State Sanitary and Epidemiological
valuation of the Russian Federation

2.1.10. Health status due to the state
ENVIRONMENT AND CONDITIONS IN

APPLICATION OF RESULTS
BIOMEDICAL RESEARCH FOR
Proof of injury to health
POPULATION negative effects of chemical
ENVIRONMENTAL FACTORS

Methodical instructions
MU 2.1.10.3165 -14

Approved 23/05/2014

The Federal Service for Supervision of Consumer Rights Protection and Human Welfare

Moscow

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1. Has the Federal Service for Supervision in the sphere of protection of the rights consumers and Welfare (G.G.Onischenko, AY Popov) Federal State Institution of Science "Federal Scientific Center health-care technology risk management health population "(NV Zaitseva, I. Mai, V.B.Alekseev, S. Klein, O. Ustinov, MA Zemlyanova, DA Kir'yanov, EV Sedusova, NV Kriulina, DV Lanin, MA Safonov) Rospotrebnadzor Perm edge (VA Horoshavin), the Office of the city of St. Rospotrebnadzora Petersburg (A. Melzer, NV Yerastova).

2. To recommend to the approval of the Commission on Public Sanitary-Epidemiological Standardization under the Federal Service for Supervision of Consumer Rights Protection and Human Welfare.

3. Approved by the Head of the Federal Service for Supervision of protect the rights consumers and welfare human The main State Sanitary Doctor of the Russian Federation G.G.Onischenko "23" May 2014

4. Enter into effect from the date of approval.

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MU 2.1.10.3165 -14

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2.1.10. Health status due to the state
Environment and living conditions

POPULATION

APPLICATION OF RESULTS OF HEALTH
BIOLOGICAL

RESEARCH FOR EVIDENCE Causing harm to health of the population NEGATIVE INFLUENCE OF ENVIRONMENTAL FACTORS

Methodical instructions
MU 2.1.10.3165 -14

1. Field of application

1.1. These guidelines establish the order applications results biomedical research for formation of evidence of negative effects of chemical environmental factors on human health (harm human health due to the negative impact of environmental factors habitat).

1.2. Methodological guidelines are designed to improve the quality performance of public functions:

- Implementation of the State Sanitary and Epidemiological oversight and control for execution mandatory demands legislation of the Russian Federation in the field of sanitary being of the population, consumer protection and in the consumer market,

- implementation of sanitary-epidemiological investigations, studies, examinations, aimed at establishing the causes and detection conditions of occurrence and dissemination Bulk non-communicable diseases;

- The organization and implementation of measures aimed at identifying and eliminating the impact of harmful and hazardous environmental factors on human health;

- The organization and management of public health monitoring.

1.3. Guidelines are intended for organizations and bodies Federal Service for Supervision of Consumer Rights Protection and human well-being, as well as research and other organizations working in the field of environmental health protection Consumer Rights and preventive medicine for improving the system sanitary qualification of doctors, medical students.

Used in the document, the terms and definitions given in the Annex 1.

Used in the document reductions are given in Appendix 2.

2. Normative references

2.1. Federal Law of 24.07.1998 № 124-FZ "On the main Guarantees of the Rights of the Child in the Russian Federation. "

2.2. Federal Law of 30.03.1999 № 52-FZ "On sanitary epidemiological welfare of the population. "

2.3. Federal law from 31.05.2001 N 73-FZ On State forensic activities in the Russian Federation. "

2.4. Federal Law of May 2, 2006 N 59-FZ "On the Procedure consideration of citizens of the Russian Federation "

2.5. Federal Law of 21.11.2011 N 323-FZ "On the basis of protection health of the citizens in the Russian Federation "

2.6. Resolution of the Government of the Russian Federation of 30.06.2004 Number 322 "On Approval of the Regulations on the Federal Service for Supervision in

Consumer Rights Protection and Human Welfare "

2.7. Resolution Government Russian Federation 15.09.2005g. Number 569 "On the Regulation on the implementation of state Sanitary and Epidemiological Surveillance of the Russian Federation. "

2.8. Resolution of the Government of the Russian Federation dated 02.02.2006 Number 60 "On approval of the conduct of social and hygienic monitoring. "

2.9. Resolution of the Government of the Russian Federation dated 17.08.2007 N 522 "On approval of rules determining the severity of the injury, to human health. "

2.10. Order of the Federal Service for Supervision in the sphere of protection of the rights consumers and Welfare from 19.07.2007 № 224 "On sanitary

epidemiological Expertise, surveys studies tests and toxicological, hygienic and other types of assessments. "

2.11. Manual P 2.1.10.1920-04 "Guidance on Risk Assessment for health when exposed to chemical pollutants environment ", approved by the Chief Sanitary RF doctor GG Onishchenko 05.03.2004.

2.12. National Standard of the Russian GOST R 52379-2005 "Good Clinical Practice »(ICH E6 GCP), approved by the Order Federal Agency for Technical Regulation and Metrology 27.09.2005 N 232-st.

These guidelines are harmonized with the following international and foreign documents:

- Declaration of Helsinki in 1975 with additions in 1983;
- Agency for Toxic Substances and Disease Registry;
- Database TSDR-Agency for Toxic Substances and Disease Registry. Database -Toxicological information by health effect or chemical class;
- US. EPA United States Environmental Protection Agency - Database TEACH (Toxicity Exposure Assessment for Children's Health);
- Database WHO. International Programmer on Chemical Safety. CICADs - Concise International Chemical Assessment Documents.

3. General Provisions

3.1. For biomedical research include:

- The qualitative and quantitative determination of the human body Chemicals characterizing contact with the habitat factors (Markers of exposure);
- quality and quantitative definition laboratory indicators that reflect the health of the body and adequate exposure to environmental hazards, and / or the level of content marker of exposure to the organism (markers response);
- Clinical studies including examination of each patient therapists / pediatricians and specialization with the aim of identify and describe the clinical manifestations of ill health, adequate exposure to environmental hazards and / or level content marker of exposure in the body;
- Functional studies and evaluation of functional disorders, adequate exposure to environmental hazards and / or level content marker of exposure in the body;
- Medical and social research aimed at identifying factor can cause infringement Health similar formed by environmental hazards

formed by environmental hazards.

3.2. The basis for biomedical research
to establish a causal relationship to the negative health disorders
the influence of environmental factors may be:

- circulation citizens individual entrepreneurs
legal persons, public authorities and local
government on the facts of harm to the life or health of citizens and
a threat of harm to the life or health of citizens;

- The establishment of unacceptable risk from exposure values
chemicals that pollute the environment to health
population in the socio-hygienic monitoring;

- The results of periodic medical examinations (surveys)
workers engaged in heavy work and work in harmful and (or)
dangerous working conditions;

- The results of socio-hygienic monitoring of the
environment and health;

- Rationale for the design and evaluation of the effectiveness of implementation
regional and municipal programs aimed at reducing
adverse effects of chemical environmental factors on health
population.

3.3. The main goal of biomedical research is
qualitative or quantitative assessment of injury to persons
to presence or absence of links with the level of harm
exposure to chemical environmental factors (air,
natural and / or drinking water, soil, food, and so forth.).

3.4. Biomedical research can be an integral
part sanitary-epidemiological examinations, investigations
surveys, studies, tests and other types of evaluations included in
substantiating materials expert advice and used in
justification to prosecute persons responsible for pollution
habitat, which entailed causing harm to human health,
at justification sanitary events Assessment
effectiveness of the latter, etc.

3.5. Organization performing biomedical research,
should have a license for medical practice and
holding laboratory Clinical Research and certificate
accreditation for conducting chemical-analytical measurement objects
habitat and / or biological media (substrates) man.

3.6. Biomedical research provides
strict compliance of national standards GOST R 52379-2005
"Good Clinical Practice» (ICH E6 GCP), with mandatory
compliance ethical Principles forth in Helsinki
Declaration in 1975 with additions in 1983, obtaining
informed consent of the volunteers (volunteers).

3.7. Organization performing biomedical research
shall ensure the confidentiality of research results within

its obligations in accordance with the legislation of the Russian

Federation. The results of biomedical research in publicly available depersonalized form of information or with the consent of patients.

3.8. All medical or chemical analytical results of health biological studies presented in the form of extracts, the results assays and protocols established and approved sample head of the institution conducting the research.

3.9. The results of biomedical research may be information basis for forensic examinations. Degree the severity of the harm caused to human health (heavy, moderate, light damage) is determined by forensic experts on the basis of aggravating circumstances referred to in Articles 111, 112, 115 of the Criminal Code using "medical criteria for determining the degree of the severity of the harm caused to human health "(app. Order Ministry of Public Health of 24 April 2008 N 194n), and also installed violations of mandatory sanitary requirements.

4. Place and role of biomedical research in the general algorithm establishing causal links between environmental factors habitat and population health

4.1. Biomedical research in conducting sanitary hygiene evaluations, studies, investigations, examinations are included in the common system of evidence linking the level of pollution habitat, mass noninfectious diseases and so on. (Fig.1).

4.2. Step establish the circumstances require you of Biomedical Studies at conduct sanitary hygiene evaluations, studies, investigations, examinations, have purpose analysis reasonableness of management decisions bodies Rospotrebnadzora.

The result of step - refusal to investigate (research, hygienic evaluation and so on.) or compiling a program of further Action.

4.3. Phase accumulation and analysis of information on the quality of habitat aims to characterize the state of the air, natural and drinking water, soil, etc. and assess the level of compliance hygienic standards.

Result stages - establishing a list of likely sources dangers and threats to public health.

4.4. Step of risk assessment for public health reveals priority hazards and the likely effects in the state Health (hazard identification), to estimate the number of population, impacted (exposure assessment) and risk level health (risk characterization).

Phase I: Establishment of circumstances, require investigation (investigation, Evaluate examination) situation

Analysis of complaints. Case Study Evaluation of compliance sanitary-epidemiological demands	Urban Development Analysis accommodation produc-governmental and residential facilities	Hygienic analysis habitat quality

No objective causes

Identified potential sources of dangers and harmful effects of conditions

Completion of investigation

Phase II: Analysis of the mechanism of the origin and evolution of the situation

Methods:

Analysis of documentation Conformity assessment of sources

potential sources
hazard.

health hazard requirements
legislation

No violation
sanitary rules and norms

Violations of sanitary rules and
norms

Completion of investigation

Phase III: Collect and analyze information about the quality of the habitat and potential impact on the population

Modeling rasprost-
injured substances

Tool
research environment

Health Risk Assessment
Population

Not exceeded hygienic
standards for calculations and measurements.
Health risk is acceptable.

Violations hygiene
regulations. Health **risk above**
acceptable level

Completion of investigation

Stage IV. Establishing the nature and extent of actual violations of individual tion and population health.

Analysis of morbidity
According to the statistics.
Calculations OR

Specialized medical and biological research
following the analysis of markers of exposure, March
Kerov response, clinical manifestations, and so forth.
r.vozd

No significant differences in
investigated the level of morbidity and
control groups. Markers of exposure
markers and response - at the level of the background.

Significant differences in
investigated the level of morbidity and
control groups. Markers of exposure and
Answer markers above the level comparison.

Completion of investigation

Phase V. Formation of a unified system of evidence. Preparation of expert conclusion. Mathematical modeling of relationships. Pathogenetic justification of violations of health. Analysis of results of jointly criteria.

Fig. 1 - The general algorithm of forming the evidence base
damage to the health of the population the negative impact factors
habitat

Stage results are:

- The parameters of the risk to health;
- Risk factors with the release of priority substances and ways to income population;
- Priority gender and age or territorial groups population;
- Critical organs and systems, the likely types of health disorders, characteristic for the set exposure (exposure).

According to the results of risk assessment forms the program of Biomedical Studies, including content, scope and duration of health biological studies, as well as local population.

4.5. Step biomedical research is to collect and compilation of data on the implementation of the health risks of a (Absence) of real harm to the individual and population level due to the influence of environmental factors.

The result of biomedical research are:

- Data on the qualitative and quantitative content in the body each individual studied and researched the chemical a group of chemicals that characterize contact with environmental factor habitat (markers of exposure);
- Data on individual and group levels of laboratory health status indicators organism, adequate Effects

environmental hazards and / or the level of the marker content
exposure in the body;

- A description and analysis of the individual and population levels
clinical manifestations of ill health, adequate exposure
environmental hazards and / or the level of a marker of exposure to
the body;

- A description and analysis of individual and group level
functional disorders, adequate exposures
habitat and / or the level of content of the marker of exposure in the body;

- Data on individual and group features image
life, production, genetic and other factors that could
cause health problems, similar harmful formed
environmental factors.

4.6. The results of biomedical research in conjunction with
data on exposure levels, sources of threats and hazards
territory, as well as background information on the types of effects
criteria influence the relationship existing models, etc. create
the foundation for a comprehensive analysis, including mathematical
processing and the establishment and description of causal relationships.

**5. Input data for the formation of health programs
biological research and building the evidence base**

5.1. The initial basis for of of Biomedical
Research results of the evaluation are sanitary
situation and health risk assessment, both qualitatively and quantitatively
describing:

- The list of threats and dangers to public health in the territory;

- The calculated levels of environmental pollution by chemical
substances with the release of populations living in
various levels of pollution;

- The results of the inventory of air emissions and discharges of harmful
substances into water bodies;

- The conditions under which the form of pollution exceeding
hygienic standards;

- The levels of pollution of the environment on materials
instrumental studies with the selection of chemicals for
which revealed violations of sanitary norms and conditions
forming pollution;

- characterization olfactory reflex impact
carcinogenicity, acute and chronic non-carcinogenic risk to
the exhibited the health of the population (with the release of sex and age groups,
and / or territorial groups with different levels of risk to health);

- Priority chemicals forming unacceptable
risks and / or equity investments in which introduce unacceptable risks to health
population.

5.2. Is optimal storage and processing of the totality
data in a geographic information system environment with the map data
vector map (or map-scheme) territory. On a map or map-scheme
displaying industrial sites, the boundaries of sanitary protection zones,
residential areas, recreational areas and other facilities that are important to
terms of assessing the exposure, place of residence of the exhibited
population

population.

As topographic GIS recommended scheme master plan for the area or territory schematic map: the population of more than 100.0 thousand. people. - The scale of 1: 10,000, with a population of 10.0 to 100.0 thousand. people. - 1: 2000 scale, with a population of less than 1.0 thous. Pers. - 1: 500 scale.

5.3. To determine the size of the exhibited population recommended formation in geoinformation the system specialized layer on the number or density of the population. The data sources can be materials of the general plan of settlement, local government fund of compulsory medical insurance and so on. The original data should include information:

- Sex and age composition of the population in the study area;

- The number of children and adults, or the structure of the population in this territory.

5.4. The sources of data on violations in health are: depersonalized data fund compulsory health insurance and documentation of the results of the individual and sample research, including specialized health biological research.

5.5. By supporting background information are

- Information about the physiological norm or regional background levels of chemicals in biological fluids of man. If there is no data in the literature as a comparison criterion may be used in evaluating the results of chemicals in biological environments similar contingent living outside exposure to the test substances;

- Data about the proven effects of chemicals in relation to human health;

- Data on critical organs and systems, the targeted chemical substances present in the environment, and the levels of reference concentrations (doses);

- Recognized mathematical models describing the relationship levels of the chemical in the environment and violations health.

The above information is contained in databases hosted on official sites of the Agency for Toxic Substances and Disease (ATSDR), National Center biotechnology Information (NCBI), the Integrated Risk Information Systems (IRIS), the World Health Organization (WHO), the World Trade Organization (WTO), Codex Alimentarius Commission, as well as can be obtained from the national scientific and normative-methodical literature).

6. Conduct of Biomedical Research

6.1. The procedure of choice for the study of the contingent

6.1.1. Preferred for the study and evaluation of injury is the method of "case-control".

Selecting populations for medical and biological Studies carried out with Given identified expected adverse effects.

Given that a large number of factors depending on age: (Susceptibility, immune status, etc.) is recommended when forming groups for in-depth medical and biological investigations

comply with the conditions:

 group should be homogeneous in age category
adopted in accordance with the inclusion of practice-gradation of both parties
sex: 0-4 years; 5-9 years; 10-14 years; 15-19 years; 20-24 years; 25-29 years; 30-34 years;
35-39 years; 40-44 years; 45-49 years; 50-54 years; 55-59; 60-64 years, etc.

 the examinees should be no acute infectious
diseases of not less than 2 weeks prior to the study,
chronic disease decompensation (group 4 health);

- The group should be homogeneous Social Welfare and
economic conditions of life;

- Lifestyle factors, production and other activities,
that can significantly affect the results of Biomedical
Studies have to be studied and taken into account when analyzing the results.

6.1.2. The sample size for the study is established on the principle of
adequacy for the statistical significance of the research and
calculated based on the necessary conditions for the existence dependence
between the compared features, namely, the reliability coefficient
determination with a given level of significance:

$$N \geq 2 \cdot t^2 \left(\frac{1}{R^2} - 1 \right) \quad (1)$$

One. Wherein

N - sample size for the study;
t - Student's coefficient;
R^2 *- Coefficient of determination;*
a - the level of significance, a = 0,05.

At a significance level of *alpha* = 0.05 quantile of the Student distribution
tends to the value of 1.96.

By setting a specific value of the coefficient of determination, by
relations determine the minimum sample size that allows
evaluate the relationship between the analyzed parameters. To assess
dependencies low severity (R^2 0.05), the total sample size
should include not less than 40 observations.

6.1.3. To obtain correct estimates should be selected
observation of at least two zones characterized by different
exposure levels of chemical environmental factors regarding
specified security criteria (experimental and control groups).
The number of cases in each area (group) should not be less than 20.

6.1.4. A prerequisite for the formation of the control group
is comparable in socio-economic, household and others.
indicators with the experimental group.

***6.2. Evaluation of group and personal exposure within the health
Biological Studies***

6.2.1. Group exposure may represent data

maximum one-time and long-term (annual average, annual mean)
concentration levels of environmental pollution, referred to

concentration levels of environmental pollution, referred to
certain area (territory), where fares study group
population. Exposure assessment is performed on the basis of calculated or
field data (see. Section 6 RD P 2.1.10.1920-04):

6.2.2. The optimum is to estimate personal exposure
particular chemical and each member of the study
control group [1]Which may be performed based on the conjugation
calculated and field data on the exposure in relation to
geographic information system (address register).

Recommended perform exposure assessment for each point,
characterizes the place of permanent residence the person for whom
performed a study of markers of exposure and markers of response. B
result for each person based on the exhibited magnitude, frequency,
duration of paths (routes) exposure is set
Individual exposure level for a particular chemical
substances or acting factor.

6.3. Evaluation of chemicals in biological media

6.3.1. As a potential marker for determining exposure to
organism (in biological media substrates) selected chemical
substances which according to the literature can register
bioenvironments within a certain time after exposure of human and
reflect the level of exposure. At the same time can be determined as themselves
chemical substances and their transformation products proved to
body.

6.3.2. Select object to the analytical study in humans -
Priority biological medium or substrate (blood, urine, hair, and
et al.) is performed based on the following principles:

- it is possible to quantitatively measure the concentration
chemical substance in biosubstrate with required accuracy
selectivity sensitivity. For tasks judicial protection
desirable results is the inclusion of a methodology for determining
State Register of measuring methods;
- substrate is informative for proxy authentication and explanations
causality. (Examples of different types of information content
biological media for the problems of biomedical research are given in
Appendix 3);
- priority is given to non-invasive method of selection of substrates.

6.3.3. Considering regularities receipts transport and
distribution of toxic compounds in tissues and organs, most

[1]The most reliable way of personal exposure assessment are the use of personal
chips, but their use is limited spectrum is determined by the components and the high cost
study.

adequate biological material is in most cases
whole blood, reflects the current exposure.

6.3.4. Collection and preservation of biological samples (blood, urine)
for research conducted in accordance with the requirements of the joint venture 1.3.2322-08
"Security work with microorganisms III-IV group pathogenicity
(Danger) and agents of parasitic diseases. "

6.3.5. Selection of biological Matter performed entity
accredited on medical investigations at Provided
informed consent of the patient (for adults) or parents (for
children) to medical intervention (informed consent form
is the model, receiving consent provides medical
organizations engaged in research).

6.3.6. Measurements of chemical substances in biological media performed standardized methods organizations accredited for this type of research.

6.3.7. Criteria to assess the levels of chemicals in biological media can be: similar performance, established for the population living outside the impact zones (Indicators of the comparison group), the literature data, the so-called "REFERENCE levels' regional background levels established for the territory of the region in a special study.

6.3.8. Statistical processing of data on the levels of chemical substances in biological fluids is carried out with regard to the nature distributions. For this test is performed on a normal distribution with using Pearson's chi-squared test.

6.3.9. In the course of statistical processing of the data are calculated the following indicators:

- Distribution parameters - mean, standard deviation, error average for variables distributed according to the normal law; median, the first and third quartiles for quantities distributed according to, different from normal;

- The maximum value of the exponent in the group;

- The proportion of samples containing chemicals in biological media study group, exceeding the average level in the comparison group (Median for non-normal distribution);

- Results of intergroup differences using Student's t test for normally distributed variables and criteria Mann-Whitney test for variables with a distribution different from normal at significance level $a = 0.95$.

6.4. Assessing the level of response in markers of Biomedical studies

6.4.1. Since the presence of chemical substances in biological media reflecting body contact with chemical agents, but the consequences

this contact, parallel and chemical analysis performed sampling and analysis of the state of the organism, which directly or indirectly reflect the impact of pollutant substance.

6.4.2. Mandatory element of inclusion marker response evidence base of health damage is biological plausibility responses established in several large-scale studies, the inclusion of these responses in the toxicological profiles of chemicals and recognized on global database level, etc.

Data for a number of chemicals and laboratory parameters biologically believable reflecting specific and non-specific effects of these substances on the obtained when analysis of international scientific materials, tested and refined in terms of epidemiological studies in Russian Federation, are given in Appendix 4.

Information on exposure markers and markers wide responses range of chemicals contained in the databases listed in clause 5.5. .

6.4.3. Statistical processing of data on the levels of laboratory indicators is based on the nature of distributions. For this test is performed on a normal distribution with Pearson's chi-squared test.

6.4.4. In the course of statistical processing of the data are calculated

the following indicators:

- Distribution parameters - mean, standard deviation, error average for variables distributed according to the normal law; median, the first and third quartiles for quantities distributed according to, different from normal;

- The worst value of the index in a group (maximum or min, depending on the type of indicator);

- The share values of laboratory parameters of the study group, characterized (above and / or below) of the average in the control group (Median for non-normal distribution), as well as from physiological norm;

- Results of intergroup differences using Student's t test for normally distributed variables and criteria Mann-Whitney test for variables with a distribution different from normal at significance level $a = 0.95$.

6.5. Conducting medical examinations and functional studies

6.5.1. Medical examinations are organized in order to identify clinical manifestations of health problems associated with probabilistic risk factors in the study area (the study group), with the level of bio-availability of chemicals - Markers

exposure level deviation from physiological norms laboratory indicators.

6.5.2. Physician examinations accompanied functional research, founded the literature on the likely negative effects of functional disorders upon exposure Chemicals.

6.5.3. During the examination the doctor recorded the presence of (Lack of) those violations that are expected at the marked level exposure and pathogenesis associated with the latter. We consider violations of critical organs and systems, for which the risk was defined as unacceptable.

6.5.4. The result of medical examinations are:

- Diagnosis for each patient (main and supporting) exposed to the light of complex laboratory parameters and results functional studies;

- Described the results for each patient physical examination;

- Are described for each patient results.

6.5.5. Statistical data processing and medical examinations Functional studies carried out in view of the scale of measurement indicators and the distribution of quantitative indicators. For This test is performed for normal distribution using Pearson's chi-squared test.

6.5.6. In the course of statistical processing of the data are calculated the following indicators:

- Absolute and relative frequency values of the nominal indicators (including exposed diagnoses, objective parameters status) in the groups;

- The parameters of the distribution of quantitative indicators - average, standard deviation error of the mean for the quantities distributed normal law; median, first and third quartile values for distributed according to the law, other than the normal;

- Frequency deviation indicators of physiological norm;

- The maximum value of the exponent in the group;

- Results of intergroup differences using

- Results of intergroup differences using
Student's t test for normally distributed variables and criteria
Mann-Whitney test for variables with a distribution different from normal at
significance level $a = 0.95$.

7. Investigation of dependencies in the "habitat - Health Population

7.1. Modeling dependencies in the "habitat - Health population "is the process of identifying the parameters mathematical models that reflect the influence of chemical environmental factors

habitat on health indicators on the basis of sample epidemiological studies.

7.2. Modeling procedure in the "habitat - Health population "is held in two phases, each of which involves construction of appropriate models.

At the first stage the dependence between exposure chemical factors of the environment and the content of substances in biological fluids of the body (a marker of exposure). The second stage constructed model of dependencies between the content of chemicals in biological media (a marker of exposure) and the deviation of the clinical, laboratory and / or functional parameters (markers of response) from the physiological norm.

7.3. To construct a model of the relation between chemical environmental factors and the content of substances in biological media organism (a marker of exposure) as a parameter of the exposure may used the concentration of substances in the environment or dose odnosredovom or multicompartment arriving path.

7.4. In the absence of published data known models relationship between the level of exposure and response:

7.4.1. In conditions of low-dose (or low level) of chronic effects of pollutants in concentrations ranging 0.1-0.5 PDKs.s. valid is the use of linear dependency of the form *(2)* :

$$x = b_1 D + b_0 \quad \text{Wherein} \qquad (2)$$

D - average daily dose averaged chronic exposure chemical mg / (kg * day);

x - the concentration of a chemical in biological media, mg / dm^3;

b_0, B_1 - Model parameters characterizing the initial level concentration of the substance in biological media and the rate of absorption.

7.4.2. In the case of the concentration pollutants in environment more than 0.5 MPC mathematical model can be given an S-shaped curve and is described by equation *(3):*

$$C = \frac{k}{1 + e^{b_0 - b_1 D}}, \text{ wherein} \qquad (3)$$

C - concentration of substances in biological media;

D - daily dose based on how a substance;

k, b_0 *and* b_1 - The parameters of the model.

7.5. Calculation of the parameters of the model and the adequacy of implemented standard procedure pair regression analysis. To test statistical hypotheses about the regression coefficients in the case of normal distribution parameters using Student's t test.

Adequacy test is performed using analysis of variance
using Fisher's exact test with a significance level of 0.05.

7.6. In determining the appropriate model reflecting investigated
dependence, the concentration of the chemical in the blood is taken in
as a marker of exposure chronic exposure.

7.7. Modeling of dependence "marker of exposure - response marker"
conducted on the basis of aggregate data on the content of chemical
substances in biological media, clinical, laboratory and functional parameters.

7.8. Simulation is performed based on the construction of the pair
Mathematical models "marker of exposure - response marker" and
is holding a computational procedure based on
Data Sample statistics studies. B resulting
statistical studies for each observation (individual from
the total sample) are fixed values and the marker of exposure
marker response.

7.9. When building a pair of mathematical models as
dependent variable response marker acts as an independent -
marker of exposure.

7.10. As a marker of a response may also be used deflection
level recorded incidence on individual nosological
forms of the average incidence in the territory. Morbidity
estimated according to health-care seeking in
clinic within 1 year prior to the survey.

7.11. Simulation depending using as marker
Answer the number of cases during the year performed in a manner
similar manner as described in Sec. 7.4. 7.5).

7.12. Determination of parameters of the mathematical model (b_0 B b_1)
produced by the method of least squares using packets
programs for the statistical analysis of data (Statistica, SPSS, SAS, and others.).

7.13. Evaluation of the reliability and adequacy of the model parameters
conducted on the basis of one-way ANOVA on
Fisher test. In constructing mathematical models implemented
determining the 95% confidence limits.

8. Application of the results of biomedical research for formation of evidence of harm to health by the negative impact of environmental factors

8.1. Biomedical studies conducted in the general system
the collection of evidence of harm to health when exposed to negative factors
environment, taking into account that in the preliminary stages of the study
the facts of environmental pollution, proved accommodation
(Stay) patients studied in conditions of exposure; calculated
health risk is above acceptable levels, detected
critical in terms of the exposure system and organs affected,

identified chemicals that form the risk to health
(Figure of section 3 of these guidelines).

8.2.

8.2. Biomedical research in addition to the identified circumstances must prove actual harm to health and communication harm from environmental factors.

8.3. Based on the definition of harm must be proved functional disorders and / or diseases associated with exposure. Deviations from the norm of individual indicators and their relationship with markers Exposure not are proof Harm and only its mediated symptoms.

8.4. Build the evidence base with regard to the criteria of causality, defined in Environmental Epidemiology (Hall, 1965, Fletcher, 1981 and et al.):

- The sequence of events in time (pollution habitat precedes the appearance of health problems); at formation of evidence under the existing long-term Exposure can be replaced by comparison groups living in different conditions of exposure;
- The effect of pronounced effect was observed in several (Many) people exposed;
- The dependence of the effect of the dose (in the amplification effects effect is enhanced, with the weakening effect of reduced exposure or disappears);
- The effect is robust and reproducible (effect observed by different researchers, regardless of the location and conditions time);
- established biological credibility connection (effect exposure is consistent with current scientific knowledge);
- The effect is specific (one cause leads to one effect). The criterion used in the case of specific effects Proved to specific chemicals;
- There are analogies (causal connection is already installed For similar exposure or disease).
- Known and eliminated other factors which might cause similar impairments.

8.5. Harmful installed on the system characteristics, shown in Table 2.

8.6. The harm can be proved on the individual and group level. Evidence of harm to the individual level requires the availability of data on the results of the study group to confirm connection exposure.

8.7. The finding of a violation of health, manifested the occurrence of disease or functional impairment associated with the negative impact of environmental factors is carried out order reflected in the diagram in Figure 2.

Tabl

Signs of injury due to the negative impact of environmental factors

Sign	I. Criteria (group level)	II. Criterion (individual level)
1. Availability of source the negative impact	1. There is a source of exposure *	1.Imeetsya source of adverse effects *
2. Accommodation (Stay) in human exposure conditions	2. A group of persons surveyed are in the conditions known chemical substance exposure * (Substance)	1. The patient is in a condition known exposure * chemical substance (s)
3. The level of risk for health of the individual or group of persons	3. The level of health risk is rated as unacceptable.	3. The level of health risk is rated as unacceptable

	4.1 scientific data confirmed the possibility the presence of the substance (s) from the environment or stable metabolite in biological media under known exposure (WHO data, EPA, regulatory methodological documents of the Russian Federation)	4.1 scientific data confirmed the possibility the presence of the substance (s) of habitat or stable metabolite in biological media under conditions kno exposure (WHO data, EPA, regulatory and procedural documents of the Russian Federation)
4. Content chemical in body	4.2. Group average rate (M ± m) content chemical in biosubstrate - marker exposure was significantly higher than the comparison ($M_k \pm m_k$) ($P \leq 0.05$)	4.2. The level of the chemical (a marker of exposure) in the patient's body above the upper border of the permissibl level comparison ($M_i > M \pm m$)
	4.3. For the study group exposed persons chemicals in biosubstrate is a significant correlation with the level of exposure ($P \leq 0.05$)	4.3. There is evidence that at the group level reliable connections of chemicals in biosubstrate with the level of exposure

Continued Table 2

Sign	I. Criteria (group level)	II. Criterion (individual level)
	5.1. A number of patients groups are unidirectional changes in laboratory indicators that reflect the impact of chemical substance ($nP > P_k \pm p_k$; $N > 5\%$)	5.1. Laboratory level indicator adequate chemical load is above (below) the upper (lower) boundaries of the physiological norm ($P > P_k \pm p_k$)
	5.2. For the studied group of exposed persons index is in significant correlation with the level exposure or a marker of exposure ($p \leq 0.05$)	5.2. There is evidence that at the group level reliable biologically justifiable depending changes from the exposure level indicator or marker Exposure
5. Level laboratory indicator functional tests (tests) results instrumental Studies	5.3. Under several patients there homogeneous (similar) complexes violations laboratory parameters indicating the the presence of functional disorders ($n > 5\%$)	5.3. The complex laboratory parameters with deviations from the physiological norm show of a patient's functional disturbance target organ (system)
	5.4. The average rate for the group of patients samples adequately reflect the effect of the chemical material is above (below) the physiological norms ($p \leq 0.05$)	5.4. Level functional test, biologically adequately reflects the effect of the chemical, is above (below) the physiological norm.
	5.5. Under several patients there unidirectional change of the index to the level of above (below) the physiological norm ($nP > P_k \pm p_k$; $n > 5\%$)	5.5. There is evidence that at the group level the relationship between functional impairment and exposure (a marker of exposure)
	5.6. There are scientific data on biological likelihood (pathogenetic link) indicator or a set of indicators for a given level exposure (a marker of exposure) (WHO data, EPA, normative and methodological documents of the Russian Federation)	5.6. There are scientific data on biological likelihood (pathogenetic link) or index a set of indicators for a given level of exposure (A marker of exposure) (WHO data, EPA, regulatory methodological documents of the Russian Federation)

Continued Table 2

Sign	I. Criteria (group level)	II. Criterion (individual level)
6. Communication "spouts effect "	6.1 In the study population (the system figures) is reliable due to the level exposure or a marker of exposure ($p \le 0.05$)	6.1 Patients included in the group in which the exponent (Scorecard) is in significant correlation with the level of exposure or a marker of exposure ($p \le 0.05$) there is scientific evidence of a sustainable significant relationship "exposition - the token response"
	6.2. There is evidence of biological plausibility (Pathogenetic link) indicators or complex performance at a given level of exposure (marker Exposure) (WHO data, EPA, regulatory methodological documents of the Russian Federation)	6.2. There is evidence of biological plausibility (Pathogenetic link) or connection indicator complex performance at a given level of exposure (marker Exposure) (WHO data, EPA, regulatory methodological documents of the Russian Federation)
7. Disease	7.1. In the group of patients exposed to several the same diagnosis due to, in addition to clinical features of laboratory system performance and functional tests with reliable biologically justified due to exposure (markers of exposure) (n> 5%)	7.1 The patient is diagnosed, the laboratory system indicators of functional tests, clinical having reliable indicators of biologically justified due to the exposure (markers of exposure)
	7.2. The frequency of the exposed (paragraph 6.1) the diagnosis was significantly exceed those in the comparison group ($p \le 0.05$)	7.2. Exposed diagnosis refers to a critical organs and systems, for which the risk was rated as unacceptable. There are scientific data similar diseases can arise in similar exposure.
	7.3 Diagnosis occurring with greater frequency than in comparison group refers to critical organs and systems, for which the risk was assessed as unacceptable. There are scientific data similar diseases can arise in similar exposure.	
8. The presence of other negative factors exposure	8. Known and eliminated other factors that could cause similar health disorders.	8. Known and eliminated other factors that could would cause similar impairments.

F1. Identification of sources of exposure

$$U: F_1 F_2 \{1, 0\}$$

$0\}$
$1;$
$\{$
F
2
F
$\vdots$
U

F2. Assessment of exposure conditions

$$U: F_2 F_3 \{1, 0\}$$

$0\}$ $0\}$
$1;$ $1;$
$\{$ $\{$
F F
2 5
F F
$\vdots$ $\vdots$
U U

F3 . Characteristics of the public health risk

F4. Measurement of chemical substances (a marker of exposure) in the body patient (patient group).

$$U: F_4 F_5 \{1, 0\}$$

$0\}$
$1;$
$\{$
F
2
F
$\vdots$
U

F5. Analysis of clinical, laboratory, functional, instrumental performance, adequate load (marker response).

$$U: F_5 F_6 \{1, 0\}$$

F6. Diagnosis and evaluation of functional disorders critical organs and systems installed in step F3

$U = 1$	$U = 0$
Injury associated with adverse impact factor **is contested** , if any represented by the sequence logical variables with a value	**Injury** associated with the negative influencing factors, it is considered **not contested** , if none of the representation of the sequence **is not allows**

logical variables with a value "TRUE" **allows to build unbroken chain from F1 to F6**

allows you to build a continuous chain of logical variables with value "true" **from F1 to F6**

Fig. 2 - The general order of proof, using health biological research harm associated with exposure adverse chemical environmental factors

8.8. The formalization presented scheme on evidence of harm Health is based on a representation of connections between individual elements in the form of logical variables. Logical variables can take two values: "TRUE" (logic 1) or "false" (Logic zero). Using the expression for the logic operations evidence of harm is as follows *(4)* :

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$$U = \bigvee_{i=1}^{N_f} U_i^{1\text{-}2} \wedge \left(\bigvee_{j=1}^{N_{Zab}} U_{ij}^{2\text{-}6} \wedge U_i^{2\text{-}3} \wedge \bigvee_{j=1}^{N_{Zab}} U_{ij}^{3\text{-}6} \wedge \left(\bigvee_{k=1}^{N_{cl}} U_{ik}^{2\text{-}5} \wedge U_i^{2\text{-}4} \wedge \bigvee_{k=1}^{N_{cl}} U_{ik}^{4\text{-}5} \wedge \left(\bigvee_{j=1}^{N_{Zab}} U_{kj}^{5\text{-}6} \right) \right) \right) \quad (4)$$

wherein:

$U_i^{1\text{-}2}$ = "The existence of the source (s) of exposure, forming exposure *i* -th factor " *I = 1..N* $_f$, N_f - The number of analyzed factors; *Proof are: meaningful Surface concentration typical source of pollutants in the ambient air places of permanent residence on the results obtained dissipation calculations on standardized methods and confirmed results of instrumental studies.*

$U_i^{2\text{-}3}$ = "Proven link exposure *i* -th factor formed with them the risk of public health " *I = 1..N* $_f$; N_f - The number of analyzed factors; *Proof is the unacceptable carcinogenic and / or non-carcinogenic acute and / or chronic risk to public health calculated according to the approved methods using criteria recognized in the Russian Federation;*

$U_i^{2\text{-}4}$ = "To prove the link between exposure *i* -th factor and content A chemical compound in the body ", *I = 1..N* $_f$ *The proof is the availability of reliable communication between indicators established by methods of mathematical statistics. Communication must be biologically plausible to be confirmed these scientific and methodical literature and other independent research.*

$U_{ik}^{2\text{-}5}$ = "Prove the negative impact of exposure *i* -th factor on the *k* th index clinical, laboratory, functional, instrumental studies " *k = 1..N* $_{cl}$, N_{cl} - The number of indicators clinical, laboratory, functional, instrumental research; *The proof is the availability of reliable communication between indicators established by methods of mathematical statistics. Communication must be biologically plausible to be confirmed these scientific and methodical literature and other independent research.*

U_{ij}^{3} = "Prove communication of health risk from the *i* -th factor with the *j* th index health " *J = 1..N* $_{Bkd}^{N}$ $_{Bld}$The number of health indicators;
The proof is the existence of a group of patients studied diagnosed in clinical trials or identified in epidemiological analysis diseases attributable to critical organs and systems identified in step health risk assessment.

The incidence of diseases should significantly exceed such in the comparison group

U_{ij}^{2-6} = "Prove the negative impact of exposure *i* -th factor on the *j* th health indicator ", *J = 1..N* $_{Bkd}^{N}$ $_{Bld}$The number of health indicators;
The proof is the availability of reliable communication between indicators Exposure and prevalence diseases established methods of mathematical statistics. Communication should be biologically plausible, supported by data and research methodological literature and other independent research. As usually considered only disease attributable to critical organs and systems identified in step health risk assessment.

U_{ik}^{4-5} = "Prove the negative impact of the content of *i* -th substance in the body on the *k* th index of clinical, laboratory, functional, instrumental studies " *k = 1..N* $_{cl}^{N}$ $_{cl}$- The number of indicators clinical, laboratory, functional, instrumental research;
The proof is the availability of reliable communication between indicators established by methods of mathematical statistics. Communication must be biologically plausible to be confirmed these scientific and methodical literature and other independent research.

U_{kj}^{5-6} = "To prove the link between the violation of *k* -th indicator of the clinical, laboratory, functional, instrumental studies with *j* -th indicator of the health of " *J = 1..N* $_{Bkd}^{N}$ $_{Bld}$The number of health indicators;
The proof is the availability of reliable communication between indicators established by methods of mathematical statistics. Communication must be biologically plausible to be confirmed these scientific and methodical literature and other independent research.

8.9. Injury associated with the negative impact factor be contested if any sequence represented logical variables with the value "true" allows to build unbroken chain from source of exposure to the establishment facts disease and / or identify functional violations critical organs and systems.

8.10. Injury associated with the negative impact factor considered is not contested when none of presented Sequences can not build a continuous chain of logical variables with the value "TRUE" from source of exposure to establish the fact of the disease and / or to identify functional violations of critical organs and systems.

8.11. The system of evidence and supporting documents are issued in established laws OK, in line with the goals and objectives.

8.12. If there is evidence of harm to health as a result of analyzed the impact of environmental factors are developed recommendations to eliminate the negative impact and / or development abatement and prevention.

8.11. Informing about results of Biomedical Studies carried out in accordance with existing RF legislation.

9. Conclusion

Applying the results of biomedical research in system evidence of injury greatly increases the objectivity and reliability the findings of the investigation, provide a focus for Planning sanitary measures to prevent and eliminate the harmful effects of environmental factors on health population and the effectiveness of measures taken.

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Appendix 1

Terms and Definitions

Injury - violation anatomical integrity or physiological function of human organs and tissues as a result of exposure to physical, chemical, biological and mental environmental factors (On approval of medical criteria determine the severity of the harm caused to human health, Order of the Ministry of Health and Social Development of the Russian Federation of April 24, 2008 N 194n)

Harmful factors - events, properties or other definable indication are: chemical which can adversely influence on human health

Dependence "exposure - response " - a link between exposure exposure mode, duration of exposure and the degree of severity, prevalence of adverse effects in the exposed population ("Guidance on Risk Assessment for Human Health effects of chemicals that pollute the environment, "P 2.1.10.1920-04)

Dependence "exposure - effect " - the relationship between exposure and severity effect in the exposed population ("Guide to assess the public health risk when exposed to chemical polluting the environment "P 2.1.10.1920-04).

Population health - a state of complete physical, mental and social well-being and not merely the absence of disease and physical defects (WHO Constitution)

Marker Answer (Effect) - figure quantitatively characterizing the biochemical, physiological or behavioral otherwise a change in the body, depending on the degree of which is determined actual or potential health impairment or disease progression ("Guidelines for assessing the public health risk when exposed chemicals that pollute the environment, "P 2.1.10.1920-04)

Marker of exposure - the exogenous chemical substance or its metabolite exogenous chemical substance or a metabolite or product and xenobiotic interaction between a molecule or a cell being targets amount whom determined in biological fluids of the body ("Guidance on Risk Assessment for health when exposed to chemical pollutants

health when exposed to chemical pollutants
environment "P 2.1.10.1920-04)

Biomedical research - the system of observation, assessment and prognosis of any changes in idividuma, group or population

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caused by exposure to environmental factors or anthropogenic
Natural Origin

Regional background level chemical matter in biological environments - Weather chemical content
substances in biological substrate a group of persons of a certain age, not
are at increased anthropogenic, including professional
loads (MU 2.1.10.2809-10. 2.1.10. The health status of the population in relation
with the state of the environment and living conditions of the population.
The use of biological markers for assessing pollution
habitat metals in the environment and health monitoring. Approved.
Ch. gos. Sanitary Doctor of the Russian Federation on 28 December 2010)

Habitat - a collection of objects, phenomena and factors
environment (natural and artificial) environment, which determines the conditions
human life

Physiological norm - a range of physiological changes, inside which the average oscillations biochemical, psychophysiological, and other genetic parameters indicate
about the safety of the morphofunctional status of the organism to maintain
given conditions at a high level of compensatory
reactive-adaptive capabilities, providing the required
level of adoptability, health and recreation (Psychophysiology.
Dictionary / Auto. M. Bezrukov, DA Farber // Collegiate Dictionary in
six volumes / Red.-comp. LA Karpenko. Under the total. Ed. AV Petrovsky. -
M .: PER SE, 2006. - 128 p.)

Exposure - Contact organism (receptor) with the chemical,
physical or biological agent (the "Guidelines for Risk Assessment
health when exposed to chemical pollutants
environment "P 2.1.10.1920-04)

Exposed population - population exposed
unfavorable factors

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Appendix 2

Abbreviations used

ATSDR	Agency for registration of toxic compounds and Diseases
CalEPA	The California Environmental Protection Agency environment
HEAST	Summary tables of estimates of effects on health
IRIS	Integrated Information System on risks
NATICH	Database Protection Agency okruzhyuaschey environment USA
WHO	World Health Organization

.

Appendix 3

Informativeness determine the number of chemical compounds in the blood, urine and hair *

Element	Blood	Urine	Hair
As	+	+	+
Al			+
Ba			+

Ba			
Bi	+		
B			+
Cd	+	+	+
Ca	+	+	+
Cr	+	+	
Co	+		
Cu	+	+	+
Fe			+
Pb	+		+
Mg			+
Hg	+	+	
P			+
Se	+		
Ag	+		
Sr			+
Tl	+		
Zn	+		+

* - "Medical and environmental risk assessment in gipermikroelementozov population megalopolis "/ AV Rocky, AT Bulls, EP Serebryansky, MG Rock. " RIC SEI OSU, Orenburg. 2003. 134.

Appendix 4

Levels (concentration) of a number of chemicals in the environment and biological environments, probabilistically forming a violation of public health

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
			0,00001-0,0001 (0,1-1 RFCcr) Acceptable risk (HQ = 0,1-1)	0,0007-0,018 * (blood) (From 0.1-0.6 reference level blood - 0,0007-0,028 * Mg / dm3)		
			0,00011-0,00026 (0,07-0,2 PDKs.s.) Unacceptable risk (HQ = 1,1-3)	0,0181-0,032 * (blood) (0,61-1,2 from reference level Blood)	□ Immunoglobulin E specific to chromium □ Eozinofilno-lymphocytic index □ total immunoglobulin E	X. Diseases of respiration, inc J30.4 allergic rhinitis, unspec J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi
Chrome	Inhaled	Organs	0,000261-0,00087 (0,21-0,6	0,0321-0,052 * (blood) (1,21-2 from		

Chrome	Inhaled	breath	PDKs.s.) Unacceptable risk (HQ = 3,1-9,0)	reference level Blood)		adenoids, incl . J35.1 Hypertro tonsils, J35.2 Hypertro adenoids; J37.1 Chronic laryngotracheit
			More 0.00087 (More than 0.6 PDKs.s.) Unacceptable risk (HQ> 9)	More than 0,052 * (blood) (2 from reference level blood	□ Immunoglobulin E specific to chromium □ Eozinofilno-lymphocytic index □ total immunoglobulin E □ Leykoformula, ESR in the blood	J38.9 disease o airway unspecified J44.8 Other refined chronic obstructive pulmonary dise

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
						J45.0 bronchial with a predomi allergic component IV. Disease Endocrine syst incl .: Protein-E46.0 energy failure E67.8 excess w a body;
Chrome	Inhaled	Endocrine System			□ total protein, glucose in serum; □ lipoproteins HDL, LDL cholesterol in serum; □ TSH, T4, svob □ Iodine in urine □ growth hormone in serum	E34.3 stunting; E34.4 tall; E01 disease thyroid associated with failure, and similar conditi E02 subclinica hypothyroidisn Iodine failure E03 other form hypothyroidisn E04.9 nontoxic goiter, unspeci
	Oral	Liver			□ albumin, C-reactive serum protein; □ total cholesterol, LDL serum □ ALT, AST, LDG3, □ γ- glutamiltransferza, alkaline phosphatase serum;	XI. Diseases of digestion incl . K71 toxic liver with cholestasis; K72 hepatic failure K73 Chronic hepatitis;

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Chrome					□ malondialdehyde Lipid hydroperoxide, alfafetoprotein in serum; □ total antioxidant activity	K74 fibrosis an liver K75 other inflammatory liver disease; K76 Other dise Liver

					superoxide dismutase, glutathione peroxidase in serum	
	Inhaled		0,000004-0,00005 (0,1-1 RfCcr) Acceptable risk (HQ = 0,1-1)	0 011-0,015 * (blood) (From 1.0-1.3 reference level blood - 0,0109 ± 0,0006mg / dm3)		X. Diseases of respiration, inc J30.4 allergic rhinitis, unspec J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids, incl . J35.1 Hypertro tonsils, J35.2 Hypertro adenoids; J37.1 Chronic laryngotracheit J38.9 disease o airway unspecified J44.8 Other refined chronic obstructive pulmonary dise J45.0 bronchial with a predomi allergic component
			0,000055-0.0002 (0.06-0.2 PDKs.s.) Unacceptable risk (HQ = 1,1-4)	0,0151-0,030 * (blood) (1,31-2,7 from reference level Blood)		
Manganese		Respiratory	0,00021-0,0005 (0,21-0,5PDKs.s.)	0,030-0,045 * (Blood) (2,71-4,0 from reference level Blood)	□ The absolute number eosinophils □ Immunoglobulin E specific to manganese □ Eozinofilno-lymphocytic index □ total immunoglobulin E	
			0.0005 (More than 0.5 PDKs.s.) Unacceptable risk (HQ> 10)	more than 0,045 * (Blood) (More than 4 from reference level Blood)		

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
						IV. Disease Endocrine syst incl .: Protein-E46.0 energy failure E67.8 excess w a body; E34.3 stunting; E34.4 tall; E01 disease thyroid associated with failure, and similar conditic E02 subclinica hypothyroidisn Iodine failure E03 other form hypothyroidisn E04.9 nontoxic goiter, unspeci
		Endocrine System		More 9,37□0,88 ** g 100 mg (blood)	□ total protein, albumin serum □ glucose in serum; □ cholesterol, lipoproteins high (HDL) and low (LDL) density Serum triglycerides blood; □ degidroepandrosteron (17KS) in urine □ TSH T4svob. serum blood; □ growth hormone in serum	
Manganese						
						VI. Diseases of the Distemic of the R45.0 asteno neurotic syndrome R53 malaise ar fatiguability G62.2 polyneu due to other toxic substances G62.9 Polyneu unspecified
	Oral	CNS		0,028-0,03 ** mg% (Brain) 1-16 mcg **% (blood)	□ dopamine, norepinephrine, acetylcholine, in serum; □ GABA serum potassium / sodium coefficient	

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Manganese	Inhaled		0,00003-0,00005 (0,6-1,0 RFCcr) Acceptable risk (HQ = 0,6-1,0) 0,000051-0,00006 (1.1-1.2 PDKs.s.) Unacceptable risk (HQ = 1,1-1.2)	0 001-0,062 * (blood) (1,0-2,2 from reference level blood - 0,001-0,028 mg / dm3) 0,0621-0,116 * (blood) (2.3-4 from the reference level in the blood)		G93.8 neurotic syndrome G92 toxic encephalopathy X. Diseases of respiration, inc J30.4 allergic rhinitis, unspec J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids, incl . J35.1 Hypertro tonsils, J35.2 Hypertro adenoids; J37.1 Chronic laryngotracheit J38.9 disease o airway unspecified J44.8 Other refined chronic obstructive pulmonary dise J45.0 bronchial with a predomi allergic component
Nickel		Respiratory	0,000061-0,0001 (1.2-2.0 PDKs.s.) Unacceptable risk (HQ = 1,4-2.0)	0,1161-0,309 * (blood) (1,0-2,2 from reference level Blood)	□ Immunoglobulin E specific to nickel □ Eozinofilno-lymphocytic index □ total immunoglobulin E	

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
		System blood hematopoiesis			□ erythrocytes (violation osmotic Resistance) □ reticulocytes in the blood, the average content □ iron, total and partial iron binding ability of serum blood; □ ferritin, transferrin serum;	III. Disease of the incl .: D50.8 Other iron deficiency anemia; D50.9 Other iron deficiency anemia, unspec D61.2 Aplastic anemia caused other external agents; D64.8 Other unspecified ane Anemia D64.9 unspecified
Nickel		Nervous system		** 2-32,7 mg% (blood)	□ LDG4-5 serum; □ potassium, sodium, serum	VI. Disease of the R45.0 asteno neurotic syndrome R53 malaise an fatiguability G93.8 neurotic syndrome IX. Diseases of circulatory incl

		Cardiovascular system			blood potassium / sodium coefficient; □ cortisol serum □ lipid hydroperoxides, malondialdehyde in serum; □ superoxide dismutase, glutathione peroxidase in serum	I10-15 disease characterized increased blood pressure; I51.6 cardio-vascular diseas unspecified; I51.0 kardiodis Heart disease I unspecified;

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
		The organ of vision (eye)			□ eosinophils in scrapings conjunctiva □ immunoglobulin E in common serum	Diseases of the adnexa incl .: N10.4 Chronic conjunctivitis H15 scleritis H16 keratitis
Nickel	Oral	Liver			□ albumin, C-reactive serum protein; □ cholesterol, lipoproteins high (HDL) and low (LDL) density Serum triglycerides blood; □ ACT LDG3, γ-glutamiltransferza in serum; □ malondialdehyde lipid hydroperoxide serum; □ total antioxidant activity superoxide dismutase, glutathione peroxidase in serum	XI. Diseases of digestion incl . K71 toxic liver with cholestasis; K72 hepatic failure K73 Chronic hepatitis; K74 fibrosis ar liver; K75 Other inflammatory liver disease; K76 Other dise Liver
		Gastrointestinal tract			□ secretory immunoglobulin A in saliva; □ alkaline phosphatase serum; □ C-reactive protein in gastric juice; □ diphenylamine assay in gastric juice; □ malondialdehyde in gastric juice;	XI. Diseases of digestion incl . K29.5 Chronic gastritis; K29.8 duodeni K29.9 gastrodu unspecified; K30 dyspepsia K83.8 Other specified disea biliary ways;

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Nickel			0.001-0.003 (0,3-1,0 RFCcr) Acceptable risk (HQ = 0,3-1,0) 0,0031-0,005	0,005-0,011 * (blood) (1-2,2 from background level - 0.005 mg / dm3)	□ serum lipid hydroperoxide serum; □ total antioxidant activity of blood plasma; □ Immunoglobulin E	K83.9 disease Biliary unspecified

			(1,0-1,7) PDKs.s.) Unacceptable risk (HQ = 1,0-1,7)	0,0111-0,049 * (blood) (2,3- 9,8 from background Level)	specific to formaldehyde □ Eozinofilno-lymphocytic index □ total immunoglobulin E	
Formaldehyde	Inhaled	Organs breath	0,0051-0,01 (1,7-3,3 PDKs.s.) Unacceptable risk (HQ = 1,7-3,3)	0,050-0,098 * (blood) (9,9-19,6 from background Level)	□ Immunoglobulin E specific to formaldehyde □ Eozinofilno-lymphocytic index	X. Diseases of respiration, inc J45.0 bronchial with a predomi allergic component
			Furthermore 0.01 (More than 3.3 PDKs.s.) Unacceptable risk (HQ> 3,3)	More than 0,098 * (blood) (Greater than 19.6 from the background Level)	total immunoglobulin E	
		CNS			□ cortisol, epinephrine serum; □ potassium, sodium, serum blood potassium / sodium coefficient	VI. Diseases of the R45.0 asteno neurotic syndrome R53 malaise an fatiguability G62.2 polyneu

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
						due to other toxic substances G62.9 Polyneu unspecified G93.8 neurotic syndrome G92 toxic encephalopathy G93.8 neurotic syndrome
Formaldehyde		The organ of vision (eye)			□ eosinophils in scrapings conjunctiva □ immunoglobulin E in common serum	Diseases of the adnexa incl .: N10.4 Chronic conjunctivitis H15 scleritis H16 keratitis
	Oral	Gastrointestinal tract			□ pepsinogen I, II serum blood □ carcinoembryonic antigen in serum □ lipid hydroperoxides in serum;	XI. Diseases of digestion incl .: K29.5 Chronic gastritis; K29.8 duodeni K29.9 gastrodu unspecified; K52.1toksiches gastroenteritis K52.9 noninfec gastroenteritis unspecified
Vanadium	Inhaled	Organs breath	More than 1 mg / m 3 8 hour exposure Vanadium pentoxide)	More ** 1.67 ng / ml (Blood)	□ immunoglobulin G peculiar to vanadium serum	X. Diseases of respiration, inc J30.4 allergic rhinitis, unspec J31hronichesky

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
					□ total immunoglobulin E in serum; □ eozinofilno-lymphocytic index blood; □ eosinophils (absolute number) in the blood;	nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids, incl . J35.1 Hypertro tonsils, J35.2 Hypertro adenoids; J37.1 Chronic laryngotracheit J38.9 disease o airway unspecified J44.8 Other refined chronic obstructive pulmonary dise J45.0 bronchial with a predomi allergic component
Vanadium						
		The organ of vision (eye)			□ eosinophils in scrapings conjunctiva □ immunoglobulin E in common serum	Diseases of the adnexa incl .: N10.4 Chronic conjunctivitis H15 scleritis H16 keratitis
		Nervous system		0,79-40,0 ** ug% (Blood)		VI Diseases of system incl .: G43 migraine

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
					□ albumin, C-reactive serum protein; □ cholesterol, lipoproteins high (HDL) and low (LDL) density in serum; □ AST, LDH, γ-glutamiltransferza, alkaline phosphatase serum; □ malondialdehyde Lipid hydroperoxide, alfafetoprotein in serum; □ total antioxidant activity superoxide dismutase, glutathione peroxidase in serum	XI. Diseases of digestion incl . K71 toxic liver with cholestasis; K72 hepatic failure K73 Chronic hepatitis; K74 fibrosis ar liver; K75 Other inflammatory liver disease; K76 Other dise Liver
	Oral	Liver				
Vanadium						
		Gastrointestinal tract			□ secretory immunoglobulin A in saliva; □ alkaline phosphatase serum; □ C-reactive protein in gastric juice; □ diphenylamine assay in gastric juice; □ malondialdehyde in gastric fluid, serum, blood □ lipid hydroperoxides in	XI. Diseases of digestion incl . K29.5 Chronic gastritis; K29.8 duodeni K29.9 gastrodu unspecified; K30 dyspepsia K83.8 Other specified disea biliary ways;

					serum; □ total antioxidant activity of blood plasma;	K83.9 disease Biliary unspecified

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Vanadium		Urinary system			□ lipid hydroperoxides in serum; □ creatinine, urea serum; □ renal epithelium in the urine; □ specific gravity, leukocytes, protein, erythrocytes in urine	XIV. Disease urogenital syste incl .: N03 chronic nephrotic syndrome; N05 nephritic syndrome unspecified; N28.9 kidney d ureter unspecified; N11.9 Chronic pyelonephritis
Cobalt	Inhaled	Organs breath		** 0.1-2.0 mg / m3 (blood)	□ immunoglobulin E specific to cobalt in serum □ total immunoglobulin E in serum; □ eozinofilno-lymphocytic index blood; □ eosinophils (absolute number) in the blood;	X. Diseases of respiration, inc J30.4 allergic rhinitis, unspec J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids, incl . J35.1 Hypertro tonsils, J35.2 Hypertro adenoids; J37.1 Chronic laryngotracheit J38.9 disease o airway unspecified J44.8 Other refined chronic

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Copper		Respiratory	0,22-14 mg / m3 (Atmospheric Air) Exposure 1-2 hours		□ leukocytes, neutrophils, monocytes, lymphocytes blood, and population lymphocyte subpopulations (CD3 +, CD4 +, CD8 +, CD16 + CD19 +, CD56 +) in the blood, □ immunoglobulins A, M, G in	obstructive pulmonary dise J45.0 bronchial with a predomi allergic component X. Diseases of respiration, inc J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids, J37.1 Chronic laryngotracheit J38.9 disease o respiratory

					□ immunoglobulins A, M, G in serum phagocytic activity Blood neutrophils	respiratory tract, unspecifi J40 Bronchitis, specified as acu or chronic; J41 simple chronic bronch J42 Chronic bronchitis, unsp
	Inhaled					VI. Diseases of the
		Nervous system		0,22-0,46 g **% (Brain) ** 64-106 mg% (blood)		R45.0 asteno neurotic syndrome R53 malaise an fatiguability G93.8 neurotic syndrome

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
					□ albumin, α-, β-, γ-globulins, C-reactive serum protein;	
		Liver	4-80 mg / l in water		□ cholesterol, lipoproteins high (HDL) and low (LDL) density Serum triglycerides blood; □ ALT, AST, LDH, Γ-glutamiltransferza, cytochrome P450, alkaline Phosphatase in Serum blood; □ malondialdehyde Lipid hydroperoxide, alfafetoprotein in serum; □ total antioxidant activity superoxide dismutase, glutathione peroxidase in serum	XI. Diseases of digestion incl . K71 toxic liver with cholestasis; K72 hepatic failure; K73 Chronic hepatitis; K74 fibrosis an liver; K75 Other inflammatory liver disease; K76 Other dise Liver
	Oral					
		Gastrointestinal tract			□ secretory immunoglobulin A in saliva; □ serum ceruloplasmin blood; □ C-reactive protein in gastric juice; □ diphenylamine assay in gastric juice; . serum □ lipid hydroperoxides in serum; □ total antioxidant activity of blood plasma;	XI. Diseases of digestion incl . K29.5 Chronic gastritis; K29.8 duodeni K29.9 gastrodu unspecified; K30 dyspepsia K83.8 Other specified disea biliary ways; K83.9 disease Biliary unspecified

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
						X. Diseases of respiration, inc

					□ leukocytes, neutrophils, monocytes, lymphocytes blood □ populations and subpopulations lymphocytes (CD3 +, CD4 +, CD8 +, CD16 +, CD19 +, CD56 +) in the blood, □ immunoglobulins A, M, G in serum □ phagocytic activity Blood neutrophils	J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids, J37.1 Chronic laryngotracheit J38.9 disease o respiratory tract, unspecifi J40 Bronchitis, specified as acu or chronic; J41 simple chronic bronch J42 Chronic bronchitis, unsp
Arsenic		Organs breath				
	Inhaled					
					□ LDH$_{4-5}$ serum; □ potassium, sodium, serum blood potassium / sodium coefficient; □ cortisol serum □ lipid hydroperoxides, malondialdehyde in serum; □ superoxide dismutase, glutathione peroxidase in serum	IX.Bolezni sys circulatory incl I10-15 disease characterized increased blood pressure: I51.6 cardio-vascular diseas unspecified; I51.0 kardiodis Heart disease I unspecified;
		Cardiovascular system				

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
					□ secretory immunoglobulin A in saliva; □ alkaline phosphatase serum; □ C-reactive protein in gastric juice; □ diphenylamine assay in gastric juice; □ malondialdehyde in gastric juice ;, serum □ lipid hydroperoxides in serum; □ total antioxidant activity of blood plasma; □ leykoformula, plasma cells blood	XI. Diseases of digestion incl . K29.5 Chronic gastritis; K29.8 duodeni K29.9 gastrodu unspecified; K30 dyspepsia K83.8 Other specified disea biliary ways; K83.9 disease Biliary unspecified
		Gastrointestinal tract				
	Oral					
					□ cortisol, epinephrine serum; □ acetylcholine in serum blood; □ Serum TSH; □ potassium, sodium, serum blood potassium / sodium coefficient	VI. Diseases of the R45.0 asteno neurotic syndrome R53 malaise an fatiguability G62.2 polyneu due to other toxic substances G62.9 Polyneu unspecified G93.8 neurotic syndrome G92 toxic encephalopathy
		CNS		1-20 mcg **% (blood)		

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Zinc	Inhaled	Organs breath			□ leukocytes in the blood, □ populations and subpopulations lymphocytes (CD3 +, CD4 +, CD8 +, CD16 +, CD19 +, CD56 +) in the blood, □ immunoglobulins A, M, G in serum □ phagocytic activity Blood neutrophils	X. Diseases of respiration, inc J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids, J37.1 Chronic laryngotracheit J38.9 disease o respiratory tract, unspecifi J40 Bronchitis, specified as acu or chronic; J41 simple chronic bronch J42 Chronic bronchitis, unsp VI. Diseases of the [illegible] system incl. R45.0 asteno neurotic syndrome R53 malaise an fatiguability G93.8 neurotic syndrome Vegeto vascula dysfunction, polyneuritis
		Nervous system		0,016-0,9 ** mg% (Blood)		

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Cadmium	Inhaled	Organs breath	More than 1 mg / m 8 Exposure hours - acute poisoning		□ immunoglobulin G specific to cadmium in serum □ leukocytes in the blood, □ populations and subpopulations lymphocytes (CD3 +, CD4 +, CD8 +, CD16 +, CD19 +, CD56 +) in the blood, □ immunoglobulins A, M, G in serum □ phagocytic activity Blood neutrophils	X. Diseases of respiration, inc J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids, J37.1 Chronic laryngotracheit J38.9 disease o respiratory tract, unspecifi J40 Bronchitis, specified as acu or chronic; J41 simple chronic bronch J42 Chronic bronchitis, unsp

		Endocrine System		2 mg / l ** (urine) Above 0.5 mg 100 ** ml (blood)	□ total protein, albumin serum □ ACTH in serum, □ 17OKS serum	IV. Disease Endocrine syst incl .: Protein-E46.0 energy failure; E34.3 stunting; E34.4 tall; Neurasthenia
		Nervous system		0.7 ug /% ** (blood)		Vegetative neu General asthen

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
	Oral	Urinary system			□ lipid hydroperoxides in serum; □ serum creatinine blood; □ Beta$_2$-microglobulin in serum □ renal epithelium in the urine; □ specific gravity, leukocytes, protein, erythrocytes in urine Blood neutrophils	XIV. Disease urogenital syst incl .: N03 chronic nephrotic syndrome; N05 nephritic syndrome unspecified; N28.9 kidney d ureter unspecified; N11.9 Chronic pyelonephritis
Toluene	Inhaled	Organs breath	Above 750 mg / m3 - Acute poisoning		□ leukocytes, neutrophils, monocytes, lymphocytes blood □ populations and subpopulations lymphocytes (CD3 +, CD4 +, CD8 +, CD16 +, CD19 +, CD56 +) in the blood, □ immunoglobulins A, M, G in serum □ phagocytic activity Blood neutrophils	X. Diseases of respiration, inc J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids; J37.1 Chronic laryngotracheit J38.9 disease o airway unspecified;
		CNS			□ cortisol, epinephrine serum; □ potassium, sodium, serum blood potassium / sodium coefficient	VI. Diseases of the R45.0 asteno neurotic syndrome R53 malaise an fatiguability G62.2 polyneu due to other

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
						toxic substances G62.9 Polyneu unspecified G93.8 neurotic syndrome G92 toxic

						encephalopathy G93.8 neurotic syndrome
Toluene		System blood hematopoiesis			□ hemoglobin, erythrocytes, color index, leukocytes, lymphocytes blood; □ iron, total and partial iron binding ability of serum blood; □ ferritin, transferrin serum;	III. Diseases of the incl .: D50.8 Other iron deficiency anemia; D50.9 Other iron deficiency anemia, unspec D61.2 Aplastic anemia caused other external agents; D64.8 Other unspecified ane Anemia D64.9 unspecified
		Endocrine System			□ LH, prolactin, FSH, Serum testosterone blood; □ leptin in the serum; □ cortisol serum	IV. Disease Endocrine syst incl .: E27.4 Other unspecified failure of the c adrenal gland;

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
						E23.3 dysfunct hypothalamic r classified in elsewhere
Toluene	Oral	Liver			□ albumin, α-, β-, γglobuliny, C-reactive serum protein; □ cholesterol, lipoproteins high (HDL) and low (LDL) density Serum triglycerides blood; □ ALT, AST, LDH, Γ-glutamiltransferza, alkaline phosphatase serum; □ malondialdehyde Lipid hydroperoxide, alfafetoprotein in serum; □ total antioxidant activity superoxide dismutase	XI. Diseases of digestion incl .: K71 toxic liver with cholestasis; K72 hepatic failure; K73 Chronic hepatitis; K74 fibrosis ar liver; K75 Other inflammatory liver disease; K76 Other dise Liver
		Urinary system			□ lipid hydroperoxides in serum; □ creatinine, urea serum; □ total protein, albumin, α-, β-, γ-globulin serum blood □ beta-2-microglobulin in serum; □ renal epithelium in the urine; □ specific gravity, leukocytes, protein, erythrocytes in urine	XIV. Disease urogenital syst incl .: N03 chronic nephrotic syndrome; N05 nephritic syndrome unspecified; N28.9 kidney d ureter unspecified; N11.9 Chronic pyelonephritis

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Xylol	Inhaled	Respiratory			□ leukocytes, neutrophils, monocytes, lymphocytes, ESR blood □ populations and subpopulations lymphocytes (CD3 +, CD4 +, CD8 +, CD16 +, CD19 +, CD56 +) in the blood, □ immunoglobulins A, M, G □ phagocytic activity Blood neutrophils	X. Diseases of respiration, inc J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids; J37.1 Chronic laryngotracheit J38.9 disease o airway unspecified VI. Diseases of the R45.0 asteno neurotic syndrome R53 malaise ar fatiguability G62.2 polyneu due to other toxic substances G62.9 Polyneu unspecified G93.8 neurotic syndrome G92 toxic encephalopathy G93.8 neurotic syndrome
		CNS			□ cortisol, epinephrine serum; □ Serum TSH; □ potassium, sodium, serum blood potassium / sodium coefficient	

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Xylol	Oral	System blood hematopoiesis			□ hemoglobin, erythrocytes, hematocrit, reticulocyte blood; □ iron, total and partial iron binding ability of serum blood;	III. Diseases of the incl .: D50.8 Other iron deficiency anemia; D50.9 Other iron deficiency anemia, unspec D61.2 Aplastic anemia caused other external agents; D64.8 Other unspecified ane Anemia D64.9 unspecified
		Liver			□ albumin, α-, β-, γ-globulins, C-reactive serum protein; □ cholesterol, lipoproteins high (HDL) and low (LDL) density Serum triglycerides blood; □ ALT, AST, LDG3, γ-glutamiltransferza, alkaline phosphatase serum; □ malondialdehyde Lipid hydroperoxide	XI. Diseases of digestion incl . K71 toxic liver with cholestasis; K72 hepatic failure; K73 Chronic hepatitis; K74 fibrosis ar liver;

					Lipid hydroperoxide, alfafetoprotein in serum; □ total antioxidant activity superoxide dismutase, glutathione peroxidase in serum	K75 Other inflammatory liver disease; K76 Other dise Liver

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Xylol		Urinary system			□ lipid hydroperoxides in serum; □ creatinine, urea serum; □ total protein, albumin, α-, β-, γ-globulin serum blood □ creatinine □ beta-2-microglobulin in serum; □ renal epithelium in the urine; □ specific gravity, leukocytes, protein, erythrocytes in urine	XIV. Disease urogenital syste incl .: N03 chronic nephrotic syndrome; N05 nephritic syndrome unspecified; N28.9 kidney d ureter unspecified; N11.9 Chronic pyelonephritis
Phenol	Inhaled	Organs breath			monocytes, lymphocytes, ESR in blood □ populations and subpopulations lymphocytes (CD3 +, CD4 +, CD8 +, CD16 +, CD19 +, CD56 +) in the blood, □ immunoglobulins A, M, G □ phagocytic activity Blood neutrophils	X. Diseases of respiration, inc J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids; J37.1 Chronic laryngotracheit J38.9 disease o airway unspecified
		CNS			□ cortisol, epinephrine serum; □ Serum TSH; potassium, sodium, serum blood potassium / sodium coefficient	VI. Diseases of the R45.0 asteno neurotic syndrome R53 malaise ar fatiguability G62.2 polyneu due to other

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
						toxic substances G62.9 Polyneu unspecified G93.8 neurotic syndrome G92 toxic encephalopathy G93.8 neurotic syndrome
					□ LDH, serum; □ potassium, sodium, serum	IX.Bolezni sys circulatory incl

					□ potassium, sodium, serum blood potassium / sodium coefficient; □ cortisol serum □ lipid hydroperoxides, malondialdehyde in serum; □ superoxide dismutase, glutathione peroxidase in serum	I10-15 disease characterized increased blood pressure; I51.6 cardio-vascular diseas unspecified; I51.0 kardiodis Heart disease I unspecified;
Phenol		Cardiovascular system				
	Oral	Gastrointestinal tract			□ leykoformula blood □ pepsinogen I, II serum blood □ carcinoembryonic antigen in serum □ lipid hydroperoxides in serum;	XI. Diseases of digestion incl . K29.5 Chronic gastritis; K29.8 duodeni K29.9 gastrodu unspecified; K52.1toksiches gastroenteritis K52.9 noninfec gastroenteritis unspecified

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Phenol		Urinary system			□ lipid hydroperoxides in serum; □ creatinine, urea serum; □ total protein, albumin, α-, β-, γ-globulin serum blood □ renal epithelium in the urine; □ specific gravity, leukocytes, protein, erythrocytes in urine	XIV. Disease urogenital syste incl .: N03 chronic nephrotic syndrome; N05 nephritic syndrome unspecified; N28.9 kidney d ureter unspecified; N11.9 Chronic pyelonephritis
Chloroform	Oral	Organs digestion (Liver)			□ albumin, α-, β-, γ-globulins, C-reactive serum protein; □ cholesterol, lipoproteins high (HDL) and low (LDL) density Serum triglycerides blood; □ ALT, AST, LDH, Γ-glutamiltransferza, cytochrome P450, alkaline Phosphatase in Serum blood; □ malondialdehyde lipid hydroperoxides serum; □ total antioxidant activity superoxide dismutase, glutathione peroxidase in serum	XIV. Disease urogenital syste incl .: N03 chronic nephrotic syndrome; N05 nephritic syndrome unspecified; N28.9 kidney d ureter unspecified; N11.9 Chronic pyelonephritis

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Chemical factor	Path receipts	Critical organs and body systems	In habitat	Concentration In biosubstrates	Laboratory parameters - marker effect	Disease by IC 10

1	2	3	4	5	6	7
Chloroform		Urinary system			□ lipid hydroperoxides in serum; □ creatinine, urea serum; □ total protein, albumin, α-, β-, γ-globulin serum blood □ renal epithelium in the urine; □ specific gravity, leukocytes, protein, erythrocytes in urine	XIV. Disease urogenital syst incl .: N03 chronic nephrotic syndrome; N05 nephritic syndrome unspecified; N28.9 kidney c ureter unspecified; N11.9 Chronic pyelonephritis
1,2-dichloroethane	Oral	Digestive (Liver)			□ albumin, α-, β-, γ-globulins, C-reactive serum protein; □ cholesterol, lipoproteins high (HDL) and low (LDL) density serum; □ AST, LDH$_3$ Γ-glutamiltransferza, alkaline phosphatase serum; □ malondialdehyde lipid hydroperoxides serum; □ total antioxidant activity superoxide dismutase, glutathione peroxidase in serum	XI. Diseases of digestion incl . K71 toxic liver with cholestasis; K72 hepatic failure; K73 Chronic hepatitis; K74 fibrosis ar liver; K75 Other inflammatory liver disease; K76 Other dise Liver

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
1,2-dichloroethane	Inhaled	CNS			□ cortisol, epinephrine serum;	VI. Diseases of the R45.0 asteno neurotic syndrome R53 malaise ar fatiguability G62.2 polyneu due to other toxic substances G62.9 Polyneu unspecified G93.8 neurotic syndrome G92 toxic encephalopathy G93.8 neurotic syndrome
Carbon tetrachloride	Oral	Digestive (Liver)			□ albumin, α-, β-, γ-globulins, C-reactive serum protein; □ cholesterol, lipoproteins high (HDL) and low (LDL) density Serum triglycerides blood; □ ALT, AST, LDH$_3$ Γ-glutamiltransferza, cytochrome P450, alkaline Phosphatase in Serum blood; □ malondialdehyde lipid hydroperoxides	XI. Diseases of digestion incl . K71 toxic liver with cholestasis; K72 hepatic failure; K73 Chronic hepatitis; K74 fibrosis ar liver; K75 Other inflammatory liver disease; K76 Other dise

					lipid hydroperoxides serum;	Liver

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
					□ total antioxidant activity superoxide dismutase, glutathione peroxidase in serum	
Carbon tetrachloride		Urinary system			□ lipid hydroperoxides in serum; □ creatinine, urea serum; □ total protein, albumin, α-, β-, γ-globulin serum blood □ renal epithelium in the urine; □ specific gravity, leukocytes, protein, erythrocytes in urine	XIV. Disease urogenital syst incl .: N03 chronic nephrotic syndrome; N05 nephritic syndrome unspecified; N28.9 kidney d ureter unspecified; N11.9 Chronic pyelonephritis
Inhaled carbon tetrachloride		CNS	6 mg / m3 (as atmospheric Air)		□ cortisol, epinephrine serum;	VI. Diseases of the System incl .: R45.0 asteno neurotic syndrome R53 malaise an fatiguability G62.2 polyneu due to other toxic substances G62.9 Polyneu unspecified G93.8 nevrozo ny syndrome G92 toxic encephalopathy G93.8 nevrozo ny syndrome

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
Chlorobenzene	Oral	Digestive (Liver)			□ albumin, α-, β-, γ-globulins, C-reactive serum protein; □ cholesterol, lipoproteins high (HDL) and low (LDL) density Serum triglycerides blood; □ AST, LDH$_3$ Γ-glutamiltransferza, cytochrome P450, alkaline Phosphatase in Serum blood; □ malondialdehyde lipid hydroperoxides serum; □ total antioxidant activity superoxide dismutase, glutathione peroxidase in	XI. Diseases of digestion incl .: K71 toxic liver with cholestasis; K72 hepatic failure; K73 Chronic hepatitis; K74 fibrosis an liver; K75 Other inflammatory liver disease; K76 Other dise Liver

					glutathione peroxidase in serum □ albumin, C-reactive serum protein; □ cholesterol, lipoproteins high (HDL) and low (LDL) density Serum triglycerides blood; □ ALT, AST, LDH, Γ-glutamiltransferza, cytochrome P450, alkaline Phosphatase in Serum blood; □ malondialdehyde Lipid hydroperoxide, alfafetoprotein in serum;	XI. Diseases of digestion incl .: K71 toxic liver with cholestasis; K72 hepatic failure; K73 Chronic hepatitis; K74 fibrosis an liver; K75 Other inflammatory liver disease; K76 Other dise Liver
Ethylbenzene	Oral	Liver				

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
					□ total antioxidant activity superoxide dismutase, glutathione peroxidase in serum	
		Urinary system			□ lipid hydroperoxides in serum; □ creatinine, urea serum; □ total protein, albumin, α-, β-, γ-globulin serum blood □ renal epithelium in the urine; □ specific gravity, leukocytes, protein, erythrocytes in urine	XIV. Disease urogenital syst incl .: N03 chronic nephrotic syndrome; N05 nephritic syndrome unspecified; N28.9 kidney d ureter unspecified; N11.9 Chronic pyelonephritis
Ethylbenzene	Inhaled	System blood hematopoiesis	30-60 mg /m3 Exposure 7 years		□ hemoglobin, erythrocytes, hematocrit, reticulocyte blood; □ the average content hemoglobin, mean corpuscular volume in blood; □ iron, total and partial iron binding ability of serum blood; □ ferritin, transferrin serum; □ Coproporphyrin, delta aminolevulinic acid urine	III. Diseases of the incl .: D50.8 Other iron deficiency anemia; D50.9 Other iron deficiency anemia, unspec D61.2 Aplastic anemia caused other external agents; D64.8 Other unspecified ane Anemia D64.9 unspecified

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
					□ total protein, glucose in serum; □ total cholesterol	IV. Disease Endocrine syst incl .: Protein-E46.0 energy

Ethylbenzene		Endocrine System			□ total cholesterol, lipoproteins HDL, LDL serum; □ TSH, T4 $_{svob}$ □ growth hormone in serum	energy failure; E67.8 excess w a body; E34.3 stunting; E34.4 tall;
Styrene	Oral	Liver		greater than 0.55 ** mg / l (Venous blood)	□ albumin, α-, β-, γ-globulins, C-reactive serum protein; □ cholesterol, lipoproteins high (HDL) and low (LDL) density Serum triglycerides blood; □ ALT, AST, LDH, Γ-glutamiltransferza,, alkaline phosphatase serum; □ malondialdehyde Lipid hydroperoxide, alfafetoprotein in serum; total antioxidant activity superoxide dismutase, glutathione peroxidase in serum	XI. Diseases of digestion incl . K71 toxic liver with cholestasis; K72 hepatic failure; K73 Chronic hepatitis; K74 fibrosis ar liver; K75 Other inflammatory liver disease; K76 Other dise Liver
	Inhaled	Respiratory, CNS	50-100 milhon l * Exposure 1-6 hours.			VII Diseases of adnexa incl .: H10 Conjuncti

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
			376 milhon l * Exposure 60 min			VI. Diseases of the Distance inc R45.0 asteno neurotic syndrome R53 malaise ar fatiguability G43 migraine
			600 milhon l * Exposure 60 min			VII Diseases of adnexa incl .: H10 Conjuncti X. Diseases of respiration, inc J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids; J38.9 disease o airway unspecified
Styrene			800 milhon l * Exposure 4 hours			VII Diseases of adnexa incl .: H10 Conjuncti X. Diseases of respiration, inc J31hronichesky nasopharyngiti pharyngitis; J35 Chronic disease of tonsi adenoids;

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
						J38.9 disease o airway unspecified
						VI. Diseases of the R53 malaise an fatiguability
						VI. Diseases of the R45.0 asteno neurotic syndrome
						R53 malaise an fatiguability
Styrene					□ cortisol, epinephrine serum; □ Serum TSH; □ potassium, sodium, serum blood potassium / sodium coefficient	G62.2 polyneu due to other toxic substances G62.9 Polyneu unspecified G93.8 neurotic syndrome G92 toxic encephalopathy G93.8 neurotic syndrome
		System blood hematopoiesis			□ hemoglobin, erythrocytes, reticulocytes in the blood; □ the average content hemoglobin, mean corpuscular volume in blood; □ iron, total and partial iron binding ability of serum blood;	III. Diseases of the incl .: D50.8 Other iron deficiency anemia; D50.9 Other iron deficiency anemia, unspec D61.2 Aplastic

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	Concentration In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
					□ ferritin, transferrin serum; □ Coproporphyrin, delta aminolevulinic acid urine	anemia caused other external agents; D64.8 Other unspecified ane Anemia D64.9 unspecified
Styrene	Inhaled	Respiratory			□ formaldehyde stimulated by cytokines IL-4,6,10 □ immunoglobulin E, G specific to formaldehyde serum blood	X. Diseases of respiration, inc J45.0 bronchial with a predomi allergic component
Acetaldehyde	Oral	Gastrointestinal tract			□ leykoformula blood □ pepsinogen I, II serum blood □ carcinoembryonic antigen in serum □ lipid hydroperoxides in serum;	XI. Diseases of digestion incl . K29.5 Chronic gastritis; K29.8 duodeni K29.9 gastrodu unspecified; K52.1toksiches gastroenteritis K52.9 noninfec gastroenteritis unspecified

						unspecified VI. Diseases of the
Benzene	Inhaled	CNS		Over 0.9 ** ug / l (Blood)	□ cortisol, epinephrine serum; □ Serum TSH; □ potassium, sodium, serum blood potassium / sodium coefficient	R45.0 asteno neurotic syndrome R53 malaise an fatiguability G62.2 polyneu due to other toxic

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
						substances G62.9 Polyneu unspecified G93.8 neurotic syndrome G92 toxic encephalopathy G93.8 neurotic syndrome
Benzene	Inhaled	System blood hematopoiesis			□ hemoglobin, erythrocytes, reticulocytes in the blood; □ the average content hemoglobin, mean corpuscular volume in blood; □ iron, total and partial iron binding ability of serum blood; □ ferritin, transferrin serum; □ Coproporphyrin, delta aminolevulinic acid urine	III. Disease of the incl .: D50.8 Other iron deficiency anemia; D50.9 Other iron deficiency anemia, unspec D61.2 Aplastic anemia caused other external agents; D64.8 Other unspecified ane Anemia D64.9 unspecified
Lead	Oral	CNS		50-100 ** (100 ml blood, ug)	□ cortisol, epinephrine serum; □ acetylcholine in serum blood; □ Serum TSH; □ potassium, sodium, serum blood potassium / sodium coefficient	VI. Diseases of the R45.0 asteno neurotic syndrome R53 malaise an fatiguability G62.2 polyneu

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Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
						due to other toxic substances G62.9 Polyneu unspecified G93.8 neurotic syndrome G92 toxic encephalopathy

	Oral		The air was 0.01 mg / m3			IV. Diseases of the endocrine syste incl .: E01 disease thyroid associated with failure, and similar conditio E02 subclinical hypothyroidism Iodine failure; E03 other form hypothyroidism E04.9 nontoxic goiter
Lead		Endocrine System		** 0.19 mmol / l (Blood) ** 0.19 mmol / L (urine)	□ TSH, T4, Antibodies to thyroid peroxidase, to serum thyroglobulin blood; □ iodine in urine	
		Liver			□ increase γ-glyutamiltranpeptidazy □ hemoglobin, erythrocytes, hematocrit, reticulocyte blood;	
	Inhaled				□ the average content hemoglobin, mean corpuscular volume in blood;	

Chemical factor 1	Path receipts 2	Critical organs and body systems 3	In habitat 4	Concentration In biosubstrates 5	Laboratory parameters - marker effect 6	Disease by IC 10 7
					□ iron, total and partial iron binding ability of serum blood;	III. Diseases of the blood and blood forming organs incl .: D50.8 Other iron deficiency anemia; D50.9 Other iron deficiency anemia, unspec D61.2 Aplastic anemia caused other external agents; D64.8 Other unspecified and Anemia D64.9 unspecified
				50-100 ** (100 ml blood, ug)	□ ferritin, transferrin serum; □ Coproporphyrin, delta aminolevulinic acid urine	
		System blood hematopoiesis			□ hemoglobin, erythrocytes, hematocrit, reticulocyte blood;	
Lead	Inhaled			40 ** (100 ml blood, g)	□ the average content hemoglobin, mean corpuscular volume in blood;	
				20 ** (100 ml blood, g)	□ increase protoporphyrin	
					□ Semen (violation spermatogenesis) □ Testosterone (decrease testosterone)	XIV Diseases urogenital syste incl: N41 Inflammat disease prostate T46 Men infertility
		Reproductive system				
				** 0.2-1.0 mg% (blood)	□ cortisol, epinephrine serum; □ acetylcholine in serum blood;	VI. Diseases of the R45.0 asteno neurotic syndrome
Mercury	Oral	CNS		** 0,013 mg% (Brain)	□ Serum TSH; □ potassium, sodium, serum blood potassium / sodium coefficient	R53 malaise an fatiguability G62.2 polyneu due to other toxic

Chemical factor	Path receipts	Critical organs and body systems	In habitat	Concentration In biosubstrates	Laboratory parameters - marker effect	Disease by IC 10
1	2	3	4	5	6	7
						substances G62.9 Polyneu unspecified G93.8 neurotic syndrome G92 toxic encephalopathy
						IV. Disease Endocrine syst incl .:
	Oral					E01 disease thyroid associated with failure, and similar conditi
					□ COP 17 in urine □ TSH, T4, Antibodies to thyroid peroxidase, to serum thyroglobulin blood; □ iodine in urine □ serum glucose	
		Endocrine System				E02 subclinica hypothyroidisn
Mercury						Iodine failure;
						E03 other form hypothyroidisn
						E04.9 nontoxic goiter
						XIV. Disease urogenital syst incl .:
					□ lipid hydroperoxides in serum; □ creatinine, urea serum; □ total protein, albumin, α-, β-, γ-globulin serum blood □ renal epithelium in the urine; □ specific gravity, leukocytes, protein, erythrocytes in urine	N03 chronic nephrotic syndrome;
		Urinary system		More ** 40-50 ug / l (Urine)		N05 nephritic syndrome unspecified; N28.9 kidney ureter unspecified; N11.9 Chronic pyelonephritis

Note: * - the child population
** - Adults

MU 2.1.10.3165 -14

UDC _____

Keywords: injury, habitat, the evidence presented

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