be either direct, or indirect. But each of them is described as a determined sequence of actions which follow established algorithms. It is necessary to point that:

- at first, initial methodology of the US EPA is recommended by its essence, but not obligatory both as a whole or in details;
- at second, distinctive feature of this methodology is its flexibility, ability to be adapted to specific tasks, new information, possibility to choose between alternative approaches to the assessment, etc.;
- at third, even US EPA guidelines on the risk assessment are modified periodically because of accumulation of the experience and/or changes of views of the EPA specialists.

The most important objective is mastering not only of the general scheme of the risk assessment, but also possibilities of creative approach which is the background of this methodology.

Identification of the hazardous factor (factors)

The first stage of the risk analysis is identification of the most serious sources of hazard (risk-factors) and their range to determine the real threat for people and environment based on the drawing of the risk maps; resistance limits of technical and ecological systems; apply the methods of mathematical statistic.

As mentioned above, the qualitative assessment of adverse impact of any factor (or factors) on people or animals have to be done at the identification stage.

E.g., it was established that lead (Pb) compounds may cause disturbances of the hemoglobin synthesis, affects peripheral nerves, vegetative and central nervous system, lead to the psychic development delay of children, affect female reproductive function, etc. The lead may be identified as a hazardous factor for health. In this example the identification is based not only on the experimental, but also vast clinical and epidemiological data. But identification of the hazardous factor is based frequently only on data of experimental toxicology. If the necessary information is absent in available bases or literature, then such identification requires special toxicological researches. As any research of such type, it is connected with previous study of chemical and physical properties of the substance, especially its reactivity. Hence, the identification stage is based on the theoretical, experimental and clinical data.

Importance of this stage means not only that on its basis may be determined those effects of adverse impact on the organism, that further will be assessed as a “dose-response” and final risk characterization will be given. But also it is necessary to choose among these effects the limited ones – which make the risk assessment the most actual, taking into account not only corresponding weight and/or both individual and social significance of effects, but also the most real of the lowest exposure levels. In other words, to solve such important task as identification, which requires registration of both qualitative and quantitative characteristics, it is necessary to return to it after analysis of the “dose-response” dependence. E.g., in case of the lead, the critical effect is the decreasing of intellectual level and behavior deviations from the norm among the babies and primary school age children, for the cadmium – the renal tubules involvement.

On the other hand, another task of the identification can be solved only analyzing both toxicological characteristics of substances and assessing (on the next stage of the work) exposure levels jointly. Such way the short list of pollutants which are emitted into the environment of this locality can be composed, for which the further stage of

analysis - the “dose-response” (the most difficult which requires the high qualification of the expert) is essential. Ordinary practice of American experts is to carry out the complete risk assessment for all registered pollutants on the specific territory (or from specific point) and then range the received risks. But native toxicologists consider that this practice is not acceptable in Russia and Ukraine. It is necessary to keep in mind that the risk assessment is necessary at first in highly industrialized zones, where emissions and waste of many enterprises pollute the environment with dozens or hundred different harmful substances. In out country, the provision of the risk assessment quality can be inadequate in such vast scales. On the other hand, the system of conservative hygienic standards of pollution of the different environmental compounds (MAC, OSIL) is developed for the most pollutants. That is why in specific conditions those pollutants which concentration is lower than these standards can be excluded from the further consideration, because they do not pose any risk. The attention, present knowledge and possible expenditures should be concentrated on those environment pollutants, which have provided adverse impacts on the population health and carry out their risk assessment (with further comparison of these risks).

E.g., in Russia the following criteria for choosing of prior pollutants (“shortlist”) were proposed on local level, applied into practice for planning of the risk assessment in towns of Sverdlovsk region.

A. Exceeding the MAC of hazardous substance by its average concentrations (for substances of unilateral action – the sum of ratios of their concentrations to corresponding MACs, which exceeds 1.0) in one of the environment components.

B. Content of hazardous substances at levels, corresponding their MACs in more than one environment component. Special attention should be given to the pollution of soil, which exceeds background one, foodstuffs of local origin. Those concentrations that do not exceed, but are “commensurable with MAC” are ranged from 0.1-1.0 MAC.

C. Especially adverse character of the provided hazardous impact of the substance (carcinogenic effect, impact on reproductive function and/or descendents, development of the child nervous system).

Environment pollutants which are present in “shortlist” of not less that two towns (territories) of the region are included to regional priorities. The pollutants of the regional “shortlist” are ranged depending on the total quantity of population living in this territory.

Conception about the work restriction based on the proposed approach can be illustrated by the example of the town Verkhnya Pushma (Sverdlovsk district). There are 29 substances which pollute the environment and are used for monitoring. Only 9 of them were chosen for the risk assessment, including: by criterion A – suspended particles, sulfurous anhydride, nitrogen dioxide, ammonia; by criterion B – benzpyrene; by criteria A and B – copper; by criteria A, B and C – lead, arsenic, cadmium.

Exposure assessment

This stage includes the assessment of the following parameters: routes and medium, quantitative level, and duration belong to real or predicted adverse impact, assessment of the population magnitude, exposed or may be exposed to such impact.

If data, received from the monitoring, for the further assessment of so called multi-medium risk connected with pollution of different environment components with one substance and different route of exposure (e.g., inhalation, oral, cutaneous), the logical approach of its assessment is determination of total dose of this substance penetrated into the organism by different routes (or at least by those which have sufficient information). The calculation of dose penetrated by each route separately is necessary for this purpose. In some cases different exposure routes lead to damage of different target-organs and doses received by such way should be considered separately. If the risk assessment of pollution is possible only for one environment component (most frequently – the air), the calculation of the dose reveals only additional ambiguities in the exposure assessment, which can be expressed in units of the pollutant concentration in this component.

The exposure level (substance concentration in the medium) and time factor are evaluated on this stage. This allows to receive the reference dose value indirectly, even if this dose can not be determined directly (e.g. chemical analysis of blood or other mediums). For the risk assessment which is not associated with the profession, the dose is calculated for the life period during 70 years (or specific period of time, e.g. childhood) as average daily value per 1 kg of body weight. E.g., average daily dose (ADD) received through inhalation or oral route is calculated according to the following formula:

$$\text{ADD} = \frac{(C_{av} \times CV \times EP)}{(BW \times AP)},$$

where: C_{av} is average (arithmetical) concentration of toxic substance in the corresponding environment medium;

CV – consumption volume of this component (in the same units of volume or mass, which belongs to this concentration);

BW – body weight;

EP and AP – total exposure and average period correspondently (in days).

For calculation of the average daily dose per life the average period equals to the life longevity. Fothis index and other exposure parameters which should be taken into account during the dose calculation (especially the volume of inspired air, consumption of water and foodstuffs), the methodology of the US EPA provides the determination of two assessment values, one of each is “central trend”, another one – “upper bound”.

“Central trend” is calculated based on the average or median exposure rate and average evaluations of its frequency, duration, other physiological parameters (e.g., breath volume or water consumption).

“Upper assessment” (more correctly “upper bound”) corresponds to upper bound of 95% confidence interval of the exposure rate (e.g., concentration of the toxic substance in the air), for the applied physiological parameters and exposure duration – values of 90^{th} or 95^{th} percentile. Other mathematical models (e.g. Monte Carlo statistics) can be used for the exposure distribution assessment if sufficient information is present.

Exposure, which corresponds to the “central trend”, is applied for the assessment of average risk affected the population. Exposure corresponds to the “upper bound” is considered as a basis for prediction of the most possible risk for certain people of this

population. In case when significant differences can be expected and on “central trend” of exposure for the separate population groups (subpopulations), it can be calculated for such groups separately. The most typical example of this is the separate exposure assessment for children and adults. The dose difference for them resulted from the higher consumption of air, water and food per unit of the body weight, differences in dietary patterns and especially the most significant value for preschool and primary school age children of the oral exposure route through the hands, polluted with soil and contained suspended from the air substances, or deviated eating patterns (consumption of soil, snow, dyed plaster, etc.).

Quantity of exposed population is not included in the dose calculation, but is the most important factor for making decision on priority of the environmental protection measures, resulted from the risk assessment results for “risk management”. Significant but complex problem is the legitimacy of the exposure distribution (calculated based on the pollution monitoring data, as usual restricted quantity of points) to wide zone, and thereby – to defined population. Significant factor of ambiguity may be the population migration (significant part of youth leaves small towns), which leads to actual restriction of the exposure duration.

Ideally the exposure assessment is based on the actual data of the different environment components pollution monitoring (atmospheric and indoor air, soil, drinking water, foodstuffs). But frequently this approach is impossible due to significant expenditures. This approach does not allow to assess the connection of pollution with its specific sources (if in the town the same pollutant is emitted from different sources, and it is necessary to assess the risk of one of them) and is insufficient for prediction of the future exposure when the data of real monitoring are absent. Due to this, different mathematical models for scattering of atmospheric emissions, their precipitation on soil, diffusion and dilution in ground water and/or open watercourses are applied in many cases. Serous problem is not only the choice of adequate model, but also the inventory reliability of industrial emission into the atmosphere and industrial waste which is the initial information for the model calculation of the toxic substances concentration in the air and water.

It is lack of models for calculation of the adverse exposure from the atmosphere through the soil (or from vegetable and animal products directly), migration models, general and reliable for application. The exposure assessment (and final risk characterization) can rarely be proper “multi-medium”, due to the data of scattering monitoring, disadvantages of reliable indices of the significant environment components pollution monitoring in real conditions, and frequently is restricted by assessment of direct impact of the atmospheric or water pollution on people. Even such incomplete exposure (and risk) assessment can bring the benefit.

Sometimes biokinetic mathematical models are used, which give the opportunity to evaluate the toxic substances accumulation in the human organism (lead concentration in the blood of children of different age) taking into account all possible route of exposure.

Assessment of the „dose-response”

This stage of the risk assessment includes search of quantitative patterns which can connect the reference dose of the substance with spreading of different adverse (for health) effect, e.i. probability of its development. US EPA glossary on the risk assessment defines the term "dose-response" dependence as "connection between dose and relative quantity (in percentage) of people with quantitatively determined evidence of defined effect in the group of people". This stage means the assessment of the "dose-response" dependence in such cases, when the risk assessment, resulted only from the atmospheric pollution, takes place. In general the same approach can be applied also for the risk assessment, resulted only from the water pollution. But in this case the pollutant concentration should be converted into its dose (taking into account the water consumption).

Patterns of the "dose (concentration) – response" (concerning rare or new pollutants) are determined in toxicological experiments frequently. Their extrapolation from the animals to the human population is connected with vast amount of ambiguities. "Dose – response" dependences, substantiated with epidemiological data, can be more reliable, but they also have their sources of ambiguities. E.g., describing some epidemiological dependence of response from the high exposure levels (usually occupational), their extrapolation on the less exposure levels can be erroneous and depend on arbitrary choice of mathematical model. Present data concerning the exposure variation inside the studied population and/or difference of exposures among comparative populations are frequently insufficient. In other words, defined response – for example, the cancer rate connected with the average exposure assessment of this population, can come from the part of population which had higher exposure level, unknown for the researcher. Dependence, found for one human population, can be different to another one due to genetic or other differences and the population being affected by other complex of factors accompanying research exposure, etc.

But epidemiological substantiations of the "dose – response" (especially using results of metaanalysis of some epidemiological researches) dependence are more reliable then experimental one. This allows to determine the "response" as a probable index of risk for the human for systemic toxic substances.

Epidemiological researches, which allow to correlate the "response" and exposure quantitatively, are not carried out often due to organizational and financial difficulties despite the intensive development of the so-called environmental epidemiology. In many cases this research is impossible due to the insufficient exposure period, low magnitude of exposed population, presence of vast amount of accompanying risk-factors which confuse the epidemiological analysis. In many cases this stage of the risk assessment is based on the experimental data, like, for example, the establishing of the MAC in Ukrainian practice.

The problems of this stage are determination of the adsorbed dose and its indicators, i.e. biomarkers. In 1987 the Commission on biological markers of National Research Council of the USA gave the definition of biomarkers as indicators of events or conditions in biological systems. Determination of such biomarkers is the task for biomonitoring. Biomonitoring assesses impact of potentially hazardous substances, measuring level of specific chemical matters, which are present in the organism during normal metabolism, substances, absent in normal conditions, and compounds resulted from damage of biological reactions. Biological markers may be the indicators of impact, effect or sensitivity.

Markers of impact are xenobiotics or their metabolites, most of them are concentrated in urine, blood and other tissues, including hair andteeth.

Markers of effect measure damage on the cell or molecular level, e.g. indices of the membrane function disturbance. Markers of effect should be found in organs and systems depending on the mechanism of xenobiotics action. Markers of nephrotoxicity are used for determination of the risk group during the heavy metals impact.

Markers of sensitivity or susceptibility may affect all stage of development after the factor impact. They are caused by the genetically determined peculiarities of the chemical substances metabolism.

Stage of assessment of the "dose – response" dependence in the US EPA methodology is different for non-carcinogens and carcinogens.

US EPA issues the concept of the threshold effect for non-carcinogenic toxic substances. It allows to establish the reference dose (RfD) or reference concentration (RfC), which impact the human population, including the most sensitive subgroups, and does not form the risk of any harmful effects development during all period of life.

The term "reference dose" means "dose for enhancement", "information dose" and does not reflect directly the idea of this dose safety. In Russian and Ukrainian languages the ordinary use of the word "referent" does not correlate with the term "reference dose" and makes it incorrect. The "reference dose" is used widely by specialists who assess the risk in Russia and even presented in some documents. The terms "allowable dose or concentration" must not be used in this context because they have legal content in Russia and Ukraine. The most adequate term is "tolerable intake" ("endurable dose"), which used in the WHO documents representing the same methodology of the risk assessment.

RfD is expressed in mg/kg/day, RfC – in mg/m^3.

Analysis of available experimental and toxicological information on the response dependence on the dose means that intake of the highest dose (exposure) reveals very earnestly, in respect to the expert, the absence of significant adverse effects statistically and biologically. This level is named NOAEL (no observed adverse effect level – level on which the observed adverse effects are absent). As a critical (limited) effect is those which is used for the lowest value of NOAEL establishing. If reliable data for this value is absent as its substitute the LOAEL (lowest observed adverse effect level) – minimal level of experimental exposure, which causes significant adverse effect statistically and biologically, can be used. In some cases LOAEL is determined based on no experimental, but "human" data (very frequently concerning occupational exposure).

These terms have clear principal conformity with the terms "noneffective" and "threshold" dose or concentration, acceptable in the native system of the MAC establishment. General disadvantage of both methodologies is probable ambiguity of accepted values. Trying to overcome this disadvantage the US EPA experts are working on the alternative approach in recent years: probabilistic analysis of the experimental "dose-response" dependences to determine the values corresponding the benchmark dose (BMD) during oral exposure to animals or benchmark concentration (BMC) during inhalation exposure. (Benchmark means checkpoint, reference point.) BMD/C is defined as a lower confidence bound of the dose (concentration), which reveals the established response level. E.g., BMD may be the lower bound of the 95% confidence bound of the dose corresponding the increasing by 1% of the rate of the determined adverse index revealing comparing to the control group. Linear model is accepted as a basic for the

experimental dependences extrapolation on lower level, but other model can be chosen. Benchmark response level, e.g. 1%, is very optional, but it is recommended to establish such level, that BMD is lower than LOAEL (sometimes it is recommended that its value lies between LOAEL and NOAEL). In general this approach corresponds to those used in Ukrainian practice of the MAC substantiation and named finding the probable threshold.

But significant discrepancy between Ukrainian methodology and the MAC substantiation practice, and the most spread cases of the risk assessment for non-carcinogenic effects is revealed by American experts during familiarization with that information presented on the US EPA database for the NOAEL or BMD/C substantiation. Fine functional and biochemical disorders which used for the determination of the "thresholds" by Ukrainian toxicologists and hygienists are not applied for this very often (or do not consider as an adverse). That is why it is true, that the dose, established as a NOAEL, may be considered for the same toxic substance both an effective (above threshold) or threshold from the point of view of Ukrainian methodology for the MAC substantiation.

Many reducing coefficients (they have the same purpose accepted in hygienic toxicology as safe factors) are used during conversion of the NOAEL (or BMD/C) to RfD or RfC. Maximum values of these uncertainty factors equal to:

10 – taking into account the extrapolation from animals to human (for inhalation RfC – 3, if dosimetric interspecific deviations or deviations of the deposition and resorption kinetics in respiratory organs are taken into account);

10 – taking into account most sensitive people;

10 and less – if data of short-term experiments are represented;

10 – if the database is incomplete;

10 – if NOAEL is used instead of LOAEL.

If the toxicokinetic and/or toxicodymanic information is presented, the extrapolation from animals to human or taking into account interspecial deviations become more seriously substantiated, first two factors are decreased. The uncertainty factor for the interspecial deviations equals to the product of the uncertainty factor of toxicokinetic (equals to 4.0) and uncertainty factor of toxicodynmics (equals to 2.5); for the interindividual deviations – both uncertainty factors equal to 3.2. E.g., significant deviations of the examined substance toxicodynamics between human and those species of animals, which were used for the identification of the "dose-response" dependence, are absent. But interspecial deviations of toxicokinetics may be present, then during the RfD conversion the corresponding uncertainty factor equals 10 instead of 2.5. All these assumptions are relative.

If the expert finds in the received information any additional uncertainties, he can use modification factor which does not exceed 10. If the product of all these factors exceeds 10 000, the database is weak for the application. If values of this divisor equal to 1 000 – 10 000, the assessment of NOAEL and LOAEL looses its significance. Each expert on the risk assessment may follow both the procedure of establishing the threshold (for animals), and than – reference (for human) doses and concentrations, and search of the toxicological information which used for this establishment. This is the way of work for the most skilled experts on the risk assessment in the USA. This assessment is also based on both application of formed and periodically revised IRIS database in the US EPA

(and many other databases), and values of NOAEL and Rf/C, recommended by this Agency for many substances (and represented in the same IRIS).

Direct use of "reference" doses and concentration, applied in the USA, may be possible as a temporary measure in Ukraine for the risk assessment due to listed above uncertainty on principles of the experimental and toxicological assessment of threshold doses (concentrations) in these countries. It is necessary to keep in mind that the list of substantiated reference doses never is presented, and appearance of the environment pollutant is always possible, for which the special substantiation of the "reference" dose is required.

The "dose-response" dependences, established based on the analysis and sometimes metaanalysis of the epidemiological researches data, may not be restricted by the LOAEL founding. These dependences are expressed as a regression equation which connects the dose (concentration) of the toxic substance with the predicted rate of any health disorders, typical for this substance impact, or hospitalization rate due to determined diseases or death, etc. Similar approach to this stage of the risk assessment was worked out for such environment pollutants as lead, dust (paniculate matters – PM), sulfurous anhydride. But this approach can be widen on other factors, if the expert finds in the available literature corresponding epidemiological data and proposes adequate way of their application.

The US EPA considers that the "dose-response" dependence for carcinogens is non-threshold (but not always). This delimitation between carcinogenic and non-carcinogenic substances is not typical for Ukrainian methodology of the MAC substantiation, because of the incontestable argument of the non-threshold (and threshold) conception of carcinogenic effect is impossible. The lowest exposure level may be found when neither epidemiologist, nor experimenter can not establish the statistical significance of increasing of the malignant tumor appearance comparing to their spontaneous level. But any hypothetical probability, that such response may be established on such lower level, is present, if more numeral (and practically impossible) cohorts of people or laboratory animals are used. This level totally corresponds to the American definitions of NOAEL (for experimental animals) or RfD (for human), which underline that these are the doses which do not cause statistically significant effect. Tendency to the paradigm of the non-threshold effects of carcinogenic substances is the barrier for the listed above parameters of determination for such matters. This paradigm is possible for those substances, carcinogenic effects of which are the consequence of their genotoxicity, but not for vast amount of non-genotoxic carcinogens.

The project of new US EPA manual on the risk assessment of carcinogenic substances determines the possibility of the threshold for those, carcinogenic effects of which are not associated with mutagenic one (e.g., is secondary consequence of toxic effect which also has a threshold).

The "dose-response" dependences have significant confidence concerning the cancer, because they are substantiated with epidemiological data. But the number of such dependences applied for the risk assessment is very low. The most significant example is arsenic. The regression coefficients are substantiated for this substance, expressed in $(mg/kg/day)^{-1}$ and different for different localizations: 1.0 – for liver cancer, 2.5 – cancer of lungs and urinary bladder, 0.86 – kidney cancer, 1.5 – skin cancer.

The assessment of the "dose-response" dependence for carcinogens means the application of experimental data if epidemiological materials are absent. These data must

be received on animals of most sensitive species or those species with reaction to this carcinogen similar to human one. Those routes of impact on animals are preferred, which are the most corresponding for the human population. But positive results of this experiment on laboratory animals groups, limited by the number, can be received only with the impact of high doses, which give high probability of tumors. The risk assessment system proposes, as a basis for the risk management, the measures to determine those doses, impact of which reveals low probability of tumors. The extrapolation of the defined "dose-response" dependence is taking place on the dose range, significantly lower than those used in experiment in real conditions. Different mathematical models are used for this extrapolation (multi-stage, logistic, probit, model of one blow, Waybull model, etc.), they assess the response in the low dose range unequally. Each model is based on the one or another general theory of carcinogenesis, but does not include data, received during the specific toxic substances assessment. Each of these models cannot be neither definitely proved nor clearly rejected.

Earlier the US EPA preferred so called linearized multistage model – a basis of uniform extrapolation form high doses to low one:

$P(d) = 1-\exp\{-[q(0) + q(1)d + q(2)d^{**}2 + ... + q(k)d^{**}k]\}$,

where, P(d) – probability of the cancer development from uninterrupted dose level;

q(i) – constants;

k – number of groups, exposed to the different doses (d^{**}) or number of stages of the cancerogenosis process. (Model is based on the hypothesis that the cancer is initiated by the cell mutation through final steps).

Main parameter for calculation of the risk for human is so called slope factor, which equals to the upper 95% confidence bound of the linear part of the "dose-response" curve. Slope factor is expressed in $(mg/kg/day)^{-1}$ and means the risk limit from the single carcinogen dose. E.g., the human was exposed to the carcinogen impact on the level 0.002 mg/kg every day during whole period of life, the slope factor equals to 0.02 $(mg/kg/day)^{-1}$. The risk, received as a product of the dose level and slope factor, can be assessed by the value 4×10^{-5}. It means probability of 4 additional cases of cancer per 100 000 population, exposed to such level of the carcinogen dose.

The following principal assumptions are accepted:

- the carcinogenesis processes are similar fundamentally both for human and laboratory rodents;
- probability of the cancer development due to any carcinogen impact per all period of life of laboratory animals is similar to the human one;
- interspecial deviations of the carcinogenic substances toxicokinetics are possible, due to their different content in the targen-organs by equivalent dosing, interspecial deviations of the toxicodynamics are also possible. Sensitivities of these organs to the same dose of this carcinogen cannot be taken into account if specific information concerning toxicokinetics and toxicodynamics for quantitative registration of these deviations is absent.

The problem of equivalent dosing is still serious due to necessity to include significant deviations of the animal and human body weight and surface. As listed above, the differences between theoretical and experimental backgrounds for different doses calculation, used in experiments, on doses for the carcinogenic risk for human were discussed. Special interdepartmental group of American experts proposes the uniform

recommendation – the equivalent doses per the body weigh unit in the ¾ degree, or equal to mg/kg/$^{3/4}$/day.

New approaches were proposed for the "dose-response" dependence analysis in 1996, which have significant differences from the previous US EPA methodology:

- initial extrapolation point on the curve, describing the "dose-response" dependence, is the lower 95% confidence bound of the dose, which corresponds to the 10% probability of the cancer development – lower effective dose (LED) proving the 10% of response (LED_{10});
- if theoretical backgrounds for the linear assumption in low doses range are sufficient (if the carcinogenity resulted from this substance impact on the DNA), the point on the curve, corresponding to the LED_{10}, is connected with the coordinate origin by the direct line. The intersection point of this direct line with perpendicular, dropped from this point on the abscissa axis, corresponds to the assessed dose for the human and equals to additional risk of the human cancer.
- if the linear dependence is not substantiated sufficiently and there are many aspects to believe that this dependence is non-linear (especially if the threshold of carcinogenic effect may be allowable), the US EPA experts reject to apply any non-linear mathematical model due to different models have significant results during the risk assessment. The extrapolation in such cases does not take place and the human risk cannot be evaluated as a probability of the cancer development or predicted number of additional cancer incidences among the population. Instead of this, the indirect criterion of the risk – ratio of the LED_{10} to the assessed dose for the human, so called Margin of exposure (MOE) – is used. This criterion is similar to the ratio of the NOAEL to the assessed dose for the human for the non-carcinogenic toxic substance.

In general, new methodological document of the US EPA approximates the approaches of the carcinogens and "systemic toxicants" assessment by many positions. But, previous methodology is widely used both in the USA and other countries.

Approximation of the US EPA approaches to analysis of the experimentally established "dose-response" dependences for carcinogenic and non-carcinogenic substances facilitates the acceptance of the risk assessment methodology by native hygienists and toxicologists, who, during the MAC substantiation both for carcinogenic and non-carcinogenic chemical substances, based on the dose threshold, lower of which the proved adverse effect is absent or cannot be identified practically.

Clear deduced paradigm of the non-threshold of the carcinogenic effect as a theoretical basis for the risk assessment is accepted by most of western experts for those substances, which carcinogenity associated with their genotoxicity. The extrapolation of the "dose-response" dependence to the zero level is proposed. This provides the calculation of any final risk during any small exposure. Inevitable consequence of this is necessity to make a decision, what risk level may be acceptable. But neither scientifically substantiated, nor accepted criteria are present for this.

The risk assessment of non-carcinogenic adverse effects of the most significant carcinogenic pollutants of the environment is of great interest. The assessment of the "dose-response" dependence for such substances, as nickel, chromium, arsenic, cadmium, etc. is represented both as a cancer rate and non-oncological adverse effects. On the other hand, western experts predict frequently the carcinogenic risk for the

population as a probable and for those substances which do not established as a "human" carcinogens. But such point of view is not approved by native toxicologists.

Risk characterization

The risk characterization is the final stage of the risk assessment. Its objective is the synthesis of all risk assessment results and drawing up the conclusions which will be submitted to the persons or organizations, which make decisions on the ecological politics.

On this stage the original US EPA methodology requires to summarize and characterize all uncertainties on each previous risk assessment stage, inform the person responsible for the management decision and community about them. The significant critic of all the risk assessment system in the USA results from multiplicity of such uncertainties and insufficient substantiation of assumptions, used for their registration.

The practically same uncertainties are typical for the Ukrainian accepted values of MACs. But these values are established as obligatory standards after discussion by strict expertship, and information on uncertainties is not brought to these standards users notice. It is necessary to accumulate the experience of real application of the risk assessment in our conditions, before establish the real necessity, possibility, volume and procedure of representation of the information on uncertainties of such assessments to user.

The form of the risk characterization can be different: form descriptive to semi-quantitative and even quantitative (rather quasi-quantitative), but the combination of such approaches is used more widely. One of the quantitative indices, used for the indirect characteristic of the non-carcinogenic risk, is the ratio of assessed daily dose to RfD, named hazard quotient (HQ). Evidence of the potential risk for health considers if HQ > 1.0. Another measure of the potential adverse exposure is its safety (MOE – margin of exposure), which equals to the ration of NOAEL to assessed dose for the human, expressed in the same units. If this value is commensurable with the product of all uncertainty factors or even exceeds this value, the necessity of the risk management is untenable.

The risk assessment from the pollution of the one environment component, i.e. the dose calculation is unnecessary and the exposure level can be evaluated with the concentration sufficiently, the $HQ = \frac{C}{RfC}$, despite of the "reference concentration" the MAC value may be used. This type of the ecological situation assessment is well known in Russia and Ukraine from hygienic positions. The HQ calculation for the "multi-component" risk assessment allows to add doses, received from different environments by different route, and compare such total dose with reference one.

During the risk assessment for some chemical substances, which have systemic toxicity and additivity of their effects may be allowable (especially if they cause the same effect, resulted from the same mechanism), the US EPA experts recommend to summarize the HQ values, corresponding to each such toxicants (if there are no deviations of effect during different exposure routes). This type of the hazard assessment from combined pollution has been applied by Ukrainian hygienists for a long time (as a sum of ratios of the substance actual concentration to their MACs). It should be kept in mind, that the dose additivity is not the prevalent type of combined

effect, especially during the low doses exposure, in particular for combined toxicity of metals, the more or less expressed antagonism is typical. Some combinations, the effect of which is higher than additive (synergism, potentiation), may be present also. If information on specific toxicans is absent, in all cases the "safe factors" are calculated as a total defensibly.

In any case, the safe factor characterizes not the proper risk for health as a probable parameter, according to its official definition, but is an indirect criterion. That is why it can be used for the risk range with many cautions, but not for absolute assessment of the risk

Only the "dose-response" dependences, based on the epidemiological data, allow to assess the substances which no carcinogenic effect on human. In this case, based on the single risk (evaluates the probability of the any adverse effect development per exposure unit on the analysis stages of "dose-response" dependence), which is multiplied by the dose (found at the exposure assessment stage), the value of "individual risk" is received. The "individual risk" means the probability of this effect development on the resident of the research territory. If the value of this probability is multiplied by the magnitude of population, the value of "population risk" of this health disorder expected cases can be measured.

E.g., the single risk of cadmium nephropathy equals to 55.9% per 1mg/kg/day, average daily dose of cadmium for the population of the Verkhnya Pushma town by all exposure routes – 0.353057 mg/kg/day. Individual risk is calculated according to the following: 55.9×0.353057 = 19.74%. If magnitude of this population is 53,000, it means that 10,500 cases of nephropathy will be registered under the condition that the exposure level is the same during all life period.

The risk characterization for the cancer development or prediction of probable additional cases of this disease during the life period is calculated as either multiplication of the dose by the slope factor, or using linear extrapolation, or MOE criterion. In Ukraine such quantitative prediction is allowable only for substances which officially are registered as carcinogenic for the human. It is rational to inform on presence of exposure to those substances, which carcinogenity for human is only specified (group B). Additional risks of the malignant tumors development, formed by separate carcinogens during combined exposure, can be summarized, if independence of mechanism of the different substance carcinogenic effect and linear "dose-response" dependence are allowable.

Connection between the risk assessment and risk management

The risk characterization is a basis for the making decision on the risk management, i.e. organizational, political, legal and other measures, directed on its prevention, liquidation or even decreasing. In any country this management depends not on the assessed or predicted risk value, but on many another factors, which are taken into account both for making decision in each case and on the environment and population health protection from the state and social mentality point of view. These factors include social, social and psychological, economic, politic, technological, etc.

Comparative assessment of risk either for the population health on different territories or different population groups (occupational, age, gender), or from the different pollution sources of the environment and/or different its pollutants, or resulted

from pollution of the different environment components with one substance, etc. the must play an important role in ranging of the environment policy priorities and sanitary inspection requirements on different levels (local, regional, state). In Russia the Common Resolution of the Principal state sanitary doctor of RF and Principal state inspector on the environment protection of RF from 10.11.1997 defines that the methodology of the risk assessment must be applied during the "state sanitary and ecological inspection, ecological and hygienic examination, ecological audit, ecological and hygienic certification, determination of zones of the ecological accidents and emergency ecological situations, social and hygienic monitoring on the environment impact assessment on the population health". These types of activities have either the risk management elements (especially, preventive sanitary inspection on the state examination of projects) directly, or form the most important initial conditions for both listed above ranging of priorities and financial or other provision of measures concerning the risk management (to establish the status of special zone for any territory).

Economical analysis of the risk management. Economical analysis of the "expenditures-efficiency" type can be a significant help for choosing the optimal "risk management scenarios". In those scenarios (i.e. system of management measures), the most significant effect of the risk decreasing per unit of future expenditures is predicted, is recommended as the best. Absolute value of the predicted effect has been attached an importance.

Special attention has to be given to objectivity and volume of the expenditure registration for the comparative management scenarios. The widespread mistake, comparing different approaches on the risk decreasing of the environment pollution from the automobile exhausts, is a statement that total recovery on lead-free fuel is not only more effective (without any doubts), but is also economically advantageous, because there are no expenditures and economical negative profits. But this problem is more complex.

The widespread approach for economical analysis of the "expenditures-benefits" type must be interpret carefully. In this case, for the prediction of the different management scenario efficiency, expenditures on corresponding measures are compared to both effect of the risk decreasing for the population health and possible decreasing of economical losses resulted from this risk. Such comparison may be only one of factors in choosing criteria of political and other decisions concerning the risk management, but not conclusive, due to great value of the health and people life for the society being not equivalent to the economical negative profits resulted from the disease and death. Assessment of these negative profits by western experts is based on the two parameters, which can be directly adopted for calculations in Ukrainian conditions. One of these parameters is the "disease cost", or average sum of expenditures and money losses connected with any disease. This parameter must be based on specific researches in Ukraine at a whole, better – for each region. It is difficult to assess the "disease cost" in conditions of economic instability. Another parameter is "ability to pay", or the sum of money, which the population representative is ready to pay psychologically for the prevention of specific risk. This value, resulted from the social researches, which never took place in Ukraine, can not be transferred from abroad, due to sharp distinctions of social and economic conditions, and social mentality.

There are cases of the significant measures attraction in the US EPA practice (expenditures of the superfoundation for those territories cleaning, which were polluted with industrial waste or after accident) even if the risk assessment is necessary for small population group health, i.e. these expenditures can be "compensated" with any financial "benefits".

Risk management and hygienic regulation. The most significant element of the operative and long-term risk management in the system of the state sanitary inspection was and still is scientific substantiation, establishment and control on compliance of standard levels of the environment pollution (MAC, OSIL). If the US EPA methodology is adapted to principles and practice of such substantiation (including the safety criteria, accepted in Ukraine, and corresponding review of American methodology concerning the "reference" doses), it is possible to prevent principal contradictions between, on the one hand, recommendations on the risk management, based on its assessment on new methodology in Ukraine, on the other hand – necessity to compliance with present standards of MACs.

Another potential possibility of these contradictions is that the risk assessment is determined by the expert position, available information, choosing mathematical models, etc., instead of unitary system of hygienic standards concerning allowable pollution. The difficult problem on rational degree of available information concerning the risk characterization uncertainties, passed to the user, should be solved, because the inspection organs demand the compliance of MAC as a deterministic value. Taking into account special attention to the state hygienic standards concerning the environment pollution in Ukraine, which do not have such development in any country of the world (abroad the CIS), it is dangerous to undermine the trust to them as a result of such collisions.

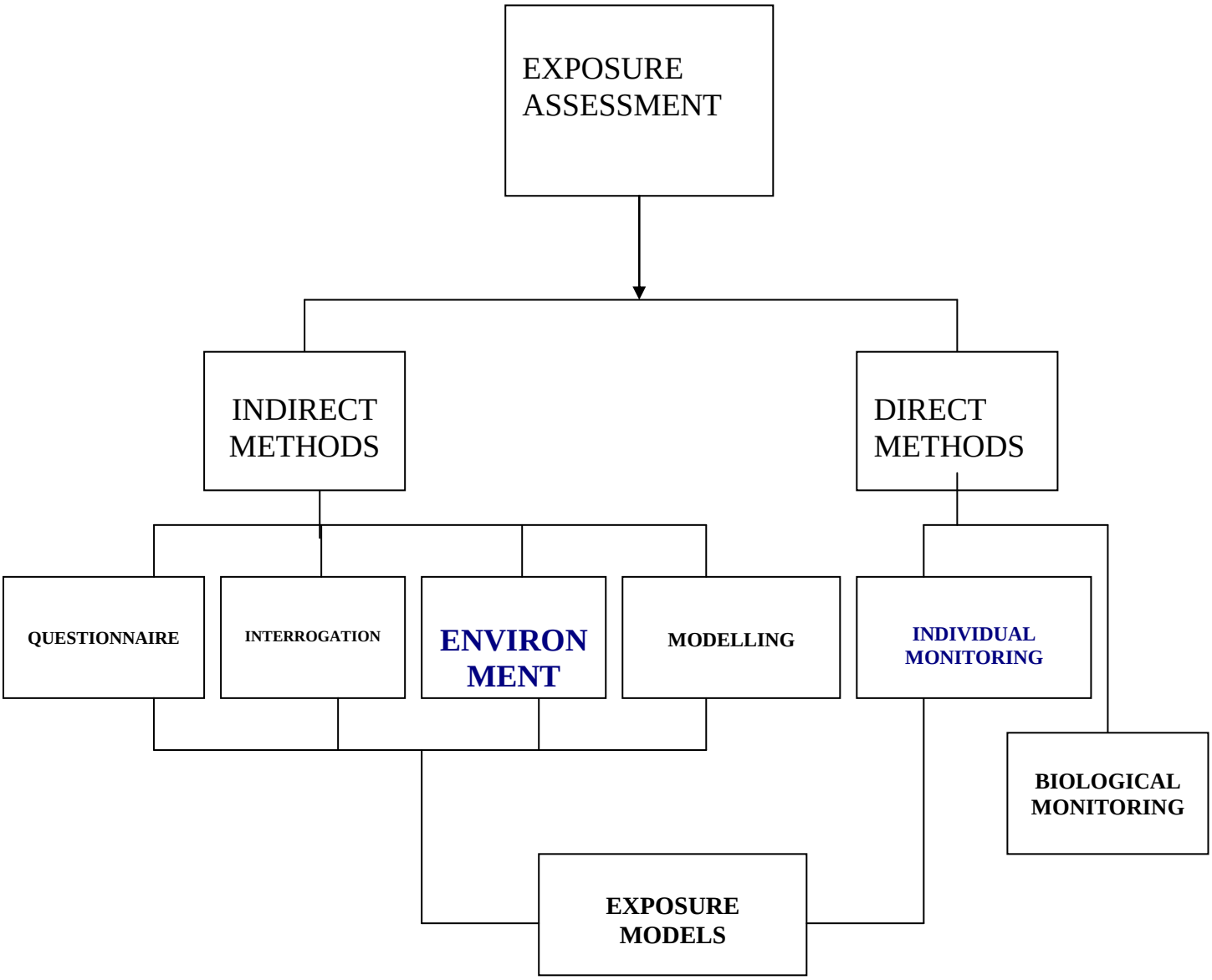
It is well known, but not eliminated in the native system of MAC, that standard value for the same pollutant from different environment components are substantiated independently, often by different researches, and are based on the safety criteria which do not comply properly. The "reference dose" determination for systemic toxicants during the "dose-response" dependence assessment forms the opportunity to calculate their corresponding reference concentrations in each environment component with different correlation of the exposure routes. These positions of the risk assessment methodology are applied in the following document – International program of chemical safety. The solution concerning this task, taking into account not only the "exposure scenarios" for human, but reliability and the experimental exposure routes for the "reference dose" determination, and similarity of effects, used for the assessment during different exposure routes, is considered in this document. There are two examples of such approach, considered in this document.

Example 1. The following data were received after the exposure assessment: 50% of total dose penetrates with food, 20% - with water and 30% - with the air. Present data are sufficient for the substantiation of both oral (RD_{or}) and inhalation (RF_{inhal}) reference doses, which are based on the similar effects and belonged to the same order of values. Each of them can be used for calculations, but RD_{or} was accepted because the main exposure route for human is oral. Allowable doses, penetrating into the human organism, are the following: 0.5 RD_{or}, 0.2RD_{or} and 0.3RD_{or}. These doses can be

converted into corresponding MAC, based on accepted levels of the water, air and foodstuffs consumption (taking into account the chemical composition of the diet).

Example 2. According to the exposure scenario the 70% of total dose penetrates with the air, 20% - with water and 10% - with food. This substance is present in some goods for consumption, but quantitative assessment associated with their exposure is impossible. There are no data concerning this substance concentration in soil, but these concentrations should be low, probably, taking into account physical and chemical properties of this substance.

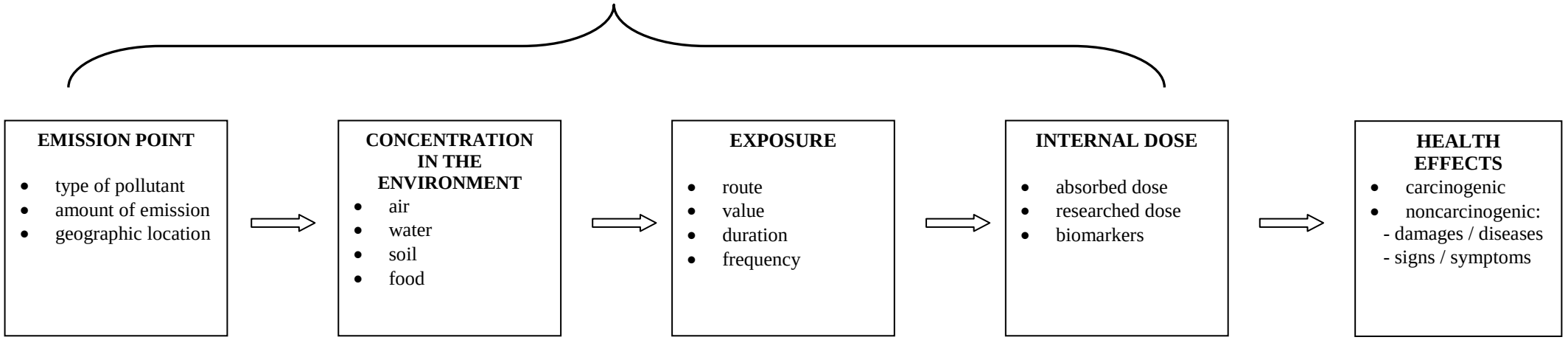
Present data are sufficient for substantiation of both RD_{or} and RD_{inhal}, which are based on the similar effects and belonged to the same order of values. Each of them can be used for calculations, but RD_{inhal} is accepted, because main exposure route is inhalation. Experimental data are used for the "reference concentration" establishment (RfC in the Us EPA notation), and RD_{inhal} must be converted into the mg/kg/day, based on such data as respiration volume, body weight, toxicological and kinetic parameters, if they are available. 10% of the RD is reserved for consumption with goods and soil (which are impossible for assessment). Other 90% of the RD is distributed the following way: 0.63 RD_{inhal} − with the air, 0.18 RD_{inhal} − with drinking water and 0.09 RD_{inhal} − with food. These doses can be converted into corresponding MAC, based on the accepted values of the water, air and foodstuffs consumption (taking into account the diet composition).


EXPOSURE ASSESSMENT
INDIRECT METHODS
DIRECT METHODS
QUESTIONNAIRE
INTERROGATION
ENVIRON MENT
MODELLING
INDIVIDUAL MONITORING
BIOLOGICAL MONITORING
EXPOSURE MODELS

Connection between the exposure assessment and impact assessment

EXPOSURE ASSESSMENT

- level
- distribution
- number of people
- emission point
- researched dose



ASSESSMENT OF IMPACT

- endogenic risk-factors
- type of effect
- dose-response

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Equipment required for the lesson

1. Schemes of research.
2. Exposure assessment.
3. Connection between the exposure assessment and effect assessment in the health paradigm caused by the environment.
4. Situational tasks for the student’s self-training for the lesson.