Ann. Ist. Super. Sanità, vol. 30, n. 4 (1994), pp. 445-455

Features of the Italian National Inventory of Chemical Substances

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Summary. - The Italian National Inventory of Chemical Substances (Inventario nazionale delle sostanze chimiche, INSC), a factual data bank on chemical toxicology produced by the Istituto Superiore di Sanità (ISS), consists of a computerized system on existing chemicals developed for routinary and emergency needs. Historical background, current status and future direction of INSC are discussed. The structure and the feature of INSC are briefly examined. Aspects of retrieval of information and the criteria for the inclusion of data and priority selection are also considered.

Key words: factual data bank, toxicology information, chemical risk data bank, existing chemical.

Riassunto *(Caratteristiche dell'Inventario nazionale delle sostanze chimiche).* - Viene presentato l'Inventario nazionale delle sostanze chimiche (INSC), la banca dati fattuale sulle sostanze chimiche esistenti, prodotta dall'Istituto Superiore di Sanità. L'INSC è stato sviluppato sia per emergenze che per ogni situazione che coinvolga sostanze chimiche. Vengono brevemente illustrate la struttura e le caratteristiche dell'INSC e presentati i criteri per la scelta dei dati da inserire e per la selezione delle priorità. Vengono inoltre esaminate le fonti di informazione utilizzate.

Parole chiave: banca dati fattuale, informazione tossicologica, banca dati sul rischio chimico, sostanze esistenti.

Introduction
The context in which the Italian National Inventory of Chemical Substances operates

As it is well known, the number of chemicals presently on the market as well as in the environment is very high. Moreover, this number is continuously increasing. This situation creates growing need for assessing the risk posed by the already existing as well as new chemicals, with the aim of eliminating or reducing their adverse effects on the human health and the environment. This assessment implies the knowledge of the intrinsic properties, of the risk factors and of exposure of human beings and ecosystems to their effects.

For this purpose it is necessary to know at least the intrinsic properties of chemicals, their environmental behaviour and fate and their potential to react with targets.

Recently, the Commission of the European Union (EU) issued a directive on risk assessment [1]. The risk assessment procedure, adopted in this framework, comprises four steps:

- hazard identification;
- dose (concentration)/response (effect) assessment;
- exposure assessment;
- risk characterization.

The purpose of this paper is to focus the attention on the first stage of the above mentioned risk assessment process with particular reference to the Italian approach in this field.

"Hazard identification", according to EU principles, is "the identification of the adverse effects which a substance has an inherent capacity to cause toward human health and environment" [1]. The EU definition focuses attention on fundamental aspects, namely the availability of relevant data regarding health effects and environmental impact of chemical substances.

Some 10 million substances are contained in the Chemical Abstracts Registry File.

Around 100,000 entries are listed and defined by the European Inventory of Existing Commercial Chemical Substances (EINECS) [2]. EINECS is a large inventory, compiled by the European Commission in application of article 13 of directive 79/831/EEC [3]. The inventory contains the generally called "existing" chemicals (all chemical substances which were on the European Community market before 18 September 1981).

"New" chemicals are all substances placed on the European market for the first time after 18 September 1981, which is the date of entering into force of the EEC notification procedure. According to the above mentioned

directive 79/831/EEC, now updated with the directive 92/32/EEC, any new chemical, not included in EINECS, must be subjected to premarketing notification in order to evaluate potential, immediate and long-term adverse effects of chemicals on humans and the environment prior to the introduction on the market [4]. Table 1 gives an example of information required in the premarketing notification dossier. Since the adoption of directive 79/831/EEC 1,112 new chemicals have been put on the European market [5].

EINECS inventory represents a legal tool for distinguishing "existing" from "new" chemicals [6]. For these latter complete data are available due to the notification procedure. The same is not always true for "existing" chemicals.

With respect to "existing" chemicals they are exempted from the new substances notification procedure, but, since 1967 [7], the European Community has been developing a body of legislation to enable the identification and control of risks presented by commercial chemicals. According to directive 67/548/EEC, the "existing chemicals" have to be evaluated and classified with regard to their intrinsic physical-chemical, toxicological and ecotoxicological properties. The directive 79/831/EEC, with the introduction of EINECS inventory and notification procedure, has initiated a new approach in this field. In this same context, the already operating system of classification and labelling of existing chemicals was extended and amended for a better control of chemicals on the European market. At the moment, around 1,400 "existing chemicals" have been evaluated and classified by an EEC working group of experts as dangerous chemicals [8]. Nevertheless, as stated above, "existing chemicals" are more than 100,000 so that it is necessary to fill the gap of information on all other "existing chemicals" for which the quantity and quality of available data may pose problems (e.g. data missing for relevant end points or produced through non-standard procedures). On the other hand, data derived from environmental monitoring and epidemiological studies, as well as from occupational surveillance may be available for the "existing chemicals", which are as yet unknown for new chemicals, and may result very useful for risk assessment purposes. Moreover, substances which are in EINECS are subjected to Council regulation 793/93 on the evaluation and control of the risks of existing chemicals substances [9].

At the Italian national level, there is an increasing need of information and evaluation concerning chemical hazards and chemical risks according to the specific necessities of the central, regional and local public institutions which have to deal with the management of human health and environmental risks. Extended and detailed information in this field is required for the environmental impact assessment of human activities, for the assessment, prevention and control of major industrial risk, as support for standard setting, for the characterization of risks during the transport of chemicals, for research, for the design, organization and interpretation of environmental monitoring surveys, for the design of experiments and tests, for the response to chemical emergencies and, in general, for all activities concerning chemical risk. This information has to be rapidly and efficiently provided, in a form easily comprehensible also to non-expert people and immediately usable. The Istituto Superiore di Sanità (ISS) receives each year hundreds of requests of providing data on chemical risk. This situation, together with the needs posed by the EU directives discussed above and by the indications and recommendations of other international bodies, such as the World Health Organization (WHO), has fostered a national data bank on chemical risk, called "National Inventory of Chemical Substances" (Inventario nazionale delle sostanze chimiche, INSC), operating for public institutions and public health services.

Table 1. - Base set information required for the notification dossier of a new chemical substance (according to 7th amendment of directive 67/548/EEC) [4] *(*)*

Physical-chemical properties

- melting point
- boiling point
- vapour pressure
- relative density
- surface tension
- water solubility
- particle size
- partition coefficient (octanol-water)
- flash point (liquids)
- flammability (solids or gases)
- explosivity
- oxidizing properties
- self-ignition temperature

Toxicological properties

- LD_{50}/LC_{50} oral/dermal/inhalation
- skin irritation
- eye irritation
- skin sensitization
- sub-acute 28 day repeated dose
- mutagenicity testing (e.g. Ames)
- screening test for toxicity related to reproduction

Ecotoxicological properties

- fish 96 h EC_{50}
- daphnia 48 h EC_{50}
- algae 72 h IC_{50}
- ready biodegradation
- bacterial inhibition
- adsorption/desorption

(*) When the volume of chemicals reaches or exceeds 10 tons/year, 100 tons/year or 1000 tons/year, different levels of more complete data are requested by authorities.

Historical background of the INSC

One of the events which at national level indicated the need for a reliable information support for the assessment and management of chemical risks was represented by the Seveso accident, which, as well known, has stimulated the promulgation of the Seveso directive [10]. Immediately after this accident, which took place on July 1976 and resulted in the release of the 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and in a severe impact of a large inhabited territory, the necessity for an appropriate system of contingency planning was recognized, together with the availability of the whole set of data useful to identify, control and prevent chemical accidents and, whenever necessary, to organize the response to emergencies they may induce [11]. In fact, one of the major problems in the management of the Seveso accident consequences, was the lack of adequate and detailed information on the health risks of TCDD and of its environmental behaviour and fate.

In the framework of a structural revision of the National Health Service this event, together with the indications deriving from directive 79/831/EEC concerning the "new chemicals", stimulated the Italian Ministry of Health to insert in the law no. 833 of 23 December 1978 the art. 9, which appoints the ISS as the institution responsible for organizing and regularly updating the INSC [12].

The INSC is today a consolidated reality; it operates in the Laboratory of Applied Toxicology of the ISS, with the task of collecting, selecting and organizing the information relevant to chemical hazard identification and risk assessment. Table 2 gives a schematic presentation of its features.

A typical characteristic of the INSC is its strict interaction and connection with local bodies of the National Health Service. Fig. 1 shows the input/output structure of the INSC.

Table 2. - Schematic presentation of features of INSC

Type	Factual, non-bibliographic data bank
Subject coverage	Physical-chemical properties: all areas of toxicology and ecotoxicology; safety; environmental fate; occupational health; standards/regulations; data on single chemical substances or families available on the European market with particular reference to "national problems" (high volume; high-toxic chemicals). Environmental pollutants, food, additives, solvents, paints, pesticides, chemical intermediates...
Producer	Istituto Superiore di Sanità, Laboratory of Applied Toxicology
Time span	1982 to date
Content	Over 2800 complete data sheets contained in 14 data fields. Available also 2000 "basic dossiers" with raw data
Sources	Primary journals; monographs; government documents; technical reports; handbooks; documents, opinions risk assessment elaborated by national and international bodies
Data access	CAS number; EU number; EINECS number; ISS number; chemical synonyms, trade names
Updating	Periodically, case by case
Comments	Complete bibliographic references for all data Data control/peer reviewed by ISS experts specialized in different disciplines Positive and negative test results are included in the INSC Flexible structure, "not rigid system"

The structure of the INSC data bank

The INSC is a factual data bank, of easy consultation, with information organized in the form of monographs, written and structured as book chapters and made of standard sections and subsections, each of them independently addressable. This format makes the INSC information easily readable and comparable to the one presented in the usual scientific literature [13].

At the present time, fourteen categories of data and more than 200 subcategories are available covering the following broad subject areas briefly described below.

Substance identity

The first step of the information gathering process is the identification of the chemical. In fact, the same chemical may have many synonyms, thus complicating the search. The Chemical Abstract Service number (CAS number) provides the most reliable key for the chemical substance identification. The INSC structure allows the concerned substance to be rapidly and exactly retrieved on the basis of the following identifiers: reference name, CAS registry number, EINECS number, EU number, IUPAC, ISO or CAS names, chemical synonyms, trade names, chemical formula, chemical structure and chemical family. Moreover, an exclusive identification number (ISS number) is assigned by INSC to identify a single chemical substance [14]. These elements allow for the entering into the INSC data bank.

A subsection provides references to isomers, similar chemicals, relevant derivatives and information on impurities and contamination occurrence.

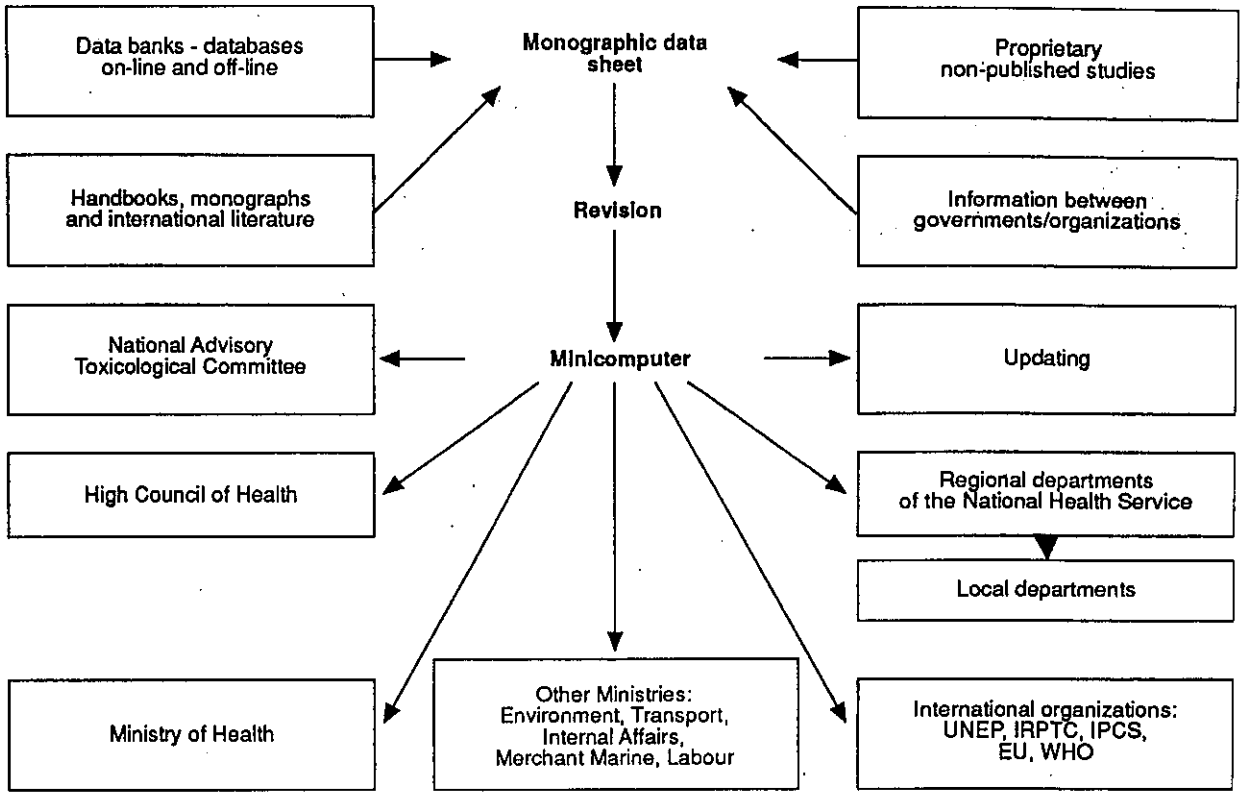

Fig. 1. - Input/output structure of the national inventory.

Another subsection contains general information on analytical methods for the identification and determination of chemical compounds and their metabolites. Furthermore, biological monitoring methods for exposure in the working area as well as in the general environment are considered in this subsection.

Use pattern, production and treatment data

Data on the major uses of the substances (e.g. as a solvent, pesticide, chemical intermediate or antropogenic contaminant) and international level production data (when available) are given.

A subsection provides information on safe handling and personal protection, hazardous reactions, incompatibility, possible violent interaction with other compounds, fire hazard, hazard prevention, engineering controls dealing with accidents and spillages, safe storage, transportation and, generally, all information or data on the hazard involved in laboratories, industrial workplaces and in the general environment during handling of chemicals.

Physical-chemical properties

Physical-chemical properties play a pivotal role from a toxicological and ecotoxicological point of view. Simple physical properties are helpful for predicting routes of potential exposure (water solubility, vapour pressure), accumulation in biota (fat solubility, octanol-water partition coefficient) and potential environmental fate. Data for physical-chemical properties vary sometimes considerably. Often, for each physical-chemical parameter more than one value is quoted as reported in the literature, when different values are given. Where available, standardized validated data are given.

This section contains also information on the main hazard characteristics (e.g. flash point, autoignition temperature) and explosion hazards.

Toxicological data on mammals

Mammal toxicity data (acute-single exposure, subacute-repeated doses up to 28 days, subchronic-repeated doses up to 90 days and chronic/long-term studies, generally up to 2 years, for rats and mice) are presented. Acute toxicity data will provide information on critical organ(s), dose-effect relationship and dose-response relationship expressed by effective dose (ED) or lethal dose (LD). Skin and eye irritation and corrosiveness data, as well as sensitization test data are also provided where available both for positive or negative results. Carcinogenic, mutagenic and reproductive toxicity data as well as metabolic and toxicokinetic studies are also included. Studies are extensively described and test conditions, animal species/strain, exposing/dosing data and substance purity are detailed.

Ecotoxicological data

This section mainly includes information on the effects of substances as primarily referred to aquatic species, even if also terrestrial species can be considered. The following major organisms are taken into account as indicators of environmental quality: bacteria, algae, protozoans, amphibians, molluscs, crustaceans, fishes, earthworms, insects, birds and plants. Data are classified on the basis of the duration of exposure as acute, subchronic and chronic. The quality of the information may vary, because for existing chemicals a large part of data are relatively old and produced not complying with the principles of good laboratory practice (GLP) and current guidelines. However, where available, the species name in Latin is indicated, together with lifestage, environmental media and test duration. Usually results are expressed as no-observed effect concentration (NOEC), median effect concentration (EC_{50}) or lowest observed effect concentration (LOEC). Particular emphasis is laid on bioaccumulation, biomagnification and bioconcentration data.

Environmental studies

Environmental fate. - Fate depends on physical and chemical properties of the chemical, environmental parameters and emission patterns [15]. In this subsection environmental fate is described on the basis of chemical reactivity, transport processes (such as dispersion, volatilization/evaporation, soil adsorption/desorption, deposition) and transformation processes (such as hydrolysis, photolysis in water and in atmosphere and biotic and abiotic transformation processes).

Contamination studies. - This section considers the four environmental compartments potentially at risk: trophic chain, soil, water, atmosphere. The type of information generally available in this section may include: laboratory-measured data according to established protocols, data on measured levels in various environmental compartments from monitoring programmes and field observations. For those chemicals for which limited amount of experimental data concerning environmental fate and transportation are available, predicted fate and exposure through model calculations or other computational procedures are provided [16,17]. They do not exactly represent the real environment, but may give reliable indications and help to quantify the expected concentrations and to interpret experimental data.

Studies on humans

This section contains data on human health effects. Occupational and non-occupational exposure, immediate effects and effects induced by prolonged/repeated esposure, kinetics and metabolism are reported here. When human data from epidemiological or clinical studies are available, they are also included as well as controlled human exposure studies in volunteers.

Emergency and/or inactivation measures

The management of accidental, occupational or environmental poisonings require the availability of appropriate information concerning methods for preventing and limiting dispersions, spillage disposal, fire extinguishing agents and personal protection to conduct the operation safely. This section includes all this kind of information, with data on medical management of victims and guidelines for treatment and adequate antidotal drugs, standard treatments (e.g. splashes on skin and eyes, burns, inhalation or ingestion accidents) and special treatments.

Complementary data for particular applications and uses

More detailed information about the detailed uses (principal and special uses) of the substances are given in this section (e.g. in the case of pesticides, technical information such as principal formulations, type of activity, mode of action, target species and quantity of application are provided).

Threshold values

Data on threshold values refer to occupational exposure limits and are obtained primarily from:

- German maximum workplace concentrations (German acronym, MAK values);
- Other European recommended limits;
- US American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit values (TLVs);
- US Occupational Safety and Health Administration (OSHA) permissible exposure levels (PELs);
- US National Institute for Occupational Safety and Health (NIOSH) recommended exposure levels (RELs).

Where available, specific laws, regulatory standards, proposals and directives banning or limiting the use of specific substances, issued by the Commission of the European Union or from specific national regulatory decisions are reported.

In addition, tolerance to pesticide residues established by the Food and Drug Administration, risk assessments carried out by the Joint FAO/WHO Meeting on Pesticide Residues and Joint FAO/WHO Expert Committeee on Food Additives and environmental quality guidelines in different media (e.g. air or drinking water) established by WHO or EPA, are reported here.

A special sub-section is dedicated to Italian limits, recommendations or prohibitions issued in different fields. These measures generally represent the implementation of EU directives or international recommendations, but may also be promulgated indipendently by the Italian government (e.g. benzene, asbestos, aromatic amines, vinyl chloride monomer, ethylene oxide or specific pesticides).

Danger classifications

This section contains mainly classifications and labellings generated by the EU according to directive 67/548/EEC.

Available assessments

Regulatory agencies and international organizations in different countries issue evaluations for different purposes. Evaluations from US National Toxicology Program (NTP), US Environmental Protection Agency (EPA), Italian National Advisory Toxicological Committee (Commissione consultiva tossicologica nazionale, CCTN) and International Agency for Research on Cancer (IARC) are presented here. Sometimes final decisions or statements may be divergent. In fact, due to differences in the scope of the different agencies or in the quality and/or quantity of investigated data, some agencies take into account only published data, other also confidential data.

Additional quantitative risk assessments both for carcinogenic and non-carcinogenic risk are summarized, as reported by Food and Drug Administration standards, US EPA reference dose (RfD), US EPA unit risk (UR).

Bibliographic references

For every piece of information reported in the INSC the original bibliographic reference is quoted in the text and the full description of the source is reported. Generally, two kinds of references are given:

base references, i.e. all those sources which are sistematically consulted (handbooks, data banks, databases, etc.);

specific references, i.e. those references which are normally quoted only once, specifically for a single chemical (monographs, articles from scientific journals, etc.).

Updating

All updating data are recorded in chronological order and for each updating process the date and the field(s) updated are reported. The names of persons responsible for the updated data are reported in the same section for each updating.

Sources of information

There is today a significant growth of data sources in the fields of toxicology, environmental sciences, public health, agriculture and industry, industrial major risks and many other topics relevant to the risk assessment of chemicals.

The information to be introduced in the INSC is obtained from both manual (Tables 3a and 3b) and computerized sources (Tables 4 and 5). A list of the different types of information sources, both manual and on-line, used by INSC, is reported in Table 6. Almost all information is presented as reported in the original sources and the bibliographic reference is fully quoted. In some cases summarized data are derived from confidential sources, journal articles or grey literature (unpublished reports). In any case, the users may obtain the original source directly addressing the INSC staff.

Manual sources

The manual sources consist in relevant books, handbooks, safety data sheets, reports, reviews, monographs, directories, data lists and, in general, scientific literature in the specific field under examination. The INSC structure includes a selected library, containing more than 300 books and about the same number of papers and documents. Past experience has indicated that the immediate availability at local level of a selected set of manual sources is essential, in particular in the case of emergencies, when information has to be collected in a very short time and the access to the central library may be difficult (e.g. overnight or during weekends). Table 3a shows some of the manual information sources mostly consulted in INSC activities.

Table 3a. - Examples of selected books on toxicology and chemical safety usually consulted by INSC

VERSCHUEREN, K. 1983. *Handbook on environmental data on organic chemicals.* 2nd ed. Van Nostrand Reinhold Co., New York (NY). (1400 chemicals).

Patty's industrial hygiene and toxicology. 4th ed.1991. Clayton & Clayton (Eds). 1991. John Wiley & Sons, New York (NY).

THE MERCK INDEX. Encyclopedia of chemicals and drugs. 11th ed. 1989. Merck and Co., Inc., Rahway (NJ).

The Pesticide manual. A world compendium. 9th ed. 1991. C.R. Worthing & S.D. Walker (Eds). 1991. The British Crop Protection Council.

SAX, N.I. & LEWIS, R.J. Sr. 1989. *Dangerous properties of industrial materials.* 7th ed.Van Nostrand Reinhold Co., New York (NY). (20,000 chemicals).

Table 3b. - Examples of selected monographs on toxicology and chemical safety usually consulted by the INSC

WORLD HEALTH ORGANIZATION. *Environmental health criteria (EHC) series.* WHO, Geneva. (1976 onward). To date 161 EHC documents have been published, including monographs on methodological aspects.

WORLD HEALTH ORGANIZATION. *Health and safety guide (HSG) series.* WHO, Geneva. (1986 onward). To date 88 HSG documents have been published.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER. *IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans.* IARC, Lyon, France. (1972 onward). To date 57 IARC monographs have been published.

US NATIONAL TOXICOLOGY PROGRAMME. *National toxicology programme technical report series on toxicology and carcinogenesis studies.* Department of Health and Human Service Public Health Service, National Institute of Health. (1976 onward). To date 434 NTP technical reports have been published.

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES. *JECFA food additives series, multivolume series.* WHO, Geneva. (1972 onward).

EUROPEAN CHEMICALS INDUSTRY ECOLOGY AND TOXICOLOGY CENTER. *Technical reports.* ECETOC, Brussels. (1982 onward). (To date 60 ECETOC technical reports have been published).

EUROPEAN CHEMICALS INDUSTRY ECOLOGY AND TOXICOLOGY CENTER. *Joint assessment of commodity chemicals.* ECETOC, Brussels. (1982 onward). To date 25 ECETOC JACC reports have been published.

BERATERGREMIUM UMWELTRELEVANTE ALTSTOFFE. *Report series produced by GDCh-advisory committee on existing chemicals of environmental relevance (BUA) of the German chemical society*. (1986 onward). To date 126 BUA chemical reports have been published.

COMMISSIONE CONSULTIVA TOSSICOLOGICA NAZIONALE. *Report series produced by the Italian national advisory toxicological committee (CCTN-Committee)* established at the Study Center of the Italian Ministry of Health. (1977 onward).

Of particular interest for INSC activity are various publications produced by international organizations, which have a major role in toxicology, environmental toxicology, ecotoxicology, health protection and chemical safety. Typical examples are the data profiles of the International Programme on Chemical Safety (IPCS) (in which UNEP, WHO and ILO also participate), and of the International Register of Potentially Toxic Chemicals (IRPTC) (managed by UNEP), monographs prepared by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the monographs produced by IARC, which provide a detailed, complete and internationally validated set of information and evaluations on a large number of chemical carcinogens.

Moreover, also the documents published by the European Chemicals Industry Ecology and Toxicology Center (ECETOC), Brussels, include detailed and useful information on the risk of chemical substances and its evaluation.

Computerized sources

The two main types of computerized sources are data banks and databases.

Data banks contain preselected factual information in the form of summary. Examples of relevant data banks routinely used by INSC are listed in Table 4. They are mainly part of the US National Library of Medicine (NLM) System Toxicology Data Network (Toxnet). The Documentation Service of ISS is the Italian national reference point for the NLM system.

If the required information cannot be found in the consulted data banks or if it is inadequate, the subsequent step is the examination of bibliographic databases.

Databases provide direct access to the literature without any preselection. Examples of databases used by INSC are listed in Table 5.

In the above mentioned list of data sources also the so-called "grey literature" has to be included, which means unpublished technical data in the form of reports or provisional documents concerning effects on health and the environment of certain chemicals. This kind of data are not published in the open literature and are made available to INSC by industry or by international or national committees in the form of provisional or confidential reports.

Priority selection

At the beginning of the 1980s a working group was established at the ISS in order to set priorities for a systematic selection of chemicals for inclusion in INSC. Chemicals were selected on the basis of the following criteria:

- chemicals suspected to pose significant risks to man, either as consumer or as worker, or to the environment;
- lists of chemicals and classes of chemicals already requiring attention at the EU level (e.g. directive 76/464/EEC concerning the pollution caused by substances discharged into the aquatic environment of the EU [18]);
- international concern for health or environment effects to several countries for different reasons;
- existing international and national priority lists developed for different purposes in other countries (e.g. German list of existing chemicals of environmental

Table 4. - Examples of relevant data banks in toxicology

Data bank	Producer	Contents
RTECS Registry of Toxic Effects of Chemical Substances	US National Institute of Occupational Safety and Health	Toxicity data on over 130,000 chemicals
HSDB Hazardous Substances Data Bank	US National Library of Medicine	Toxicity, environmental fate, exposure, chemical safety, emergency on over 4000 chemicals
GEN-TOX Genetic Toxicology	US Environmental Protection Agency	Genetic toxicology (mutagenicity) data on over 4000 chemicals
CCRIS Chemical Carcinogenesis Research Information System	National Cancer Institute	Short- and long-term bioassays on 2000 chemicals
ECDIN Environmental Chemicals Data Information Network	European Commission, Joint Research Centre	Ecology/ecotoxicology/toxicology Occupational health Standards/regulations on 104,000 chemicals
IRIS Integrated Risk Information System	US Environmental Protection Agency	Carcinogenic and non-carcinogenic health risk on 400 chemicals
MHIDAS Major Hazard Incident Data Service	UK-Health and Safety Executive	Accidents involving hazardous material
BEILSTEIN On-line	Beilstein Institut für Literatur der Organischen Chemie, Berlin	Physical data on 3.5 million organic compounds

Table 5. - Examples of relevant bibliographic databases used by INSC

Toxline Toxicology Information on-line	Pharmacological, biochemical, physiological and toxicological effects of drugs and chemicals. Producer: NLM
Medline Medlars on-line	Biomedical problems Producer: NLM
Cancerlit Cancer literature	Literature covering all aspects of cancer (1963 onward) Producer: International Cancer Research Data Bank (ICRDB) of NCI
CAS-on-line Chemical Abstract Service on-line	All substances indexed by Chemical Abstract Service since 1965 Producer: American Chemical Society
DART Developmental and reproductive toxicology	Teratology and other aspects of developmental and reproductive toxicology Producer: EPA and US National Institute of Environmental Health Sciences

relevance (BUA-list)) or US priority lists of hazardous substances (e.g. superfund priority lists developed by EPA and other federal agencies [19, 20]);

- chemicals for which IARC evaluations indicate positive or suspected carcinogenicity evidence to humans and/or animals;

- chemicals for which NTP carcinogenicity bioassays provide positive, suspect or equivocal evidence of carcinogenic activity;

- concern in workplace environment or in general environment;

- specific requirements concerning chemical emergencies coming from regional departments;

- classes of chemicals considered to be of priority because of widespread exposure and/or evidence of carcinogenicity (e.g. polyciclic aromatic hydrocarbons, PAH, or nitro-PAH);

- EU legislation and/or programmes already carried out as regards dangerous substances (e.g. national implementations of EU directives, such as the directive on carcinogenic agents in workplace).

This selection procedure resulted in a first priority list of 140 entries regarding individual chemicals or families of substances. This list was left open and continuosly updated, even if over the last few years requests of assistance from the regional bodies of the National Health Service have reached such a high number that most resources are devoted to satisfy these daily requests.

Update of INSC

On-line data banks and databases are generally updated on a regular basis.

INSC is usually updated periodically on a case-by-case basis according to the specific requests made by the users.

In addition, for more than 300 substances specific sections (such as EU classification, EPA, IARC, NTP evaluations and TLV values) are updated sistematically, at least yearly.

Quality control of data is performed in different ways, usually by having a systematic verification of the data introduced by the documentarist who was charged with the task of preparing a monographic data sheet by another INSC staff member. After these corrections are made, further reviews are performed by a different person when the monographic data sheet has been completely entered into the INSC computerized system. In addition, for specific requirements and for specific fields (e.g. epidemiological studies, reproductive toxicity studies, analytical methods) ISS scientists specialized in various areas give their contribution in reviewing the different parts of a monograph.

Table 6. - Sources of information

Handbooks and textbooks
Monographs from international agencies (IARC, IRPTC, IPCS)
Monographs from national bodies (CCTN-Committee)
Monographs from industrial organizations (ECETOC)
Primary journal literature
Articles published on scientific reviews
Proceedings
Proprietary unpublished reports
Information exchanged between governments/ organizations
Data banks on-line
Bibliographic databases on-line

Number of chemicals included in INSC

The INSC data bank became operative on January 1981.

At the present time (September 1994) INSC contains information on more than 2800 chemicals and for ca. 2000 more substances raw data are available, consisting of bibliographic references, specific articles collected in the open and grey literature, etc. This dossier is kept easily available and updated in view of the preparation of a computerized data sheet. Often this material proves to be very useful in the case of emergencies, when time is no sufficient for the elaboration even of a short monograph.

Each monographic data sheet in INSC contains at least the CAS number, ISS number, EU index number and EINECS number, if available; molecular formula, structure and synonyms; physical and chemical properties; EU classification and labelling; IARC, EPA, CCTN Committee, NTP evaluations; workplace recommendations and international and national standards.

Chemicals can be retrieved through their chemical names and synonyms, CAS number, EINECS number, EU number and ISS number.

Typology of chemicals included in INSC

According to the original project elaborated by the working group charged to assess the feasibility of a national inventory, the objective was to provide ready-to-use relevant information in each situation where chemical substances are involved.

The substances covered by the INSC are individual chemicals and comprise solvents, chemical intermediates, environmental pollutants, pesticides and generally all those substances which might pose serious and significant adverse problems to man and the environment.

The following substance categories are generally excluded from the scope of the INSC:

- active ingredients used in medicinal products for human use;
- active ingredients used in medicinal products for veterinary use;
- cosmetic products.

Also occupational processes are generally excluded. Nevertheless, sometimes, on the basis of specific requirements, *ad hoc* monographic data sheets are prepared to cover even these needs.

Users of the INSC

The INSC is not a commercially available data bank; it is restrained to the national authorities responsible for the management of legislations on chemicals control (Table 7).

As already said, originally the objective of INSC was to systematically store information on substances relevant from a toxicological and ecotoxicological point of view.

As the structure of the inventory grew up, it became more and more evident that the peculiarity of INSC was the possibility of direct interaction with the users, in order to modulate the quality and quantity of the information collected as a function of the actual needs of the peripheral bodies of the National Health Service.

At present, INSC is an interactive structure totally open to users. Once a problem arises, specific or generic information is gathered depending upon the request.

Current status and future direction

At the moment, the INSC data bank is involved in "ordinary" as well as in "emergency" situations. Recently, efforts have been made to introduce new kinds of information, with particular reference to national and international legislations, regulations and standards.

All data are stored in a minicomputer using a database specifically designed by a software supplier. This software was firstly written in COBOL and recently translated into Microfocus in order to be run in Unix environment.

It is now possible to access INSC on-line via a modem system through a dedicated telephone line; provisional access has been allowed to the Ministries of Health and of Environment. In the near future a national network will be created in order to be connected with all regional authorities, so that information will be available in real time, even overnight in case of emergencies.

By 4 June 1994, the EU regulation no. 793/93 on risk assessment of existing chemicals was adopted for a systematic evaluation of high production volume chemicals (HPVCs) [9].

Table 7. - Users of INSC

Regional departments of the National Health Service → Local departments
High Council of Health (Consiglio Superiore di Sanità)
Italian National Advisory Toxicological Committee (Commissione consultiva tossicologica nazionale)
Ministry of Health and other ministries: Environment, Transport, Internal Affairs, Merchant Marine, Labour
International organizations: EU, OECD, UNEP, IPCS
ISS researchers

Such regulation foresees the definition of a European data bank on HPVCs on the basis of the data provided by the concerned industry. Apart from process of risk assessment for priority chemicals foreseen by the regulation, it is anyway very important that this data bank (International uniform chemical information database, Iuclid) be made available to all member states. As far as Italy is concerned, ISS will surely play a very important role in managing this tool. It is evident that the Iuclid databank will become in the future a relevant base for any control activities in the field of chemical substances, and that INSC, which started as a national programme, will become part of an international action in chemicals control.

Submitted on invitation.
Accepted on 12 October 1994.

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