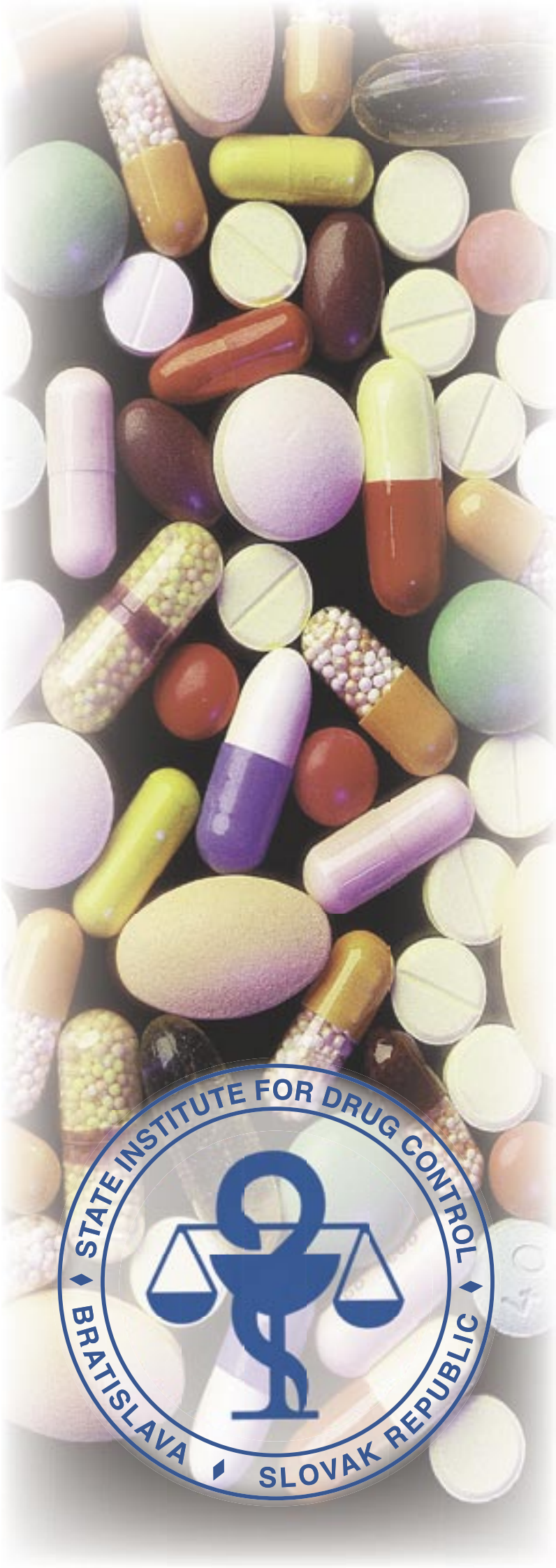
The State Institute for Drug Control

Slovak Republic



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ANNEXES:

1. Identification of SIDC

Name:	State Institute for Drug Control
Reporting to:	Kvetná 11, 825 08 Bratislava 26
Governmental Department:	Ministry of Health of the Slovak republic
Director:	Assoc. Prof. Ľudevít Martinec, PhD

Main activities:

The State Institute of Drug Control (in following text only „SIDC“) is according to the article 58 of the Act No 140/1998, Coll. on medicinal products and medical devices the authority of the state administration in the field of human pharmacy.
SIDC is a state budget organization directly reporting to the Ministry of Health of the Slovak Republic (in following text only „MHSR“). The head of SIDC is a director, appointed according medicinal act (No 140/1998) and a head of Service Office appointed according the Civil Service Act (No 312/2001).

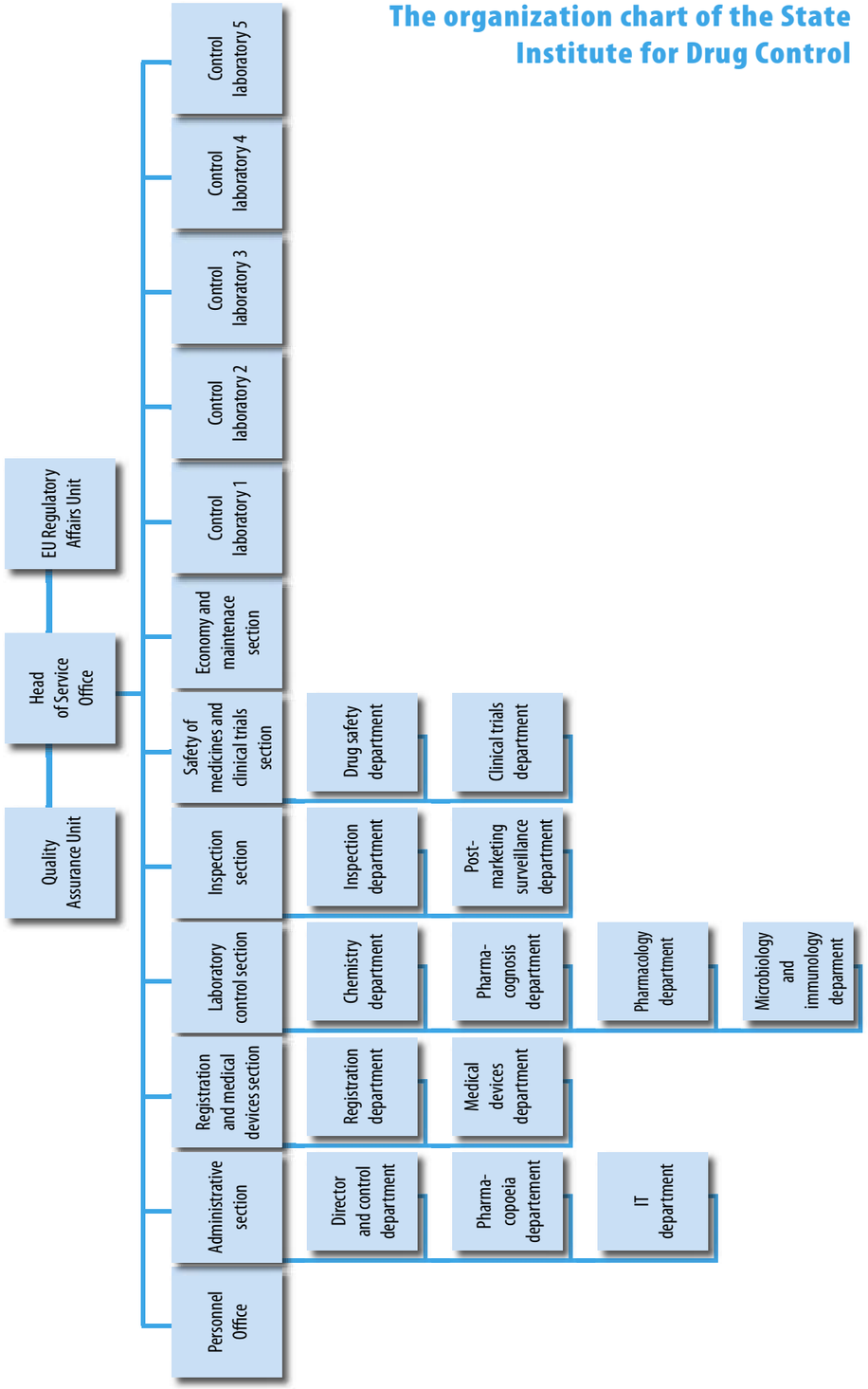
SIDC is an organization that ensures the state supervision and inspection of all pharmaceutical activities in the area of Good Manufacturing Practice (GMP), Good Distributing Practice (GDP), Good Laboratory Practice (GLP), Good Clinical Practice (GCP) and Good Pharmacy Practice (GPP) in the SR. The supervision over the quality, safety and efficacy, decisions making on registration of human medicines and issuing of certificates on assessment of compliance and testing of medical devices is being a part of it.

The cooperation with international institutions within the European Council, that we are the righteous members, The European Pharmacopoeia Committee, the European network of pharmaceutical activities in field of quality of drugs and its monitoring but also within the scope of activities connected with cooperation of the OECD authorities in the area of GLP, where we are connected with cooperating authorities and organizations, all this is an integral part of the main activities of SIDC.

Government Decree No. 1067, dated December 12, 2001 authorises to ministers and head of central bodies to conclude contracts with budget and contribution organizations in area of competence of their department.

The SIDC concluded a contract with the Ministry of Health of Slovak Republic for the year 2003, which was signed bilaterally on January 29, 2003.

The organization chart of the State Institute for Drug Control



Advisory bodies

For management and decision-making in particular fields of SIDC activities the following advisory bodies are established:

- Assembly for Drug Quality
- Pharmacopoeia Committee
- Committee for Safety of Medicines
- Committee for Medicinal Products
- Sub-committee for Immunological Products of the Committee for Medicinal Products
- Sub-committee for Phytotherapeutics and Homeopathics of the Committee for Medicinal products

2. The mission and perspective of SIDC

SIDC mission is the state supervision of the field of pharmacy, the control of manufacture and wholesale distribution of medicinal products and medical devices, the issuance of human medicines registrations, monitoring and assessment of data about reported accidents, defects and failures of medical devices. SIDC approves and controls the execution of clinical trials, testing of medical devices, regulates advertising including the sample medicine provisions.

In addition to above mentioned activities, SIDC carries out inspections of adherence to the principles of good manufacturing practice, good clinical practice, good laboratory practice, good distributing practice and good pharmacy practice and to the observance of provisions of the Slovak Pharmacopoeia and the Slovak Pharmaceutical Codex in the process of preparation of the mass- and individually-prepared medicines. Furthermore, SIDC compiles the Slovak Pharmacopoeia and the Slovak Pharmaceutical Codex (§45), imposes fines for shortcoming being disclosed and keeps the list of registered medicinal products and approved medical devices.

Being a member of PIC/S Scheme since 1996, SIDC was delegated for the first time to organize the annual seminar „The Inspection of Quality Control Laboratories“, which was held on the 2nd – 6th June 2003 in Bratislava, Slovakia. The seminar was highly appreciated by the PIC presidency as well as by the participants from 38 countries (pictures 1 and 2).

picture 1 ▲

picture2 ▼

As a part of pre-accession activities, special audits – so called benchmarking – were conducted in the bodies of regulation and control of medicinal products (drugs). The director of SIDC and the head of Quality Assurance Unit participated in the audits in Bulgaria and the Czech Republic. SIDC finally enjoyed the highest rating from the conducted audit among all ten accessing countries.

Due to the necessity of implementation of the quality systems complying to the criteria EC specified in ISO/IEC 17025 and

ISO 9004, the SIDC have received the approval of relevant financial budget and started appropriate reconstruction and enlargement of SIDC premisses (pictures 3 - 4 see the page 26).

Currently, the transformation of SIDC is being prepared. The material about transformation was discussed and ratified by the session of minister of health of the SR in December 2003. The material has been submitted for inter-ministerial procedure. After the incorporation of the comments, the completed document will be submitted to the Government of the SR. The document includes some new responsibilities of SIDC e.g. licensing of the manufacturers, more sanctions in cases of the violation of the law, and the name of Institute might be changed to the "Office for pharmacy the SR". If the proposed document will get governmental approval, SIDC will be independent from Ministry of Health of the SR and will be on the same official level as the other central governmental institutions.

The proposed variant guaranties that the state organization will be responsible for ensuring supervision of the quality, efficacy and safety of human medicines and medical devices. New office will be more professional and politically independent than the present SIDC in relations with European institutions and international institutions, e.g. OECD, PIC/S, WHO, EMEA and others. Several EU member countries already have institutions of similar type.

After SIDC transformation, the new office will get these new increased responsibilities:

- preparing the draft proposals to the Government of the SR on principal direction and priorities of national pharmaceutical policy
- to issue Official publication of the Office for Pharmacy of the SR
- to grant licenses for manufacturing medicinal products, manufacturing medicinal products from blood, licensing the blood banks, licensing medicines, medical devices and licensing health care in hospital pharmacies
- to issue GMP certificates according to WHO resolution No. WHA 50.3. (Annex 2) of May 1997, and EU: Commission directive 2003/94/EC, of the 8th October 2003
- providing corresponding information and data in the pharmaceutical policy for the interested stakeholders
- publishing the Slovak Pharmacopoeia, the Pharmaceutical Codex and other standard documents concerning the medicines, medical devices, problems of pharmacy and the policy in the area of medicinal products
- to cooperate with the European and other supra-national structures functioning in the area of the quality assurance, efficacy, safety and control of human medicinal products and related activities.

3. Activities / products of SIDC

3.1 Quality Assurance Unit

The international cooperation with EMEA has been focused on the exchange of information, participation in the implementation of the project of quality and assessment systems with the purpose of unified policy to be employed by the European agencies and mutual recognition. Within the project, 17 regulation institutes for human and veterinary drugs in 10 accessing countries were inspected. The inspections (Benchmarking visits) were conducted by the inspectors from EMEA, EU member countries as well as from candidate countries. Assoc. Prof. Ľ. Martinec in Bulgaria and Dr. I. Šidlíková in the Czech Republic participated in the benchmarking visit as the inspectors from the Slovak Republic.

The main effort was focused on the assessment of quality system and the benchmarking visit at SIDC was conducted in the 27th – 29th October 2003.

The results of the assessment of all the 17 agencies in 10 accessing countries were presented at the Integrated Quality Management Benchmarking Network Meeting held in December 2003 at EMEA, London, where SIDC enjoyed the highest rating. It means that our institute will be accepted in EU as an equal partner in the field of human medicines.

For the purpose of objective information and assessment of the contacts between the SIDC employees and clients, specific questionnaires have been prepared out and evaluated. The questionnaires were focused on the improvement of quality of the services:

- a client satisfaction questionnaire,
- an employee satisfaction questionnaire.

Our objective was to receive feedback for our assessment of the quality system. The conclusion of client questionnaires was that 80% of respondents are satisfied with the quality of our services and 71% of respondents have the confidence to the SIDC decisions and statements. The plan was developed and "the management review" was conducted in compliance with STN EN ISO 9004 for the purpose of assessment of efficiency of the implementation of the quality system and the execution of changes and improvements. The subsequently made management review report included the proposals of corrective measures, related responsibilities and deadlines.

Internal audits of individual units were performed according to the predetermined plan. *Inspections* made for the purpose of supervision over the operations having the SIDC authorization for pharmaceutical, toxicological and pharmacological testing were performed in compliance with the approved annual plan. Currently, 10 laboratories obtained the SIDC authorizations that are being audited year by year. The updated list of laboratories was published at the SIDC web site.

3.2 EU Regulatory Affairs Unit

On the 1st September, the EU Regulatory Affairs Unit reporting directly to the head of service office – i.e. to the SIDC director – was established. The main objective of the unit is the coordination of conceptual works in the field of human pharmacy of the state administration body, carried out in the programs of incorporation into EU. The coordination of activities related to the incorporation into the European structures, in particular DG-III-Enterprise and the coordination of harmonization with EU legislation and the SIDC statements towards legislative and other issues of the European Union and statements towards the EU legal disputes in the field of medicines and medical devices belong to many important tasks of the unit.

From its establishment, the unit worked in the area of coordination of EU legal documents related to the free movement of persons and documents related to the amendment of EU legislation and in the area of the transfer of current information from the sessions of the Pharmaceutical Committee, advisory bodies of the European Commission, in particular in EMEA. As a part of the coordination activity, the unit has started to prepare the proposals of nomination of SIDC representatives into the EMEA and EC advisory bodies, to become effective on the date of the SR access into EU.

3.3 Administrative Section

Director and Control Department

Control Division

In terms of the Act of the National Council of the Slovak Republic No. 85/1990 Coll. on petitions and Act No. 152/1998 Coll. on complaints, Control Division keeps the central registration of petitions and complaints and organizes scrutinizing the petitions and complaints that have been delivered to the institute. Control Division elaborated the report referring to the numbers, types and method of handling and justness of petitions and complaints for the year 2003 and presented it to the Ministry of Health of the SR. Three of the total nine complaints were assessed as justified and the measures eliminating the disclosed shortcomings were adopted.

Public Relations

Starting from the 1st July 2003, Public Relations Division was established as a part of Director and Control Department. Public Relations Division provides statements for media, monitors the press information, monitors the web sites of the institutions involved in drug policy and executes the agenda according the Act of the free access to information.

Metrology

Quality of measuring instruments and measuring equipment being in use in the Laboratory Control Section has been ensured in compliance with the requirements of Act No. 142/2000 Coll. in particular and with other related legislative standards of the Slovak Republic in the field of metrology as well as in compliance with the STN ISO standards for the demonstration of quality system operation in this area.

Our metrologist participated, as a member of the inspection group of Good Laboratory Practice (GLP), in the special GLP inspection of our institute which was a part of the OECD audit. With reference to this audit, the GLP SR monitoring program was recognized to be fully compatible with the OECD requirements.

Metrological quality of measuring instruments and measurements was systematically assessed as a part of both internal audits and external inspections of Good Manufacturing Practice conducted in the organizations supervised by SIDC.

The ongoing monitoring of microclimatic conditions in the 31 selected places of the institute is conducted and related records are being registered.

Pharmacopoeia Department

Pharmacopoeia – translations of pharmacopoeia monographs S–Z, general methods of analysis and standard terms of dosage forms to be included in the 6th volume of Slovak Pharmacopoeia 1 were elaborated in a unified style, the structural formulas were incorporated into the monographs and the editorial revision of technical style was conducted. The two-grade professional review was performed and the Slovak terminology of active substances was defined. Technical and editorial comments were incorporated into the text. The revision of the identity of the Slovak text with the applicable original of the European Pharmacopoeia was executed.

The 6th volume of Slovak Pharmacopoeia 1 was published in June 2003.

In line with the decision of the Slovak Pharmacopoeia Commission, the preparation of the 7th volume of Slovak Pharmacopoeia 1 has started with summarization and revision of the titles of reagents and methods of analysis The comprehensive index of Latin and Slovak titles of the monographs of active substances and excipients summarizing previous six volumes was elaborated. The purpose is to provide the users with a practical help for easier orientation in individual volumes of the Pharmacopoeia.

Upon manufacturer's request 23 translations of monographs were made.

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The following tasks related to the cooperation with EDQM were conducted from time to time: generation of standard terms of dosage forms, comments and the work schedule of the European Pharmacopoeia Commission.

Pharmaceutical codex - A preliminary list of monographs of the officinal and magistral preparations has been specified on the basis of documentation from the control laboratories 1-5 and the hospital pharmacies. To revise the monographs, ingredients necessary for the sample preparation were purchased. So far, 15 of 38 assigned preparations have been experimentally verified in accordance with the pharmacopoeia monographs; the achieved results of analysis confirmed that the revision was well-founded.

Information Technology Department

In terms of electronic processing of the registration documentation, the department was assigning SIDC codes and performed ongoing processing and updating of the database of registered medicinal products. The approved package leaflets and SPC from manufacturers were electronically processed and the operation of IT equipment in the institute was organized.

As for the publication activity, the department carried on with editorial works, publishing and distributing printed information materials (The Drug Risk, The Reports on Drug Quality, Annual Report).

The department participated in the technical processing of documents necessary for specialized seminars, conferences, trainings, lectures and presentations organized by other institute's departments.

3.4. Registration and Medical Devices Section

Registration Department

Granting of the Marketing Authorisations on registration was focused on improving the coordination of assessment of documentation related to the applications for registration, renewal and variation of human medicinal products. Standard working procedures for the individual activities of Registration Department were practically completed. Instructions for applicants as well as the application forms for a new registration, variation and renewal were updated and published at the SIDC web page.

The time-schedules of the Committee for Medicinal Products and its sub-committees introduced last year have been consistently respected. Written materials for negotiations have been sent to the members of committees and e-mail form has been used. The materials sent prior to the commission session facilitated and shortened the negotiations and generated more available time for discussion.

Within the internal trainings of the Registration Department the individual parts of Notice to Applicant have been discussed, which had significant impact on the improved work quality of the Registration Department employees.

Most important attention was paid to the EU pre-accession activities. Such activities were based on Methodical Instruction No. MP 5/2002. Due to the massive amount of documents submitted for individual phases and the necessity to impute the data into a database developed for this specific purpose in cooperation with the Information Technology Department, the corresponding works were time-, physically- and mentally-consuming.

Further tasks that were to be fulfilled in the framework of the pre-accession phases had been set in Methodical Instruction No. MP 3/2003 and covered submitting of complementary applications to the applications for registration that are currently being processed. Analyses made at the Registration Department resulted in the generation of new tasks that must be conducted prior to the access into EU. The pending applications have been separated into the 2 groups as "perspective" and "non-perspective" pending applications. The recommendation

of SIDC related to "non-perspective" pending applications has been followed by applicants. Most of the pending applications with granted marketing authorisation in other EU member states have been withdrawn by applicant.

Due to the fact that candidate countries will automatically take over the medicinal products being registered by a centralized procedure after their accession into EU, it was necessary to harmonize the Slovak versions of SPC, PIL and packages of the respective medicinal products with current conditions in EU, as to comply with QRD instructions. Five employees of the Registration Department contributed to above-mentioned activity.

Committee for Medicinal Products

The Committee for Medicinal Products had eleven sessions in 2003. At the sessions, totally **300** applications were discussed, thereof **288** were recommended and **12** postponed. In addition to the assessment of applications, current problems of registrations of human medicines were discussed, if necessary.

The conclusion as for the above information is that the standard of documentations submitted to the Committee on Medicinal Products has improved significantly and the number of postponed medicinal products has fallen accordingly, which applies particularly to the former „generic drugs".

Review of the medicinal product registrations in the year 2003

Total number of applications for registration	417
Decisions on marketing authorisation issued	381
Total number of applications for renewal	404
Decisions on renewal issued	536
Total number of applications for variation	1591
Decisions on variations issued	807
Decisions on rejection of applications for registration	1
Decisions on withdrawal of registration issued	190

Medical Devices Department (MDD)

The Medical Devices Department keeps the central database of registered medical devices being launched to the market in SR under obligatory reporting of the representatives of foreign and domestic manufacturers according to the Act No. 140/1998 Coll. in its later amendments and Orders No. 569/2001 Coll., 570/2001 Coll. and 572/2001 Coll. which are the modifications of directives No. 93/42 EEC, 90/385 EEC and 98/79 ES.

Step by step, Medical Devices Department took over the functions of a competent authority which monitors and processes reports of adverse effects of medical devices and keeps databases of notified of clinical trials of Medical Devices. Data from the respective Medical Devices registration application forms and declarations of conformity have been continuously processed and added into individual databases and registries in terms of given legal regulations.

Overview of the Medical Devices Department in the year 2003

accepted applications for certification	937
reports of adverse events	17
inspection requests	4
complaints	1
clinical trial notifications	3
assessment related to the wholesale activities	28
codes related to the reimbursement system assigned	5 470
codes related to the reimbursement system updated	4 990
inspections related to the wholesale activities	28
expert opinion of new standards	22
consultations related to governmental ordinances	184
repeated inspections related to the wholesale activities	3

3.5 Laboratory Control Section

Being a part of the state authority, the Laboratory Control Section is an executive section of SIDC in field of registration of medicinal products (drugs) as well as in the area of laboratory analysis of medicinal products during the process of registration and in the postmarketing surveillance.

The Laboratory Control Section is divided into Chemistry Department, Pharmacognosis Department, Pharmacology Department, Microbiology and Immunology Department and House of animals. All the departments focused their activities on fulfilling tasks related to major orientations in 2003.

The employees of the section participated in three international laboratory tests monitoring the laboratory performance within a given method.

The marketing authorization holders submitted, due to having of the upgraded registration documentation according to "acquis communautaire" on place, either confirmation or supplement of particular part of documentation. These both documents were in the section assessed.

Chemistry Department performed chemical, physical and pharmaceutical tests within the scope of control of medicinal products in registration proceeding and domestic and foreign medicines on market. Market surveillance was performed through the assessment of the submitted certificates of the imported drug batch. Methodical Instruction No. MP 6/2003 has been prepared. According to this Instruction, the test protocols issued by authorized laboratories will no longer be assessed.

Pharmacognosis Department evaluated herbal medicinal products, herbal substances and preparations obtained from herbal substances or herbal extractions. In addition, drugs containing narcotic and psychotropic substances, homeopathics as well as the medicines of assigned pharmacological groups containing active chemical substances were checked. Employees of the department organized the disposal of wastage from narcotic and psychotropic substances and precursors.

Pharmacology Department performed biological control of drugs on the market - mostly as a part of long-term orders. The reconstruction of the house for keeping animals started in September.

Microbiology and Immunology Department was monitoring efficiency and safety of blood derivates, vaccines and diagnostics produced in Slovakia. The control of foreign immunological products was carried out in a form of the assessment of certificates or as a part of registration proceedings. Microbiological purity of drugs from domestic and foreign producers was checked in various types of samples.

As a part of registration proceedings, **325 new registration documentations and 708 variations** of registration, **7 clinical batches, 22 certificates** as a part of systematic controls and **27 certificates** as a part of import were assessed and **434 test reports, 985 confirmations and assessment reports were issued within the updating procedure** of the registration documentations.

Five clinical complaints concerning clinical problems and 10 complaints related to the pharmaceutical quality of the medicinal products were assessed in the light of the samples analysis results. The following defects were disclosed: presence of pyrogens, fail in quality of drug substance, an unregistered medicinal product on the market, incorrect pH, presence of live insect.
Total number of processed items are 3 188.

3.6 Inspection Section

Inspection Section activities have been focused on supervising the practical implementation of the principles of Good Manufacturing Practice (GMP), Good Wholesale Practice (GWP), Good Pharmacy Practice (GPP) and meeting the standards of the Slovak Pharmacopoeia in the processes of preparation of mass- and individually-prepared medicines in terms of applicable legislation.

In the Q1, the tasks concerning the preparation and organizing of the annual training seminar for the PIC/S 2003 inspectors were performed. The seminar was held in Bratislava under the commission of the PIC/S executive bureau and the topic was: the GMP inspection in quality assurance laboratories of pharmaceutical producers.
In connection with the organization of the international seminar, the section carried out the following tasks:

The draft program was prepared and expert lecturers were invited. The PIC/S executive approved and adopted the draft program. Program was divided into four sections: International aspects; Specific aspects; Inspection aspects; Future. 19 lectures with 18 lecturers were included in the program. 4 workshops with following topics were prepared: Preparation of Aide Memoire; Microbiological monitoring, Validation, Documentation.
The internal document for seminar participants was prepared: Abstracts and lectures.
The inspection section coordinated scientific program at the seminar. An SIDC employee was authorized to coordinate the group and submit the document to the PIC/S executive bureau in Geneva.

95 delegates from 38 countries participated at the seminar. Scientific program more or less followed the plan. The participants highly appreciated the seminar, thus, this task could be considered as fulfilled. However, further tasks had to be fulfilled in Q2. It was necessary to coordinate the activity of working group for the preparation of Aide Memoire: „GMP inspection in quality assurance laboratories at pharmaceutical producers" and to present the first proposal of the group to the PIC/S executive bureau.

Inspections focused on the implementation of the principles of Good Manufacturing Practice were executed in compliance with the schedule of inspections at the Slovak manufacturers of pharmaceuticals. The regular inspections are carried out every two years and, on their basis, a producer may receive the GMP certificate.

Total number of inspections performed at Slovak manufacturers of pharmaceuticals was 15, two of them were joint international inspections carried out in cooperation with the inspectorates of Italy and Latvia as a part of harmonization of inspection procedures in relation to our access to the European Union. 3 inspections were conducted at international pharmaceutical manufacturers.

In 2003, total number of inspections was 63 in all types of medical facilities - manufacturers, wholesalers, hospital and public pharmacies, opticians, dispensaries of medical devices and facilities of the transfusion service. Total number of documents issued was 180. It covers the expert reports on equipment, premises and personnel, opinions on expert reports on equipment, premises and personnel, statements on handling of chemical substances that can be misused for non legal production of narcotic and psychotropic substances, opinions on the equipment and premises of opticians, certificates of products and WHO certificates concerning the fulfilment of GWP requirements.
Total number of assessed registration documentations in 2003 was 1580.

Post-marketing surveillance department

The Post-marketing Surveillance Department activity was focused on the control of pharmaceuticals imported to the territory of Slovak Republic, receiving and sending off information on insufficient quality of drugs that are presented for the discussion to the Assembly for Drug Quality.

The sessions of the Assembly for Drug Quality were on 16th January 2003, 29th April, 2nd September and 3rd December 2003. Members of the assembly discussed 146 cases, 19 of them were medicinal products and 13 of them were medical devices recalled.
25 interventions were carried out between the sessions of the Assembly for Drug Quality, 4 of them were sent by fax and 21 by post. Medicinal products were postponed in 2 cases, recalled from circulation in 14 cases and 4 medical devices were recalled; release into circulation was announced in 3 cases, fast information on medical devices in 2 cases. Remaining interventions were conducted through the Reports on Drug Quality.

The Reports on Drug Quality 36/2003, 37/2003, 38/2003 and 39/2003 are published at www.sukl.sk. Moreover, they were distributed through the database e-mail and mail addresses. The quality information is published on monthly basis at „The Health News Paper" and „The Pharmacist".

The assembly covers also receipts of the international RAPID ALERTS – fast recalls of a medicinal product from circulation within EMEA, PIC/S and WHO. According to the requirement of the European Agency for the Evaluation of Medicine Products EMEA and recommendations of WHO, the 24-hour service in 365 days a year is provided. 4 employees of the institute participated at the 24-hour service. In 2003, 77 notices from international institutions were received, 6 of them covered the recall of medicinal products from the market in the Slovak republic.

The summary of received and processed analytical certificates and samples is listed in Annex No. 1.

3.7 Safety of Medicines and Clinical Trials Section

In the area of clinical trials with investigated as well as registered medicinal products and with medical devices and Good clinical practice (GCP), the Institute ensures reviewing applications for clinical trials and study protocols, issuing the decisions on approval of clinical trials, surveillance over its performance and approving of study centers.

Overview of the activities in the year 2003:

Activity	Number
Application for clinical trials	148
Authorization of clinical trials of drugs	183
Rejection of application for clinical trial	3
Notification on clinical trial in phase IV	17
Application for approval of amendment to protocol	164
Application/notification on changes in Investigator's Brochure	81
Application for approval of a new study center	67
Submission of agreement of ethical committee	95
Notice on beginning of clinical testing	100
Notice on end of clinical testing	95
Annual report on the process of clinical testing	82
Confirmation for custom purpose	508
Report on adverse event from Slovak workplaces	222
Notice on adverse event from abroad	281
Own activity	10
Other	179
Application for clinical trial with medical device	3
Authorization of clinical trial with medical device	1
Rejection of application for clinical trial with medical device	1

Department of Drug Safety is a coordinating center for pharmaco-vigilance and monitoring of adverse drug reactions in Slovakia. Its main task is identification, monitoring, analysis, assessment and evaluation of new information on safety of medicinal products (drugs), so called safety signals. New signals are formed from international system of information exchange (DRS, Information Exchange Service, WHO), EMEA and FDA, from available domestic and foreign literature, from Periodical Safety Update Reports (PSUR), from passive monitoring of adverse drug reactions in Slovakia. The Committee on Safety of Drugs takes part on assessment and evaluation of new safety signals.

In the year 2003 the Institute received 772 reports on adverse reactions from health professionals. Reports are included into ADR database. The information on 365 medicinal products from the database was forwarded to WHO (Uppsala) drug monitoring center and to 17 companies in purpose to prepare the Periodic Safety Update Reports (PSUR).

SIDC received also another 6971 spontaneous reports on adverse reactions that occurred in other countries than Slovakia. These reports as well as reports from clinical trials are not included in our database.

Laboratory control of drug samples in connection with incidence of adverse reactions (so called clinical complaints) has been done 16 times. No deficiencies have been found out in the quality of drugs.

We received totally 366 PSURs. Other 454 PSURs were submitted with application for renewal of registration. These reports were checked for content. About 5% of them were not accepted.

Reporting adverse reactions to drugs has been promoted via direct posting of letters to physicians and state county physicians and directors of hospitals. Two issues of the bulletin „The Drug Risk" have been prepared and they are also available on Internet. The web site has been rearranged so that information on safety of drugs could be easily accessible.

The Committee for Safety of Drugs has 3 meetings in 2003. The committee evaluated reported cases of adverse reactions and signals and accepted 2 statements on adequacy of free sale medicinal products of some therapeutic groups.

International cooperation in monitoring of the adverse drug reactions developed especially well with WHO. The information from our database on adverse reactions has been transmitted to WHO. Cooperation has been also ensured with the EU authorities, especially with The Drug Agency in London (EMEA). Cooperation was developing on the basis of the PERF III (Pan European Regulatory Forum) project.

Promotion and advertising of medicinal products is also subject of surveillance. The Promotion Act No. 147/2001, Coll. states the Institute to be responsible for the surveillance of advertising medicinal products, infant milk preparations, infant food formulas and supplements. SIDC reviewed 11 cases of possible violation of the act. SIDC issued 11 decisions involving penalty of 541 000 Slovak crowns and three announcements in press. Some of these decisions did not yet come into force.

3.8 Control Laboratories 1- 5

The activity of Control Laboratories in the year 2003 was focused on:

Inspection activity:
in facilities providing medical care, in wholesale organizations and the other facilities.

Total number of inspections performed:	741
Total number of samples taken:	288

In 2003, the activity of control laboratories 1 - 5 covered mainly:

- inspection
- controlling and analyses
- other specialized activities

Inspection activity:
In the facilities providing medical care:
- public pharmacies and branches
- hospital pharmacies
- dispensaries of medical devices, opticians

in wholesale organizations
in other organizations which subject of activity also includes handling of precursors of narcotic and psychotropic substances and at poppy growers

Analytical control activity
Control testing of randomly taken samples was focused on the quality monitoring of medicinal preparations, purified water and packages with respect to chemical and microbiological properties of randomly taken samples.

The main reasons for non-compliance report on samples randomly taken in pharmacies:
- incorrect content of active substances
- non-complying labelling of preparations
- insufficient quality of purified water

Other professional activities
Advisory and consulting activities for public pharmacies, hospital pharmacies, wholesale distribution organizations, poppy growers and other organizations were carried out.
Standard working procedures were developed, updated and mutually commented between CL 1 - 5.
Quality assurance activity proceeded with stability studies of reagent and volumetric solutions.
Pre-attestation trainings for the employees in pharmacies were organized.
Professional education of employees was provided in a form of internal and external trainings in line with all-year schedule.

4. Budget of SIDC

Budget of SIDC and its utilization in the year 2003

Budget classification	Budget approved	Utilization adjusted	(in thousands SKK)
Incomes from the others SIDC activities	14 100	8 000	8 453
Incomes from registration			65 204
Incomes of SIDC[1]			**73 657**
Common expenses	85 037	93 651	93 651
Capital expenses	38 000	43 226	43 226
Expenses of SIDC[2]			**136 877**

Development of selected budget indicators for the period of 2000 - 2003
(in thousands SKK)

	2001	2002	2003
Incomes	**18 245**	**16 273**	**8 453**
Common expenses	**78 955**	**78 998**	**93 651**
Capital expenses	**4 646**	**16 273**	**43 226**
Exchange rate 1 EUR / 40 SKK			

5. Personnel policy

In 2003, our Personnel Office provided exercising of Act No. 312/2001 Coll. on Civil Service and amendments to certain acts in their later amendments (hereafter called „Civil Service Act") and Act No. 313/2001 Coll. on public service in its later amendments (hereafter called „Public Service Act"). The main activity carried out by the Personnel Office was exercising of legal relations of civil servants related to civil service, i.e. exercising of rights and obligations of state and civil servants resulting from the execution of civil service or related to the execution of civil service. The Personnel Office organized exercising of legal relations of employees executing public service, assessed economic effectiveness of work and kept records and statistics related to the above activities which are submitted to the Institute of Health Information and Statistics, the Statistical Office of SR, the Civil Service Office and the Ministry of Health of SR.

1 total incomes which are not utilized by SIDC, they are going directly to the state budget
2 total budget allocated from the Ministry of Health of Slovak Republic

Number and structure of SIDC employees
Limit for SIDC employees in 2003 and filling of capacity:

Indicator	Civil service	Public service	Total
Limit 78	***124***	***202***	
Reality – natural persons	***77***	***128***	***205***
- average	74.17	118.25	192.42
- records as of 31 December 2003	76.50	121.84	198.34

The fact that the capacity of civil service employees has not been filled originates in time-consuming process of selection procedure and particularly in the fact that announced selection procedures for the years 2002 and 2003 that should have been conducted for SIDC in 2003 by the Ministry of Health of SR started as late as Q2 of 2003.

The capacity of public service employees has not been filled due to the fact that 5 employees retired and will be replaced by new employees later in 2004.

Age structure of employees in the year 2003

20 years and less	2
20-29 years	12
30-39 years	28
40-49 years	53
50-59 years	96
60 years and more	14

Educational structure of employees

university	90
complete secondary school	97
secondary specialized school	3
elementary + training	8
elementary	7

Comparison of the number of employees in the last 4 years in re-counted number and in natural persons:

year	average registered number of employees re-counted	in natural persons
2000	197.35	202.62
2001	194.30	202.80
2002	194.76	199.26
2003	192.42	198.00

Comparison of average month salary

year	
2000	11 409 SKK
2001	12 207 SKK
2002	14 674 SKK
2003	15 677 SKK

Employee fluctuation

In course of the year 2003, totally 45 employees terminated the employment, thereof:

19 employees left for retirement
2 employees terminated temporary employment
19 employees changed job
1 employee - other reasons (death)

In course of the year 2003 the Institute concluded the working contract with 54 employees:

31 public service
23 appointed to state service

Education of employees

a) Obligatory education activities for new employees

In 2003, 54 new employees were accepted. All newly accepted employees completed *„Entry briefing on work safety and fire protection"*. Within the adaptation process of Organization guideline OG No. 6/2001 (*Adaptation process for new employees*) they completed professional and practical preparation in individual sections/departments to which they were accepted. Every employee has an *„Education file"* in which all the education and trainings are recorded.

b) Continuing education

Serious attention was paid to the continuing education of our employees of both internal and external form.

The education was conducted in accordance with Organization guideline OG 5/2001 *„System of education of SIDC employees"*.

Internal education

Within the framework of regular education of the employees of the Institute the all-year-round program of training has been elaborated. According to this program the all-institute internal courses on actual topics of professional area as well as in the area that refers to the activity of the institute and new legislation have been performed.
Besides the whole institution workshops, in every section/department planned education oriented to particular activities has been organized.

External education

External education has been ensured through participation of employees in courses, workshops, conferences of domestic and foreign character.
In the year 2003, employees of the Institute elaborated 62 different lectures, 11 publications, they took part in 114 professional business trips to various professional congresses abroad, to working sessions within the OECD, EU, EMEA, OMCL, PIC, WHO and worked as lecturers of the Slovak Medical University.
All actions of this kind have being recorded and registered.

6. Aims and overview of their fulfilment

International cooperation was focused on the European pre-accession activities. Being one of important areas, PERF III program was the framework for the preparation of experts from the bodies of regulation and control of drugs in accessing countries for the activities and participation in EU structures after accession of SR into EU.

Representatives of institute participated in the sessions of advisory bodies of EMEA, London, and in the European Commission, such as Pharmaceutical Committee, „Head of Agencies" group, Interview, etc. On behalf of the Health Minister of the SR, the director of institute actively participated in the meetings of Ministers of Health from the member and accessing countries in Milano.

Another important task was the participation at regular sessions of the European Pharmacopoeia Commission and cooperation in EDQM projects concerning the preparation of the European Pharmacopoeia.

Legislative activity focused on the amendment of Act No. 140/1998 Coll. on medicinal products and medical devices in its later amendments and on the implementation of decisions and recommendations of OECD and the European Commission on chemical substances.
Works on quality manual, organizational guidelines and standard working procedures necessary for accreditation were carried out.
Pharmacopoeia- and standard-related activities covered the publishing of the 6th volume of the Slovak Pharmacopoeia 1 in June 2003 and commencement of works on the 7th volume of SP 1.

As for the medical product registration, standard working procedures necessary for improving, coordination and assessment of documentations attached to the registration application were completed.

The Medical Devices Department conducted a centralized records of registered medical devices in terms of Act No. 140/1998 Coll. The department carried on with the work on the construction and development of functions of a competent authority. As before, the Slovak and European standards were continuously harmonized.
Informatics – processing of registration documentation has started in a new program. The database of registered medicinal products was continuously updated and code allocation work was carried on. Internal information system was completed in cooperation with MCR Company. The institute proceeded with editorial work.
Inspection of GMP, GLP, and GCP was conducted in compliance with applicable legislation and focused particularly on issues that might influence negatively the quality, safety and efficiency of medicines. Following the commission of the PIC/S executive bureau, SIDC arranged an annual training seminar of PIC/S 2003 inspectors under the name „GMP inspection in quality assurance laboratories at pharmaceutical producers" and focused its attention to it.
Coordination sessions of inspectors and control laboratories continued.
Laboratory control was focused on tasks arising from the main scope of activity of individual departments, i.e. application of laboratory methods and procedures of drug control particularly with respect to alternative chemical and biological methods. The employees of the section participated in three international laboratory tests focusing on monitoring a laboratory performance in the use of a given method. Registration documentations delivered in order to complete original documentation of already registered medicinal products were evaluated.
Monitoring of adverse effects of drugs focused on stimulating adverse effects reports and taking necessary measures. Cooperation of the institute and WHO at International Drug Monitoring project and involvement in EU system proceeded.

As for clinical testing of medicines and medical devices, SIDC was providing assessment of applications for clinical testing, issuing decisions on clinical testing permissions, approving work places and conducting supervision.

The institute supervised the advertising of drugs, infant milk preparations, infant food formulas and supplements.

Control laboratories 1 - 5 conducted inspection in compliance with applicable legislation that was coordinated with reference to the requirements of the Ministry of Health of the SR in cooperation with the Inspection Section.
Analytical control activity was particularly focused on monitoring chemical and microbiological quality of random samples of medicinal preparations, purified water and packages.

Economical department supported uninterrupted activity of SIDC and monitored expenses of individual units and control laboratories and made a quarterly list of bad payers.
In accordance with Act on Public Procurement of Goods and Services, the head of Economy and Maintenance Section completed a specialized training necessary for enhanced professional capability.
Experts from EMEA, EU member and candidate countries made a benchmarking visit in SIDC. SIDC received the highest rating among all the participating institutes.
Quality Assurance Unit –carried on with the implementation of quality management in standard of STN EN ISO 9000: 2000 and ISO 9004: 2000 under the recommendation of the European Agency for the Evaluation of Medicine Products EMEA as a part of harmonization of quality provision.
The Public Relations Division has been established as a part of the Director and Control Department.
A new concept of SIDC was developed and it is currently discussed at interdepartmental level.
In line with control activity plan, heads of each unit in the institute conducted control activity and complaints from citizens and organizations were inspected and settled in compliance with the act on complaints.

7. Evaluation and analysis of the Institute's development

In recent years, SIDC has worked systematically on the improvement of quality of its services. Appropriate feedback is essential for developing the quality system. Therefore, SIDC decided to make its own research of information from its clients in order to get the necessary feedback. The research was made in the form of a questionnaire distributed to 400 clients. SIDC received 137 responses, representing 34.25% of respondents. The research was made in the period of June to September 2003.
The results of the quantitative research confirm that SIDC activities have been evaluated as very good. SIDC decided that the research should be made regularly, at least once a year. The repeated research will help to monitor trends in quality of services provided and to compare similar time periods.

In 2003, SIDC fully used the state budget resources distributed into current and capital expenditures. The results having been achieved by SIDC in 2003 were regularly evaluated in the activity reports and submitted to the Ministry of Health of SR.

8. Main groups of users of the Institute's outputs

External clients:

patients,
legal persons (pharmaceutical producers, medical devices producers, distributors of medicinal products and medical devices),
natural persons (owners of pharmacies and dispensaries of medical devices etc.)
others (e.g. applicants for information).

Services provided to the clients:

registration of medicinal products and medical devices,
issuing of binding opinions for permissions for wholesale distribution,
issuing of permissions for clinical testing,
initial inspections at pharmacies and dispensaries of medical devices.

SIDC outputs are made for and used by the Health Ministry of SR and wide range of users, in particular pharmaceutical producers, wholesale distribution companies of medicinal products and medical devices, owners of public and hospital pharmacies, opticians, and dispensaries of medical devices as well as general public.

Individual sections and departments provide specialized advisory services and consultancy in the area of registration of medicinal products and medical devices, Slovak Pharmacopoeia and Pharmaceutical Codex issues and other specialized services.

Agenda related to Act No. 211/2000 Coll. on Free Access to Information is handled in the Public Relations Division. In 2003, totally 53 requests for information were received (information provided 52-times, 1 decision on withholding information was issued in compliance with the act).

In 2003, editorial activity was represented by quarterly publishing „the Reports on Drug Quality" that are published for the benefit of general medical community. The reports inform about non-compliant medicinal products and measures resulting from it, and/or about products consequently released for medical use.

Database of registered medicinal products being used by the Ministry of Health of SR and health insurance companies represents an electronic form of the output.

9. Publication of the Annual Report

Publication of the Annual Report is realized in two forms: in the form hard copy (paper copy) in Slovak and English language, that is delivered to Ministry of Health of the SR, Slovak Medical University and to the other domestic and foreign institutions. The second form is the publication of the Report on the web site of SIDC - www.sukl.sk.

Annex No. 1

Overview of analytical certificates and samples accepted and processed

Total number of analytical certificates accepted was **148**
Total number of samples accepted for testing was **1273**
Total number of registrations and amendments in registration accepted was **1407**
Number of registered approval decrees **979**
Number of registered EDQM **6**

Analytical certificates processed	Complying	Non-complying	Elaborated	Total
Import	**78**	**13**	**58**	**149**
Domestic Producers	**18**	**0**	**4**	**22**
TOTAL	**96**	**13**	**62**	**171**

Samples processed in laboratory testing	Complying	Non-complying (showing discrepancy or defect)	Elaborated	Total
Imported drugs	**102**	**3**	**96**	**201**

Samples processed	Complying	Non-complying	Elaborated	Total
MIS*, Pharmacies	**421**	**1**	**11**	**433**
IMUNA, s.e.	**14**	**0**	**0**	**14**
SLOVAKOFARMA	**44**	**0**	**8**	**52**
CHIRANA PREMA	**18**	**0**	**0**	**18**
VULM, j.s.c.	**80**	**1**	**0**	**81**
ADSR	**16**	**0**	**2**	**18**
Starting substances	**3**	**0**	**1**	**4**
Complaints	**4**	**8**	**5**	**17**
Clinical trials	**11**	**0**	**3**	**14**
Other companies on request	**21**	**0**	**1**	**22**
Center of drug dependences	**2**	**0**	**0**	**2**
Attests	**400**	**22**	**9**	**431**
PTS, CS testing	**3**	**0**	**3**	**6**
Internal testing	**22**	**1**	**33**	**56**
TOTAL	**1059**	**33**	**76**	**1168**

* MIS (Manufacture of infusion solutions)

Annex No. 2

Overview of inspections and sample takings carried out by Control Laboratories 1-5

Medical facilities	Inspections	Number
Public pharmacies	Entry inspections	60
	Targeted inspections	283
	Follow- up inspections	252
	Sample takings	272
Branches of public pharmacies	Entry inspections	1
	Targeted inspections	1
	Follow- up inspections	26
Hospital pharmacies	Entry inspections	4
	Targeted inspections	6
	Follow- up inspections	5
	Sample takings	11
Dispensaries of medical devices	Entry inspections	21
	Follow- up inspections	25
Distribution organizations	Entry inspections	9
	Targeted inspections	2
	Follow- up inspections	4
Opticians	Entry inspections	20
Other facilities		
Producers of poppy	Entry inspections	4
Precursors of NPS	Entry inspections	6
Manufactures of medicines	Sample takings	5
TOTAL:	Inspections	741
	Sample takings	288

NPS*- Narcotic and Psychotropic Substances

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ANNUAL REPORT 2003 SIDC

CURRENT BUILDING (picture 3) ▲

VISUALISATION OF THE NEW BUILDING (picture4) ▼

The State Institute for Drug Control

Report on the SIDC's activity for the year 2003

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