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Review

Toxicological information on chemicals published in the Russian language: Contribution to REACH and 3Rs

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ABSTRACT

This review is reporting on the current situation of publicly available toxicological and ecotoxicological information on chemicals published in Russian language in various libraries, databases as well as in the Internet. This information can be beneficial for the new EU chemical policy REACH and for the development of intelligent testing strategies (involving also QSAR and QAAR) that enable a significant increase in the use of non-testing information for regulatory decision making, thus minimizing the need for animal testing according to the 3R's strategy. Currently, the access to this information is limited due to the language barrier and low level of digitalization of respective journals and books. Fortunately, on-line translation services are overcoming language barriers already now.

Contents

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1. Introduction

When the USSR launched the world's first satellite in 1957, the US government searched for explanations. One reason was that Russian scientists were using Western scientific literature whereas Western scientists were unable to handle the Russian language, leading to a very low citation frequency and citation impact of most Soviet published materials compared to analogous Western journals (Garfield, 1972).

Russia is the largest country in the world, covering more than 17 million square kilometers and is home to 142 million people. Russia had worldwide power and influence starting from the time of the Russian Empire under Peter the First, through the period of the Soviet Union and currently as the Russian Federation. Russians have a long tradition of excellence in most aspects of the arts and sciences. Some Russian universities are world-famous, such as the State Universities of Moscow, St. Petersburg and Novosibirsk. In the field of the natural sciences, Russia is recognized from the contributions of famous scientists, including Mikhail Lomonosov (1711–1765), who made an important contribution not only to literature and education, but also to science, particularly to chemistry and physics. G. S. Kirchhoff (1764–1833) discovered, in 1812, the conversion of starch into glucose by acidic hydrolysis. Dmitri Mendeleev (1834–1907) was the creator of the periodic table of elements. Nikolay Zelinsky (1861–1953) was one of the founders of the theory on organic catalysis. In 1904 Ivan Pavlov (1849–1936) received the Nobel Prize in Physiology and Medicine for his pioneering studies on the physiology of digestion and conditioned reflexes. Sergei Winogradsky (1856–1953) pioneered the cycle of life concept and discovered the biological process of nitrification, the first known form of chemoautotrophy. More recently, Mikhail Mashkovsky (1908–2002) was a famous pharmacologist and worked as an expert for the World Health Organization (WHO) on quality control of drugs. In addition, scientists from Russia and the former Soviet Union have devoted numerous studies to the toxicology of different compounds.

During the years of the Cold War Soviet scientists were also involved in research related to properties of chemical and biological warfare (see below). In the area of civil research, Soviet toxicologists were active in creating various hygienic and occupational standards for (chemical) industries.

Numerous available Internet resources provide guidance and other information on *in vitro* and other alternatives to animal testing (Hakkinen and Green, 2002; De Marcellus, 2003; Aggrawal, 2005). Despite that, valuable toxicological data published in the Russian language have remained non-cited in recent scientific papers (Hakkinen and Green, 2002; Schwela and Hakkinen, 2004; Poppenga and Spoo, 2002; Junghans et al., 2004; Young, 2002; Russom, 2002; Winter, 2002; Wolfgang and Johnson, 2002; Felsot, 2002; Gilardi and Fubini, 2005) except when these were the only information sources available concerning a particular compound (Polifka and Faustman, 2002). Within the frame of the EC FP6 Integrated Project OSIRIS, the Estonian partner (research group of Dr. A. Kahru) proposed to collect those materials due to their knowledge of the Russian language and their access to the corresponding literature archived in Estonian libraries during the last century. Multilanguage training of Estonians was common even during the Soviet time: schools and universities taught in Estonian but Russian was learned for 11 years and English, German or French for 6 years in school by every child.

Therefore, the aim of this paper is to upgrade the information concerning the sources of toxicological literature published in the Russian language and to contribute to filling the gap, focusing on mapping of the main publicly available sources of toxicological information. Although a number of other republics of the former USSR, such as Ukraine, Belarus or Lithuania are also active in toxicology (see Supplementary material), this review focus only on Russian and Estonian resources. It concerns mainly web-sourced, peer-reviewed articles and books (the URLs are listed as additional material in Table S1). This review contributes to the 3R strategy (reduction, replacement and refinement), a worldwide acknowledged and EU-level prioritized strategy for the reduction of the use of laboratory animals in scientific studies.

2. Toxicological research in Russia and chemical weapons

A brief but important overview of the history of toxicology as well as on current research activities and education in toxicology in Russia (including a list of national bodies and research institutes, laws, regulatory documents and databases in toxicology) has been published in the Elsevier journal "Toxicology" by Kurlyandskiy and Sidorov (2003). However, according to ScienceDirect as well as to the ISI Web of Science, this paper has not been cited yet.

An interesting aspect of toxicology in the Soviet Union, analogous to the situation in the US and other major Western countries, was the close dependence of its development on military applications, particularly concerning chemical weapons (Kobyakov and Orlov, 2005). The history of chemical and biological warfare agents has been recently reviewed by Szinicz (2005) For a few decades now, discussions have taken place at the highest levels between Russia and Western or World organizations for redirecting Russian toxicologists towards civil scientific activities. In 1997, the Russian Federation ratified the

Chemical Weapons Convention (CWC, 1993) and created, in 1999, the Russian Munitions Agency. With the help of the European Commission (http://ec.europa.eu/research/nis/en/istc.html), the International Science and Technology Centre (ISTC) in Moscow and the Science and Technology Centre of the Ukraine (STCU) in Kiev were established in 1992 and 1993, respectively. Since then, the majority of projects were and still are funded through these two research centers to redirect Russian and NIS (Newly Independent States) scientists formerly working on chemical and biological weapons to peaceful scientific activities as well as to support fundamental and applied research. Since 1998 the international series of conferences – Chemical Weapons Demilitarization (CWD) Conferences – have been held annually in order to address and provide potential technical and practical solutions to the key problems associated with chemical weapons disposal (http://www.dstl.gov.uk/conferences/cwd). In addition, the special program "The Strengthening the Global Partnership project" (Center for Strategic and International Studies, 2002) was adopted by the leaders of the Group of Eight industrialized countries (G8) at the Kananaskis summit in Canada in June 2002 (Kobyakov and Orlov, 2005). This program aimed at dismantling excess weapons and weapon-related infrastructure left in Russia and other former Soviet States since the end of the Cold War. In order to counter the risk of proliferation the West has taken a number of initiatives to increase financial support to Russia. The US focus has been on threat reduction and the EU is aiming more at civil R&D (Roffey et al., 2003). For example, in 1991, a US Cooperative Threat Reduction Program (CTR) was launched together with Russia, also known as the Nunn-Lugar CTR Program with a goal to lessen the threat posed by weapons of mass destruction, to deactivate and destroy these weapons, and to help the scientists formerly engaged in the production of such weapons to start working for peace (http://nunn-lugar.com). Since 1992, the European Commission and member states (European Communities, 2000–2005) have also intensively developed cooperation with various NIS and Russia.

3. The current key actors in toxicological research in Russia and in Estonia

As mentioned above, national bodies and major research institutes dealing with issues of toxicology and related disciplines are listed in the review of Kurlyandskiy and Sidorov (2003) and thus will not be repeated here. In addition to governmental organizations, an All-Russian Public Organization of Toxicology (Russian Society of Toxicology) was established in 1996. This organization succeeds the former All-Union Society of Toxicologists, which existed at the time of the USSR. The Russian Society of Toxicology has about 300 members (Kurlyandskiy and Sidorov, 2003).

Within the framework of former cooperation programs, several Russian institutes were engaged in cooperation with the US and Europe concerning toxicological research:

- Institute of Physiologically Active Compounds (IPAC), Russian Academy of Sciences, Chernogolovka, http://www.ipac.ac.ru
- The Institute of Toxicology, St. Petersburg, http://toxicology.ru
- Research Institute of Hygiene, Occupational Pathology and Human Ecology (RIHOPHE), St. Petersburg
- Research Center for Applied Microbiology and Biotechnology (SRCAMB), Obolensk, Moscow region, http://www.obolensk.org
- Research Center for Toxicology and Hygienic Regulation of Biopreparations (RCTandHRB), Federal Medico-Biological Agency, Serpukhov (Moscow region), http://www.toxicbio.ru
- Research Institute of Hygiene, Toxicology, and Occupational Pathology (RIHTOP), Volgograd, http://www.rihtop.ru

A non-profit partnership "Orchemed" (Organic Chemistry and Medicine) was also created as a consortium of research institutes of the Russian Academy of Sciences. This consortium is collaborating with almost all the major Western industrial groups producing chemicals and pharmaceuticals. For commercial activities, a joint scientific center TRUST (Testing and Revalidation of Unique Substances and Technologies) has been funded in Chernogolovka. Both together provide certified preclinical trials including animal experiments (Bachurin, 2007). One of the main foci of current toxicological research in Russia is the harmonization of Russian chemical legislation with the EU new chemical management policy REACH, as well as the Globally Harmonized system of Classification and Labeling of Chemicals (GHS). The "Chemicals management policy of the Russian Federation" has recently been summarized (Eco-Accord, 2006). The Russian Chemists Union (RCU), together with the Russian Industry and Enterprise Union, decided to organize a permanent working commission of experts. In addition, a national REACH Centre was established in connection with the RCU (Kinnunen, 2008). This REACH center organizes informative seminars and publishes recommendations for methodologies. It has also created an information system on IUCLID 5, computer software which plays a central role in the IT environments of all organizations that have to cope with the data submission requirements of REACH. Finally, a Committee "REACH" of the All-Russian Organization for Quality is promoting REACH directive and supports Russian exporters (http://www.reach.ru).

To give also a short overview of Estonian scientists contributing to toxicology within the Soviet Union and after that period, one should know that Estonia is a country of 1.3 million people and the history of industrial toxicology in Estonia dates back to the beginning of 1950s. The first experiments on industrial toxicology in Estonia were started in 1951 at the Institute of Experimental and Clinical Medicine and were related to the investigations of Estonian oil-shale, oil-shale phenols and different derivatives such as adhesives, resins, mastics, softeners and solvents (Loit and Jänes, 1984). Most of these oil-shale derivatives are now defined as new chemicals and are listed in the European List of Notified Chemical Substances (ELINCS) (European Communities, 2006). During the Soviet period (about 50 years), Estonian researchers were mainly publishing in the Russian language. Currently, the search in the web-database of the Estonian Research Portal ETIS (http://www.etis.ee) using the keyword "toxicol" yields 138 scientific papers and proceedings published by Estonian scientists since 1977. At present, toxicological research in Estonia is made mainly in the groups lead by Prof. A. Zharkovsky (Tartu University), Prof. M. Karelson (Tallinn University of Technology) and Dr. A. Kahru (National Institute of Chemical Physics and Biophysics, Tallinn). The Estonian Society of Toxicology (ETS; http://www.kbfi.ee/ets) was created in 1997 and has 50 members. ETS is a member of EUROTOX (Federation of European Toxicologists and European Societies of Toxicology) and IUTOX (International Union of Toxicology).

4. Bibliometrical analysis of toxicological information published in the Russian language

In 1972, the first analysis of citations of and by Russian journals was published by Garfield (1974). The citations analyzed were extracted from the Science Citation Index (SCI) data bank. This analysis showed that many highly cited articles by Soviet scientists have been published in foreign or international journals. The most highly cited Russian journal articles published during 1961–1972 were almost exclusively in physics and mathematical physics (Garfield, 1975). It was pointed out already in 1975 that the citation life of Soviet literature by Western scientists was unfairly shortened at the outset by an overlong gestation period due to the translation from Russian to English (Garfield, 1976). The analysis of the 1000

Table 1
Scientific papers published in Russian and in English in toxicology and ecotoxicology (number of hits obtained by search in various databases).

Database	Keywords	Russian language	English language	All languages	% Russian[a]
Google books	Toxicology[b]	3590	51100	52400	6.56
	Ecotoxicology[c]	28	2142	2147	1.29
ISI Web of Science	Toxicology	71	97244	>100000	0.07
	Ecotoxicology	4	2528	2641	0.16
ISI Web of knowledge	Toxicology	88	97 773	>100000	0.09
	Ecotoxicology	13	25277	25797	0.05
Science Direct	Toxicology	n.a.	n.a.	99251	n.a.
	Ecotoxicology	n.a.	n.a.	1265	n.a.
PubMed[d]	Toxicology	59	4731	5025	1.23
	Ecotoxicology	0	3	3	0.00
Scopus	Toxicology	10748	489865	578737	2.15
	Ecotoxicology	36	10263	11014	0.35

n.a. – not applicable due to the search engine used.
[a] Calculated on the total of Russian and English published papers.
[b] Keywords: toxic OR toxicology OR toxicity.
[c] Keywords: ecotoxic OR ecotoxicology OR ecotoxicity.
[d] Covers 327 journals in Russian.

most cited articles in the period 1961–1982 in the SCI showed that the vast majority of these papers were published in English (976) and only four were written in French and two in Russian (Garfield, 1986). During 1973–1988, physics dominated Soviet science, followed by chemistry and life sciences. Indeed, the word "toxicology" was absent in all previously cited documents. Interestingly, only 35 of the top 100 Soviet scientists belonged to the USSR Academy of Sciences (Garfield, 1990).

To obtain numerical data on toxicological scientific papers published in Russian, an initial bibliometrical search was performed in October 2008 with several commonly used search engines using the same keywords (Table 1). The results varied depending on the search engine used but the number of documents for "toxicology" was always greater than for "ecotoxicology" (Table 1). In addition, according to this search Russian papers represented always less than 1% of the scientific literature and less than 7% of the books. Hence, Russian scientific literature is poorly visible by commonly used search engines. However, this "low visibility" could be partially due to the choice of the keywords, as in Russian language literature the word "toxic" was not often used. Instead, terms such as "negative effect" or "harmful" were applied.

The bibliometrical analysis of the toxicological scientific papers in two subject areas was performed in October, 2008 using the SCImago Research Group search engine in the Scopus® database. The data showed that the Russian and Estonian toxicological literature were both cited less than the US or French literature, reflected also by lower H indexes (Table 2).

During 1997–2007, toxicological scientific papers contributed 18.6% in North America, 15.5 % in Europe and 20.1 % in Estonia to the subject area "Pharmacology, Toxicology and Pharmaceutics" of the SCImago classification. By contrast, less than 7% were contributed by Russia. In addition, 4 years after their publication, the percentage of non-cited documents is low (less than 20%) for Western countries (including Estonia) contrary to Russian papers (almost 60% not cited) (Fig. 1).

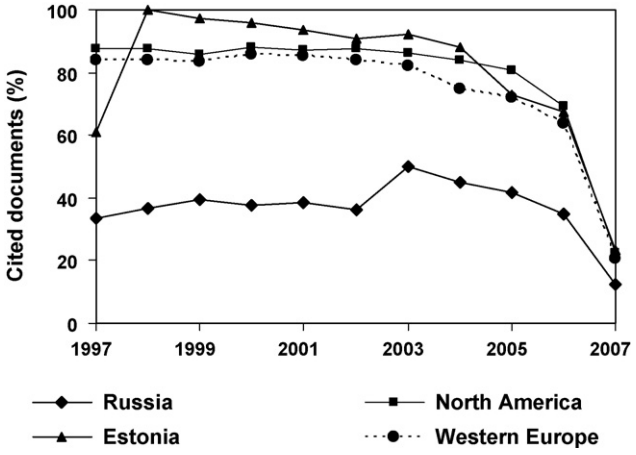

Fig. 1. Percentage of cited documents of Russian, Estonian, North American and Western European scientists in the subject area "Pharmacology, Toxicology and Pharmaceutics". Source: Scopus®, 2008. Available at: http://www.scimagojr.com.

This situation is even worse when comparing Russian and Western scientific journals. For the comparison, two high level Western scientific journals ("Toxicology" and "Toxicology Letters") were compared with similar high-rank Russian journals ("Doklady Akademii Nauk" and "Doklady Biological Sciences"). The comparison showed that more than 70% of documents from Western journals were cited compared to less than 20% of papers from Russian journals (Fig. 2A). However, a slight improvement of citation percentages may be observed for the "Doklady Biological Sciences" between 2003 and 2007. For those two Russian journals, the average number of citations per document (Fig. 2 B) is very low (less than 0.27) in contrast to the two Western journals mentioned above (more than 2.5).

Indeed, Van Raan (2008) in his comparison of the performance of the 100 largest European research universities within the period 1997–2004 on the basis of all publications (published in journals covered by the Citation Index) states: "we have left out Lomonosov University of Moscow. As far as number of publications concerns, this university is one of the largest in Europe (about 24000 publications in the covered 8-year period) but the impact is so low that it would have a very outlying position in the ranking".

5. Main resources for collecting toxicological and ecotoxicological documents in Russian language

For the mapping of the resources for collecting documents published in the Russian language, first the web-resources were

Table 2
Selected bibliometrical data on scientific toxicological literature from Russia: comparison with Estonia, US and France. Time-frame: 1996–2007.

Subject area	Pharmacology, toxicology and pharmaceutics			Environmental sciences		
Subject category:	Toxicology			Health, toxicology and mutagenesis		
Country (population, millions inhabitants)	Number of documents	Cites per doc.	H index	Number of documents	Cites per doc.	H index
United States (305)	41640	13.2	173	20233	10.6	113
France (65)	4164	12.8	77	2072	11.2	56
Russian Federation (142)	425	8.8	27	306	7.8	22
Estonia (1.34)	79	7.7	12	60	6.0	9

Source: Scopus®, 2008. Available at: http://www.scimagojr.com.

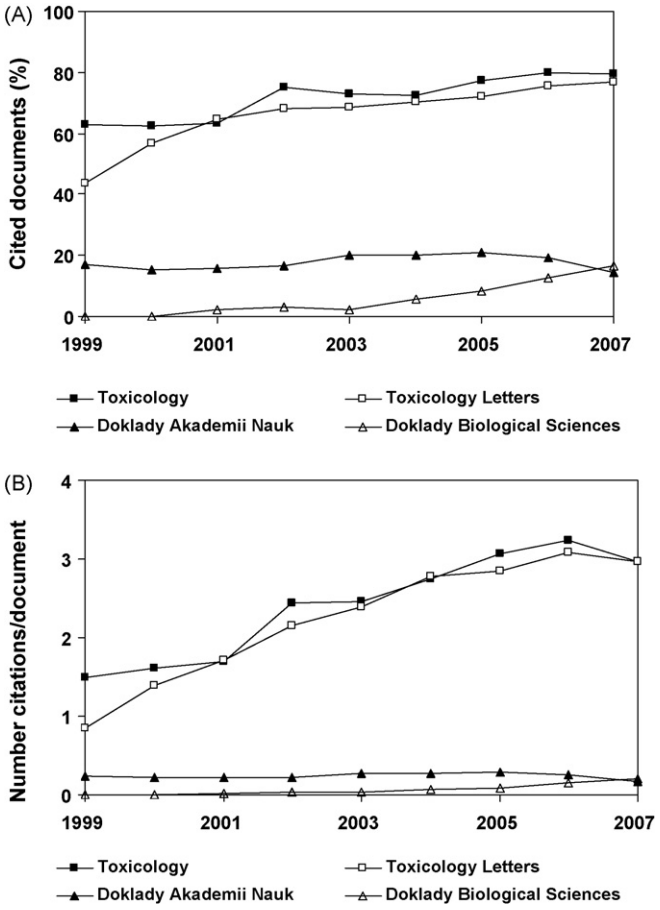

Fig. 2. Comparison of Russian and Western scientific journals by the percentage of documents cited (A) and by the number of citations per documents (B). Time-frame: 1999–2007. Source: Scopus®, 2008. Available at: http://www.scimagojr.com.

searched both in Roman and Cyrillic characters. In addition, the resources of libraries in Estonia and of the State Library of Russia (Moscow) were explored.

5.1. Institutions

5.1.1. Russian Academy of Sciences

The Russian Academy of Sciences (Российская Академия Наук, http://www.ras.ru) consists of the National Academy of Russia and a network of scientific research institutes from across the Russian Federation as well as auxiliary scientific and social units like libraries, publishers and hospitals. Headquartered in Moscow, the Academy is incorporated as a civil, self-governed, non-commercial organization chartered by the Russian Government. It combines the members of the Russian Academy of Sciences and scientists employed by institutions. This institution holds several sources of information (see below).

5.1.2. All-Russian Institute of Scientific and Technical Information (VINITI)

(Всероссийский институт научной и технической информации РАН, ВИНИТИ РАН)

VINITI (http://www2.viniti.ru/) is the leading information centre in Russia and CIS countries supplying scientific and technical information since 1952. During the Soviet era, Referring Journals (Реферативный журнал) of VINITI were the main source of scientific information for Soviet scientists as they covered the contents of the main international journals, providing even the abstracts of papers translated into Russian, and enabled ordering of full copies of original papers. Currently VINITI implements an analytical search in data flows in various natural and technical sciences, receiving information from 130 countries in 66 languages. On that basis, it prepares about one million documents a year, presenting them both as printed publications and computer-readable databases. The unique feature of VINITI is that it collects, creates abstracts and stores all scientific and technical materials which were not published anywhere (deposited manuscripts, dissertations, etc). VINITI can provide printed or electronic copies of these materials. VINITI RAN is one of the largest databases in Russia for natural, exact and technical sciences. It includes the materials of VINITI since 1981 and has more than 26 million documents (periodicals, books, conference proceedings, theses, patents, normative documents, deposited scientific works, etc), 30% of which are from Russian sources.

5.1.3. International Science and Technology Centre (ISTC), Moscow

ISTC (http://www.istc.ru/) is an international organization established by an international agreement in November 1992 to prevent the proliferation of nuclear and other weapons of mass destruction. The ISTC supports innovative projects that are expected to induce business opportunities by launching new commercial joint ventures that link the demands of international markets with the highly qualified scientific talent pool available in Russian and the Commonwealth of Independent States (CIS) institutes. The ISTC is a non-profit organization with a sister organization called the Science and Technology Center of the Ukraine (STCU, http://www.stcu.int/).

5.2. Libraries

Two Russian largest libraries with online catalogues are following:

5.2.1. Russian State Library (RSL), Moscow

From 1925 to 1992, this library was named V.I. Lenin State Library of the USSR and is currently one of the largest libraries in the world with more than 42 million items in 247 languages. Digital library and on-line catalogue are available (http://www.rsl.ru/index.php?f=97).

5.2.2. National Library of Russia (NLR), St. Petersburg

The National Library of Russia in Saint Petersburg holds the most complete collection of publications in Russian. Special attention is traditionally paid to the acquisition of foreign works about Russia and publications in languages of the Russian Federation printed in different countries of the world. Today the National Library of Russia houses more then 34.5 million items, of which 6.2 million items are in foreign languages. Electronic catalogues of books and journals are available in Russian (http://www.nlr.ru/res/cat/) and in English (http://www.nlr.ru/eng/opac/).

5.3. Websites

A well-documented list of web-based resources was previously reviewed by Kurlyandskiy and Sidorov (2003). Additional websites of toxicological and/or ecotoxicological interest are listed below.

5.3.1. Russian section of the Cheminformatics and QSAR Society

In 2006 the Russian section of the QSAR and Modeling Society (http://www.ndsu.edu/qsar_soc/aboutsoc/russia.htm) included members from Moscow, Novosibirsk and other cities of the Russian Federation. The main purpose of the Russian section is the promotion of collaboration between Russian and foreign scientists in the fields of bioinformatics, (Q)SAR, molecular modeling,

and computer-aided drug discovery. Therefore, the Russian section intends to provide its activity in close collaboration with the International Board of the QSAR and Modeling Society.

5.3.2. Laboratory of Structure-Function Based Drug Design, Department of Bioinformatics, Institute of Biomedical Chemistry RAMS

This laboratory focuses on bioinformatics and computer design of drugs, particularly on the identification of "structure-activity" and "structure-property" relationships, on the predictions of biological activity, toxicity and the biotransformation of pharmacological substances. Several software and associated databases were developed in the laboratory and are available on the web (http://www.ibmc.msk.ru/en/departments/drug_design/) after registration:

- PASS (PC/Web), for prediction of the biological activity spectrum for a compound on the basis of its structural formula.
- GUSAR (PC) – for the quantitative prediction of physical chemistry properties, biological activity and toxicity.
- PharmaExpert (PC/Web) – to describe the relationship between pharmacological effects and mechanisms of physiologically active substances.
- METAPREDICT (PC) – to predict classes and biotransformation sites of substances.

5.3.3. FSI "Research and Applied Toxicology Centre (RTIAC)" (Научно - практический Токсикологический Центр), Moscow

The main purpose of this center (http://web.mac.com/sktors/rtiac/index.html) is to improve the quality of medical care in cases of acute chemical poisoning. It provides information regarding the treatment of human poisonings to the general public and health care professionals. This centre has developed an information bank of toxicological data "IPCS INTOKS" for doctors and toxicologists on providing health care for acute chemical poisonings.

5.3.4. 'MAIK Nauka/Interperiodica", Russian Academy of Science, PMG Enterprises Ltd.

"MAIK Nauka/Interperiodica" (http://www.maik.ru/) is a company that publishes more than 180 academic journals in English in cooperation with Pleiades Publishing Inc. with the support of the Russian Academy of Sciences, and more than 200 journals in Russian in cooperation with Akademizdattsentr Nauka. The system of electronic publication allows the world scientific community to access full-text electronic versions of Russian scientific journals published under the logo of the Russian Academy of Sciences, and provides Russian and foreign scientists with up-to-date world-standard information services. Indeed, MAIK is part of Pleiades Publishing, uniting 10 Russian publishing entities with a combined overall volume of 1000 titles per year. In addition to "MAIK Nauka/Interperiodica", the holding includes the following publishing houses: "Akademkniga" (Chemistry, Biology, Transport, Metallurgy); "Fizmatlit" (Mathematics, Physics, Information Science); "Zoomedlit" (Veterinary Science, Cattle Breeding, Microbiology); "KolosS" (Agriculture and Mechanical Engineering); "Medkniga" (Medicine); and the humanitarian and educational publishing houses "Flinta," "Yurist," "Economist," "Gardariki," and "Akademkniga/Uchebnik". Recently Pleiades Publishing has acquired Allerton Press, which publishes English translations of 45 scientific and technical journals originating from Russia. Both Pleiades Publishing and Springer Science + Business Media entered into a contract, the main project being called "Russian Library of Science" – an online library in English, which became a part of Springerlink (see Section 5.5.4).

5.3.5. eLIBRARY.RU – Scientific electronic database

This database is accessible on the website of eLIBRARY.RU after registration (http://www.elibrary.ru/defaultx.asp?lng=EN). It contains more than 27,000 journals of which almost 5100 are Russian. Full texts are available for about 790 Russian journals.

5.4. Russian web-based toxicological databases

A search of databases was made through websites of the Ministry of Health of the Russian Federation (http://www.mzsrrf.ru/) and of the Ministry of Natural Resources of the Russian Federation (http://www.mnr.gov.ru/) using various search engines both in English and Russian. The Russian language website of the noncommercial organization of Sciences – Center for the Environment – Risk – Health, has links to foreign toxicological and risk databases (http://www.erh.ru/dbchemicals.php). In addition, two other potentially useful Russian language databases for collecting toxicological data were identified and are described below:

5.4.1. "ARIPS Hazardous substances" (Опасные вещества, http://www.rpohbv.ru/arips/online/)

This on-line database in Russian language of the Russian Register of Potentially Hazardous Chemical and Biological Substances contains toxicological data on more than 3100 substances handled in the territory of Russia (individual chemical and biological compounds produced and/or imported into Russia). The database includes data on toxicity and hazard to humans and the environment, and also occupational and environmental standards. These data are available after paid registration. Literature references used in this database originate not only from Russian sources but also from various international databases including:

- EU Uniform Chemical Information Database (IUCLID),
- monographs of the International Agency for Research on Cancer (IARC),
- database of the International Labor Organization (ILO),
- International Register of Potentially Toxic Chemicals (IRPTC),
- Registry of Toxic Effects of Chemical Substances (RTECS).

In this database, references are presented as a separate paragraph and are not linked directly with the data and so the origin of data (Russian or foreign) is not always clear. This database will be characterized in more detail below (see Section 8).

5.4.2. "Chemistry and Toxicology" (Химия и токсикология, http://chemister.da.ru/)

This personal website was created by Mr Ruslan Kiper in 2001 and is constantly updated. It contains well documented information on organic and inorganic synthesis, toxicology and pharmacology. The website is in Russian, although there is a demo version of chemical database in English (http://chemister.da.ru/Database/search-en.dbp). The website contains an impressive collection of data on 5158 chemicals, including toxicity data for 341 chemicals and toxins with literature references) (http://chemister.da.ru/Toxicology/ld50.htm). For 119 highly toxic substances and venoms, there is also information on physico-chemical properties and the chemical formula (http://chemister.da.ru/Toxicology/Toxins/toxins.htm). In addition, the physico-chemical properties and toxicities of 31 chemical warfare substances are documented (http://chemister.da.ru/Toxicology/BOV/bov.htm). Symptoms of poisoning are given for 128 toxic substances and venoms. For 19 chemicals, treatment methods are also given. Moreover, there is a page on laboratory safety and even laws concerning occupational chemical exposure limits.

5.5. Western websites containing Russian data or papers

In few public access Western databases, papers or abstracts in English from Russian scientific papers are available.

5.5.1. US TOXNET and US EPA ECOTOX databases

TOXNET is an US integrated system of toxicology and environmental health databases available free of charge on the web. In turn, several other databases are available for searching via TOXNET. TOXLINE covers the scientific literature in toxicology including literature in Russian published in the former socialist countries (Poland, Czechoslovakia, Hungary and GDR). ChemIDplus provides access to structure and nomenclature information for the identification of chemical substances of over 380,000 chemical records, of which over 289,000 include chemical structures. In addition another US database, the US EPA ECOTOX contains also data from Russian origin.

5.5.2. US PubMed

PubMed is a well-know service of the US National Library of Medicine (NLM) that includes over 18 million citations from MEDLINE and other life science journals for biomedical articles dating back to the 1950s. The search through the PubMed journal database with "russian" as a keyword yielded altogether 342 journals published in former socialist countries (Russia, Poland, Czechoslovakia, etc.) (data not shown). The PubMed journal database contains also English-translated titles of the papers published in Russian and in some cases also abstracts are available. For example, almost 7500 reference titles in English from the journal "Industrial Hygiene and Occupational Diseases" (Гигиена труда и профессиональные заболевания) can be found for 1960–1992. Abstracts in English are partially available only for the period 1989–1992. More information on this Russian journal can be found in the Section 6.2.

5.5.3. French INIST's catalogue of articles and monographs: Article@INIST database

This French on-line database contains about 15 million bibliographic records of documents held in the INIST/CNRS collections starting from 1973 and covering all fields of worldwide research in science, technology, medicine, humanities and social sciences. Freely accessible, Article@INIST provides a direct link to a document copy ordering service. In total 76 Russian journals and almost 140,000 articles published in Russian are indexed in this database.

5.5.4. Springer's "Russian Library of Science", http://www.springer.com/life+sci?SGWID=0-10027-12-129141-0

Springer is one of the largest publishers and distributors of cover-to-cover translations of Russian-language journals, all peer-reviewed and authoritatively translated. The aim of the "Russian Library of Science" is to publish the best articles and papers from research institutes and scientific societies in Russia and the surrounding countries. The "Russian Library of Science" contains more than 200 journals of which 29 are covering various topics of life sciences. The table of contents of the Journals is available online. The recent cooperation agreement between Pleiades Publishing (i.e. Allerton Press) and Springer Science + Business Media, Inc. expands the "Russian Library of Science" (see also Section 5.3.4).

5.6. Estonian libraries and databases

5.6.1. National Library of Estonia, Tallinn

The acquisition of collections in the National Library of Estonia (http://www.nlib.ee/) began with the foundation of the State Library in 1918. Since then, the Library started receiving deposit copies of all Estonian publications. Also, the collections were increased via international book exchange. During the Soviet period, communication with foreign libraries ceased and the collections were dominated by Russian language publications received as deposit copies (that the authors of the current paper also used as information for mapping the toxicological literature sources). Currently, the collections may be searched through the online catalogue "ESTER".

5.6.2. ETIS – Estonian Research Information System

The Estonian Research Information System ETIS (http://www.etis.ee) collects and stores information on research and development institutions, researchers, research projects and various research results. Researchers use also ETIS for submitting applications for grants, for reporting and archiving their documents/projects. In addition, Estonian R&D institutions can submit through ETIS applications and introduce their research results more widely. Research funding organizations use ETIS for evaluating and processing applications and giving feedback. This database allows searches in English and in Estonian by names of scientists and/or institutions, by keywords or by projects.

6. Main documents containing toxicological data published in the Russian language

6.1. Books

The search was performed mainly via card catalogues of the Academic Library of Tallinn University, the former Medical Library of Estonia and electronic catalogues (common electronic catalogue of Estonian libraries ESTER) of different libraries in Estonia, via on-line electronic catalogues of the Russian State Library and the National Library of Russia. Limited search was also made via the e-catalogue of the US National Library of Medicine. One of the most valuable documents in terms of REACH and industrial chemicals is a series of handbooks for chemists, engineers and doctors entitled "Hazardous substances in the industry" (Вредные вещества в промышленности). The first volume of this series was published by Lazarev and Astrachanzev in 1933 and there is a lot of updated editions. Each book of this series is about 600 pages. The first editions of the reference book were entitled as "Hazardous chemical substances in the industry" ("Химически вредные вещества в промышленности"). In 1954 it was renamed as "Hazardous substances in the industry" ("Вредные вещества в промышленности"). These handbooks contained toxicological information on industrial chemicals not only from Russian sources but also from US and Western sources. During the period of 1954 –1964 this handbook was translated and published in Polish, Czech, Romanian and Chinese (Filov, 1987). In Estonian libraries, 18 different editions of this series of handbooks are available (the titles listed as additional material in Table STable S2).

6.2. Journals

The search for scientific journals was carried out mainly via various Russian language internet sites and electronic catalogues of different libraries in Estonia and in Russia, but also by using PubMed databases. As a result, 37 different Russian language peer-reviewed scientific journals published between 1928 and 2007 were identified. Most of these journals are available in Estonian libraries. As no search engines were available for these journals, the journals were partly or fully screened by reading titles, abstracts and in most of the cases, contents. The most important journals among them are:

- "*Doklady Akademii Nauk SSSR*" (Proceedings of the USSR Academy of Sciences, ISSN 0002-3264) was published from 1933 to 1992. Since 1992 it has been continued as "*Doklady Akademii Nauk*" (Rossiĭskaia akademii nauk, Proceed-

ings of the Russian Academy of Sciences, ISSN 0869-5652). Since 2001, several sub-series have been translated into English and are available on-line (http://www.maik.ru/cgi-perl/journals.cgi?lang=eng&action=alphabet#). Main toxicological information can be found in "*Doklady Biochemistry and Biophysics*" (ISSN 1607-6729), "*Doklady Biological Sciences*" (ISSN 0012-4966) and "*Doklady Earth Sciences*" (ISSN 1028-334X).

- "*Hydrobiological Journal*" (Гидробиологический журнал, ISSN 0018-8166 print version), published since 1965 until now by the Institute of Hydrobiology, National Academy of Sciences of Ukraine (http://hydrobiolog.narod.ru/). The journal is simultaneously translated into English and published under the title "Hydrobiological Journal", Begell House, Inc. Pub., USA. Abstracts from 1998 are available in English at http://www.begellhouse.com/journals/38cb2223012b73f2.html. The volumes of the journal published up to 1971 are available in the National Library in Tallinn (Estonia).
- "*Hygiene and Sanitaria*" (Gigiena i sanitaria, Гигиена и санитария, ISSN 0016-9900) has been published since 1922 and covers all aspects of hygiene and sanitary practices. The focus is on hygiene of the environment, communal hygiene, the hygiene of children and teenagers, the hygiene of labor and nutrition, organization and planning of sanitary affairs as well as training of sanitary doctors. The tables of contents are available on http://www.medlit.ru/medrus/gigien.htm. The journal up to 1993 (except 1947) is available in the National Library in Tallinn (Estonia).
- "*Inland Water Biology*" (Биология внутренних вод, ISSN: 1995-0829 (print version) ISSN: 1995-0837 (electronic version) is published since 1995 till now. The journal is published in Russian and in English (http://www.springer.com/life+sci/ecology/journal/12212) under the authority of the Office of Biological Sciences, Russian Academy of Sciences. The journal covers fundamental research on aquatic organisms, from viruses to fish and aquatic mammals.
- "*Modern problems of Toxicology*" (Современные проблемы токсикологии, ISSN 1609-0446 print version, ISSN 1609-0470 on-line version). Since 1998, this journal has been published by the Medved's Institute of Ecohygiene and Toxicology in Kiev, Ukraine. The full content in Ukrainian or Russian is available on the web and the abstracts are translated into English (http://www.medved.kiev.ua/MAG/arhiv.HTM).
- "*Occupational medicine and industrial ecology*" (Meditsina truda i promyshlennaia ekologiia, Медицина труда и промышленная экология, ISSN 1026-9428). This journal was previously named "*Industrial hygiene and occupational diseases*" from 1957 to 1992 (Gigiena truda i professional'nye zabolevaniia, ISSN 0016-9919) and includes papers on theoretical and practical problems of occupational health and diseases, including toxicology. The journal also publishes the description of different test methods and literature reviews from Russia and abroad. Since 2008 the *table of contents is* available online (http://www.niimt.ru/publishing/magaz_contents2008.php?lang=en). The volumes of the journal up to 1992 are also available in the National Library in Tallinn (Estonia).
- "*Pharmacology and Toxicology*" (Farmakologiia i toksikologiia, Фармакология и токсикология; ISSN 0014-8318) was published from 1939 to 1991. Since 1992, the journal continues as "*Experimental and clinical pharmacology*" (Eksperimental'naia i klinicheskaia farmakologiia, Экспериментальная и клиническая фармакология, ISSN 0869-2092). The tables of contents of this journal for 2000–2006 are available on the web (http://ekf.folium.ru/contents.htm). The volumes of the journal up to 1991 are available in the National Library in Tallinn (Estonia), although some volumes are missing (1942–1945, 1950–1956).
- "*Toxicological reviews*" (Токсикологический вестник, ISSN 0869-7922) has been published since 1993 by the Federal State-owned Establishment of Public Health (FSEH) "Russian Register of Potentially Hazardous Chemical and Biological Substances (RRPHCBS)". It highlights scientific and practical issues related to chemical safety and publishes legislative and regulatory documents concerning chemicals (http://www.rpohbv.ru/magazin/). It should be noted that it is different from the "Toxicological reviews" (ISSN 1176-2551) published since 2003 by Adis International (New Zealand).

In January 2009 we performed a search in PubMed using a combination of the keywords (toxic*) AND ("russian"[Language]) and obtained 16374 hits. The bibliometrical analysis in PubMed for some of the above described journals using the keyword "toxic*" showed that those Russian journals (Table 3) accounted in total for 37% of the hits for the combination "toxic* AND Russian" (6075/16374) and that the "Doklady. . ." titles seem to be the least representative for toxicological studies (Table 3).

6.3. Scientific reviews of Soviet literature on toxicity and hazard of chemicals

The International Register of Potentially Toxic Chemicals (IRPTC or UNEP Chemicals) has collaborated with the Government of the USSR to publish in English and in Russian a series of Scientific Reviews of Soviet Literature on Toxicity and Hazards of Chemicals (http://www-cger.nies.go.jp/cger-e/db/info-e/InfoDBWeb/db/irptc.htm). The current availability of these papers

Table 3
Visibility of the toxicological research published in Russian scientific journals indexed in PubMed database. Indices a and b show the change of the name of the Journal (see also Section 6.2).

Journal	Number of documents in PubMed	Number of documents containing "toxic*"	% of documents found with keyword "toxic*"
1. Hygiene and sanitary (Gigiena i sanitaria)	18622	2980	16.0
2.a. Industrial hygiene and occupational diseases (Gigiena truda i professional'nye zabolevaniia)	7426	1375	18.5
2.b. Occupational medicine and industrial ecology (Meditsina truda i promyshlennaia ekologiia)	2187	207	9.5
3.a. Pharmacology and toxicology (Farmakologiia i toksikologiia)	6350	989	15.6
3.b. Experimental and clinical pharmacology (Eksperimental'naia i klinicheskaia farmakologiia)	2059	329	16.0
4. Doklady Akademii Nauk SSSR	9859	101	1.0
5. Doklady Akademii Nauk	1378	54	3.9
6. Doklady biological sciences	1283	32	2.5
7. Doklady biochemistry and biophysics	815	8	1.0
Total:	49979	6075	

Source: PubMed, 2009. (http://www.ncbi.nlm.nih.gov/pubmed/).

is problematic even though these are constantly cited in various reports and reviews.

6.4. Dissertations

The Russian State Library (RSL) has a unique collection of scientific dissertations. The All-Russian (former All-Union) Collection of Dissertations was founded by the Decree of the All-Union Committee for Higher School. Around 17,000 Candidate of Sciences (*Russian:* кандидат наук, more or less equivalent to Ph.D. degree) and 8000 Doctor of Sciences (*Russian:* доктор наук, the highest post-graduate academic degree in the Soviet Union, Russia and in many post-Soviet states awarded in recognition of a substantial and sustained contribution to scientific knowledge) dissertations in all fields of research are collected every year. At the moment the full access is possible in the reading rooms of the RSL. Digital versions of dissertations have been available since 1996. The search can be performed via the electronic catalogue of the RSL.

7. Impact factor of Russian scientific journals

The impact factor of a journal is a measure of the frequency with which the "average article" in a journal has been cited in a particular year or period (Garfield, 2006). Based mainly on papers published in English, it is calculated each year by Thomson Scientific, previously known as The Institute for Scientific Information® (ISI®). And thus, it was recommended by Garfield (1997) that all Russian journals could provide keywords and abstracts in English.

A Russian Impact Factor of Russian scientific citation index (Impact factor RINTS) has also been established by the Scientific Electronic Library of Moscow (eLIBRARY.RU). The comparison of those two impact factors jointly available for 24 Russian journals shows that these indices are not correlated (data not shown). It should be noted that none of these 24 journals were related to toxicology. However, all journals considered relevant for toxicology (listed in Section 6.2) belonged to top-1000 Russian journals and had a RINTS factor above 0.200 (http://www.physchem.chimfak.rsu.ru/index-eng.html).

8. Comparison of the Russian database "Hazardous Substances" with European and American databases

In order to compare the Russian database "Hazardous Substances" (see also Section 5.4.1.) with the analogous US TOXNET (http://toxnet.nlm.nih.gov/) and US EPA ECOTOX (http://cfpub.epa.gov/ecotox/) databases, three lists of chemicals were used:

- two lists of chemicals from the European Chemical Substances Information System, i.e. the PBT (persistent, bioaccumulative and toxic chemicals) list and the ORATS (Online European Risk Assessment Tracking System) list
- a list consisting of 373 phenolic compounds (Phenols list) was created by the authors of this paper. The list is a result of the search in US EPA database ECOTOX using "phenol" as a keyword.

For all three lists, less than 23.4% of the compounds were registered in the Russian database (Table 4).

Among the Phenols list of 373 chemicals, only 8.3% were recorded in the Russian database whereas 317 chemicals (84.9%) were recorded in the US TOXNET database (data not shown). However, for those 317 chemicals, 207 were associated with toxicological data.

For the Phenols list, the search in TOXNET was also done with the language restriction criterion "limit to: Russian" (years: 1900–2008) using Toxline (Toxicology Literature Online) subdatabase. In this case the hits obtained included articles published in Russian from Russian journals and in addition also from those of former socialist countries (Poland, Czechoslovakia, Hungary, GDR). As a total, 317 chemicals of the Phenols list had 130610 references in Toxline of which only 2372 (1.8 %) were in Russian. However, these Russian references concerned only 112 chemicals (38.7%) of the Phenols list. The comparison of the use of test organisms in toxicological research showed that the pattern of use of test animals is similar in Russian "Hazardous Substances" and TOXNET databases with rodents as the most often used group of animals (Table 5).

Among the 373 chemicals of the Phenols list, 297 had aquatic toxicity data for algae, fish, protozoa, molluscs and crustaceans. In contrast, only 21 of those 373 chemicals had ecotoxicological data in the Russian database. Crustaceans, fish and algae are the most used ecotoxicological test organisms in both databases (Table 6).

Table 4
Availability of toxicity data for different types of chemicals in the Russian database "Hazardous Substances" (Опасные вещества, http://www.rpohbv.ru/arips/online/).

List of chemicals	Total number of chemicals in the list	Number and percentage of chemicals present in Russian database "Hazardous Substances"
PBT list[a]	127	17 (13.8%)
ORATS list[b]	141	33 (23.4%)
Phenols list[c]	373	31 (8.3%)

Search in the Russian database was performed compound-by-compound using CAS numbers.
[a] Persistent, bioaccumulative and toxic chemicals.
[b] Chemicals from Online European Risk Assessment Tracking System.
[c] Phenolic compounds from EPA ECOTOX database.

Table 5
Comparison of Russian on-line database "Hazardous Substances" (Опасные вещества, http://www.rpohbv.ru/arips/online/) and US TOXNET database in terms of usage frequency (%) of test organisms in toxicological research.

Species	Usage frequency (%) in the toxicological research	
	US TOXNET database	Russian database
Dog	4.8	4.8
Cat	4.1	4.0
Guinea pig	8.4	14.4
Mouse	29.7	24.0
Rabbit	10.7	22.4
Rat	27.0	23.2
Hamster	0.4	5.6
Chicken	4.1	0.8

Table 6
Comparison of Russian on-line database "Hazardous Substances" (Опасные вещества, http://www.rpohbv.ru/arips/online/) and US EPA ECOTOX database in terms of usage frequency (%) of test organisms in ecotoxicological research.

Species	Usage frequency (%) in the ecotoxicological research	
	US EPA ECOTOX database	Russian database
Algae	15.3	29.8
Fish	41.5	35.1
Protozoa	8.9	1.8
Mollusks	13.2	1.8
Crustaceans	21.1	31.6

9. Conclusions

The reviewed Russian data sources contain a considerable amount of toxicological information on different pure chemicals, mixtures and preparations, including pesticides and pharmaceuticals. The major limitation of access to this information is knowledge of the Russian language. However, this limitation could be par-

tially overcome by using on-line translation services (translation websites) such as Google™ Translate (http://translate.google.com). Another limitation of the access to Russian toxicological data might be that this information is usually not digital and is available only in libraries. Fortunately, in the libraries of former Soviet republics now part of the EU, such as Estonia, large collection of Russian language literature has been preserved. This makes access to original documents much easier.

In addition to the problems linked to apparently limited access, CAS numbers or IUPAC names of chemicals are not always provided and thus identification of compounds may be difficult for non-chemists. More positively, references to test guidelines are usually given at least in the list of literature references. As a rule, toxicity studies have been or are conducted according to standardized methodologies of the former USSR (Sanotski, 1970) and in the Russian Federation (Ministry of Natural Resources of the Russian Federation, 2001). Currently, many ISO international standards and EPA standard procedures are also used (http://www.bioassay.narod.ru/standards/standards.html).

This review demonstrates that considerable amounts of information from Russian language data sources of potential benefit for the new EU chemical policy REACH (European Parliament, 2006) remains unexplored, mostly due to language barriers. Those hidden data may be used for the development of intelligent testing strategies (ECETOC, 2007) that enable a significant increase in the use of non-testing information for regulatory decision making, thus minimizing the need for animal testing (3R: reduction, replacement, refinement). Indeed, the Annexes VII-X of the REACH directive state: "all available *in vitro* data, *in vivo* data, historical human data, data from valid (Q)SARs and data from structurally related substances (read-across approach) shall be assessed first".

Conflict of interest

There are none.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tox.2009.05.001.

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