The State Institute for Drug Control

Slovak Republic

ANNUAL REPORT

2004

CONTENTS

ANNEXES

1. Identification of SIDC

Name	The State Institute for the Drug Control
Reporting to	Kvetna 11, 825 08 Bratislava 26
Governmental Department	Ministry of Health of the Slovak Republic
Director	Assoc. Prof. Ludevit Martinec, PhD

Main activities

The State Institute of the 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, on the amendment of the Act No 455/1991 Coll. on small trade business (Small Trade Business Act(, as amended from time to time, and on the amendment and supplement of the Act of the National Council of the Slovak Republic No 220/1996 Coll. on advertising as amended, 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 „MH SR“). The head of SIDC is a head of Service Office and a director, appointed and recalled by the minister of health of the SR.

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 (GPhP) in the SR. The supervision over the quality, safety and efficacy, decisions making on registration of human medicines, registration of medical devices with the statement of compliance and since 1.5.2005 also registration of medical devices on the basis of CE certificates of the notified persons of EU, as well as the other activities following the current legislation 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 Committee, in the framework of which the SIDC closely cooperates with The European Agency for the Evaluation of Medical Products, London (in following text only “EMEA”), WHO, PIC/S (Pharmaceutical Inspection Cooperation Scheme), 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.

Detailed Organization chart is stated in following overview

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 ensuring and control of the quality, efficacy and safety of medicinal products and medical devices, issuing the decisions of the registration of human medicines, performing the state supervision in the field of pharmacy, the control of manufacture and wholesale distribution of medicinal products and medical devices and the cooperation with the EU organisations.

In addition to above mentioned activities, SIDC carries out inspections of compliance with the principles of good manufacturing practice, good clinical practice, good laboratory practice, good distributing practice and good pharmacy practice and to the compliance with the 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.

International cooperation is focused on the activities following the access of the SR to the EU as well as on the development of the cooperation and the exchange of information with the member states of OECD.

Another important activity is the cooperation with the European Directorate for the Quality of Medicines (EDQM) and the Offical Medical Control Laboratories (OMCL), in the view of the unified implementation of the quality system in the laboratories in the framework of the mutual recognition of the results, as well as the cooperation and the participation in the periodical sessions of the EMEA.

The nominated employees participated in the regular sessions of the working groups and committees according to the requirements of the above mentioned organisations and agencies (EMEA, EDQM, OECD, and EC).

No less important part is the Good Laboratory Practice. The director of the Institute represents the SR in the working group for the GLP in the framework of OECD and in the working group in the EC. He ensures the implementation of the regulations and decisions and the coordination of the monitoring.

In the framework of the international cooperation the special importance has the representation of the SIDC and SR by the expert lectures in the various international and domestic conferences, seminars and workshops, which are performed mainly by the director of the Institute and by the employees of the Registration section, Medical devices section, the

Safety of medicines and clinical trials section, the Laboratory control section and the Quality Assurance Unit.

In the framework of the mission and perspective SIDC is proposed to be the central agency of the state administration in the field of human pharmacy, as it is subsequently realised in the member states of EU with the new name "Office for Human Pharmacy of the SR".

In this regard the Office for Human Pharmacy apart of the competencies stated in the current legislation and the statute of SIDC should fulfil following tasks:

- 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 Human Pharmacy of the SR
- to grant licenses for manufacture of medicinal products and medicinal products from blood, licences for wholesale distribution of medicinal products and medical devices and licenses for providing health care in hospital pharmacies
- to issue GMP certificates according to WHO resolution No. WHA 50.3. (Annex 2) of May 1997
- providing corresponding information and data in the pharmaceutical policy for the interested stakeholders
- publishing the Slovak Pharmacopoeia and other standard documents concerning the medicinal products 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.

The new tasks arising from the legislation, which have the statewide character would require also the changes of the personal occupation of the institute by the extension of the number of employees especially in the unit of the registration of human medicines and the information technology department.

3. Activities / products of SIDC

3.1 Quality Assurance Unit

In general the cooperation and exchange of information between the members states of OECD proceeded, the comments to the documents were given according to the requirements of the OECD Environment Directorate. The review and assessment of the inspection activity "Annual Overview of GLP in Slovak Republic 2004" was worked up and was submitted to the Environment Directorate OECD, to the member states and to the European Commission according to the requirements.

The reports on the activities and the status of SR in the field of GLP were worked up and were presented by the director of the SIDC at the session of the working group for GLP of the European Commission in Brussels.

On 18th Meeting Working Group on GLP in Paris were assessed the conclusions of the follow-up inspection of SR and the decision was accepted by the delegates, that the SR complies with the requirements of OECD and the GLP programme was fully implemented.

The international cooperation with the European Directorate for the Quality of Medicines (EDQM), European Network of Official Control Laboratories (OMCL) was focused on the development of the cooperation, effort on implementation of the unified system of quality assurance and the exchange of information. The preparation continued for the audit, which was performed in July 2004 with the purpose of the unified procedure in the testing of drugs and subsequent mutual recognition of the results. In the final assessment it was stated the improvement in the field of implementation of the standard ISO/IEC 17025 in the laboratories of the Institute. The deficiencies were found out especially in the premises and equipment. It was stated, that the requirements for the premises will be fulfilled after the finalization of the additional building of the Institute.

The international cooperation with the EMEA continued in the framework of the Benchmarking according to the requirements.

The results of the cooperation with both of the European agencies (EMEA, EDQM) outlined, on the basis of audits, that the SIDC is on a very good level in the framework of the implementation of the quality systems and that in full extent performs the National quality programme of SR. SIDC is a member of the Slovak Society for Quality, too.

The legislative activity was realised by the cooperation with the health, environmental, economy and agriculture departments in the framework of the implementation of the decisions and recommendations of OECD and European commission on the field of chemical substances. For the 36th Joint Meeting of the Chemical Committee and he Working Party of Chemicals, Pesticides and Biotechnology OECD the data were worked out for the report on the status and transposition of the legislation in the field of the chemicals including GLP "Progress Report", which was submitted in the session of the Joint Meeting OECD in Paris the sponsor – Ministry of Environment. The Progress Report was accepted positively.

The implementation of the quality system continued according to STN EN ISO 9000:2000 and STN EN ISO/17025 in the laboratories. The new internal directives, guidelines were worked out and updated and were published at the website. In order to assess the efficiency of the implementation of the quality system and subsequently to perform the changes and improvement the Management Review was realised and Self-assessment was worked out. The corrective measures which resulted from the conclusions will be realised according to the plan and the results will be assessed.

For the objective assessment and knowledge in the contact with the personnel, the purpose of which is the improvement of the quality of service the questionnaire on client´s satisfaction was worked out and evaluated. The purpose of it was to obtain the feedback in the evaluation of the quality systems. The assessment of the questionnaire outlined that 80% of the respondents are satisfied with the level of the service and 71% trust in the results produced by the Institute.

The internal audits of the particular sections of the Institute were performed according to the plan ad furthermore the audits were performed in the laboratories, which have the authorisation of SIDC for the pharmaceutical and toxicologically-pharmacological testing. 6 organisations are authorised at present. Their actual list is published at a website.

3.2 EU Coordination Unit

EU Coordination Unit was involved as a separate unit to the Organisation structure of the SIDC reporting directly to the head of service office and the director of SIDC since 1st September 2003.

In the year 2004 the main activity of the unit was focused mainly on the pre-accession activities, which culminated on 1st May 2005 by the access of the SR to the EU and by the integrating of SIDC into European structures in the field of human pharmacy.

In 2004 EU Coordination Unit ensured on the quality level not only the pre-accession activities, but assured also the liabilities of SIDC resulting from the membership in the international schemes and organisations.

The main activities of the EU Coordination Unit

- nomination of 30 representatives of SIDC to the advisory bodies of European Commission (EC) and European Medicines Agency (EMEA) and its updating
- participation and coordination of the transfer of the actual information about implementation of the decisions of the particular bodies of EU in the field of regulation and control of medicinal products from the sessions of the Pharmaceutical Committee EC, Head of Agencies and Management Board EMEA, EMACOLEX, including the coordination of the preparation of the documents for the regular sessions,
- coordination of the programme conceptions of the incorporating to the EU structures,
- coordinating activity in the elaborating the documents for the sessions of the advisory bodies of EMEA,
- coordination of documents and active participation in the framework of the incorporation to the EU structures and mainly to DG-III-Enterprise, industry, free movement of persons and goods,
- coordination of the practical implementation of the EU legislation to the national legislation and active part in the harmonisation of the EU Member States legislation including the statements of SIDC,
- coordination of activities of the SIDC representatives in the advisory bodies of EMEA London, EC, EDQM, PIC/S, WHO, OECD, and European associations in the field of human pharmacy,
- coordination in the elaboration of the database of the SIDC representatives and external experts SR in the field of human pharmacy,
- training of the SIDC employees directly involved in the European structures, theme: "Position and importance of the EU Regulatory Affairs Unit in the SIDC",
- coordination in the elaboration of the European database in the field of human medicines, elaboration of the expert questionnaires (total number 17),
- realisation of the foreign official journeys of the nominated SIDC employees and external representatives in the total number 461, which means the increase to 158% after the accession to the EU structures,
- realisation of the working meeting on the occasion of the access of SR to EU with the participation of the SIDC, MH SR representatives and the SIDC employees, which took place on 6th May 2004.

3.3 Administrative Section

Director and Control Department

Control Division

In the terms of the Act No 242/1998 Coll., which amends the Act No 85/1990 Coll. on petitions and the terms of the Art.10, paragraph 1 of the Act No 152/1998 Coll. on complaints the central registration of petitions and complaints is kept separately from the other documents in the way to provide the data required for the control of the handling with complaints and petitions.

The Institute received totally 12 complaints, 8 of them were assessed as justified and 4 as unjustified. 3 anonymous complaints were received, 1 of which was assessed as justified.

The subject of justified complaints was mainly dispensing of the expired medicinal products, marking of incorrect dosage, dispensing of the medical device by the unqualified person without the valid licence. The administrative proceedings started in 5 cases and the penalties were imposed in the total sum 102 000 thousands Slovak crowns. The proposal for suspension of the activity of the dispensary of medical devices was submitted in one case.

According to the plan of the control activity for the year 2004, 15 control actions were performed focused mainly on:

- performing of the subsequent financial control,
- observing the Act No 312/2001 Coll. on civil service
- control of the fire protection and work safety
- drawing of the capital and common expenses
- control of the cash economy
- updating of the overview of civil servants and public servants – retained exceptions.

Apart of the mentioned control actions controls of the fulfilling of the corrective measures connected with the subsequent financial control in the terms of the Art.11 of the Act No 502/2001 Coll. and drawing of the holiday leaves for the calendar year 2002-VIII/2003.

It is stated that the findings resulting form the control activity were removed in the appointed term.

Public Relations

Public Relations Division ensured the performing of the tasks resulting from the position of the division as the press body of the head of Service Office and director and continuously performed the monitoring of media. Public Relations Division coordinated the communication between the Institute and media. 86 applications received from the print and electronic media were executed.

In cooperation with the other units of the Institute the Division participated in the realisation of the Annual Report of the SIDC. The activities connected with the translation were coordinated and the works related to the publishing of English version were ensured. Public Relations Division in cooperation with the Information Technology Department regularly updated internet and intranet websites of the Institute on the basis of the requirements of the expert units. Furthermore the Division elaborated the internal directive No 8/2004 "Publishing of the information on intranet and internet of SIDC". The Division monitored the internet websites of the important institutions in the field of drug policy and legislation.

Public Relations Division kept the registration and performed agenda related to all applications submitted to the SIDC in the terms of the Act No 211/200 Coll. on the free access to information. 206 applications for information were received and executed, in one case was issued the decision about non-providing of the information.

Summary of the submitted applications for information

Number of the submitted applications for information	206
Number of provided information	204
Appeal for completion of the application	1
Issue of the decision about non-providing of information	1

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.

The update and prescribed revision of the control documentation was performed. In the framework of it the 4th update of the Metrology order SIDC was executed.

Metrology assurance of the Institute was presented and checked in the framework of the "Blank audit" EDQM.

Our metrologist participated as an expert in the EU GMP pre-inspection, which took place from 6.9.2044 to 17.9.2044 and has been the presumption for the MRA visit.

On deputy of the Quality Assurance Unit two inspections were performed with the purpose of the licensing, resp. keeping of the authorisation for the determined scope of activities.

In cooperation with the Pharmacopoeia Department and Laboratory Control Section the comments were elaborated to the revised article Ph.Eur. (physically-chemical methods); European Pharmacopoeia article 2.2.25 **Absorption spectrophotometry, ultraviolet and visible.**

Our metrologist participated regularly in the sessions of the Commission for certified reference materials, which is the advisory body of director of the Slovak metrologist institute.

Metrological quality of measuring instruments and measurements was assessed as a part of internal audits of the Laboratory Control Section departments, as well as Control Laboratories 1-5.

The ongoing monitoring of microclimatic conditions in the 33 selected places of the Institute is conducted and related records are being registered.

For the needs of the Laboratory Control Section and Control Laboratories 1-5 calibration of 3 hot-air sterilizers was performed.

Metrologist of the Institute performs the function of the quality manager of the Administrative Section, too.

Information Technology Department

In terms of electronic processing of the registration documentation, the department was assigning SIDC codes and preformed ongoing processing and updating of the database of medicinal products. The comments from the users were processed continuously to the programme "VIS-medicinal products". The employees of the department participated in the working meetings with the supplier of the information system and the Registration Section related to the further development of the programme for processing of the registration documentation. The help was provided to the employees of the Registration Section in the work with the mentioned programme according to their needs.

On the basis of the requirements of the MH SR the current lists of the medicinal products were supplied. The approved package leaflets and SPC from manufacturers were electronically processed. New application for faster searching in the database SPC and PIL was developed.

The works connected with the ongoing processing and updating of the internet website of SIDC were performed. New certified firewall and more efficient email server were introduced.

The cooperation between SIDC and AISLP creator in the form of data exchange continued.

The department ensured the operation of the information technology of SIDC. Minor failures were removed by employees themselves. In the occurrence of major technical failures the service was ensured by the selected suppliers. The department ensured the technical part of the transformation of the Institute to the exchequer system.

The expert help to the users of the IT in the work with the installed programmes was provided.

IT employees of the Institute developed simple programme modules for internal purposes of the Institute. In cooperation with the system integrator the department ensured the processing of electronical notifications in the terms of the Act No 140/1998 Coll.

The system of attendance registration was improved. In the framework of this activity the department cooperated with the Personnel Office by printing of attendance sheets.

On the basis of the requirements of the employees the steps were taken for providing and modernisation of the programme equipment for processing of the wage and personnel agenda and for introducing of the electronical processing of the ISO documents.

The department participated in the technical processing of documents necessary for specialized seminars, conferences, trainings, lectures and presentations organized by particular departments of the Institute.

In the field of cooperation with EMEA the supporting software was installed for the project Eudravigilance for the transfer of information about adverse effects of medicinal products (ICSR). The project EudraCT for registration of clinical testing in EU was introduced as well.

In the field of the registration of medicinal products the system CTS for the registration of the medicinal products registered in the mutual registration procedure MRP was introduced in cooperation with EMEA.

IT employees of the department participated in the expert meetings and trainings of the working group Telematics Implementation in EMEA.

In order to increase the public awareness of the registered medicinal products the cooperation with the external supplier was established on the project Nobel. The purpose of this project is the creation of the interactive internet database of medicinal products.

3.4 Registration Section

The activity of the Registration section in 2004 has been strongly influenced by the access of SR to EU. This required organisation change – from the original Registration and medical devices section was separated the Registration section with two departments: **National registrations department and EU procedures department.**

In pre-accession period the activity of section was focused mainly on:

- Control of the registration documentation of medicinal products, submitted according to the requirements SIDC Guideline No 5/2002 with "aqcuis communautaire", which were registered until the Act No 10/1998 Coll. on medicinal products and medical devices came into force. In connection with this the database of supplied documents was created and their correctness was checked in cooperation with the Laboratory Control Section and Inspection Section.
- Checking of the correct translation of the medicinal products registered via centralised procedure. In connection with this 71 Summary product characteristics, Patient information leaflets and other documentation related to the medicinal product have been checked.
- In the framework of pre-accession activity the project with the Dutch medicines agency was organised focused on the registration procedure and process of MRP coordination in two weeks duration. The employees regularly participated as the observers in the key commissions and working groups in EMEA (MRFG, QRD, NRG, TIG, CHMP, commission for phytopharmacs, working group for homeopathics, and others) as well as European Commission (NtA).

In post-accession period:

- In connection with the amendment of the Act on medicinal products and medical devices and changes in the registration conditions, which came into force since 1.5.2004 two SIDC guidelines were prepared: SIDC guideline for the centralised and simultaneously national

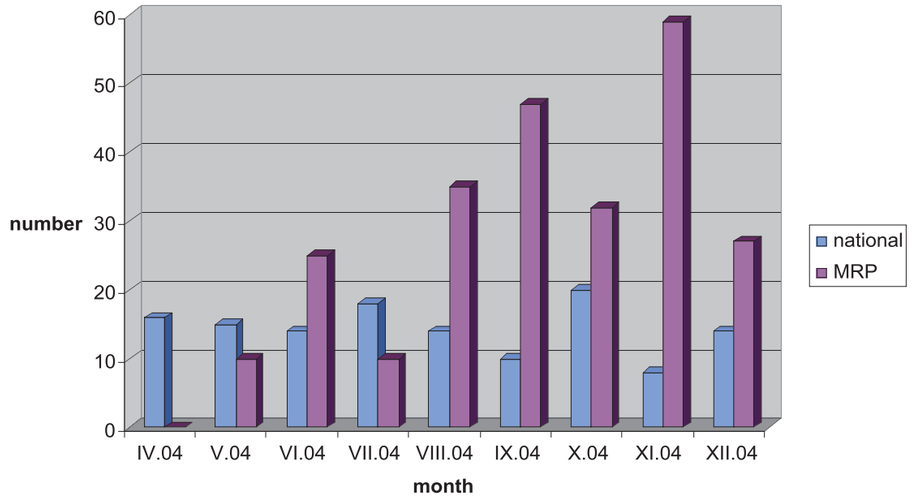
medicinal products and SIDC gudeline on the degree of completion of the submitted national registration applications. At the same time new SOPs were prepared.

- Informing of the applicants was realised by the two-day seminar in the cooperation with the Slovak Health University (29.-30.9.2004), whereas the materials are published at the internet. Questions given during the seminar were elaborated and published document "Questions and Answers" in the internet on 12.10.2004, whereas this document is periodically updated according to the requirements of applicants.
- For the centralised medicinal products the withdrawal of national registrations were subsequently issued according to the publishing of the particular medicinal products in EMEA. Up to now 139 withdrawals of registrations were issued.
- The assigning of SIDC codes of registered medicinal products and amending of missing medicinal products to the database was ensured.
- The withdrawal of national registrations of medicinal products was issued, the documentation of which was not complying with the "aqcuis communautaire", totally 150 medicinal products.
- The documents for the sessions of CHMP commission for the CHMP member representing the Slovak Republic were prepared monthly.
- For the purpose of the creating the cooperation system of SIDC with the patient organisations started the work on the list of patient organisations in the Slovak Republic.
- The session of the Commission for Drugsat SIDC took place 10 times in the planned terms. During the sessions were assessed new registration applications, renewals of registrations, variations in registration and the changes in the way of dispensing.
- The sessions of the subcommission for immunopreparates and preparations from human blood and plasma took place twice.
- The session of the subcommission for phytopharmacs and homeopathics took place once. 79 medicinal products were assessed.

Review of the medicinal product registrations

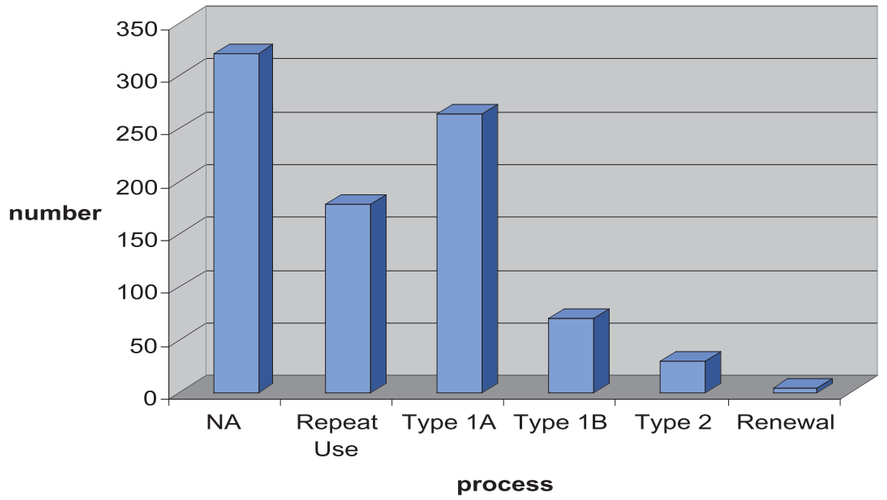
	MRP	National procedure
Total number of applications for registration Decisions on marketing authorisation issued	372 90	232 206
Total number of applications for renewal Decisions on renewal issued	0 0	684 184
Total number of applications for variation Decision on variation isued	67 31	1732 759
Decisions on rejection of applications for registration	0	3
Decisions on withdrawal of applications for registration	8	506

Overview of applications for registration



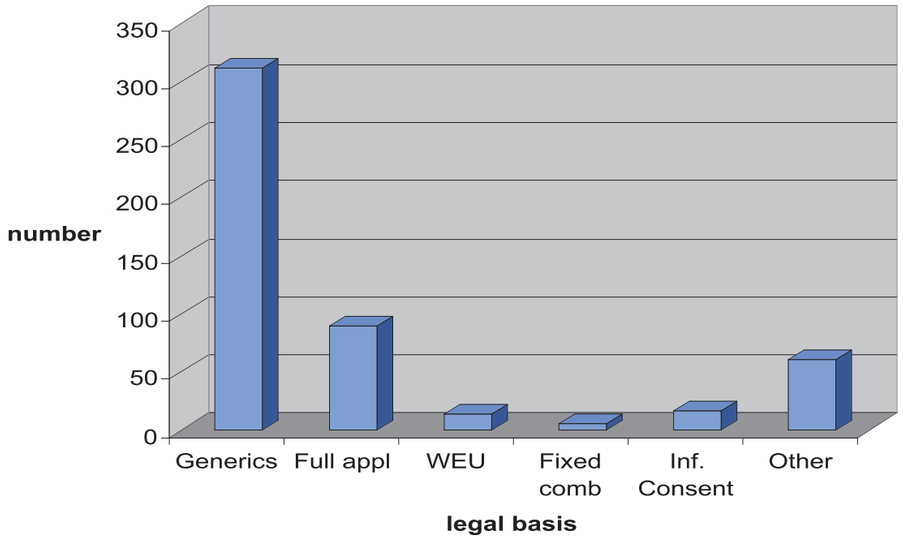
The number of applications for registration via MRP was extremely higher than via national procedure.

Overview of applications for registration, variation and renewal



Statistically the most of the applications were submitted as a new application. From Variations, the Type 1A was very frequently submitted.

Legal basis of the applications



The applications with legal basis „generic aplication" were mostly submitted and evaluated by SIDC assessors.

3.5 Laboratory Control Section

The Laboratory Control Section is an executive expert section of SIDC divided into Chemistry Department, Pharmacognosis Department, Pharmacology Department, Microbiology and Immunology Department and Pharmacopoeia Department.

One of the main tasks of the section is the assessment of the chemical, pharmaceutical and biological part of the registration documentation submitted together with the registration application. After the access of the Slovak Republic to the EU the assessors elaborated the assessment reports from the position of the concerned member state (CMS). At the same time the assessors performed the laboratory analysis of the samples of medicinal products being on the market together with the substances for the manufacture of the medicinal products.

Employees nominated to the particular working groups of the European Commission, Council of Europe, EMEA (European medicines Agency) and EDQM (European Directorate for the Quality of Medicines) performed 29 foreign bussiness trips. As OMCL (Official Medicines Control Laboratory) of the SR the section participated in the four circle tests organised by EDQM, so called PTS studies. Experts from the Dutch agency performed one week training of the assessors concerning the elaborating of the European assessment reports on the registration documentation in the MRP procedure and processing the applications for variation according to the new Regulation EC 1083/2003. In June an audit was carried out by the OMCL/EDQM network inspectors. Recommendations from this audit were implemented into the tasks of the main aims of the section for the year 2005 and in the same time on the basis of these recommendations internal guidelines concerning the validation of analytical methods No 9/2004 and out of specifications results No 12/2004 were elaborated.

OMCL of the SR participated in the CAP programme for testing of authorised medicinal products, directed by EDQM in Strasbourg. The analysed medicinal product was RAPAMUNE, sol. por.

In cooperation with the Slovak health university the section has been a sponsor of the thematic course "Physical-chemical methods in the analysis of medicinal products according to the SPh. 1" (April) and of a discussion meeting in November. Employees of the section participated in the 33th annual international conference Synthesis and analysis of drugs connected with the 7th congress SFS, which took place in Nitra, 9 -11 September.

In the Laboratory Control Section was totally processed **534** samples (tab.1) and **1 650** assessment reports (tab.2). 2 of the analysed samples were assessed as unacceptable, one for nonconformity in appearance and the second for the nonconformity in bacterial endotoxins testing. The activity of section expressed financially represents **8.240 538** Slovak crowns.

Tab.1

Number of samples	Pharmacology Department	Microbiology and Immunology Department	Pharmacognosis Department	Chemistry Department
Foreign registration	-	-	1	13
Domestic registration	-	-	-	1
Obligatory control	-	10	1	24
Import	-	17	10	30
Domestic manufacture	-	1	-	-
Ordered	302	33	7	7
Clinical complaint	-	-	-	3
Reclamation	-	10	6	3
Internal needs (QA)	-	17	6	6
PTS/MSS/CS	-	-	2/0/0	2/0/0
Others	-	-	8	14

Tab.2

Number of Assessment Reports	Pharmacology Department	Microbiology and Immunology Department	Pharmacognosis Department	Chemistry Department
Foreign registrations	4	47	95	199
Domestic registrations	-	-	4	12
Variations	3	35	203	523
Clinical batches	-	-	2	1
Analytical certificates	8	101	4	67
Assessments and reviews	-	-	25	17
"Upgrade"	-	63	47	137
Others	2	51	-	-

In 2004 the Pharmacopoeia Department was associated to the section. In this department the 7th and the last volume of Slovak Pharmacopoeia 1 was elaborated, which contains the updated complete part about reagents according to the supplement Ph. Eur. 4.7., list of all monographs, control methods and names of dosage forms contained in the volumes I – VI of Slovak Pharmacopoeia1 and in addition the list of monographs of the latest supplement Ph. Eur. 4.8. The 7th volume is a brief summary of the 1st edition of the Slovak Pharmacopoeia. Complete edition of all VII volumes of the Slovak Pharmacopoeia 1 is available in the electronical version CD-ROM, too.

On the basis of the analytical results the pharmacopoeia monographs were elaborated for the preparations, which will be included into the 2nd edition of the Slovak Pharmaceutical Codex. In the purpose to perform stability tests for the selected preparations the time schedule was elaborated for the period 2 - 4 months.

3.6 Inspection Section

The main part of the Inspection section activity was the performing of inspections focused on the compliance with the principles of the Good Manufacturing Pracice, Good Pharmacy Pracice, Good Distribution Practice and the provisions of the Slovak Pharmacopoeia in the terms of the valid legislation.

In connection with the pergorming of the international GMP audit of European Commission and the international convention PIC/S in the Inspection section (6.9. – 17.9.2004) the activity of the section was mainly focused on the organisation and realisation of the audit.

GMP department

In connection with the preparation of the audit the activity of the department was mainly focused on the following tasks:

- revision and addition of the Quality manual in the terms of the document EMEA/INS/GMP/3351/03/Rev.1/corr. „Compilation of Community procedures on Inspections and Exchange of Information".
- Revision and addition of the standard operating procedures according to the above mentioned document
- Revision and addition of the inspection documentation system
- Organisation and performing of GMP inspection of the domestic manufacturer by SIDC GMP inspectors under the supervision of the international inspector focused on the inspection of the Quality Assurance system in the manufacture of medicinal products and inspection of the manufacture of solid dosage forms

Inspection section adopted all corrective measures to remove the deficiencies according to the conclusions of the Audit Report:

- implementation of the requirements of the EU legislation in the field of inspection activity into the legislation of the Slovak Republic and especially to the Act No 140/1998 Coll. on medicinal products and medical devices as amended and the Order of the Ministry of Health SR No 274/1998 Coll. laying down the principles of the good manufacturing practice and good distribution practice
- revision, addition and elaboration of the required inspection documentation at the inspection section in the field of GMP and quality system control of the inspection activities.

Another important task was the performing of the inspections of the Slovak and foreign manufacturers of medicinal products according to the plan.

GMP inspectors actively participated in the joint audit programme organised by the European Commission, EMEA, PIC/S and EDQM. The document „Aide-Mémoire: Inspection of Pharmaceutical Quality Control Laboratories" was elaborated.

The total number of the GMP inspections of the Slovak manufacturers was 14.

3 GMP inspections of the importers from third countries (batch release) and 19 inspections of manufacturers of transfusional preparations were performed. In 2004 GMP inspectors participated in 11 foreign GMP inspections.

GPhP and GDP department

The department performs the state supervision and inspection of compliance with the principles of good pharmacy practice and good distribution practice in the health facilities. The supervision and inspection in non-health facilities as opticians, popy producers, licence holders on handling with certain substances which can be misused for non legal production of narcotic and psychotropic substances and others, was executed , too.

The main activity was focused on performing the tasks resulting from the Act No 219/2003 Coll. on handling with the chemical substances which can be misused for unlegal production of narcotic and psychotropic substances. In the terms of this act the inspections of all public pharmacies and their branches and inspections of distributors on the basis of the application of the licence holders on handling with medicinal products and medical devices were performed until 31.8.2004. In the terms of the Act No 219/2003 Coll. arised as well

the inspections of health and non-health facilities handling with the certain substances from group I.

On the basis of the suggestion of the State Control bodies, patients and for the reason of the new legislation provisions the focused inspections were executed. In 2004 the arised number of focused inspections was noticed. The performing of the inspection was focused on the specified requirement, suggestion. In the case of justified requirment, the suggestion for further administration was submitted to the relevant bodies – MH SR, Regional Office, legal department of SIDC. The focused inspections were performed also in connection with the new legislation provisions: Art.8 par.9 of the Act No 138/2003 Coll. and No 633/2004 Coll. The regular inspections of the wholesale distributors were focused on the compliance with the good distribution practice in the terms of the Order of MH SR No 274/1998 Coll.

On the basis of the amendments of the legislative provisions in December were executed inspections in public pharmacies for the reason of the change of owner – the transposition of the licence from the physical person to legal person.

The inspection activity of the section is summarised in the annex No 7.

Post-marketing surveillance department

The activity was focused on the control of the medicinal products imported and distributed in the terrirory of SR, especially medicinal products imported from third countries, distributed blood derivates and vaccines. The fluent reception and transmission of information on quality defects of medicinal products, which were subsequently the subject of the sessions of the Assembly for Drug Quality.

The sessions of the Assembly for Drug Quality took place three times: on 17th March 2004, on 23rd June 2004 and on 21st October 2004. The members of Assembly discussed 203 cases, 14 medicinal products and 5 medical devices were recalled from the market.

25 interventions were carried out between the sessions of the Assembly for Drug Quality, 3 of them were sent by fax and 24 by post. Medicinal product was suspended in 1 case, recall of medicinal products in 13 cases and recall of medical devices in 3 cases, release for the market was notified in 7 cases, rapid information on medicinal products in 3 cases. The other interventions were performed through the Reports on Drug Quality.

The Reports on Drug Quality 40/2004, 41/2004 and 42/2004 are published at a website www.sukl.sk. Moreover, they were distributed through the database of e-mail and post addresses. The quality information is published monthly at „The Health News Paper".

The activity of the Assembly covers also the reception of the international RAPID ALERTs – fast recalls of the medicinal products from the market within EMEA, PIC/S and WHO. 24-hour service 365 days a year according to the requirements of the European Medicines Agency (EMEA) and the recommendations of WHO. 6 employees of SIDC participate in the 24-hour service.

118 notifications from the international inspectorates were received, 4 of them concerned the recall of medicinal products in the Slovak Republic.

The summary of the received and processed analytical certificate and samples is in the annex No 6.

Control laboratories 1 – 5

Control laboratories performed in the health facilities inspection control-analytical and other expert activity.

Inspection activity was carried out:

- in the facilities providing pharmacy care: public pharmacies and their branches
  hospital pharmacies
  dispensaries of medical devices
- in the distribution organisations
- in the other facilities (poppy producers, opticians, Reginal Offices of Public Health, non-state health facilities etc.)

Total number of inspections performed: 1 629
Total number of samples taken: 197

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

Analytical control activity was focused on:

- chemical and microbiological control of the active substances and excipients on the basis of the order for distribution organisations and hospital pharmacies (issuing of analytical cerificates),
- chemical and microbiological control of medicinal preparations , purified water and packaging material on the basis of random choice,
- chemical and microbiological control of the purified water for pharmacies on the basis of the order

The most frequent reasons of the non-compliance statement were:

- incorrect content of the active substance
- incomplete labelling
- not complying total amount of the medicinal preparation
- not comlying conductivity, microbiological purity of the purified water

Other expert activity

- elaboration, updating and mutual preparing of comments for the standard operating procedures,
- advisory and consulting activities for public and hospital pharmacie, dispensaries of medical devices, wholesale distribution organisations, poppy producers, opticians and the public,
- performing of regular audits by the quality managers of the control laboratories,
- ensuring of the calibration and verification of the measuring instruments and equipment according to the valid requirements by the metrologists of the laboratories,
- ensuring of the expert training of the employees in the form of the internal and external training according to the training plan,
- performing of the qualification examination by the civil service employees,
- realisation work on the monographs for the Slovak Pharmaceutical codex,
- elaboration of the articles for the magazine „The Pharmacist".

3.7 Safety of Medicines and Clinical Trials Section

Department of drug safety

Department of drug safety is a coordinating center for pharmacovigilance and monitoring of adverse drug reactions in Slovakia. Its main task is identification, monitoring, analysis, assessment and evaluation of new information on safety of drugs, so called safety signals.

Overview of the activities

Reporting ADR from Slovak republic (spontaneous)	860
Expedited reporting of ADR (post-registration)	23 047
Clinical complaints including laboratory control	9
Submitted PSURs	548
Control of PSURs for renewal of registration	463
Published statements on drug safety	9

Reporting adverse reactions to drugs has been promoted via direct posting of letters to physicians. Two issues of the bulletin „The Drug Risk" have been prepared and issued that are also available on Internet. A guideline on reporting ADR (spontaneous, solicited and from literature resources) has been issued on Internet.

The Committee on safety of drugs has met 2 times. The Committee evaluated reported cases of adverse reactions and signals and accepted 2 statements on adequacy of free sale drugs of some therapeutic groups.

Department of clinical trials

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

Since May 1, 2005 directive No. 2001/20/EC on clinical trials has been implemented to our act No. 140/1998 Coll.

Overview of the activities

Activity	Number
Application for clinical trial	120
Authorization of clinical trials of drugs	144
Rejection of application for clinical trial	1
Notification on clinical trial in phase IV	1*
Application on approving of amendment to protocol	230
Application/notification on changes in Investigator's Brochure	105
Application on approving of a new study center	50
Submission of agreement of ethical committee	92
Notice on beginning of clinical trial	65
Notice on end of clinical trial	79
Annual report on process of a clinical trial	84
Confirmation for custom purpose	48*
Report on adverse event from Slovak trial sites	498
Notice on adverse event from abroad	444
Own activity	5
Other	136
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

* Not required from May 1, 2005

Advertisement Supervision

Promotion and advertising of medicinal products is also subject of control. The Promotion Act No. 147/2001, Coll. states the Institute to be responsible for control the advertising of medicinal products, infant milk formulae and infant follow on formulae. We reviewed 13 cases of possible violation of the act. We issued 2 decisions involving with penalty 100 000 Slovak crowns, 5 decisions on non-violation of law. 6 times the administrative procedure was stopped.

3.8 Section of Medical Devices

After the changes in the organisational structure of SIDC since 1.7.2004 due to the increase of the work connected with the access of the SR to the EU and due to the legislation changes the Medical Devices depatrment became a section with two departments: department of the registered medical devices and department of the safety of medical devices.

The section performed the registration of the medical devices in the form of submission of the Registration form for medical devices, which was adopted for the registration of medical devices in the terms of the Government Regulation **No 569/2001 Coll., No 570/2001 Coll. and 572/2001 Coll.**

Since 1.5.2004 on the basis of free movement of certain products after the accession of SR to EU, the registration formats were received also on the basis of the CE certificates issued by the notified bodies, resp. CE Declaration of Conformity of the manufacturer. The notifications of the manufacturers , competent EU authorities and distributors about Vigilance Report of medical devices and registered formats of diagnostical medical devices in vitro sent by the manufacturers after the registration at the authorised person in the country of manufacture were processed. At the section were registered also notifications of the clinical testing from the EU manufacturers in the framework of the multicentric studies.

Various lists of manufacturers, abbreviations of manufacturers, resp. distributors of medical devices according to the requirements of the MH SR, health facilities were elaborated. For the needs of helth insurance is performed especially the verification of the compliance with the legislation norms for the exceptions on the reimbursement of the medical devices exceeding the cathegorisation list.

During the year were updated and published on internet SIDC websites actual formats in English language for the foreign clients.

In the system of the quality management based on the norm ISO No 9004/2000 was at the section developed new system of records documentation, which improves the quality, monitoring and effectivity of the system in the framework of the process approach.

One employee of the Laboratory Control section and one external employee were nominated to the advisory bodies of the European Commission as external representatives of SIDC in the field of medical devices.

The processing of the quartal notifications from the distributors on the consumption of the medical devices was continued.

The summary list of the consumption of medical devices is regularly submitted to the MH SR.

Summary of the activies of the Medical Devices section

Number of received registration formats for medical devices	1066
Notifications of Vigilance Report of medical devices	124
New assigned codes for medical devices	4141
Updated codes for medical devices	6220
Registration of formats for diagnostical medical devices in vitro from EU	801
Inspections of the wholwsale distributors	12
Suggestions for the inspections of the wholesale distributors	10
Repeatd inspections of wholesale distributors	22
Assessment reports for the wholesale distribution licence	19
Notification of the clinical testing	2
Clinical complaints	11
Comments on the drafts of new STN	12
Updating of the norm database	66

4. Budget of SIDC

Budget of the Institute and its utilization in the year 2004

Budget classification	Budget approved	Utilization adjusted	(in thousands SKK)
Incomes from the others SIDC activities	12 000	8 100	7 715
Incomes from registration			99 972
Incomes of SIDC[1]			**107 687**
Common expenses	92 844	95 462	95 438
Capital expenses	59 051	69 082	69 082
Expenses of SIDC[2]			**164 520**

Development of selected budget indicators for the period of 2001 - 2004
(in thousands SKK)

	2001	2002	2003	2004
Incomes	**18 245**	**16 273**	**8 453**	**7 715**
Common expenses	**78 955**	**78 998**	**93 651**	**95 438**
Capital expenses	**4 646**	**16 273**	**43 226**	**69 082**

Exchange rate 1 EUR / 40 SKK

5. Personnel policy

Personnel Office provided exerising of Act No 312/2001 Coll. on Civil Service and amendments to certain acts in their later amendments (hereafter called „Civil Service Act"), Act No 552/2003 Coll. on performing the work in public interest in later amendments, Act No 311/2001 Coll. Labour Code in later amendments (hereafter only „Public Service") and Act No 553/2003 Coll. on remuneration of certain employees exercising the work in public interest in later amendments. The Personnel Office provided keeping of records and statistics related to the above mentioned ativities which are submitted to the Statistical Office of SR, the Civil service Office, the Ministry of Health of SR and to the Institute of Health Information and Statistics according to their assignment.

[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 and filling of capacity:

Indicator	Civil service	Public service	Total
Limit	***81***	***124***	***205***
Reality – natural persons	***77***	***128***	***205***
- average	74.98	120.5	195.48
- records as of 31 December 2004	77	128	205

Age structure of employees

	Civil Service	Public Service
20 years and less	-	1
20-29 years	9	7
30-39 years	10	19
40-49 years	18	29
50-59 years	34	63
60 years and more	6	9

Educational structure of employees

	Civil Service	Public Service
university II. degree	74	21
university I. degree	2	4
complete secondary school	1	87
secondary specialized school	-	5
elementary + training	-	-
elementary	-	11

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
2001	194.30	202.80
2002	194.76	199.26
2003	192.42	198.00
2004	195.48	205.00

Comparison of average month salary

year	
2001	12 207 SKK
2002	14 674 SKK
2003	15 677 SKK
2004	16 177 SKK

Employee fluctuation

During the year 2004 totally 23 employees terminated labour relation or civil service relation, thereof:

5 retirement
8 agreement
2 termination of temporary civil service
3 termination in trial period
4 termination of the certain period
1 change of the job

During the year 2004 the Institute entered the labour relation or civil service relation with 24 employees, thereof:

13 in public serice
11 appointed to state service

TRAINING OF EMPLOYEES

Training of state employees

According to the government decree of SR No 79/2004, which approved the Conception of education of state employees, was at the service office developed the Plan of education of the state employees for the year 2004.

In the year 2004 continued the specialised training of the state employees in the temporary and permanent civil service. The purpose of the training was the completion of the knowledge and abilities of the civil employees in performing of the civil service tasks in the required field of civil service before the qualification examination.

In the specialised training partcipated 34 state employees in temporary civil service and 10 state employees in preliminary civil service. The training was performed in the scope of 5 service days, one part of it was focused on the common basis (Constitution of SR, constitutional law, Act on Adminisrative proceedings, other generally binding legal provisions and Act on civil service) and the second part was focused on the specified provisions related to the concerned section of the civil service.

Internal training

In the framework of the regular training of the SIDC employees the Quality Assutance Unit developed the year-round plan of inernal training approved by the head of Service Office and the director. According to this plan seminrs were performed on actual topics related to the expert, legislative questions concerning the SIDC etc. The seminars took place always after the gremial session and were notified in advance in the protocol from the previous session.

The heads of the particular units of the Institute had at their disposal year-round plan. Apart from the whole-institute seminars was at each section/department performed the training

focused on the specific topics according to the elaborated plans. Year-round plans of the internal trainings, attendance lists and copis of the training plans of the particular organisational units are kept at the Quality Assurance Unit.

External training

External training was ensured by the participation of the employees at the expert events (seminars, conferencies, workshops, etc.) in the SR and abroad.

6. Aims and overview of their fulfilment

International cooperation was focused on the European pre-accession activities and participation in EU structures after accession of SR to the EU, development of the cooperation and exchange of information between the OECD member states.

Another important task was the coopertion with the European Directorate for the Quality of Medicines (EDQM and OMCL), in the purpose of the unified implementation of the quality system in the laboratories in the framework of the mutual recognition of the results, as well as the cooperation and participation in the regular session of EMEA.

Nominated employees participated in the regular sessions of the working groups and committees according to the requirements of the European organisations and agencies (EMEA, EDQM, OECD, EC).

Legistative activity was realised in the framework of the cooperation with the department of health, environment, economy and with the Centre for chemical substances in the framework of implementation of the decisions and recommendations of OECD and European Commission in the field of chemical subsatnces.

Elaboration of the control documents continued: quality manuals, internal directives and standard operation procedures in the purpose of accreditation, as well as the publication of the 7th volume of the Slovak Pharmacopoeia I.

The Quality Assurance Unit continued the realisation of the quality mangement implementation in the terms of STN ISO 9000, the quality system in the laboratories in the terms of STN EN ISO 17025 and the preparation for accreditation.

At the coordination of the tasks in the framework of the particular quality sytems in the purpose of the mutual recognition of the results the cooperation with the OMCL, EMEA, OECD proceeded. The supervision was performed of the laboratories with the SIDC authorisation for pharmaceutical and toxicologically-pharmacological testing. Simultaneously the quality systems criteria were consequently applied.

The EU Coordination Unit coordinated the activities related to the access of SR to the EU in the field of human pharmacy and ensured the realisation of the obligations resulting from the SIDC membership in the international organisations.

Administrative section according to the control activity plan realised the control activity and ensured the complaints and petitions agenda in the terms of the valid legislation.

Moreover the section ensured the performing of the tasks in the field of the public relations, metrological activity, as well as in the field of fire protection, work safety and civil deference.

Informatics: The processing of the registration documentation started in new programme. The updating of the database of registered medicinal products and assignation of SIDC codes was performed continuously. In cooperation with the MCR company continued the work on the internal information system. The works related to the editorial activity were carried on.

Registration section was influenced by the access of SR to the EU. This required the organisational change. In the framework of the registration section two departments were established: department of EU registrations and department of national registrations. At the same time the separate Medical devices section was established.

Laboratory control was focused on the assessment of the chemical, pharmaceutical and biological part of the registration documentation submitted with the registration application within the MRP procedure.

Pharmacopoeia- and standard-related activities covered the finalisation and transmitting for publication of the 7th volume of the Slovak Pharmacopoeia I. and processing of the data for the electronical version of the Slovak Pharmacopoeia. Translation of the articles from Ph.Eur.5 started. The work on the Pharmaceutical code was carried on by the experimental verification of the tests on 50 products and stability tests started.

Inspection activity in the field of GMP, GPhP, GCP was performed according to the valid legislation focused especially on the problems related to the quality, safety and efficacy of medicinal products. The coordinating sessions with the control laboratories were carried on. Control laboratories 1 - 5 performed the inspection activity according to the valid lagislation coordinated on the basis of the requirements of MH SR and in cooperation with the Inspection section. Analytical control activity was particularly focused on monitoring of the chemical and microbiological quality of random samples of medicinal preparetions, purified water and packages.

Monitoring of adverse effects of drugs was focused on stimulating of adverse effects reports and taking necessary measures. Cooperation with WHO at International Drug Monitoring project and involvement in EU system proceeded.

In the field of clinical testing of drugs and medical devices and Good Clinical Practice SIDC was providing the assessment of the applications for clinical testing, issuing of the decisions on clinical testing permissions, approving of work places and conducting supervision. The institute supervised the advertising of medicinal products, infant food prearations and supplements.

Medical devices section performed tasks related to the registration of medical devices. Within the organisational changes two departments were established: department of registered medical devices and department of safety of medical devices.

Economy section ensured the SIDC activity connected with the monitoring of the expenses of the particular units and control laboratories, as well as the monitoring of the working schedule regarding the development and extension of SIDC to be in compliance with the termination date of building. The list of non-payers for provided service was prepared quarterly.

Personnel Office – the main activity was focused on the realisation of the act on civil service and act on works performed in the public interest.

7. Evaluation and analysis of SIDC development

In recent years, SIDC works on the improvement of the quality of its activities. Appropriate feedback is essential for development of the quality system. Therefore, in 2004 was performed regular annual research of information in the form of questionnaire. The results of the research were published at the SIDC website.

The results of the quanitative research confirm that SIDC activities have been evaluated very positively. SIDC decided to perform the research 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. The results of the research will be used as one of the tools for improvement of the quality of SIDC acivities.

For ensuring of the planned tasks the Institute used the state budget resources divided into current and capital expenditures. The results achieved by SIDC were regularly evaluated in the activity reports and submitted to the Ministry of Health of SR. On the basis of these evaluations the following conclusions could be presented:

Drawings from the state budget for the particular items and subitems were realised in the way to ensure the continuous peforming of the SIDC tasks together with the effective using of the vested resources.

Total current expenditures were drawn according to the approved budget, mainly for ensuring of the material, services, energy and official journeys.

Capital expenditures were drawn according to the pescribed limit. Small investments in the machine and equipment cathegory were finished, which improves the technical and technological equipment of the institute. The crucial investment of the institute was Extension of SIDC, for which was invested 62 982 thousand Slovak crowns. By finishing of this action premises and technical equipment of the institute will be resolved according tho the requirements of the EU.

In the field of income for the year 2004 the determined limit for SIDC was 8 100 thousand Slovak crowns. Actually the income for the provided services presents 7 715 thousand Slovak crowns, which were delivered to the state budget.

8. Main groups of users of SIDC outputs

External clients:
- patients,
- legal persons (pharmaceutical manufacturers, medical devices manufacturers, distributors of medicinal products and medical devices),
- physical persons (pharmacies, dispensaries of medical devices),
- applicants for clinical testing
- others (e.g. applicants for information, applicants for authorisation).

Services provided to the clients:
- registration of medicinal products and medical devices,
- issuing of binding opinions for licences 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 manufacturers, 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. Totally 206 requests for information were received (information provided 205-times, 1 decision on withholding information was issued in compliance with the act).

The 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. Partial outputs from the mentioned database are provided to the applicants for the registration and to the Ministry of finance for the purpose of the pricing of medicinal products.

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 processedin

Total number of analytical certificates accepted was **226**
Total number of samples accepted for testing was **564**
Total number of registrations and amendments in registration accepted was **1287**
Number of registered approval decrees **41**
Number of registered EDQM **5**

Analytical certificates processed	Complying	Non-complying	Elaborated	Total
Import	72	24	130	226
Domestic Producers	0	0	1	1
TOTAL	72	24	131	227

Samples processed in laboratory testing	Complying	Non-complying (showing discrepancy or defect)	Elaborated	Total
Imported drugs	79	1	31	111

Samples processed in laboratory testing	Complying	Non-complying (showing discrepancy or defect)	Elaborated	Total
MIS*, Pharmacies	212	1	15	228
ZENTIVA, s.e.	55	1	56	112
CHIRANA T. INJECTA, s.e.	3	0	20	23
VULM, j.s.c.	29	0	3	32
ADSR	11	0	3	14
Starting substances	1	1	0	2
Complaints	4	8	5	17
Clinical trials	4	0	0	4
Other companies on request	24	0	32	56
Attests	40	0	8	48
PTS, CS testing	4	0	3	7
Internal testing	58	13	24	95
TOTAL	456	24	167	641

* 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 and branches of public pharmacies	Entry inspections	153
	Targeted inspections	109
	Follow- up inspections	211
	Precursors of NPS	934
	Sample takings	177
Hospital pharmacies	Entry inspections	12
	Targeted inspections	5
	Follow- up inspections	7
	Precursors of NPS	33
	Sample takings	15
Dispensaries of medical devices	Entry inspections	22
	Targeted inspections	1
	Follow- up inspections	9
Distribution organizations	Entry inspections	4
	Targeted inspections	12
	Follow- up inspections	37
	Precursors of NPS	20
Opticians	Entry inspections	22
Other facilities	NPS	10
	Precursors of NPS	4
	Authorisation of ORPH**	1
	Targeted inspections	2
	Sample takings	5
Producers of poppy	Entry inspections	20
TOTAL:	Inspections	1629
	Sample takings	197

* NPS - Narcotic and Psychotropic Substances
** ORPH - Office of Regional Public Health

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