Centre for Economic
and Financial Research
at New Economic School

#38

December 2013

Formation of the Institutional Base and Providing Creation of the System of Good Laboratory Practice in accordance with OECD Requirements

G.Besstremyannaya, O.Bondarenko, M.Ananyev, M.Kartseva

CEFIR Policy Paper series

G.Besstremyannaya, O.Bondarenko, M.Ananyev, M.Kartseva

Centre for Economic and Financial Research

Formation of the Institutional Base and Providing Creation of the System of Good Laboratory Practice in accordance with OECD Requirements

Introduction

One of the instruments used for harmonizing regulation of chemicals in OECD are Principles on Good Laboratory Practice which are used for Mutual Acceptance of Data (MAD). Additionally, there are OECD's Guidelines for the Testing of Chemicals, which contain standards for testing the safety of chemicals.

As a part of this project we carried out expert evaluation of international experience of GLP usage. Evaluation and summary of international experience of GLP implementation in legislation of a number of countries allow to assess their applicability for Russian Federation and to choose the most optimal method of implementing them for the purpose of making regulatory decisions by authorities. Aside from that, we prepared proposals for optimization of system of product admission, testing of which is conducted in Russia in accordance with GLP principles.

In the course of research we carried out analysis of possible positive and negative effects of implementing GLP principles in Russia and joining agreement of mutual acceptance of data from non-clinical testing for economic agents.

For this purpose we conducted survey and interview of the following groups of agents:

- Firms that produce industrial chemicals, pesticides, medicines and cosmetics (275 respondents).
- Laboratories that conduct registration studies of industrial chemicals, pesticides, medicines and cosmetics (25 respondents).
- Regulatory authorities (3 respondents).

These data were used for qualitative and quantitative statistical and econometric analyses of the following issues:

- Major problems of Russia's joining MAD/GLP OECD system and possible change in area of regulation of regulatory authorities.
- Influence of Russia's joining MAD/GLP OECD system on industries and admission of their production to the market.
- Influence of Russia's joining MAD/GLP OECD system on simplification or complication of registration regime.
- Change in competition intensity.
- Allocation of exporting firms and firms with an R&D department.
- Change in amount of documentary for product registration.
- Change in output, services prices, information availability and research potential.
- Measures for offsetting possible negative influence on economic agents.

1. Analyses of international experience of using GLP principles in implementing regulatory decisions by authorities

Principles on Good Laboratory Practice – GLP principles (Principles on Good Laboratory Practice, 1998) apply to conduction of non-clinical test studies and organization of the test facility. They guarantee quality and reliability of test data for registration of chemical substances. GLP principles regulate detailed aspects of laboratory activities: organization of the test facility where studies are conducted; handling and calibration of apparatus; reporting and storage of test data and etc.

GLP principles served as an instrument of harmonizing testing procedures of chemicals in OECD countries for the Mutual Acceptance of Data (MAD) which was adopted by OECD in 1981. The legal basis of GLP principles in OECD and Member countries is outlined in figure 1.

Mutual Acceptance of Data was established in OECD Council Decision of May 12, 1981 (updated in 1997) as follows: '…data generated in a Member country in accordance with OECD Test Guidelines and Principles of Good Laboratory Practice (GLP) shall be accepted in other Member countries for assessment purposes and other uses relating to the protection of human health and the environment' [C(97)186/Final]. Countries can conduct additional tests but a foreign company does not have to do it. Figure 2 depicts the process of mutual acceptance of data between two members of the agreement.

Figure 1 – International System of Building GLP Legal Basis

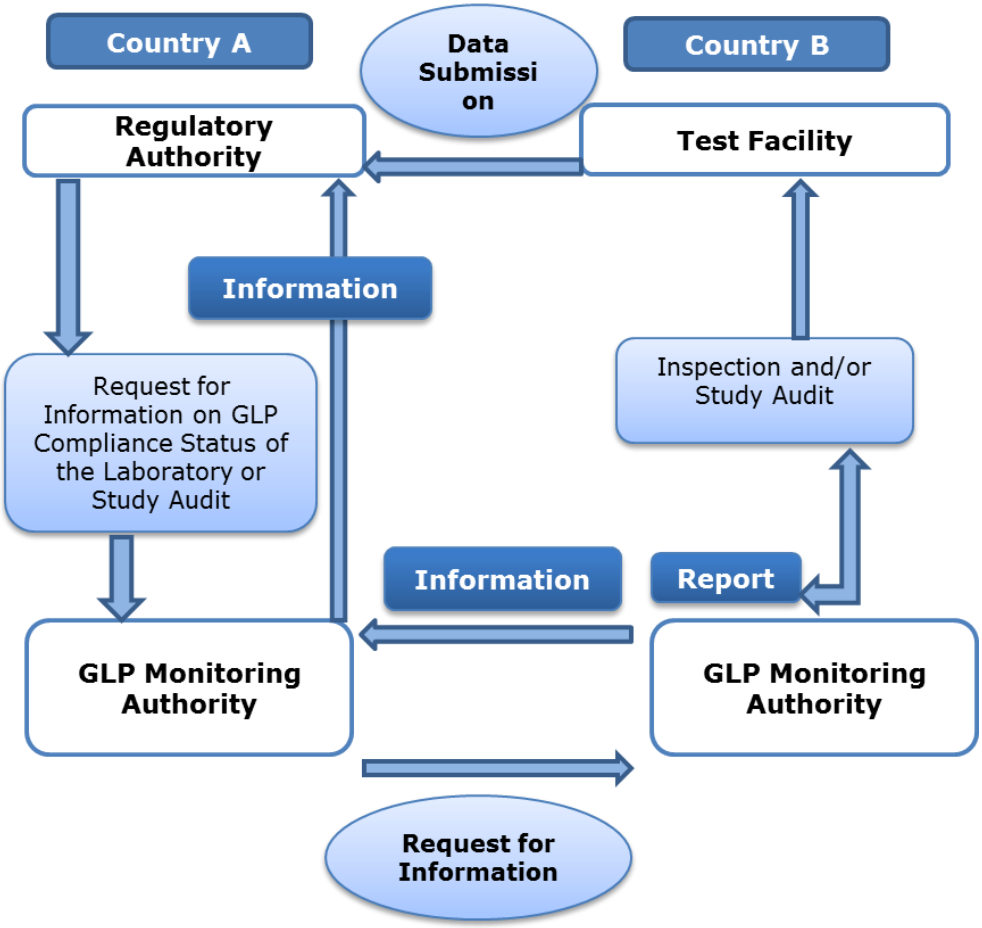

Figure 2 –Mutual Acceptance of Data Mechanism

The main OECD documents which the countries should rely on during the implementation of national policy are the annexes to the OECD Council Decision: Guides for

Compliance Monitoring Procedures for Good Laboratory Practice and Guidance for the Conduct of Test Facility Inspections and Study Audits.

Non-OECD member countries with developed chemical industry may join the agreement on the mutual acceptance of data since November 26, 1997 when the Decision of the OECD Council on compliance with the regulations relating to MAD by non-OECD countries was adopted. It may be noted that Israel and Slovenia have adopted an agreement on the mutual acceptance of data shortly before they became the OECD members, while Argentina, Brazil, India, Singapore and South Africa are members of the agreement on mutual recognition of data without being the members of OECD.

OECD documents contain norms whereby the countries wishing to become members of the OECD or full-fledged participants in the MAD Programme must organize and implement measures aimed at creating a national system of Good Laboratory Practice including the procedure of conducting non-clinical research, a system of compliance monitoring, recognition of the results of non-clinical research and empowering the national bodies to implement these measures.

Decision C(81)30 confirmed the principle of mutual acceptance of the results of non-clinical tests by OECD member countries whereby the data obtained during the tests of chemicals in an OECD country, in accordance with the OECD guidance for tests and OECD Good Laboratory Practice, are accepted by another OECD country for audit and other purposes connected with the protection of man and the environment.

Decision C(81)30 sets down the legal force of OECD guidance for tests and OECD Good Laboratory Practice principles which have been equated to guidance and principles adopted by the Council for the OECD member countries. These guides have been recommended for direct use by the OECD member countries.

Decision C(81)30 is an international normative legal document effective for the OECD member countries and its potential participants in the area of non-clinical tests of chemicals contained in pesticides, food and fodder additives, cosmetics, medicines, veterinary drugs and industrial chemicals.

Supplement I to Decision C(81)30 was published separately. It contains recommendations on the conduct of tests, a set of key internationally agreed test methods used to determine the safety of chemical substances and chemical preparations and industrial chemicals. They cover tests of the physical-chemical properties of substances, the impact on human health, the environment, decomposition and accumulation in the environment.

These recommendations contain description of the specific methods classified into five sections:

Section 1: Physical-chemical properties;

Section 2: Impact on biotic systems;

Section 3: Degradation and accumulation;

Section 4: Impact on health;

Section 5: Other guiding test principles.

In 1995 the OECD formed a panel of experts which revised the Guidance for Good Laboratory Practice (GLP) previously set forth in Supplement II of Decision C(81)30. From the results of the work of the panel of experts the Guidance for Good Laboratory Practice (GLP) was developed and approved by decision of the OECD Council on 26 November 1997 C(97)186(Final) (hereinafter Decision C(97)186(Final)), which replaced Supplement II to Decision C(81)30.

The Good Laboratory Practice principles were subsequently adopted as the national standard of the Russian Federation GOST P 53434-2009 and put into effect by Executive Order of the Federal Agency for Technical Regulation and Metrology № 544-ст of 2 December 2009.

Decision C(97)186(Final) provides an exhaustive definition of Good Laboratory Practice: the organization process and the conditions under which laboratory tests are planned, conducted, observed, recorded and reported. Effectively it means that the principles of Good Laboratory Practice cover the entire process and stages of non-clinical research beginning from planning, execution, follow-up monitoring and recording of results.

Non-clinical tests and pharmacological, toxicological and other biological laboratories must comply with the Good Laboratory Practice principles. Compliance of laboratories with GLP principles ensures acceptance of the results of non-clinical research. The principle of data acceptance of GLP guarantees the validity and reliability of the data used and obtained in the process of tests as well as humane treatment of animals in developing new drugs.

OECD documents serve the following main purposes:

a) ensuring safety for man and the environment,

b) removing trade barriers.

OECD documents regulate the conduct of non-clinical study of objects contained in pesticides, drugs for medical and veterinary use, food and fodder additives, cosmetics and industrial chemicals.

An analysis of OECD documents makes it possible to divide them into the following groups:

I) OECD documents that directly establish GLP principles (OECD Council Documents №№ 1-3 as per list in Table A.1 – Supplement A to this final report);

II) OECD documents establishing requirements to test centers and non-clinical studies they conduct (OECD Council Documents №№1 (OECD Principles of Good Laboratory Practice), 6-10, 12, 13, 15-17 as per list in Table A.1 – Supplement A to this final report);

III) OECD documents establishing requirements to the creation of a national system of compliance to GLP principles (OECD Council Documents №№ 4, 5, 11, 14 as per list in Table A.1 – Supplement A to this final report).

OECD documents can be classified by the character of the norms they contain into those establishing “horizontal” requirements and those establishing “vertical” requirements. The former include documents that establish general fundamental requirements including the principles of Good Laboratory Practice, requirements to the test centers and studies, the national GLP as well as the system of GLP compliance monitoring. The latter include OECD documents that regulate specific test methods contained in Supplement I to Decision C(81)30.

The norms and requirements set forth in these documents, although having a recommendatory form, are binding for the countries that wish to take part in the MAD programme or seek full-fledged membership of the OECD.

Mutual acceptance of data is possible if the national GLP programme complies with the GLP principles set forth in Group I documents. Such compliance is ensured by incorporating the normative requirements of Groups II and III documents in the national legislation and compliance therewith.

An analysis of the OECD documents warrants the conclusion that their system is clear-cut and the norms they contain are legally correct;, however a study of the substantive normative aspects has revealed the existence of contradictions and gaps.

Analyses of foreign legislation concerning requirements for conducting nonclinical test studies in accordance with GLP OECD principles

Here we analyze, how OECD requirements which are contained in above mentioned documents are described in legislation of the UK, Germany, Switzerland and Slovakia.

We paid special attention to the following aspects of national legislation concerning regulation of non-clinical studies and fulfilling OECD recommendations in GLP area:

- National GLP compliance monitoring authorities.
- Statutory acts regulating implementation of GLP principles.
- Mutual acceptance of data.
- Process of monitoring test facilities.
- Conducting inspections.
- Payment for inspections.
- Appeal for inspection results.
- Obtaining GLP certificate by the test facility.

In all EU countries GLP principles (and all OECD documents from GLP series [1]) are an acknowledged international standard for conduction of non-clinical safety studies. In Switzerland GLP is legally required for safety testing of medicines [2], agrochemicals [3], industrial chemicals [4], biocides [5]. In UK GLP principles are obligatory for regulatory studies. Such studies are aimed at safety testing of a chemical and are necessary for placing it on the market. These regulation requirements are contained within Statutory Instruments of 1999 [6] and 2004 [7].

Being an EU member country, Germany employs GLP principles as a legal requirement for carrying out non-clinical testing, as is stated in the Chemicals Act [8]. In Slovakia, according to Article 5 of the Chemicals Act, testing of chemicals should be carried out in compliance with requirements of EU Directive No 1907/2006 concerning REACH. If production is under REACH regulation, its testing should be carried out according to GLP principles.

In India GLP principles are voluntary; however, there are constant arguments about changing national legislation and making certification according to GLP principles obligatory. It is possible that along with further development of chemical industry and increase in number of GLP-certified laboratories GLP monitoring system will be legally required for all test

facilities. There are 1100 contract research organizations which conduct clinical and non-clinical studies in India. 30% of these organizations carry out non-clinical studies.

In countries where GLP principles are not implemented into legislation and non-MAD members any laboratory can carry out testing according to GLP principles and make it obligatory for internal use as a quality assurance system. Some national legislation frameworks provide a chance to obtain a GLP-compliant status for a laboratory from a foreign national GLP compliance monitoring authority.

GLP compliance monitoring is carried out in accordance with the Decision of OECD Council of October 2, 1989. Countries should first, establish national GLP compliance monitoring program based on test facilities inspection and study audits; second, establish one or several national GLP monitoring authorities responsible for conducting compliance monitoring and, third, receive declarations signed by the directors of test facility proving that chemicals test studies were carried out according to GLP principles and other legal acts related to GLP.

According to the Decision of OECD Council of 1989 countries can assign the full list of chemical products or part of it to production testing of which is conducted under GLP principles. In the considered countries (UK, Germany, Switzerland and Slovakia) the following categories are included in the list:

- Medicinal products
- Veterinary medicines
- Industrial chemicals
- Agrochemicals
- Cosmetics
- Pesticides
- Food additives

The expertise area of GLP OECD looks as follows:

- Physical-chemical testing
- Toxicity studies on human health
- Ecotoxicity studies on effects on short- and long-term effect on environment
- Ecologic studies on behavior in water, soil and air; bioaccumulation.

Analyses of mechanisms of providing mutual acceptance of data generated from non-clinical studies conducted according to GLP principles in countries which joined the MAD agreement

According to the Decision of OECD Council of 1981, test data generated in accordance with GLP Principles is accepted by all members of the MAD agreement. Countries that are not members of the OECD may join the agreement on mutual recognition of data according to the OECD Council Decision C (97) 114. OECD Council Decision C (89) 87/Final establishes the legal advice of the non-clinical studies for the purpose of recognition of the members of the agreement in accordance with the Principles of Good Laboratory Practice.

Membership in this agreement automatically assumes that testing data for registration of chemical production is accepted from members of the agreement. Necessary conditions for MAD also include existence of national authority for interactions in GLP area (regulatory authority), existence of information exchange and information about GLP compliance status of the test facility (see Figure 2). For instance, article 18 of Swiss ordinance on GLP regulates the process of interactions between Federal Office for the Environment, Federal Office of Public Health and Swiss Medicines Office with foreign regulatory and OECD authorities.

Some countries that are not in OECD but are the members of MAD agreement conclude international agreements with regulatory authorities of some countries. For instance, Switzerland entered bilateral agreements about mutual acceptance of GLP compliance monitoring with important trade partners and their offices: with Germany, Japan and USA.

Country A will accept data from country B only if it obtains information of GLP compliance monitoring procedures from the country where the data came from. If the country is a full member of the agreement on mutual acceptance of data, test results obtained in the GLP-certified laboratories of that country may be forwarded to the national regulatory authorities of other countries for the recognition in the EU and OECD. For this purpose, each member of the agreement should prepare a GLP report on its territory. This report includes the list of test centers, which have been carried out the inspection, inspection date and a brief description of the results of inspections. In case of any problems with mutual recognition of data the laboratory must notify the national authority for monitoring.

For every country OECD acts (C(81)30(Final) и C(97)114/Final for non-members) particularly are basic legislative norms. There are no specific legislative instruments providing implementation of MAD on national level. The country states its readiness to

accept testing data under membership in the Working Group on GLP OECD. It is one of the stages of the process of joining the agreement.

Absence of harmonized statutory instruments often becomes a problem, which was noted by international experts. Let us consider the case when a German company which produces chemicals conducts safety tests in a GLP-certified laboratory in the country that is not an EU or MAD member. The company can send request to the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety so that the test facility could be monitored for GLP compliance. That is how test facilities from Thailand and India are certified. However, if the country is not a MAD member or a member of a bilateral agreement between separate countries, data generated in its laboratories will not be accepted in EU and OECD.

Similar difficulties may appear when GLP studies take a number of steps and are conducted in laboratories from different countries (so called multisite studies). A German test facility often conducts multisite pesticide tests in other non-MAD countries. If a pesticide is registered neither in the US nor in the EU but is used in India, treated crops can only be imported to the US or Europe if an import tolerance study has been conducted according to GLP in the respective country of origin.

Analysis of Common GLP Compliance Monitoring Procedure

National GLP compliance monitoring authority checks whether laboratories conduct testing in accordance with GLP principles and whether they can guarantee due quality of generated data. 'Monitoring' means carrying out various kinds of inspections, issuing GLP certificates, management of GLP compliance monitoring programs test facilities take part in, training of GLP inspectors, organization of inspections order, etc. Its duties may also include inspecting foreign laboratories when it is requested to do so.

The order of conducting inspections is usually contained in legal acts and fully in the text of GLP programmes. Frequency of inspections may differ slightly between countries but types of inspections are the same. Requirements for qualification of GLP inspectors are similar; experience and training under national GLP programme play an important role. National legislation lists the appeal and complaints procedure when inspection results are not satisfactory. Table 1 provides a description of the national monitoring systems, identifying the legislative and normative documents on the issue.

Table 1 — Procedures for monitoring compliance with GLP Principles

Country	Order of monitoring procedures	Source
United Kingdom	– Laboratories willing to conduct GLP studies must first join the Compliance Monitoring Programme. The process of accession to the Compliance Monitoring Programme is the following: 1. Implementation of appropriate systems to ensure that the laboratory can operate in accordance with the Principles of GLP. 2. The completion and submission of the application form to the monitoring body (GLPMA). 3. Consideration of the application by the national monitoring body. 4. Acceptance of the facility as a prospective member of the Programme. 5. Implementation of the inspection of test facility by the monitoring body. 6. Preparation of the report on the inspection and identification of any inconsistencies. 7. Recognition as a full member of the UK GLP Compliance Monitoring Programme and issue of the GLP Certificate. – Prior to the inspection, inspectors should familiarize themselves with the inspected testing facility. Any existing information on the facility should be reviewed. Such information may include previous inspection reports, site plan, organizational charts, study reports, biography (CVs) of the staff. – The documents should provide information on: 1. Type, size and location of the object. 2. Number of studies that may be encountered during the inspection. 3. The structure of the enterprise management. – Inspectors should note any deviations from the previous inspections of the laboratory. In the absence of previous inspections, Pre-Inspection visit can be made to obtain relevant information. – During the inspection the laboratory's compliance to the GLP Principles is verified for the following items: 1. Organization and personnel. 2. The quality assurance program. 3. Equipment. 4. Service, providing storage and containment of biological test systems.	Statutory Instrument 1999 No. 3106: The Good Laboratory Practice Regulations, Statutory Instrument 2004 No. 994: The Good Laboratory Practice (Codification Amendments Etc.) Regulations, Guide to the UK GLP, Medicines and Healthcare Products Regulatory Agency[1].

[1] http://www.mhra.gov.uk/index.htm

Country	Order of monitoring procedures	Source
	5. Apparatus, materials, reagents and testing samples. 6. Test systems. 7. Standard operating procedures. 8. Implementation of the study. 9. Reporting of study results. 10. Storage and preservation of documentation and research. – The report on the results of the inspection is prepared and it is the basis of a decision on the UK GLP Principles compliance of the laboratory, and on the decision to include the laboratory into the UK monitoring programme. – Laboratories that are members of the Monitoring Program should be checked on compliance with the GLP Principles to maintain membership in the program each 1-2 years.	
Switzerland	– For participating in the GLP Compliance Monitoring Programme, a written application in accordance with article 5 OGLP should be submitted to the Notification Authority for Chemicals (NAChem). – The competent GLP Compliance Monitoring Unit will discuss the request with the applicant and outline the further procedure (e.g., preparation meeting, pre-inspection visit, etc.). – The prospective test facility should already posess good experience in GLP studies, having completed two studies per area of expertise (exceptions to this rule might be granted by the GLP authorities). – Prior to conducting an inspection, the responsible GLP Compliance Monitoring Unit requires the test facility to submit the following documents: 1. (actual) name and address of the test facility; 2. site plans documenting the use of the individual premises; 3. organization charts documenting the name and position of the test facility management, the personnel in charge of quality assurance and the study directors; 4. name and address of a contact person; 5. standard operating procedures for quality assurance; 6. a list of all standard operating procedures; 7. the relevant study categories; 8. a list of all studies planned over the next six months with the relevant schedules; 9. a list of all studies conducted over the last six months, or still being carried out, in the relevant	Swiss GLP Compliance Monitoring Programme, Ordinance on Good Laboratory Practice, Guidelines on the interpretation of the GLP Principles

Country	Order of monitoring procedures	Source
	study categories. In case of routine inspection, the list should cover all studies conducted since the last inspection. – Based on the statement of the inspectors in the final report, the Notification Authority for Chemicals then issues the decision concerning the compliance with the Principles of GLP. – If the GLP compliance is confirmed for an inspected test facility or an audited study, and the decision becomes effective the test facility (if it was a first inspection), or the study will be listed in the GLP register. – Laboratories listed in the registry are regularly checked on compliance with the GLP Principles for further presence in the Swiss GLP Registry.	
Germany	– Test facilities must submit to the Regional Authority of GLP: 1. The completed form in English. The form must contain detailed description of the tests conducted in the laboratory. 2. Documented characteristics of the test center. 3. Information on contacts with foreign laboratories and with regulatory bodies of other countries in the exchange of research results. – During the inspections the following documented characteristics of the test center / information on past GLP inspections are checked: 1. Organizational and administrative structure. 2. Qualifications of staff. 3. List of GLP tools, test systems, standard procedures. 4. Schedules of all the ongoing trials at the moment of inspection. 5. An example of a research plan. 6. An example of the final report on the study. 7. Type and size of the laboratory (e.g. number of personnel, the scope of testing, any sponsors). 8. List of all completed, ongoing and stopped studies at least since the last inspection. 9. Quality assurance program. 10. Plans for the buildings / locations (marked GLP areas).	Manual for Inspectors Monitoring Compliance with the Principles of Good Laboratory Practice[2]

[2] http://www.bfr.bund.de/cm/349/glp_manual_insp.pdf

Country	Order of monitoring procedures	Source
	– The report with the results of the inspection report should be prepared. Based on the report a decision is made about compliance of testing laboratory with the GLP Principles. – Laboratories that are members of the Monitoring Program should be checked on compliance with the GLP Principles.	
Slovakia	– A laboratory that wants to be a member of the national program (SN GLP CP) sends to the Slovak National Accreditation Service (SNAS) a completed application form for a statement of compliance with GLP Principles, including the application (TL 501 / G and TL 502 / G), signed by the legal representative. – SNAS Secretariat checks all the documents of the applicant and, in accordance with the current legislation, forwards them to the GLP Department. SNAS also issues an invoice for acceptance to the applicant. – If the application meets all the requirements of the GLP Department, the Department calculates the cost of services required and, after payment by the applicant, forms an inspection team. – The report with the results of the inspection should be prepared. The report contains conclusion of the presence of any deviations from the GLP Principles. In case of the presence of any deviations from the Principles, a letter indicating deviations that need to be corrected and the timing to eliminate these deviations is sent to the test facility. – The GLP Committee discusses the inspection results and verification of corrections, and recommends the SNAS Director whether to issue or not a certificate of compliance with the GLP Principles and to include or not the laboratory into the national program. – Laboratories involved in the GLP Principles compliance monitoring program are regularly checked for the compliance with the Principles.	Slovak National GLP Compliance Programme[3]
India	– A Test Facility desirous of obtaining “GLP Certificate” from the National GLP Compliance Monitoring Authority (NGCMA) shall submit an application in a prescribed Application Form (Document No. GLP-102) along with the prescribed non-refundable application fees of Rs.10000. – Copies of all documents submitted along with the application (e.g., organizational charts, floor plans, master schedule etc.) should be authenticated with dated signature by the laboratory's management.	Terms and Conditions of NGCMA for obtaining and maintaining GLP certification by Test Facilities

[3] http://www.snas.sk/e/files/pdf/Slovak_National_GLP_Compliance_Programe_2011.pdf

Country	Order of monitoring procedures	Source
	– The applicant laboratory shall offer its records and facilities under the scope of certification open for inspections by NGCMA. – If the application is found complete and eligibility criteria are met, NGCMA will organize inspection of the test facility. Test facility Inspection means an on-site examination of the laboratory's procedures and practices by inspectors appointed by NGCMA to assess the compliance with GLP Principles. – The report containing the results of the inspection should be prepared. Based on the report a decision on laboratory's compliance with GLP Principles is made. – GLP certification awarded to a test facility will be valid for a period of three years. After receiving a GLP compliance certificate the laboratory becomes a member of the National GLP Programme and has to maintain its membership by paying an annual membership fees of Rs.10,000. – Laboratories having the GLP Certificate have to be checked each three years for the compliance with GLP Principles.	

To obtain GLP-compliant status laboratories should get a GLP-certificate and before that – send a special application form for inspection to prove it. GLP-certificates last 3-4 years and have to be obtained again after expiration date. The number of GLP-compliant laboratories differs between the countries we analyzed: in Germany there are about 200 such test facilities, in India – 24, in Slovakia – 6 and in Switzerland around 30 ones.

Test facilities pay all costs and fees for obtaining a GLP-certificate and inspections for that purpose. National GLP programs and principles of price calculation for statutory services contain fees range for inspections and membership in the GLP program. They vary depending on the type of inspection and laboratory classification. In India the application fee for carrying out an inspection for obtaining GLP-compliant status is 1000 rupees or 144 euro plus inspectors' transport costs. In Slovakia the first application costs 233 without VAT while the re-inspection costs 180 euro. The inspection fee is calculated according to a special formula. In the UK annual fee is determined by the laboratory classification and depends in the number of days the inspection takes. In 2011-2012 the fee for one inspection day amounted to £2583 (3036 euro). The costs of GLP inspections are shown in Table 2.

Table 2 — Costs of GLP inspections in the countries

Country	**Procedures and costs for obtaining GLP Certificate**	**Source**
United Kingdom	In the UK, the annual contributions are determined by the classification of laboratories. Laboratories are classified according to the number of inspection days required for the inspection of the premises. Charges correspond to that part of the cost of the UK GLP Monitoring Authority, which can reasonably be attributed to the cost of the inspection and delivery of services. Fees for 2012 – 2013 were, depending on the classification of test facilities (£2583 (€3036) for inspection-day): – (inspection lasts more than 6 days) — £15504; – (inspection lasts from 4 to 6 days) — £10336; – (inspection lasts from 2 to 4 days) — £5168; – (inspection lasts from 1 to 2 days) — £2584; – (inspection lasts less than 1 day) — £1380.	Website of Medicines and Healthcare Products Regulatory Agency
Switzerland	The cost of inspection is determined individually, typically paid for by participant with a per diem and expenses charge. Neither exact numbers nor any methodology for price calculations were found.	ELAB GLP Subcommittee Executive Summary and Final Report (LabLynx laboratory information management system)[4]
Germany	The cost of inspections varies among federal lands.	Decree on the

[4] http://www.epa.gov/elab/pdfs/archives/glp02697.pdf

Country	Procedures and costs for obtaining GLP Certificate	Source
	For Bayern: — Issuing the GLP certificate– 1500–15000 €; — Change or addition to GLP certificate – 125 – 10.000 €; — Routine inspection, verification of the compliance the provisions of the basic GLP (Art. 21 of the Law on Chemical Substances) – 750 –15.000 €; — Request for inspection (Art. 21) – 50 –200 €; — Action on a request from the authorities – 150 –5.000 €; — Issuing the regulation on prohibiting activities – 50 –500 €; — Recall or return of GLP certificate – 75 –2.000 €	classification of costs
Slovakia	Fee for consideration of primary application is 233 euros without VAT, secondary – 180 euros. There is a special formula to calculate the cost of inspection GLP: C = H*(D + M + U), where D –cost of the work of the head of the inspection team, M – the cost of work of an inspector, U – the cost of work of an expert, H – the number of hours spent on inspection. According to the formula the minimal cost of one hour of the inspection is 33 euro without VAT Number of hours spent on inspection depends on the number of employees. There are several steps usually distinguished: preparation and review of the documents, inspection, and preparation of the report.	Principles of Price Calculation of the SNAS Services
India	– non-refundable registration fee — Rs. 10,000 when submitting an application; – when test facility becomes a member of the National GLP Programme and has to maintain its membership by paying an annual membership fees of Rs.10,000. All the costs are paid by test facility; it also pays for the inspection to obtain or renew the certificate. The costs of inspections are not publicly listed.	Terms and Conditions of NGCMA for obtaining and maintaining GLP certification by Test Facilities

Overview of general issues in implementing GLP

It is useful to point out similar characteristics and special features of GLP principles implementation in five countries. Each country assigns one or a few regulatory authorities

responsible for GLP implementation in chemicals regulation as a part of the national GLP compliance monitoring program. These are environment and human health safety authorities. Regulatory authorities fully support test facilities and other agents in the area of their responsibility. One or a few national GLP compliance monitoring authorities are established under the responsibility of the regulatory authority. Its quantity often depends on the federal structure of the country. This authority is usually statutory. Web pages of national monitoring authorities contain lists of GLP-compliant test facilities. In each country chosen for analysis laboratories from non-members of MAD can take part in their monitoring programmes.

The structure of national GLP compliance monitoring authorities is similar. They determine precise mechanisms of laboratories' monitoring, requirements for inspections of test facilities and study audits. In the UK, India, Slovakia and Switzerland GLP policy is carried out by one or two national monitoring authorities while in Germany due to its territorial characteristics monitoring is provided by authority in every federal land.

Each country alters its own legislation in accordance with OECD recommendations: adopts new acts and ordinances (related to GLP) or changes existing regulations of chemicals (acts related to chemicals).

Mutual acceptance of data is provided by the decisions of OECD Council while there are no specific national legal instruments for this purpose. This often results in harmonization of process of mutual acceptance of data.

GLP compliance monitoring organization is similar in the countries we considered. Inspections are conducted on average every 1-2 years. Their types are the same in all countries because they comply with OECD standards (first inspection, routine inspection, inspection without delay, re-inspection, final inspection, study audit). The appeal procedure also possesses the same pattern (oral discussion, sending appeal to the national GLP compliance monitoring authority, processing the appeal and notification).

In each country the test facility obtains a GLP certificate with data similar for all the countries. The fee for the certificate differs. In India where GLP system is parallel and voluntary the fee is the lowest while in the UK – the highest.

GLP Principles are an acknowledged international standard for conduction of non-clinical test studies. We analyzed how Germany, UK, Switzerland, India and Slovakia successfully deal with implementation of OECD's recommendations, establish national GLP systems and become members of MAD agreement. UK was the earliest one to establish GLP principles (1990) whereas India was the latest (2003). In Germany, UK, Switzerland and Slovakia GLP principles are obligatory for specific studies (non-clinical regulatory studies). Legislation of these countries

contains ordinances that involve obligatory following GLP principles. In India GLP compliance monitoring system is voluntary and parallel.

The number of GLP-certifies laboratories increases worldwide and more and more countries with advanced chemical sector successful in export join the MAD agreement. This category includes Germany, Switzerland, UK. Chemical sector in Slovakia and India persistently accelerates and actively improves. GLP-certificate mainly obtain large laboratories that find the costs for re-equipment according to GLP principles acceptable. Each country implements OECD recommendations in its own way: establishes national GLP compliance monitoring authority and GLP national program, changes national legislation and adopts new legal acts. Such national characteristics as federal structure, quality of international affairs, status of research and chemical sector play an important role.

Economic effects of usage of GLP principles are not yet fully studied but so far international experience shows that GLP and MAD implementation bears important advantages for its members. They include absence of duplicative testing, mitigating non-tariff trade barriers, creating a level playing field for chemical firms, development of integration and, in addition, limiting the use of testing on animals, providing sustainable development and green growth and improving risk assessment and management methods.

2. Assessment of possible risks and consequences for operation of Russian laboratories and for other economic agents due to the ensuring of recognition of non-clinical studies conducted in accordance with OECD Principles of Good Laboratory Practice

According to international studies on the impact of changes in management of chemical substances on economics agents (Table 3) to analyze the effects of Russia's accession to the system of MAD / GLP three groups of subjects of economic activity were selected:

- Laboratories conducting non-clinical studies.
- Chemical enterprises that use their services.
- Regulatory authorities (Federal Executive Authorities — FOIV hereafter).

Table 3 – Review of research analyzing impact of REACH and GLP principles on chemical industry

Article/Working paper	Dependent variable	Explanatory variable, input data	Data	Model, impact	Notes
Ackerman, Stanton, Massey (2006)	- Direct and indirect employment in US-EU chemical export; - Volume of chemical export (monetary and as a GDP share)	- share of production exported to EU - share of production affected by REACH - employment in chemical sector	Calculations cover 2002 and 2004 r. for 43 states	Quantitative estimation of exporters' costs	Forecast costs are relatively small (10% of export on average)
Little (2002)	Output of German chemical industry, % change Value added of German economy Innovation Investment Export Forecast number of substances 'on exit'	**Costs** –registration of substance, registration for use; Number of intermediaries; Number of categories for specific use **Time** – time costs for registration, registration for use; **Authorization** – restriction on number and area of use of hazardous chemicals **Transparency** – level of information transparency Restriction on use of dangerous chemicals	2 industries: raw textile, processing/manufacture of textile	Significant variables: negative effect – registration costs, registration process for intermediaries. Time costs are significant for firms with a high innovation share (idle period – loss of competitiveness) – increase in costs Registration for use – categories for use; number of parallel registrations of one substance increases costs Substitution effect of more costly substances not depending on their hazard to human health or environment (elimination of some substances from the market)	3 scenarios – depending on the degree of implementation of standards – low, medium and high level of 4 variables. It is important to understand, which substances are registered – based on one or several essences– because all costs are associated with the substance.
Ministry of Economic Affairs and Labor, Poland (2005)	Average annual costs of Polish chemical Innovation Costs of laboratories	The higher the total output of the firm is; price per unit of production; longer the period of allocation of REACH implementation	Producers of chemicals and chemical production; Distributors; Importers; Final consumers of	Large firms with diverse production will be least affected. Some small firms can quit the market due to unbearable	Considered stages – pre-registration; registration; testing; authorization

Article/Working paper	Dependent variable	Explanatory variable, input data	Data	Model, impact	Notes
	that carry out registration testing of chemicals Employment in laboratories	costs, the lower annual costs are. Costs are higher for importers; Information exchange: the lower awareness is, the higher the costs are	chemical production (textile, electronic, automobile industries) Survey of 78 firms, 28 of them – large (более 250 чел.) and 50 small ones	increase in costs Decrease in innovation potential and и competitiveness Decrease in employment level Change of business profile	
Canton, Allen (2003)	Estimation of effect on final consumers (share of chemicals which will crowded out from the market) Number of firms Production price	Turnover Value added Overheads Marginal costs Individual demand elasticity Elasticity of aggregate demand Number of submarkets Elasticity of substitution between chemicals in the market	5 industries: Basic chemicals Pesticides Dyes Pesticides Soaps and detergents Other chemicals	Microeconomic model of monopolistic competition (Dixit, Stiglitz (1977)) Differented production, returns to scale 2 scenarios. Normal expectation – Higher substitution costs-chemicals are crowded out from the market due to increase in the total industry costs (due to price increase)	The following process stages are considered: registration, testing Only impact of costs is analyzed and not international competitiveness
Ackerman, Massey (2004)	Price elasticity of demand Price elasticity of supply Costs/revenue ratio		Single chemicals market	Microeconomic model. Response of market to increase in costs is estimated	

The general population was classified as chemical enterprises and testing laboratories, selected from the RUSLANA database (Ruslana, Bureau van Dijk) according to the following codes of *Russian National Classifier of Economic Activities* (OKVED):

- Manufacture of chemicals (OKVED codes 24.XX.XX).
- Technical testing, certification and research (OKVED codes 74.30.XX).

Chemical enterprises have been selected as the general population, as the chemical manufacturing sector that produces goods is most likely to fall under the influence of the GLP principles. The choice of RUSLANA database is explained by the presence of most comprehensive set of the characteristics of the firms in RUSLANA compared to the other sources of similar information[5]. Total number of the firms from the selected industries is 5725 (3423 if testing laboratories are excluded), but the number of firms with present contact details is 4733 (2821 if testing laboratories are excluded).

Firms that produce:

- Chemical substances for industrial use account for 76.3%[6] of total population (2090 firms);
- Pesticides account for 2.9% of total population (79 firms);
- Medical substances (including substances for veterinary use) account for 7.3% of total population (199 firms);
- Cosmetics – 13.4% of total population (368 firms).

The sample was constructed employing the methodology developed by the World Bank based on the population described above.

We conducted survey and interview of the following economics agents: firms (275 respondents), laboratories (25 respondents) and regulatory authorities (3 respondents). Interview on the phone was used as a survey method. The list of 25 surveyed state laboratories is in the Annex M (coordinated with the Customer).

Chemical firms were selected from the sample firms from 11 regions of Russia (see Annex in Part 2 of the Final Report for methodology description): Moscow and St-Petersburg;

[5] Examples of other Russian databases: EGRUL, SPARK, FIRA. Of all the listed, RUSLANA is the most comprehencive.

[6] Percentage is computed as a share of the firms (%) to the total number of firms that satisfy criteria of the selected industry classification. This (latter) number does not include firms that produce ink, artificial and synthetic fibers and other chemical products (OKVED codes 24.66.2, 24.66.4 and 24.70) and the laboratories for technical testing, certification and research (OKVED code 74.30).

Moscow, Nizhny Novgorod, Samara, Sverdlov, Rostov, Novosibirsk and Volgograd regions and also Krasnodar and Tatarstan regions. Table 4 shows the shares of the firms from the sample exporting their products abroad, importing products as inputs and spending on R&D among small, medium and large enterprises.

Table 4 — Shares of firms exporting their products abroad, importing products as inputs and spending on R&D among small, medium and large enterprises, %

Firms	Exporters	Importers	Spending on R&D
Small (less than 20 employees)	37.50	41.00	66.00
Medium (20–100 employees)	47.97	52.50	67.50
Large (more than 100 employees)	65.96	68.18	81.82

Regulatory authorities that have been surveyed are the following:

- Russian Ministry of Health (Minzdrav Rossii)
- Russian Consumer Watch (Rospotrebnadzor)
- Federal Accreditation Service (Rossakkreditatsiya).

The questionnaires and interviews focused on the following aspects:

- Main problems of Russia's accession to the OECD system of MAD / GLP and the possible changes in the responsibilities of the federal executive authority;
- The impact of Russia's accession to the OECD system of MAD / GLP on different sectors of the economy, and the admission of products of various groups of producers to the market;
- The impact of Russia's accession to the OECD system of MAD / GLP (complication or alleviation);
- Change in the intensity of competition;
- Change in the volume of documentation for product registration;
- Change in the output, in the price of services, in the availability of information, and in the scientific potential;
- Measures to counteract the possible negative impact on economic agents, etc.

Surveying of economics agents

Laboratories

1) 56% of laboratories spend money on R&D.
2) Laboratories conduct on average from 3 to 60000 studies for Russian firms, and 52% conduct more than 10000 studies (14550 on average). 20% of laboratories

conduct studies for CIS countries and 16% of laboratories conduct studies for companies from EU and USA. 31.58% of respondents conduct studies for Russian exporters.

3) 28% of respondents evaluated competition in their market as insignificant and the same number – as serious, 12% evaluated competition as highly intensive and 32% of respondents – as average. Figure 3 shows the distribution of the evaluation of competition intensity for all respondents as well as for laboratories spending money on R&D. 71.43% of laboratories which spend money on R&D evaluate competition as insignificant or average whereas almost the same share (78.57%) expect that it will increase.
4) Under GLP Principles implementation:
    a. 36% of respondents expect an increase in provided services;
    b. 52% of respondents consider raising prices for services whereas the remaining 48% are not going to do it;
    c. 36% respondents believe the information to become more available (60% do not expect it).
5) Under unilateral acceptance of data:
    a. 68% expect increase in amount of registration documentation
    b. 60% expect their research potential to rise when Russia enters one-sided MAD agreement.

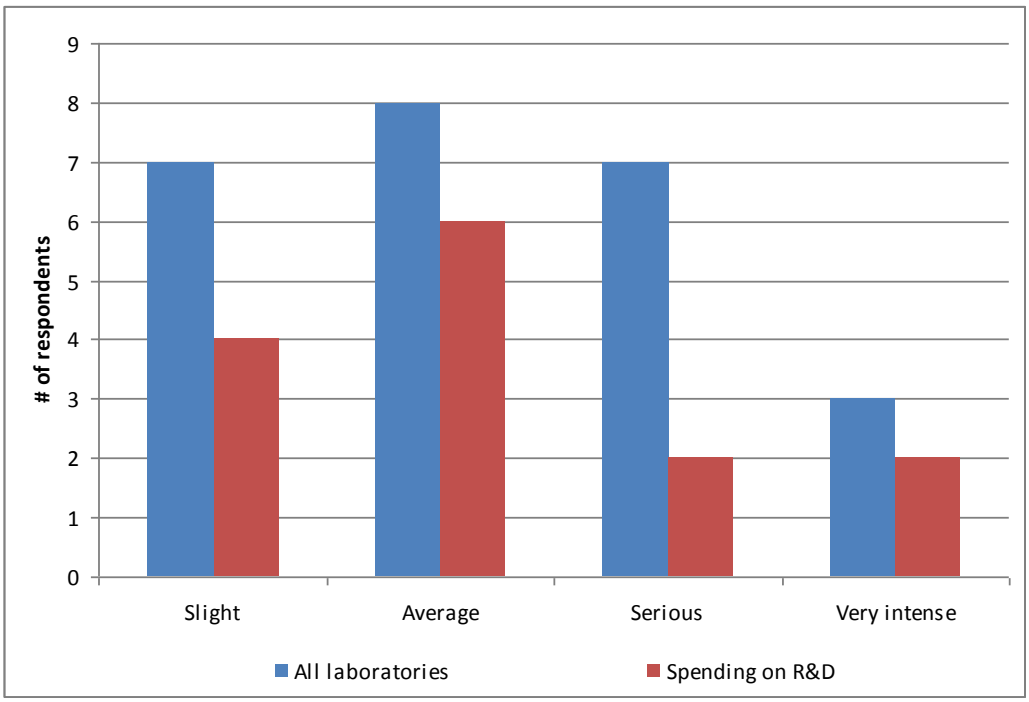

Figure 3 — Evaluation of competition intensity by laboratories

Figure 4 shows distribution of the laboratories' expectations about changes in admission of various substances to Russian market.

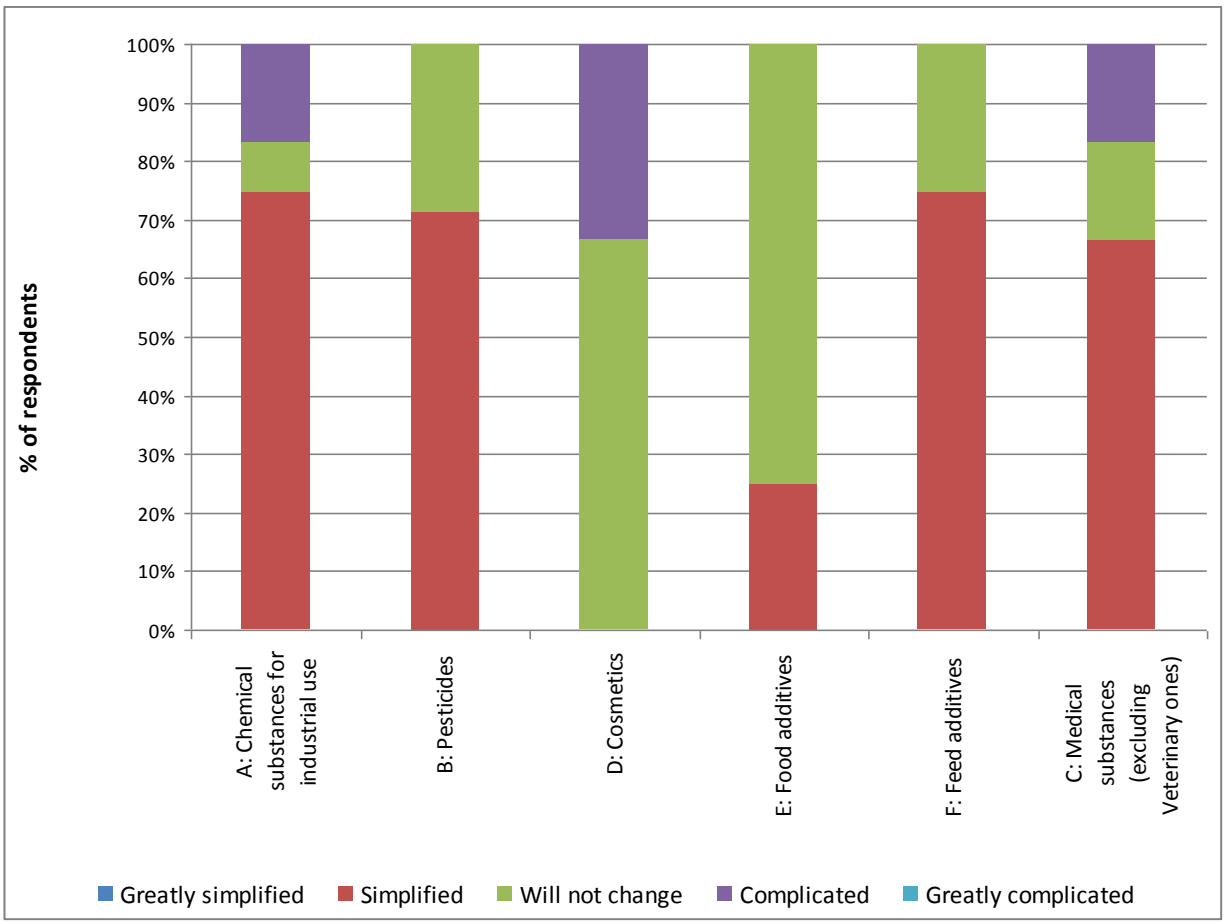

Figure 4 — Evaluation of expected changes in admission of substances to the market by laboratories

Chemical Enterprises

1) Large firms believe that they face more intensive competition than small and medium enterprises.
2) Two thirds of large firms export their products abroad and import foreign products as inputs for production while 80% of large firms do their own R&D. 66% of small and medium enterprises also do their own R&D, while half of medium and 40% of small import products as inputs. At the same time only 33% of small and around 50% of medium enterprises export their products abroad.
3) Firms that produce food and feed additives face the highest level of competition while the firms that produce medical substances, veterinary substances and cosmetics face a slightly lower level of competition (Figure 5).
4) Under GLP Principles implementation:
    a. Rise in the costs for registration is more likely for the exporters.

b. Rise in the costs for registration is less likely for the enterprises that conduct their own R&D.

c. 40% are going to increase their prices.

5) Under unilateral acceptance of data:

a. Around 25% of all respondents expect negative consequences in the product admission to the market and in the change of competition intensity.

b. Investments in the following areas will be demanded (categories are listed in the decreasing order in the amount of investments): education of employees, administration, marketing research and new technologies.

c. One third of the enterprises are going to hire new employees.

6) Half of all respondents do not expect any consequences in the sphere of change in competition intensity of in admission of products to the market under unilateral acceptance of data or under GLP implementation, and are not going to respond to the new standards in any way.

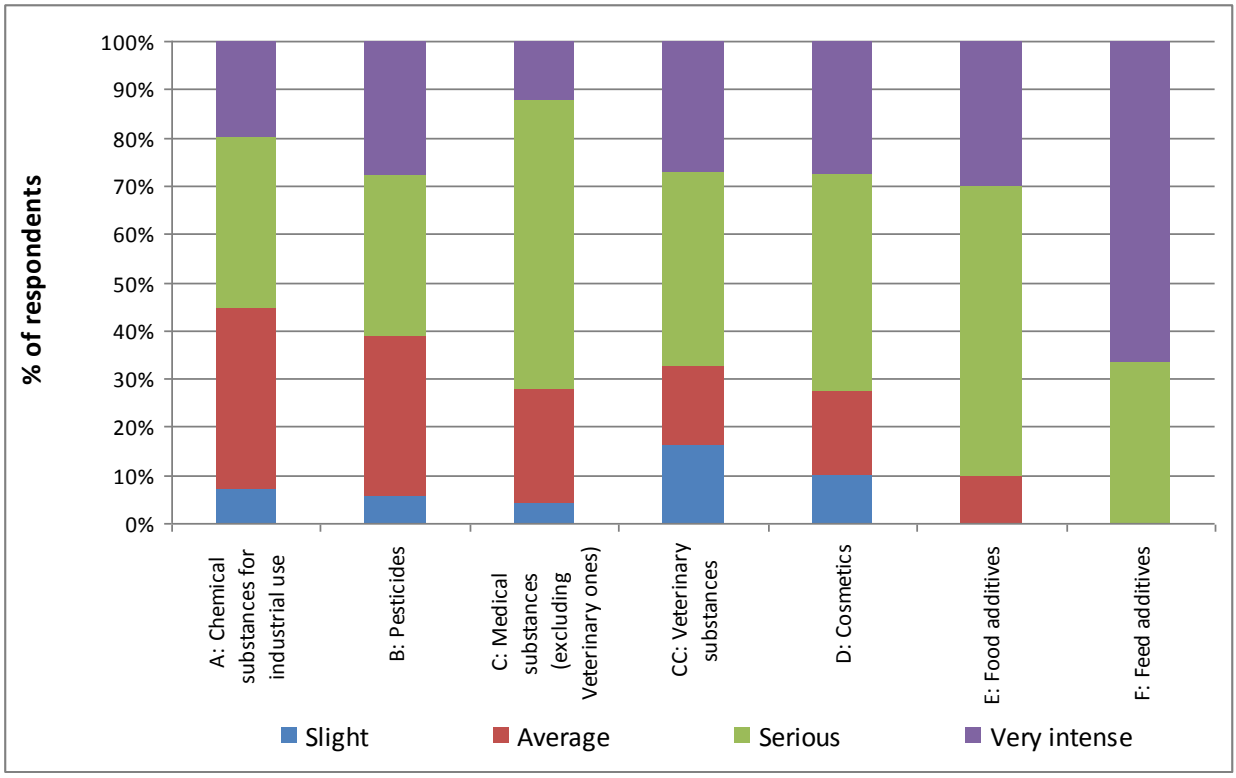

Figure 5 — Evaluation of competition intensity by chemical enterprises by product type

Regulatory Authorities

Federal Executive Body has noted the following consequences of unilateral acceptance of data and implementation of GLP Practice for agents:

1) Reduction of the competitiveness of products of Russian manufacturers and testing

laboratories;

2) Cost of equipping Russian laboratories, as well as costs of audits and inspections;
3) Slow innovative development and deterioration of the capacity of Russian scientific complex;
4) The GLP system is particularly relevant for Russian exporting laboratories, as well as for non-governmental laboratories wishing to demonstrate the level of compliance of the research according to international standards.

Interviewing Economic Agents

Laboratories

1) One third of the respondents expect an increase in output, 66 per cent expect an increase of the volume of documentation for new substances registration, but at the same time only half of the respondents are going to raise their prices (the other half is not going to change prices);
2) 66 per cent expect an increase of scientific potential under unilateral acceptance of the data of results provided by foreign laboratories.
3) More than the half of the respondents believe that the competitiveness on the market (figure 6) and the documentation volume to register new substances are going to increase.

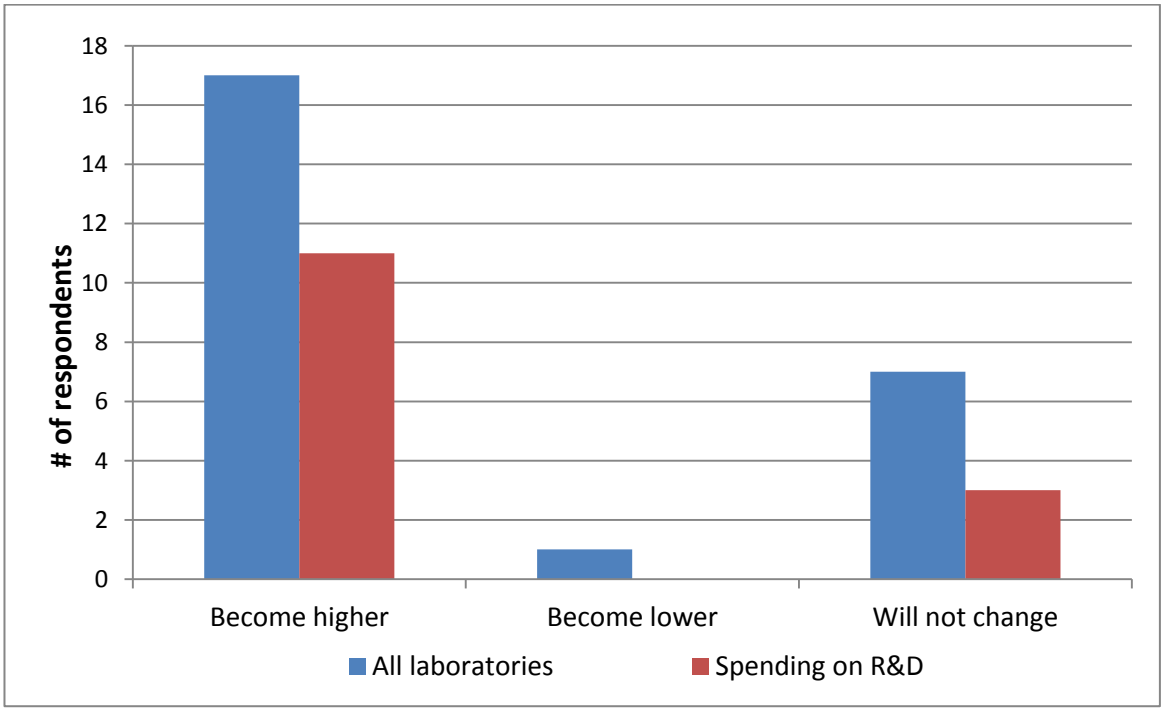

Figure 6 — Laboratories' expected competitiveness change

Chemical Enterprises

1) Under GLP Principles implementation small and medium enterprises expect a significant decrease in output, but insignificant for large ones;
2) Under GLP Principles implementation an increase in the costs for registration is less probable for the enterprises exporting their products.
3) Under GLP Principles implementation an increase in the costs is less probable for the enterprises providing their own R&D in comparison to all the rest.
4) Unilateral acceptance of the results provided by foreign laboratories will lead to the following types of investments (the categories are listed according to the decreasing order of the value of investments): education of employees, administration, marketing research, and new technologies. One third of the respondents are planning to hire new employees.
5) Unilateral acceptance of the results provided by foreign laboratories will not affect the prices, but the GLP Principles implementation will lead to the increase of prices.

Figure 7 shows the distribution of time-associated costs to register new substances according to the answers of interviewed chemical enterprises.

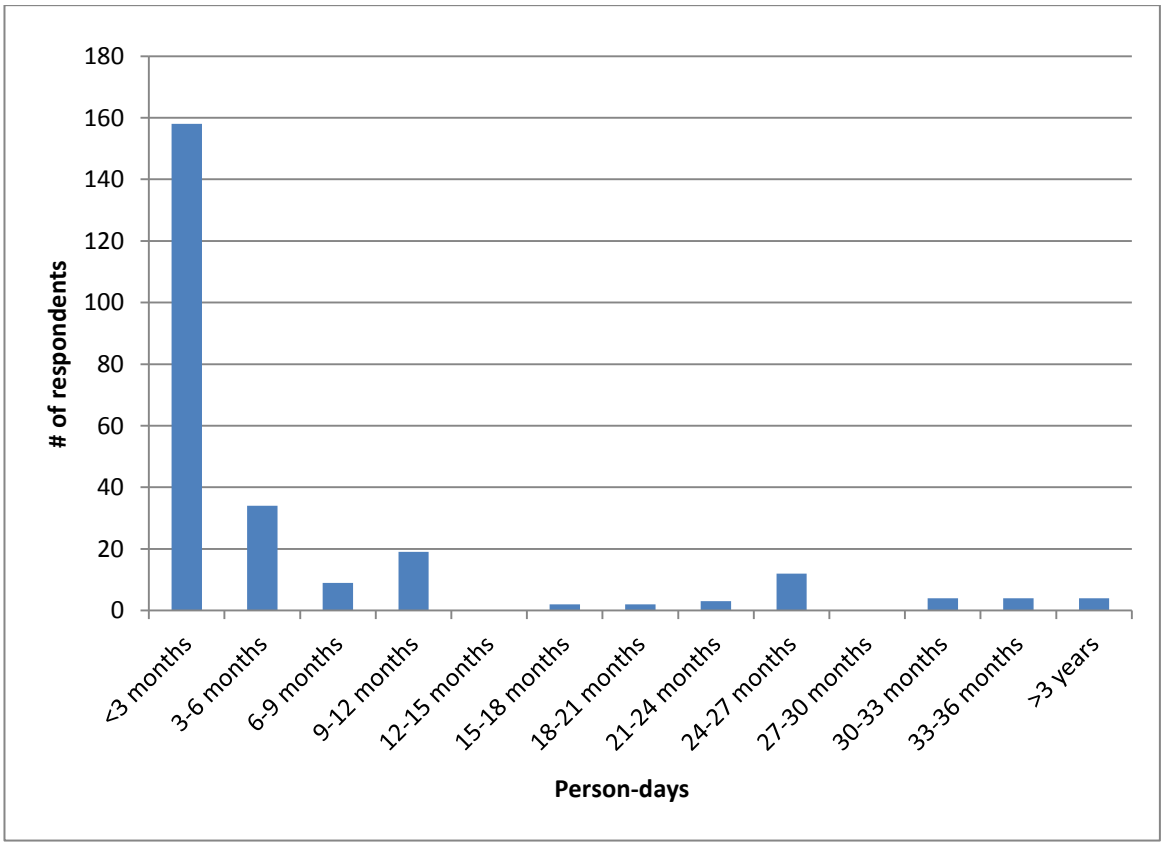

Figure 7 — Distribution of time-associated costs to register new substances according to the answers of interviewed chemical enterprises

Figure 8 shows the distribution of responses on the existing registration regime as an obstacle for the activity of chemical enterprises.

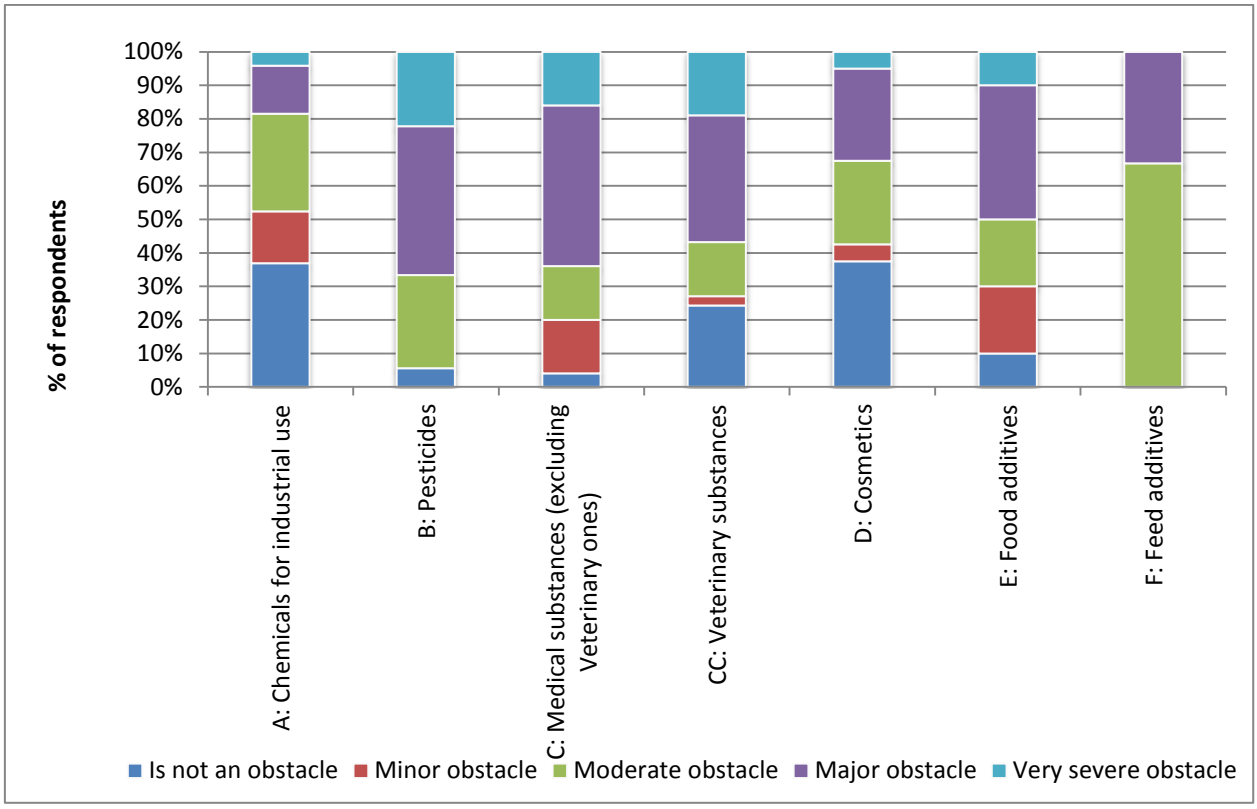

Figure 8 — Existing registration regime as an obstacle for enterprises

To assess the macroeconomic impact of the introduction of the GLP Principles for the chemical industry weighted average change in turnover and investments have been calculated. Thus, assuming that the answers of the respondents are representative for the whole industry, that is, that the entire chemical industry production estimates the consequences of the introduction similar to the respondents' answers, the following results were obtained. The expected change in turnover in the industry is 89 billion, or 5% (of the turnover in 2011), and the expected change in the volume of investment is 13.1 billion rubles, or 11% (of the total investments in 2010.) At the same time, the average rate of growth of trade volume in the chemical industry in 2009 was 30% per year, while investment growth rate — 6%. As can be seen from these figures, the expected increase in turnover from the implementation of the GLP Principles is not as large compared to the average annual growth rate in the sector, while the share of the necessary investment is almost two times higher than the average growth rate of investment in the industry.

General conclusions on the effects of the introduction of the principles of GLP, according to the survey of chemical enterprises, are presented in Table 5a, for testing laboratories - in Table 5b. Possible risks and competitive advantages that chemical enterprises and testing laboratories

will face under mutual acceptance of data and GLP Principles implementation are listed in Table 5c.

Table 5a — The positive and negative effects for the enterprises

Positive effects	Negative effects
Under GLP implementation – increase in the quality and quantity of products, – withdrawal of low-quality products and companies from the market, – improving the quality and facilitating the control of laboratory studies.	*Under GLP implementation* – increase in competition, – tightening the regime of registration, – increase in the share of foreign veterinary products in the Russian market, – risks of unfair competition, – increase in financial costs.
Under unilateral acceptance of data – increased exports among firms that export products abroad	*Under unilateral acceptance of data* – increase in competition (especially for exporters

Table 5b — The positive and negative effects for the laboratories

Positive effects	Negative effects
Under GLP implementation – increase in scientific capacity, – increase in the availability of information, – increase in the quality and quantity of research.	*Under GLP implementation* – increase in competition, – increase in the volume of required documentation, – additional costs, – higher risks, possible new ones.
Under unilateral recognition of data – simplified market admission of most of chemical products	*Under unilateral recognition of data* – increase in competition

Table 5c — Risks and competitive advantages of chemical enterprises and laboratories

	Enterprises	Laboratories
Risks	Unfair competition, increased competition, bankruptcy risks	Insufficient funding
Competitive advantages	Competitive prices, quality and volume of production, the uniqueness of products	Quality and the amount of research
Positive legislation	Improving the efficiency of registration, ensuring the reliability of results, increasing tariffs to protect domestic producers	Assurance of compliance with the international rules of research

Source: data from interviews of chemical enterprises and testing laboratories

Here we briefly point out the main findings of the survey of enterprises and laboratories. In general, the impact of the implementation of requirements for research in accordance with the GLP Principles will be significant for the most enterprises. The costs of registration of new substances will increase, the new conditions will require firms to invest significant amounts of money, and in addition, some firms expect to face new risks. A lot of legislative initiatives that would facilitate the activities of enterprises were suggested.

Compared to chemical enterprises, test laboratories expect serious consequences of the unilateral recognition of data on the competition and admission of products to the market, but do not intend to respond actively to the new standards. While most firms believe that their output will not change, more than half of responded laboratories tend to believe that competition in the market and the volume of the necessary documentation for the registration of substances will increase, and plan to raise prices for their services. The majority of laboratories expect to increase their own scientific capacity and facilitate admission of substances on the market. However, the additional costs associated with the implementation of GLP standards, hiring and retraining of personnel, purchase of new equipment and laboratory facilities will be needed. In addition, more than half of respondents expect to face new risks.

Regulatory Authorities

1) Part of the legal basis for the adoption of non-clinical research results obtained in the GLP laboratories already exists, the system of mutual recognition of data is voluntary;
2) GLP System in Russia must be coherent to existing state standards and technical regulations;
3) Creation of the Russian GLP system will improve product quality and safety. It will allow to receive accurate information on substances, archive the results of studies, and allow laboratories to enter the foreign market;
4) It is not recommended to introduce GLP System in the Custom Union — it is successfully replaced by the technical regulations.

Regression analysis

The regression analysis was conducted in the survey analysis. The analysis included building econometric dependence of changes in output, costs of registration, financial volume of necessary investments, the expected changes in competition, as well as changes in export and import on the selected explanatory factors.

The regression results show that the expected increase in output increases with the investment required, and that unilateral recognition and tightening of registration regime lead to the decrease in the expected output. However, the percentage change in the expected output is described by the equation which includes only the annual turnover. Also it is worth noting that small enterprises tend to assume greater expected change in output, compared with medium and large ones given the rest equal. The results for the estimation of expected changes in output are presented in Table 6.

Table 6 — Regression results for the expected change in output

Variables	**Change in output, %**	**Change in output (1 if will increase, 0 otherwise)**
	(1) [a]	(2) [b]
Annual turnover, mln. rub.	0.0475***	
	(0.00348)	
Required investment, mln. rub.		0.0123**
		(0.00543)
Reported low competition		0.894*
		(0.467)
Small firm	-10.60	-0.471
	(12.85)	(0.491)
Assumed price increase by MAD		-0.846**
		(0.388)
Expected tightening of registration regime		-0.660**
		(0.291)
Constant	22.73**	-3.512***
	(9.704)	(0.611)
Number of observations [c]	57	100
R^2	0.212	
Robust standard errors in parenthesis *** p-value <0.01, ** p-value <0.05, * p-value <0.1		

Note: [a] – OLS, [b] – Ordered Logit, [c] – number of observations is less than the number of surveyed firms because not all respondents answered some questions.

The expected change in costs is determined by the expected price change under the GLP principles implementation as well as by the expected tightening of registration regime. However, firms that export their products abroad believe that an increase in costs is less likely for them than for other firms given the rest equal, and small enterprises believe that their costs will increase by an amount greater than that of medium or large ones. In addition, firms engaged in their own research find that their costs will be lower than for the rest under the same conditions about holding all the other parameters equal. The results for the estimation of expected changes in costs are presented in Table 7.

Table 7 — Regression results for the expected change in costs

Variables	Cost change, %	Change in costs (1 if will increase, 0 otherwise)
	(1) [a]	(2) [b]
Output change, %	2.299***	
	(0.655)	
Total costs for registration, mln rubles	9.346	
	(4.992)	
Required monetary investments, mln rubles	2.204***	
	(0.617)	
Annual turnover, mln rubles	-1.530**	
	(0.440)	
Low competition	321.7***	
	(88.00)	
Small enterprise	52.63	0.164
	(29.14)	(0.282)
Expect increase of prices under MAD	-259.0***	
	(67.50)	
Expect increase of prices under GLP	81.19***	-0.701***
	(19.05)	(0.238)
Expect tightening of registration regime for substances	-259.4**	-0.496***
	(75.40)	(0.167)
Expected complication of product admission	203.4**	
	(59.84)	
Conduct own R&D	-208.7***	
	(58.41)	
Exporter		-0.584**
		(0.278)
Constant	-123.1*	0.350
	(55.91)	(0.245)
Number of observations [c]	19	264
R^2	0.834	
Robust standard errors in parenthesis *** p-value <0.01, ** p-value <0.05, * p-value <0.1		

Note: [a] – OLS, [b] – Ordered Logit, [c] – number of observations is less than the number of surveyed firms because not all respondents answered some questions.

Cash amount of additional investment is described by the following factors: time costs for registration of substances, annual turnover, total cost of registration and proposed changes in prices under the implementation of GLP principles. Small firms require much smaller investment than large and medium ones given the rest equal. The results for the estimation of required investments are presented in Table 8.

Changes in the intensity of competition are described by the equation that includes change in the expected costs, and change in the regime of production admission. The enterprises engaged in their own R&D expect a lesser increase in competition compared to other firms given the rest equal. The results for the estimation of the intensity of competition are presented in Table 9.

Table 8 — Regression results for the required investments

Variables	Required investment, mln rubles
	(1) [a]
Time costs, man-days	0.0587*
	(0.0334)
Total registration costs, mln rubles	-0.183
	(0.111)
Annual turnover, mln rubles	0.119**
	(0.0517)
Small enterprise	-13.31
	(8.079)
Expect price increase under GLP implementation	17.93**
	(8.995)
Constant	-3.772
	(9.211)
Number of observations [c]	86
R^2	0.266
Robust standard errors in parenthesis *** p-value <0.01, ** p-value <0.05, * p-value <0.1	

Note: [a] – OLS, [c] – number of observations is less than the number of surveyed firms because not all respondents answered some questions.

Table 9 — Regression results for the intensity of competition

Variables	Change in intensity of competition
	(1) [b]
Expected cost change, %	-0.0110**
	(0.00488)
Small enterprise	-0.383
	(0.391)
Expected complication of product admission	0.463*
	(0.265)
Conduct own R&D	-1.364***
	(0.501)
Constant	-1.807***
	(0.530)
Number of observations [c]	111
Robust standard errors in parenthesis *** p-value <0.01, ** p-value <0.05, * p-value <0.1	

Note: [b] – Ordered Logit, [c] – number of observations is less than the number of surveyed firms because not all respondents answered some questions.

Percentage change in export is described by the equation including change in output and turnover (Table 10), whereas the (bivariate) change in import depends only on the toughening of registration regime and complication in product admission (Table 11). Also, given the rest equal, an increase in the volume of the required investments has a positive effect on reducing import of inputs.

Table 10 — Regression results for the expected change in export

Variables	Change in export, %	Change in export (1 if will increase, 0 otherwise)
	(1) [a]	(2) [b]
Change in output, %	0.460***	
	(0.0894)	
Annual turnover, mln. rub.	-0.0199***	
	(0.00444)	
Small firm	-20.78	-0.0517
	(15.52)	(0.444)
Reported low competition		-1.064**
		(0.423)
Constant	21.57*	-1.386***
	(11.74)	(0.314)
Number of observations [c]	15	111
R^2	0.525	
Robust standard errors in parenthesis *** p-value <0.01, ** p-value <0.05, * p-value <0.1		

Note: [a] – OLS, [b] – Ordered Logit, [c] – number of observations is less than the number of surveyed firms because not all respondents answered some questions.

Table 11 — Regression results for the expected change in import

Variables	Change in import, %	Change in import (1 if will increase, 0 otherwise)
	(1) [a]	(2) [b]
Change in output, %	0.971***	
	(0.0246)	
Required investment, mln. rub.		-0.0175**
		(0.00736)
Small firm	-2.397	-0.745
	(4.720)	(0.913)
Expected tightening of registration regime		0.939*
		(0.487)
Expected complication of product admission		-1.056*
		(0.556)
Constant	5.469	-1.592***
	(4.588)	(0.522)
Number of observations [c]	11	54
R^2	0.988	
Robust standard errors in parenthesis *** p-value <0.01, ** p-value <0.05, * p-value <0.1		

Note: [a] – OLS, [b] – Ordered Logit, [c] – number of observations is less than the number of surveyed firms because not all respondents answered some questions.

Conclusion

The aim of the research was an expert assessment of the international experience of exploiting the principles of good laboratory practice for the purposes of regulatory decisions by the authorities of the Russian Federation. The research was also targeted at assessing the applicability of GLP for the Russian Federation and at preparing proposals for optimizing the market admission of products, which were researched according to the OECD's principles of good laboratory practice.

The following tasks were accomplished during the research:

a) The analysis of the legislation of a number of countries on the requirements for conducting non-clinical tests, including procedures and rules for admission of products to the market.

b) The analysis of normative and methodological documents by OECD.

c) The analysis of the mechanisms for accepting the results of non-clinical tests, conducted according to GLP principles in the countries, which joined the system for Mutual Acceptance of Data, MAD.

d) The analysis of the procedures for monitoring the compliance with GLP, based on inspections of laboratories.

e) The analysis of agreements and technical regulations of the Customs Union on the safety of products, which contain objects, tested according to GLP OECD.

e) The analysis of the legislation by the Russian Federation on products, which contain objects, tested according to GLP OECD.

f) The preparation of proposals for optimizing the system of admission of products, tested according to the GLP, on national market and on the territory of the Customs Union.

g) The development of the concept for the draft Agreement of the Customs Union on GLP.

h) The development of a draft Agreement of the Customs Union on GLP.

i) The development of draft legislation on implementing OECD's GLP in national laboratory practice, including requirements for laboratories and administrative procedures for monitoring.

g) The development of a draft methodology for assessing Russian laboratories in their ability to follow the requirements of OECD's GLP.

k) The assessment of Russian laboratories in their ability to follow the requirements of OECD's GLP.

It may be noted that formation of the institutional foundations for creating the system of good laboratory practice according to OECD requirements is directly linked to the necessity of creating national legislation, aimed at providing correspondence with the rules and procedures by

OECD. The national legislation should incorporate special issues, related to national regulation and regulation at the Customs Union. At the same time, to assess the readiness of Russian laboratories to the participation in GLP, the research conducted the study of Russian economic agents (including laboratories), according to the developed methodology.

The results of the research may be used by national authorities in developing various measures for perfecting administration and regulation of good laboratory practice in Russia.

References

1. Development. Environment Directorate. The OECD Principles of Good Laboratory Practice. – Organisation for Economic Co-operation and Development, Environment Directorate, 1992. – №. 45. http://www.oecd.org/chemicalsafety/testing/oecdseriesonprinciplesofgoodlaboratorypracticeglpandcompliancemonitoring.htm
2. Medicines Act. http://www.admin.ch/opc/de/classified-compilation/20011787/index.html
3. Agrochemicals Act. http://www.admin.ch/opc/de/classified-compilation/20100203/index.html
4. Chemicals Act. http://www.admin.ch/opc/de/classified-compilation/20021519/index.html
5. Biocide Act. http://www.admin.ch/opc/de/classified-compilation/20021524/index.html
6. The Good Laboratory Practice Regulations 1999. http://www.legislation.gov.uk/uksi/1999/3106/contents/made
7. The Good Laboratory Practice Regulations 2004 http://www.legislation.gov.uk/uksi/2004/994/introduction/made
8. German Chemicals Act. http://www.iuscomp.org/gla/statutes/ChemG.htm
9. Ministry of Economic Affairs and Labour, Poland. (2005) Results of the polish impact assessment of implementation of the REACH system (Registration, Evaluation and Authorisation of Chemicals) on the Polish chemical industry and downstream users
10. Ackerman F., Massey R. The true costs of REACH. – Nordic Council of Ministers, 2004.
11. Ackerman F., Stanton E. A., Massey R. European chemical policy and the United States: the impacts of REACH. – Tufts University, 2006.
12. Canton J., Allen C. A microeconomic model to assess the economic impacts of the EU's new chemicals policy //DG Enterprise. November. – 2003.
13. Little A. Economic Effects of the EU chemicals policy on the German textile industry. Report on the BMWA research project. 2002.