Ústav pro státní kontrolu veterinárních biopreparátů a léčiv
Institute for State Control of Veterinary Biologicals and Medicaments
Hudcova 56a, Brno-Medlánky
Postal Code: 621 00, Czech Republic

ANNUAL REPORT

On Activities of the Institute for State Control of Veterinary Biologicals and Medicaments Brno

2008

In Brno 28. 2..2009

Basic Information about ISCVBM, Position of ISCVBM

Founder:	Ministry of Agriculture of the Czech Republic
Name:	Institute for State Control of Veterinary Biologicals and Medicaments
Address:	Hudcova 56a, Brno-Medlánky, postcode: 621 00
Phone:	00420- 541 518 211
Fax:	00420- 541 212 607
E-mail:	uskvbl@uskvbl.cz
URL:	http://www.uskvbl.cz
Identification No:	00019453
Bank Account – Current:	31229641/0710
Bank Account - Special:	35-31229641/0710

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1. Introduction

Dear partners and customers of Institute for State Control of Veterinary Biologicals and Medicaments,

Let me introduce the report on activities of the Institute in 2008. Although it may not be evident at first sight from the data and numbers stated in the report, I am convinced that over the last year the Institute made further qualitative advancement in professional spheres, which are entrusted with responsibility of the Institute. Therefore I believe that the Institute will play a dignified role within oncoming year and activities which are going to be organised within the frame of CZ PRES.

In 2008 the Institute invested in informational technologies with the aim to install the informational system which will enable more efficient managing of procedures, decrease administrative burden, enable more efficient control and also enable better utilization of veterinary products data, both from the perspective of internal needs of the Institute and from the perspective of regulated subjects and public. Therefore I assume that in the second half of 2009 the Institute will be able to offer a significantly higher informational service related to authorised veterinary medicinal products to individual concerned parties.

Further improvements should be done in the coming period in laboratory section instrumentation, in the Division of Laboratory for Monitoring of Veterinary Drug Residues where it was decided to purchase two new chromatographic devices corresponding to the current requirements on instrumentation of laboratories for monitoring. It is also worth mentioning that year 2008 meant significant progress in the sphere of monitoring of extraneous substances residues within the scope of the Institute namely due to scheduled moving of laboratory for monitoring to modernized premises of former State Veterinary Institute Brno. It would not be able to realize this significant step without cooperation of all main concerned partners – namely Ministry of Agriculture, State Veterinary Administration, Regional Veterinary Administration for South Moravia Region and ISCVBM.

Year 2008 and namely its second half was already in token of preparations for the first half of 2009 – the period of Czech Republic´s presidency of the Council of the European Union.

As well as in the previous periods the Institute will greatly appreciate all suggestions and comments which will further help us improve the level on which the Institute ensures its assigned tasks.

Prof. MVDr. Alfred Hera, CSc.
Director

2. The Quality Assurance System and Organisation Structure of the Institute

The Institute was maintaining the construction and developing of quality assurance system in 2008. The scheduled internal audits were carried out.

The Institute was also audited by the external auditors namely by the Czech Accreditation Institute which conducted the regular supervisory visit within the frame of the Institute and the extra supervisory visit in which the new methods were accredited and new employees evaluated. This audit was carried out on 20.11., 21.11. and 24.11. 2008.

Mutual Joint Audit was the second external audit, which was realized in the Institute in 2008. Within the frame of this audit the European Directorate for the Quality of Medicines (EDQM) based in Strasbourg evaluated the competency of Official Medicines Control Laboratory which works within the Laboratory Control Section of the Institute, for the activities of OMCLs in European network. This audit took place on schedule 2. – 4. September 2008. Pursuant to this audit and after the ensuring of corrective actions the Institute will ask the EDQM for official final audit.

During the 2008 the updating of management documentation of the Institute was updated (revisions, variations, adoption of new documents).

With regard to provisions set by the Ministry of Agriculture the Institute took the measures and adjusted organisational structure in compliance with its organisational scheme (see Annex No 1).

3. Activities and Active Co-operation with National, European and Other International Organisations

HMA

The Institute took part in HMA meetings namely in contributions to antibiotic policy issues and measures in the sphere of antimicrobial resistance. From October 2008 the Institute actively participated in the preparation of HMA meetings namely by the participation in the working in HMA Management Group (HMA_MG). The Institute set as a priority the issues associated with the antimicrobial resistance following the Slovenian and French Presidency and the on-coming Swedish Presidency and the main endeavour will be presentation the necessity of integration of both veterinary and human medicinal product sphere.

Further issues which may be considered as pivotal from the view of Czech Republic are the issues associated with the training of assessors of dossiers, issues associated with the testing of veterinary medicinal products, efficient use of resources, vaccination against bluetongue and the activity associated with Task Force Group on Veterinary Legislation may be appraised as the principal sphere of veterinary medicine. Its ambition was to prepare the opinion and the base for revision of pharmaceutical legislation in the sphere of veterinary medicinal products for future revision of legislation which is expected around 2012 – 2014.

The activity within the frame of HMA will be ranked among the pivotal tasks of on-coming CZ PRES when the Czech Republic will arrange two HMA meetings in accordance with the established rules.

The Council – Working Party for Veterinary Experts – Public Health

The Council Working Party meetings were in process in 2008 where the entrusted experts of the Institute (Mgr. Pokludová, MVDr. Bureš and Mgr. Rejtharová) were participating actively and regularly. The various stages of legislative regulation suggestions were discussed together with the deputies of State Veterinary Administration. During the 2008 the intensive discussions devoted namely to the proposal of EP regulation relating to EC approach to residue limit determination of pharmacologically active substances in food of animal origin and annulling the regulation 2377/90/EC. First reading passed in the EP and in the second half of 2008 the intensive discussions took place on the level of CVO, Coreper and the Council pointing to finalization of the proposal. The employees of the Institute took part in all meetings in cooperation with SVA, Permanent Representation of the CR to the EU in Brussels (SZ) and also General Secretariat of the Council (GS) and were preparing the opinions representing the positions of CR. In the last quarter 2008 the communication with General Secretariat of the Council and Permanent Representation of the CR to the EU in Brussels got intensified within the frame of preparation of on-coming CZ PRES.
New directive 2008/97/EC of the European Parliament and the Council was published in the Official Journal of 19 November 2008 amending Council Directive 96/22/EC concerning the prohibition on the use in stockfarming of certain substances having a hormonal or thyrostatic action and of beta-agonists, on its discussing they took part in 2007 and 2008.

3.1 Preparing and Amending of legal regulations

During the year 2008 the Institute participated in the preparation and approval of all implementing legislation which is administered by the special provisions of Act on Pharmaceuticals.

The decree No:

- 54/2008 Coll. on the method of prescription medicines, data stated on the prescription, use and the rules of the medical prescription, which was amended by the Decree 405/2008 Coll.
- 84/2008 Coll. on good pharmacy practice, further conditions of medicines treatment in pharmacies, medical services and in further operators and plants
- 85/2008 Coll. on making a list of active ingredients and excipients which may be used for preparation of medicinal products
- 86/2008 Coll. on application of good laboratory practice principles in the sphere of medicinal products
- 106/2008 Coll. on good practice of sellers of selected medicinal products and on specialized course for sellers of the selected medicinal products
- 226/2008 Coll. on good clinical practice and further conditions of clinical evaluation of medicinal products
- 228/2008 Coll. on marketing authorisation of medicinal products
- 229/2008 Coll. on manufacturing and distribution of medicinal products
- 344/2008 Coll. on use, prescription and dispensing of medicinal products while veterinary care is provided
- 427/2008 Coll. on the amount of reimbursement for professional acts performed within the scope of the State Institute for Drug Control and the Institute for State Control of Veterinary Biologicals and Medicaments

Except the implementing legislation in the sphere of medicinal products the Institute participated on the preparation, making comments and approval of the regulations which responded to repealing Directive 84/539/EC in the sphere of electric veterinary technical devices, amendments to an Act on Pharmaceuticals and to others, from the perspective of the Institute less important regulations.

3.2 Ministry of Agriculture, State Veterinary Administration and Other Partners of the Institute in CR

3.2.1 Ministry of Agriculture

During the firs half-year 2008 the Institute and Ministry of Agriculture were intensively discussing the field of change in conditions of putting the medicinal products into circulation with reference to the new rules which allow in compliance with the rules set by the Act on Pharmaceuticals the distribution of medicinal products towards breeders which is unprecedented practice in the Czech Republic. The negotiations resulted in the compromise which was consequently realized in the form of amending act 54/2008 Coll.

Within the frame of activities connected with the CZ PRES the list of activities was repeatedly submitted to the ministry on behalf of ISCVBM. Czech Republic will have to ensure these activities within the scope of CZ presidency of the Council of the European

Union. There were the following pivotal activities: two meetings of HMA (in cooperation with the SIDC), provision of informal CVMP meeting, active participation in meetings of WGs of the Council following the on-coming CCRVDF meeting (Codex Alimentarius – Codex Committee for Residues of Veterinary Drugs in Food).

On behalf of the Institute second and third category experts were nominated, who were called to ensure the professional support for the negotiations relating to the VMP issues and the sphere of VMP residues in food of animal origin (Mgr. Rejtharová, Mgr. Pokludová, MVDr. Bureš). Within the scope of preparation for CZ PRES the above-mentioned employees passed the exams themed EU basics degree I and II, and also the English language exam level C1.

Committee on Treatment of Genetically Modified Organisms and Products in the Department of Ministry of Agriculture

Committed on Treatment of Genetically Modified Organisms and Products has been acting as a advisory body of Ministry of Agriculture and has participated in the elaborating of opinions to submitted applications for contained use of GMO or release of GMO into the environment or putting into circulation.
Aside from the agenda according to Act 78/2004 Coll. on the use of genetically modified organisms and genetic products further.the issues relating to amending act on agriculture were discussed and the results of feed inspections from the view of permitted level of GMO or the controls of compliance with the regulations relating to cultivation of genetically modified crops were discussed as well.
In genetically modified veterinary medicinal products the quality, safety and efficacy are henceforth ensured by the EMEA by the co called centralised procedure. Eventual need of identification of genetically modified medicines is ensured and established by the agreement with State Veterinary Institute Jihlava.
Commission meetings were held 2.4.2008 and 7.7.2008.
One employee of the Institute works in Commission.

3.2.2 State Veterinary Administration and Regional Veterinary Administrations

The cooperation with the State Veterinary Administration was carried out in traditional spheres as a monitoring of extraneous substances, the control of usage, prescription and dispensing of veterinary medicinal product including medicated feedingstuffs, monitoring of usage of chosen veterinary medicinal products or the sphere of exceptions from marketing authorisation of veterinary medicinal products.
During 2008 the SVA in cooperation with the Institute made definitions of the veterinary surgeons and breeders inspections which will enable more sufficient controls of adherence of requirements set for the sphere of medicines, in case of breeders this will enable the evaluation of compliance with the European directive 96/22/EC given in the Cross-Compliance program.
In terms of preparations of these definitions the seminary for State Veterinary Administration and Regional Veterinary Administration was held by the Institute 19.11.2008 which was attended by the deputies of all Regional Veterinary Administrations and also SVA.

3.2.3 State Institute for Drug Control

Implementing legislation to Act on Pharmaceuticals was prepared in conjunction with SIDC in 2008.
In cooperation with the SIDC the steps for successful organisation of activities practised within the CZ PRES were also made.
No joint inspections in the sphere of GMP were executed within the cooperation with SIDC, inspection schedules and prepared regulations were interchanged.

3.2.4 Central Institute for Supervising and Testing in Agriculture (CISTA)

There were two workshops of Inspection Section employees carried out during 2008 (June, November) with CISTA employees where the issues relating to anticoccidials and their residues in feeds for nontarget animals were discussed.

Further cooperation proceeded between CISTA in the sphere of medicated feedingstuffs and the assessment of so called border products.

Together with CISTA and Ministry of Agriculture the opinions to EU legislation draft were prepared by which the transfers of residues of additives for nontarget animals determined.

Within EU (Greece as a guarantee) the cooperation of Laboratory Control Section of ISCVBM with CISTA, SVA Prague and VFU Brno on the joint project on quality, efficacy and safety assurance of some plant substances has also begun.

3.2.5 Ministry of Health

Ministry of Agriculture was a partner for the Institute in the sphere of preparation, making comments and approval of legislation implementing the Act on Pharmaceuticals. Except this sphere it is further necessary to mention the cooperation in the area of antibiotic policy where the Ministry of Agriculture plays the key role of the coordinator of the activities (for further details on antibiotic policy see the relevant part).

Pharmacopoeia Committee – activities of the Institute for Pharmacopoeia in 2007
In 2008 ISCVBM participated in the pharmacopoeia activity in compliance with the task which are lay out by the Act on Pharmaceuticals.
Among these main tasks pertained the participation in activity of Pharmacopoeia Committee at Ministry of Health CR (prof. MVDr. A. Hera, CSc. As a vicechairman, MVDr. Jana Jeřábková as a member), and the activity of Section for Veterinary Immunologicals and Pharmacuticals and the Expert Group of European Pharmacopoeia Committee activities (MVDr. Jana Jeřábková and PharmDr. Jaroslav Maxa, PhD)
In the year 2008 analogous to previous years the crux of the work consisted in the preparation of new edition of Pharmacopoeia Bohemica 2009. This work included translations of new and revised articles and sections for European part of Pharmacopoeia Bohemica (this part will contain texts corresponding to sixth edition of European Pharmacopoeia including its addenda 6.1 and 6.2) and preparation of national part of PB 2009, where the updated review of doses of some active ingredients used in veterinary practice.
The pharmacopoeial activity was mediated and coordinated by the Section for Veterinary Immunologicals and Pharmaceuticals of the Pharmacopoeia Committee at Ministry of Health CR, whose official administrative place is the ISCVBM. The Institute ensured its work via the Department of Pharmacopoeia at ISCVBM, Dr. Jeřábková is charged with its management. In the Section for Veterinary Immunologicals and Pharmaceuticals of the Pharmacopoeia

Committee at Ministry of Health CR there were nine ISCVBM employees working in 2009 and another six members from other workplaces, the total number of members in this section was 15 in 2008. The external employees which the Institute made a contract with considerably took part on the translations and translation revisions of the pharmacopoeial articles. MVDr. Jana Jeřábková and PharmDr. Jaroslav Maxa, PhD as a member of the Expert Group of Pharmacopoeia Committee took active part in this Committee including the participation in negotiations in Strasbourg.

3.2.6 Chamber of Veterinary Surgeons of the Czech Republic

In case of the Chamber of Veterinary Surgeons in the first half-year 2008 the joint negotiations with the Ministry of Agriculture deputies and breeders deputies took place. These negotiations were relating to conditions under which it is possible to put medicinal products under circulation, namely with regard to new rules which recently enabled the distribution of medicinal products towards the breeders.

3.2.7 Central Committee for Animal Protection

Expert Committee for Animal Protection

During the year 2008 the Committee was ensuring entire activity of the ISCVBM experimental plant provided by the act related to protection of animal against torture No 246/1992 Coll. as amended.
The Expert Committe experessed its opinion on two experimental projects. Pursuant to data stated in the eperimental project the Expert Committee approved the performance of both submitted experiments.

1/2008 Evaluation of efficacy of various ways of slaughter of killing animals
2/2008 Chloramphenicol kinetics studies

With respect to the submission of experiment 2/2008 at the end of 2008, by that time only the experimental project 1/2008 was approved by the competent authority. The positive opinion is anticipated as well at the project 2/2008, it is approval of animal usage.

The Expert Committee has 5 members, one employee was replaced this year. Nine ISCVBM employees has qualification provided by law according to article 17 of the act 246/1992 Coll. related to protection of animals against torture and 5 employees passed the required course for laboratory assistants, technicians and tenders, re-examination of professional qualifications regarding animal maintenance, also provided by the law.

The Committee checked the process of approved experiment projects, checked and ensured welfare of experimental animals and checked and ensured required data records.
In the investigation protocol there was no fault detected by governing body it is Regional Veterinary Administration Inspectorate for South Moravia region (from day 23.5.2007).
Welfare of experimental animals after attended time was again ensured by trained and professional employees from the Institute.

The following documents were elaborated by the Committee for the Ministry of Agriculture CR: Summary Report for Calendar Year 2008, Evidence of animals for experimental purposes in 2008 and Sixth statistical report on usage of laboratory animals in 2008. The numbers of experimental animals used in 2008 were following:

Animal Category	Year 2006	Year 2007	Year 2008
mice	1310	3949	2340
guinea pigs	17	12	23
rabbits	22	7	-
birds	109	4	100
dogs	9	-	-
cats	4	-	-
Total	**1471**	**3972**	**2463**

The disposal of cadavers and contaminated materials after termination of the experiment were ensured by contract with these companies – AGRIS s.r.o. Medlov and SITA Brno.

3.3 EU Organizations and Other Foreign Partners

3.3.1 European Medicines Agency (EMEA)

Activity in the Committee for Veterinary Medicinal Products (CVMP) and its Working Parties

Eleven CVMP meetings took place in 2008. Committee for Veterinary Medicinal Products was assessing the applications for determination of Maximal Residue Limits, applications for centralized marketing authorisation of veterinary medicinal products, prepared or approved new guidelines in the sphere of quality, safety and efficacy of veterinary medicinal products, solved referral procedures and worked out further expert opinions or reports.

To the most important issues, which were solved by the Committee during 2008 was the marketing authorisation of bluetongue vaccines, further guideline on anticancer medicinal products, guideline on the conduct of bioequivalence studies, guideline on risk/benefit assessment. In the sphere of antimicrobial resistance was the document administering the risk resulting from the usage of third and fourth generation cephalosporins was issued and at the end of year 2008 the preparation of the document administering the issues relating to methicillin-resistant Staphylococcus aureus was finished.

The significant development have been further done in the sphere of guidelines on immunological veterinary medicinal products – namely considering two recent concepts – rules for so called "multistrain dossier" which is suspected to be used namely in the event of foot and mouth disease, influenza or bluetongue and rules for "antigen master file".

Joint CHMP/CVMP Quality working party (QWP)

Joint CHMP/CVMP Quality working party being engaged in quality of human and veterinary medicines met four-times in 2008 (from that one meeting was shared with GMP working party and one meeting with industry deputies). Within the scope of working party the revisions of current guidelines were discussed relating to VMP quality, elaboration of new guidelines, cooperation QWP with EDQM, ICH and VICH and solving of quality issues in specific preparations authorised mainly by the centralized procedure.

Namely the following guidelines were solved in 2008:

- the preparation of guideline on the stability testing (EMEA/CVMP/846/99-Rev1)
- the elaboration of guideline on the quality aspects of single-dose veterinary spot-on products(EMEA/CVMP/QWP/544461/2007)
- working on revision of the guideline relating to bioequivalence (in conjunction with EWP) is in process
- working on the preparation of guideline relating to quality requirements of anticancer medicinal products
- working on new guideline VICH GL 45 is in process – Bracketing and matrixing designs for stability testing (in conjunction with EWP)
- working on preparation of new guidelines in connection with new regulation of the Commission relating to variations to MA

Safety Working Party

Following the meetings and agenda from the previous period there were 4 meetings of the working group carried out (three in London, one in Amsterdam). The meetings were focused on safety issues of veterinary medicinal products from the perspective of user, from the perspective of safety for target species of animals and residues safety as well. Working group has continued to work on the sphere of preparation of guidelines relating to marketing authorisation of VMP, prepared opinions for CVMP and discussed the professional themes of given issues. Part of the January meeting was also the workshop inquired into approaches of MRL determination within EMEA and its comparison with JECFA approaches.

The following guidelines were solved and prepared in 2008:

- guideline on alternative thresholds for MRL establishment
- guideline on evaluation whether the substance is pharmacologically active
- guideline on evaluation of pharmacological/pharmacokinetic data with regard to pharmacological ADI establishment
- dossier requirements on the anticancer medicinal products
- revision of the guideline on microbiological ADI establishment
- guideline on user safety assessment
- revision of the guideline on bioequivalence
- update of EMEA summary report on penicillins

The issues of VICH guidelines drafts related to evaluation of metabolism and kinetics of VMP residues in food producing animals were annotated.

The following issues were discussed:

- alternative referential limits and exposure assessment (TTC, ArfD)
- injection site residues assessment
- new data relevant for evaluation of safety factor for amoxicillin
- guideline on establishment of withdrawal period for milk in DC preparations
- new template for MRL Summary Reports
- N-methylpyrrolidon carcinogenity (NMP)
- Faecal binding studies

The opinions to discussed issues were sent and at the last group meeting Mgr. Pokludová was appointed co-rapporteur of the negotiations on MRL opinion of monensin and of the issues relating to residues of pharmacologically active substances in honey. Active participation was also done in the sphere of background papers providing for new guideline on establishment of withdrawal period for milk in DC preparations

Efficacy Working Party

The working party works on elaboration of new guidelines for efficacy evidence, making comments on them and implementation. It cooperates with other groups on common themes. EWP met four times in 2008 on two-day meetings, where the following issues were solved:

Newly formed guidelines:

- guidelines on dossier requirements for anticancer medicinal products

Revised guidelines:

- efficacy evaluation of veterinary medicinal products used in aquaculture
- bioequivalence studies for veterinary medicinal products

- safety evaluation for target animal species
- efficacy evaluation of products controlling Varroa jacobsoni in bees

Implementation of guidelines:

- guideline on testing and evaluation of the efficacy of antiparasitic substances for the treatment and prevention of tick and flea infestations in dogs and cats

Immunological Working Party (IWP)

The working party for immunological veterinary medicinal products met three times in 2008. The main task of the group was first of all preparation of guidelines on evaluation and marketing authorisation of immunological veterinary medicinal products.
The following current issues were solved at IWP meetings:

- the draft guideline on requirements on multi-strain dossiers
- guideline on need for requiring data to demonstrate the influence of maternally derived antibodies on the vaccination of very young animals was discussed
- continued work on guideline on preparation of master seeds to replace established master seeds already used in authorised immunological veterinary medicinal products
- the VICH guideline on target animal safety for veterinary live and inactivated vaccines was finished
- the VICH guideline on target animal safety - examination of live veterinary vaccines in target animals for absence of reversion to virulence was finished
- the guideline on minimum data requirements for an authorisation under exceptional circumstances for vaccines for emergency use against bluetongue was finished
- the preparation of guideline on variation categorization in immunological veterinary medicinal products was initiated
- early in December the joint meeting of IWP deputies and deputies of expert group for veterinary vaccines and sera of European Pharmacopoeia in Strasbourg in order to harmonize the requirements stated in VICH and IWP guidelines and European Pharmacopoeia articles

Pharmacovigilance Working Party

In the year 2008 five pharmacovigilance WP meetings were held. The most remarkable activity was the finalization of Volume 9B “EU Pharmacovigilance Rules for Medicinal Products – Pharmacovigilance for Medicinal Products for Veterinary Use”. This document has the great importance to harmonisation of approaches in the sphere of pharmacovigilance for VMP for marketing authorisation holders, for EMEA and for concerned medicines agencies in EU member states. Part of the document is also guideline on electronic submission of adverse reaction reports to veterinary medicinal products and Group for implementation of EudraVigilance Veterinary was charged with the preparation of this guideline. The members of this group are the deputies of particular EU member states and deputies of major pharmaceutical companies. Indispensable contribution of this document is the fact that it contains all relevant and applicable information (documents) for all interested parties involved in pharmacovigilance in one place.
This document has been passed along to European Commission for approval, afterwards it will be publicly available.
Further after the consultation with the deputies of pharmaceutical industry the working party finished the document “Recommendations for Management and Assessment of Periodic Safety

Update Reports (PSURs) of Veterinary Medicinal Products", the document was published on EMEA website at the end of 2008. The document also includes the template of PSUR and the table helping to analyse submitted pharmacovigilance data within the frame of proper PSUR assessment. In November 2008 EMEA arranged the training to this topic which was attended also by the employee of pharmacovigilance department.
Working party has been responding to actual situation in the sphere of marketing authorisation of bluetongue vaccines by the centralised procedure and vaccination schemes in EU member states including CR and elaborated the document "Review of field data on bluetongue vaccines safety from the emergency national vaccination schemes in 2008". This document is helpful within the authorisation procedure to the "rapporteur" and also to member states during the evaluation of adverse events after administration of these so far unauthorised vaccines.
Five meetings of Pharmacovigilance Working Party is scheduled for the year 2009.

Pharmacovigilance Inspection Working Group
In 2008 two meetings of this working group were held, on which the issues relating not only to pharmacovigilance inspections – human medicines, but also to pharmacovigilance inspection – veterinary medicines were discussed.
Among the major documents which were discussed falls the following:

- preparation and coordination of pharmacovigilance inspections – veterinary medicinal products authorised by the centralised procedure
- execution of pharmacovigilance inspections – veterinary medicinal products authorised by the centralised procedure
- review of findings within the pharmacovigilance inspections – veterinary medicinal products authorised by the centralised procedure
- reporting of results from pharmacovigilance inspections – veterinary medicinal products authorised by the centralised procedure.

For the year 2009 four meetings of the working group are scheduled, from that two will be again addressed to veterinary medicinal products issues.

Environmental Risk Assessment Working Group (formerly ad hoc)

The group works on preparation of new guidelines on executing trials and tests which are necessary for higher phase of environmental risk assessment. The group continues to collect suggestions to the guideline which should simplify the approach to environmental risk assessment for veterinary medicinal products within the frame of authorisation process. The group provides the experts for solution of specific issues associated with the impact of active ingredients on environment during their actual way of usage, cooperates with other working groups on common themes. The group cooperates with OECD and SETAC. ERA WG meets irregularly, in 2008 the chosen members met to discuss ERA issues raised by the industry and whole working group met three times and the following current issues were addressed:

- explanatory guideline on simpler usage of VICH guidelines GL6 and GL38 for environmental impact assessment
- guideline on studies in dung and dung soil for veterinary medicinal products
- in cooperation with EMEA and European Commission the group processes the interpretation of ERA solution for various types of applications for authorisation, according to rules of current legislation
- guideline on anticancer medicinal products – solution of environmental risk assessment using these medicinal products
- elaboration of public assessment report from the perspective of environmental impact assessment

- in cooperation with OECD the discussions to draft guidelines on tests for dung beetles and dung flies

On needs basis the working group engaged in issues relating to degradation of medicines in dung and toxicity of substances to dung fauna.
Further the group provides consultations for IFAH and for other external clients, consultations are guided by EMEA.

Other Activities of the Institute within the scope of EMEA

Ad Hoc Meeting of GMP Inspection Services – GMP/GDP Inspector working group

Within the harmonisation of procedures and approaches in the sphere of inspections in manufacturers of pharmaceuticals the GMP and GDP Inspectors Working Group is organised by EMEA. During the year 2008 four meetings of the group took place.
The members of the group are the deputies of inspectorates from the EU/EEA countries, observers are the deputies of EDQM, EU acceding countries and third countries with the agreement on mutual recognition of certificates and results of inspections (MRA).
During the regular meetings the new and revised chapters and amendments of guidelines on good manufacturing practice, documents relating to MRA, impact of new legislation on the sphere of active ingredient manufacturers, documents on harmonisations of inspection procedures and the sphere of cooperation with other working groups even with another organisations as a PIC/S, EDQM, PDA, ISPE are discussed.
Mgr. J. Holý took part in these meetings in 2008. In terms of Joint Audit Program EMEA the Czech Veterinary Agency (Mgr. Jiří Holý) was charged with the audit management of the French Veterinary Agency in 2007, this evaluation was got done by the audit in situ and by elaboration of final audit report.

QRD

The Quality Review of Documents (QRD) Working Group consists of deputies of the national agencies of EC member states, EC deputies and EMEA deputies. The main aim of the group is to ensure intelligibility, conformity and accuracy of the information on medicinal products (summary of product characteristics – SPC, package leaflet and labelling) and its translation, which is enclosed to opinions of the committees.
In 2008 all SPC, PL and labelling translations for VMP whose marketing authorisation expired during this year were revised. Also in cases of the approved variations and marketing authorisation renewals when changes in these tests happen, the accuracy was checked.
During the firs half-year the tests to 3 new marketing authorisations, to 3 marketing authorisation extensions, to 5 marketing authorisation renewals, to 6 type II variations and to 1 referral procedure were revised. During the second half-year 2008 the tests to 8 new marketing authorisations, to 1 renewals, to 5 type II variations were checked.

Working Group on Medicinal Products and Medical Devices at the Council of Europe
In connection with the implementation of the control procedure even for the sphere of veterinary medicinal products, the Institute cooperated on changes whose implementation induced the changes in Directive 2001/82/EC, further on changes, which were induced by the newly implemented system and in regulations administering the whole variation system.

3.3.2 European Commission

European Commission – Committee for Veterinary Medicinal Products and Standing Committe on Veterinary Medicinal Products
In 2008 a CVMP session was called whose aim was the finalisation of EC directive, which amends the Annex I of the Directive 2001/82/EC.

Notice to Applicants Working Group at the European Commission

In the year 2008 the deputy of the Institute took part in the meeting of the NTA Working Group at the EC which was held once during the year in Brussels in Centre Borschette.
The spheres of human and veterinary medicinal products were discussed together. Agenda was especially centred on the amendment of Volume 6, Chapter 1 (procedural issues), Chapter 7 (national validation requirements), further theme was the solving of issue relating labelling/PL in the human and veterinary sphere.
Participation in meetings was very important with respect to the fact that rules stated in approved guidelines for applicants are asserted in marketing authorisation procedures of VMP in Czech Republic and they are implemented into guidelines issued by the Institute.

3.3.3 Institutions Ensuring the Cooperation of Member States

HMA Meeting – Heads of Medicinal Agencies (human and veterinary) of EC member states
(see page 3)

Coordination Group for Mutual Recognition and Decentralised Procedures – Veterinary (CMDv)

The Institute deputy as a nominated member took part in the regular meeting of CMDv which were held ten times in 2008. The meetings were held always once a month at European Medicines Agency in London and nominated members of particular medicines agencies of EU member states, IFAH and EMEA deputies took part in.
The main function of CMDv is the work on new guidelines preparation, making comments and suggestions on them and subsequent finalization for its practical use. The CMDv cooperates with other EMEA working groups on common issues within the scope of coordination of authorisation procedures and standard operating procedures.

The negotiations in connection with the implementation of Directive 2004/28/EC amending the Directive 2001/82/EC continued and were finished. Coordination Group CMDv has been also dealing with the current issues of this year together with the IFAH-Europe, with the European Group for Generic Veterinary Products (EGGVP) and with working groups and EMEA deputies. Among the main discussed issues belonged the issues associated with the updating of documents for mutual recognition procedure and decentralised procedure which are the main authorisation procedures in the EU, improvement of cooperation among the main concerned parties during the authorisation procedures – reference member state/concerned member state/applicant, solving of national validation requirements of member states, issues relating to harmonisation of QRD/CMDv templates for SPC/PL/labelling, preparation of new guideline on variations to a marketing authorisation, generic VMP sphere, documents relating to improvement of veterinary legislation and development of communication resources among EU member states.

3.3.4 Other Institutions

EDQM

MVDr. Jana Jeřábková and PharmDr. Jaroslav Maxa, PhD. as members of the Expert Group of the European Pharmacopoeia Committee worked on the activities ensured by EDQM in 2008. Considering MVDr. Jana Jeřábková´s expertness she ensures namely the agenda relating to the immunological veterinary medicinal products, further employee of the Institute - Jaroslav Maxa, PharmDr., PhD ensures the activities relating to the quality of medicinal products and pharmaceuticals.

MVDr. Jeřábková as a 15V Group member (Expert Group for Veterinary Vaccines and Immune Serums) took part in 2 workshops in 2008 whereon the following topics were solved in the course new pharmacopoeial articles elaboration and revisions of current articles of European Pharmacopoeia:

- new draft on new article relating to live vaccine against Bordetella bronchiseptica in dogs was elaborated
- the work on revision of the article relating to vaccine against vibriosis in salmonids
- the work on new article relating to live vaccine against Salmonella enteritidis continued, the meeting of 15V Group with deputies of manufacturers of this vaccine took place
- the work on new article relating to live vaccine against Salmonella typhimurium continued, the meeting of 15V Group with deputies of manufacturers of this vaccine took place
- the draft of new article relating to live vaccine against infectious Turkey Rhinotracheitis was elaborated, the meeting of 15V Group with deputies of manufacturers of this vaccine took place
- the revision of the article relating to substances of animal origin used for the preparation of veterinary vaccines was finished
- the revision of the article relating to vaccine against Chicken Infectious Anemia was finished
- the new article relating to vaccine against Enzootic pneumonia in pigs was finished
- the work on guideline on elaboration and use of European Pharmacopoeia articles designed for immunological veterinary medicinal products continued
- on the beginning of December 2008 the joint meeting of EDQM, 15V Group and IWP deputies in Strasbourg took place in order to harmonize the requirements stated in the VICH guidelines and IWP guidelines and in the European Pharmacopoeia articles, the activity concerning harmonisation of requirements on the immunological VMP is going to continue even in 2009

Jaroslav Maxa, PharmDr., PhD on behalf of Group 7 (Antibiotic Group) of European Pharmarmacopoeia Committee took part in meetings of this group which met three times in 2008. During 2008 the group elaborated and finished several new monographs, e.g. rifaximin. The group was working on revisions of many current monographs, e.g. sulphonamides and cephalosporins. More extensive revision of penicillin and tetracycline monographs was initiated. The employee of the Institute - Jaroslav Maxa, PharmDr., PhD also took part in this revision, namely in the monograph relating to chlortetracycline hydrochloride and demeclocycline.

Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S)

The Institute has been PIC/S member from the year 2005. The membership contribution is partly access to seminars and trainings for inspectors on required level and partly the increase of the international reputation of the Institute and approval of its inspection results also by the authorities outside the EU/EEA (Australia, New Zealand, Israel, Iran, Egypt and others) and thus the simplification of Czech industry access to these markets. In terms of PIC/S membership the Institute has been participating in the preparation of guidelines within the PIC/S and in the harmonisation of inspectional procedures worldwide. Inconsiderable contribution is the possibility of participation in highly professional seminars and obtaining of many contacts on

GMP inspectors.In 2008 the head of Inspection Section, Mgr. J. Holý took part in two PIC/S committees (Switzerland – Geneva, Poland – Cracow) and in one seminar in Cracow together with MVDr. Bronislava Midrlová. The assessment in cooperation with Swiss agency (as a second assessor) of application for PIC/S membership made by French medicines agency was finished by the auditing made in place (joint also with the JAP EMEA schedule) and by the elaboration of report. The final report was received by PIC/S on the meeting held on May in Geneva and it was appraised with a very positive evaluation.

3.4 Activity of the Institute in Relation to Regulated Subjects

In 2008 the Institute by means of Czech Society for Medical Technology arranged 5 workshops for distributors, manufacturers of veterinary medicinal products, manufacturers of medicated feedingstuff and for marketing authorisation holders (2 seminars), the current issues were negotiated over in the sphere of VMP regulation in EU and CR, enforcing act on pharmaceuticals, new or newly prepared guidelines, frequently asked questions and experiences from inspections and authorisation procedures.

Pursuant to possibilities and needs based on Act on Pharmaceuticals the Institute issued 16 guidelines in 2008, from that 4 were generally applicable guidelines, there were 5 guidelines on marketing authorisation sphere, 4 guidelines for manufacturers of VMP and 3 guidelines for distributors of VMP.

The review of ISCVBM guidelines issued during the year 2008:

Generally Applicable Guidelines

UST – 04/2008	Administrative fees and reimbursement of expenses for professional operations performed within the scope of ISCVBM
UST – 03/2008	Syllabus of the Course for sellers of selected medicinal products
UST – 02/2008	Amendment of Annex No 1 of the guideline ÚSKVBL/UST – 01/2008
UST – 01/2008	Reimbursement of costs for operations connected with information providing

Guidelines on Marketing Authorisation of VMP

REG – 05/2008	Summary of the dossier – Part 1A of Application Form
REG – 04/2008	Specific information on variations to marketing authorisation of veterinary medicinal products
REG - 03/2008	Updated version of application form for approval of type II variation/variation type IA/1B notification
REG – 02/2008	Updated version of application form for renewal of marketing

	authorisation of VMP
REG – 01/2008	Application for import of veterinary medicinal product authorised in other member state

GMP Guidelines

INS/VYR – 04/2008	Guidelines on Good Manufacturing Practice – Amendment 20 – Quality risk management
INS/VYR – 03/2008	Guideline on Good Manufacturing Practice – Revision of Amendment 1 – Manufacturing of Germ-free Medicinal Products
INS/VYR – 02/2008	Amendment of guidelines on GMP – Part I, Chapter 1
INS/VYR – 01/2008	Variation to Annex No 1 of the guideline ÚSKVBL/VYR – 2/2003

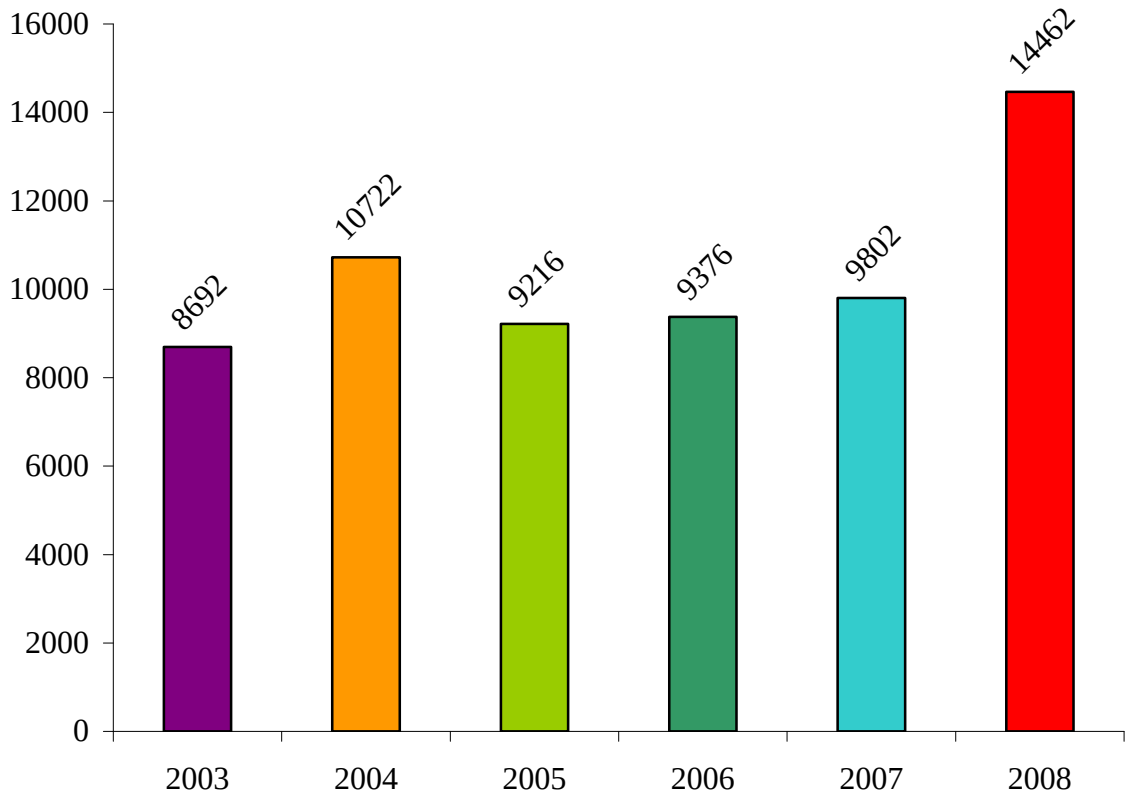
GDP Guidelines

INS/DIS - 03/2008	Revocation of the guidelines ÚSKVBL/INS/DIS – 01/2008 and ÚSKVBL/INS/DIS – 02/2008
INS/DIS - 02/2008	Validity Suspension of the guideline ÚSKVBL/INS/DIS – 01/2008
INS/DIS – 01/2008	Distribution process of veterinary medicinal products to breeders

4. Agenda of the ISCVBM

In 2008 the registry and forwarding office of the Institute started to work with new informational system of the registry office called Magion. This system enables the evidence and tracking of information relating to methods of document execution and persons who took part in the execution of the document at any time.
The total of 14462 papers were registered in the ISCVBM registry and forwarding office in the year 2008, compared to past years there was a significant increase of registered papers, with regard to the year 2007 the increase was 4660 papers.

Picture 4/1 Number of Registered Papers by the ISCVBM Registry and Forwarding Office in Years 2003 - 2007



5. Activity of Section of Marketing Authorisation, Approval, Register of VTD and Clinical Evaluation

5.1 Marketing authorisation of VMP

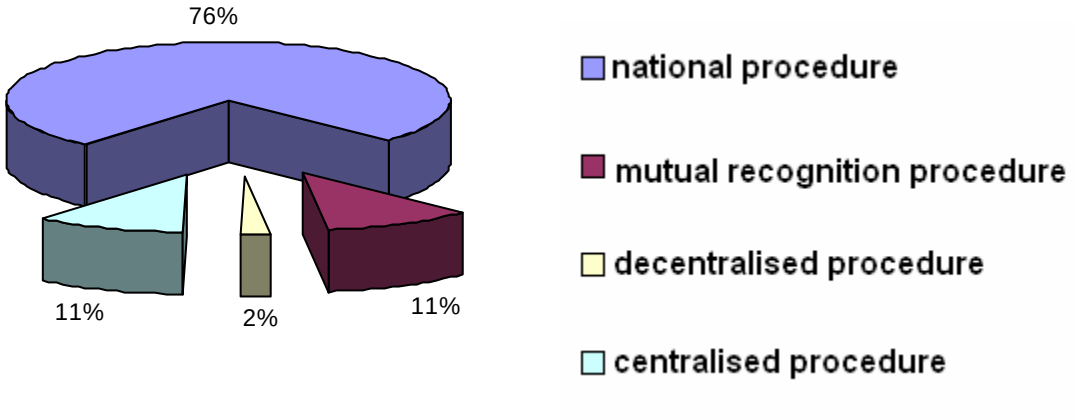
5.1.1 Incorporation of the CR to European Procedures of Marketing Authorisation

During the year 2008 in the course of marketing authorisation of VMP the European procedures of marketing authorisation were applied in compliance with the regulations of the consolidated Directive 2001/82/EC (dated 1.11.2005 as amended by the Directive 2004/28/ES) - national procedure, mutual recognition procedure and decentralised procedure. VMP authorised by centralised procedure were also placed on the market in CR in compliance with the Regulation 726/2004.

Table 5/1 Number of authorised VMP based on procedure type on the 31. 12. 2008

TYPE OF PROCEDURE	TOTAL
NATIONAL PROCEDURE	982
MUTUAL RECOGNITION PROCEDURE/ DECENTRALISED PROCEDURE	143/27
CENTRALISED PROCEDURE	140
TOTAL NUMBER OF AUTHORISED VMP IN CR	**1292**

Picture 5/1 Percentual representation of marketing authorisation procedures in 2008



Within the frame of foreign marketing authorisation procedures of European Union – the mutual recognition procedure and decentralised procedure, the system of application submission remained the same and unchanged.
Applications for new marketing authorisation are submitted by the decentralised procedures, application for new marketing authorisation, applications for renewal and for variations to marketing authorisation type IA, IB and type II are submitted by the mutual recognition procedure.

The Czech Republic has been in both mentioned procedures in the position of both concerned member state (CMS) and reference member state (RMS). In case that CR is in the position of concerned member state the number of applications has increased in new authorisations by the decentralised procedure in this year, in mutual recognition procedure the number of applications for new authorisations using first use procedure, applications for renewal and for variations to marketing authorisation type IB and type II has also increased. On the contrary the number of applications for new marketing authorisation using the repeat use procedure and application for variation to a marketing authorisation type 1A has decreased. The administrative procedure of repeat use has not already been used. In case that CR is in the position of reference member state the number of applications in the sphere of applications for new marketing authorisation and in the sphere of variations to marketing authorisation of all types has increased in comparison with the last year.

Mutual recognition procedure and decentralised procedure has been used by the foreign applicants for marketing authorisation of VMP and by the marketing authorisation holders so far, but this year the first intentions of Czech applicants for marketing authorisation of VMP has already been consulted as well.

Table 5/2: Summary of total number of submitted applications and cases when MA was granted in 2008– Decentralised Procedure and Mutual Recognition Procedure

Type of marketing authorisation	Category of VMP	Number of Applications			
		CR/CMS		CR/RMS	
		Submitted Applications	MA granted	Submitted Applications	MA granted
Mutual Recognition Procedure – First Use	Pharmaceuticals	14	9	0	1
	Immunologicals	4	11	0	0
Mutual Recognition Procedure – Repeat Use	Pharmaceuticals	4	5	0	0
	Immunologicals	3	4	1	1
Decentralised Procedure	Pharmaceuticals	31	15	8	1
	Immunologicals	0	3	0	0
Mutual Recognition Procedure – Variation Type IA	Pharmaceuticals	35	46	0	0
	Immunologicals	0	7	1	0
Mutual Recognition Procedure – Variation Type IB	Pharmaceuticals	38	47	0	0
	Immunologicals	5	7	1	1
Mutual Recognition Procedure – Variation Type II	Pharmaceuticals	22	10	0	0
	Immunologicals	35	27	3	0
Mutual Recognition Procedure – Renewal	Pharmaceuticals	16	3	0	0
	Immunologicals	9	1	0	0

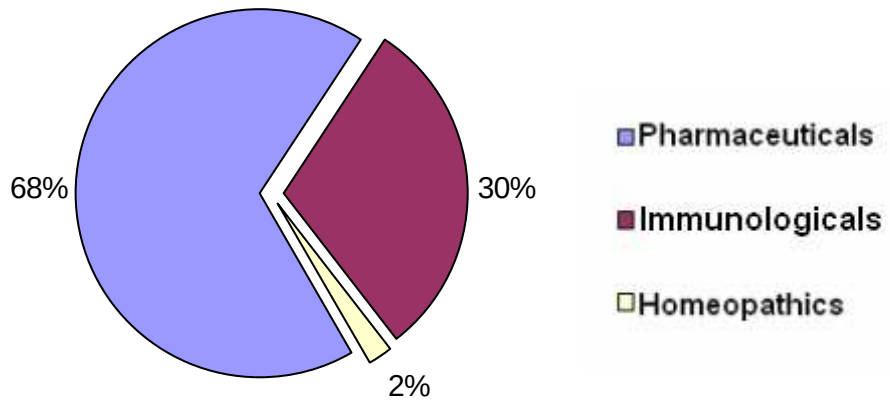
5.1.2 The situation of authorised VMP, agenda of submitted applications, results from the marketing authorisation proceedings

In total 1292 VMP were authorised on the 31.12. 2008, from that 874 were pharmaceuticals, 388 immunologicals and 30 homeopathics. There were 6% of OTC preparations and that represents 56 pharmaceuticals and 15 homeopathics.

Table 5/3 Total number of authorised VMP and the way of their release on the 31.12.2008

Type of VMP	Total	Total (percentage)	From that OTC	Total (percentage)
Pharmaceuticals	**874**	**68**	**56**	**6**
Immunologicals	**388**	**30**	**0**	**0**
Homeopathics	**30**	**2**	**15**	**50**
Total	**1292**	**100**	**71**	**6**

Picture 5/3 Percentual representation of authorised VMP



Total of 1138 applications were accepted by the Department of Administrative Affairs during the year 2008, which is 44% more than in the year 2007. Especially the applications for MA variations outweighed. In total 148 applications for the new marketing authorisation were submitted, which is much higher number than in recent years. The increased number is caused by the fact that for 61 preparations belonging to category of preparations approved according to Veterinary Act the application for marketing authorisation was submitted according to new legislative rules. In applications for renewal, variation to a marketing authorisation and transfer of the marketing authorisation there was significant increase in comparison with the past years. The applicants have also started to claim the mechanism of application withdrawal

according to Administrative Regulations. The number of issued decisions and resolutions by which the administrative proceedings are executed has increased by around 55 percent compared to the year 2006.

Table 5/4 Number of submitted applications and the number of cases when MA was granted in 2008 in comparison with the year 2007 and 2006

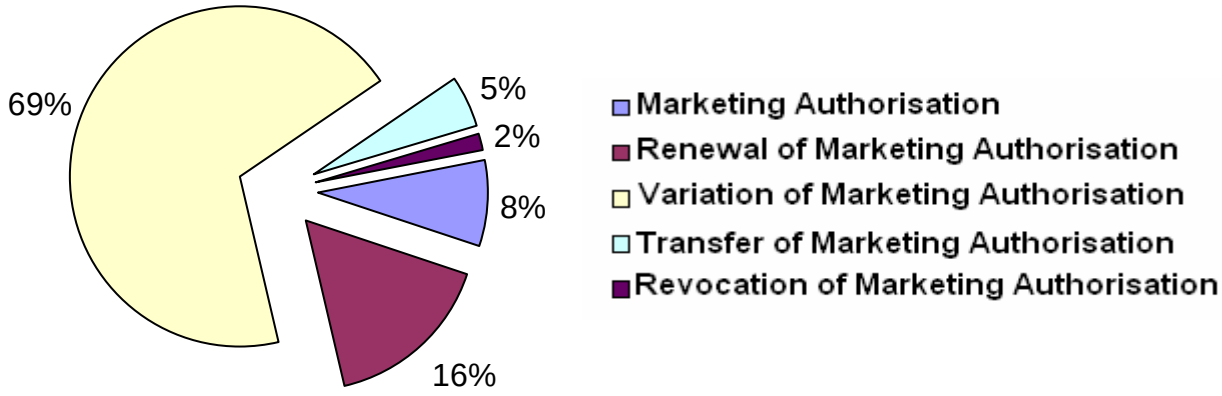
Type of Application	Year	Submitted Applications	MA Granted
Application for new MA	**2008**	**148**	**77**
	2007	87	58
	2006	60	46
Application for renewal of MA	**2008**	**282**	**145**
	2007	201	133
	2006	198	92
Application for variation to MA	**2008**	**590**	**679**
	2007	543	462
	2006	453	449
Application for transfer of MA	**2008**	**45**	**45**
	2007	13	10
	2006	13	13
Application for revocation of MA	**2008**	**17**	**17**
	2007	12	11
	2006	25	25
Application for discontinuance of administrative proceeding	**2008**	**29**	**29**
	2007	21	21
	2006	11	11
Appeal against the MA decision	**2008**	**2**	**2**
	2007	2	8
	2006	12	6
Administrative corrections in the MA decisions	**2008**	**25**	**25**
	2007	20	20
	2006	15	15
Summary	**2008**	**1138**	**1019**
	2007	899	723
	2006	788	657

The following table 5/5 shows the results of marketing authorisation procedures and as evident the absolute majority of the proceedings had the possitive result. Some of the proceedings were staying at the Institute for a longer time and were discontinued because the applicant did not completed the required documentation. The revocated proceedings were related to type I variations above all.

Table 5/5 Results from marketing authorisation procedures in the numbers of VMP in 2008

Result / Type of VMP	Approved	Approved in total	Discontinued	Refused	Executed in total
MARKETING AUTHORISATION					
Pharmaceuticals	**42**	**63**	**14**	-	**77**
Immunologicals	**21**		-	-	
RENEWAL					
Pharmaceuticals	**104**	**132**	**13**	-	**145**
Immunologicals	**28**		-	-	
VARIATION					
Pharmaceuticals	**455**	**640**	**18**	**21**	**679**
Immunologicals	**185**		-	-	
TRANSFER					
Pharmaceuticals	**23**	**45**	-	-	**45**
Immunologicals	**22**		-	-	
REVOCATION BY REQUEST					
Pharmaceuticals	**12**	**17**	-	-	**17**
Immunologicals	**5**		-	-	

Picture 5/5 Percentual Representation of Outputs of MA Proceedings in 2008



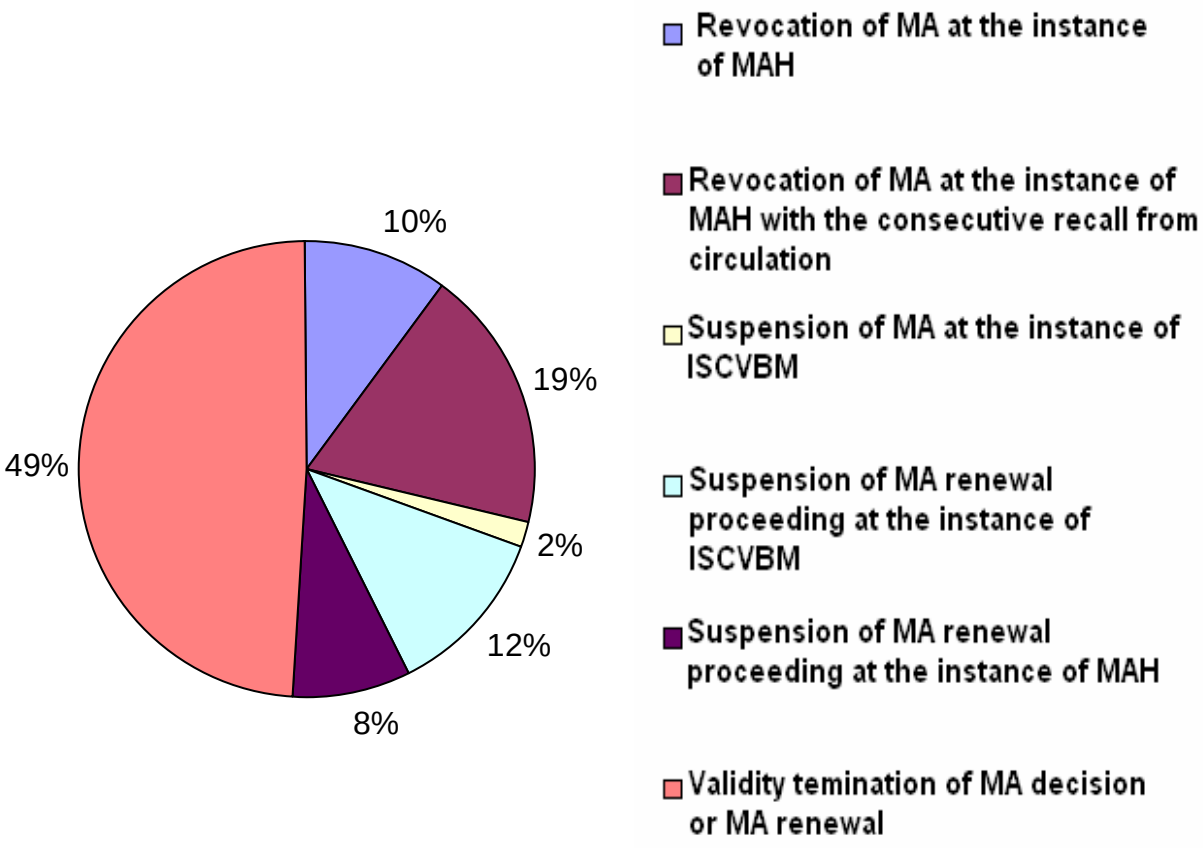
There are several reasons on the basis of which the VMP can be discarded from the register of authorised VMP which can be placed on the market in Czech Republic. Characterization of the reasons and the numbers of VMP which were discarded from the register of authorised VMP in 2008 is stated in the following table 5/6.

Table 5/6 Revocation of MA, Suspension of MA, Discontinuation of MA Proceeding and Termination of Validity of MA Decision or Renewal of MA

Reason	**Type of VMP**	**Number of VMP**	Total	**Total**
Revocation of MA by request of MAH	Pharmaceuticals Immunologicals	**2** **4**	**6**	**59**
Revocation of MA by request of MAH with the consecutive recall from circulation	Pharmaceuticals Immunologicals	**8** **3**	**11**	
Suspension of MA at the instance of ISCVBM	Pharmaceuticals Immunologicals	**1** **-**	**1**	

Suspension of MA renewal proceeding at the instance of ISCVBM	Pharmaceuticals Immunologicals	**7** **-**	**7**	
Suspension of MA renewal proceeding by the request of MAH	Pharmaceuticals Immunologicals	**5** **-**	**5**	
Termination of Validity of MA Decision or Renewal of MA	Pharmaceuticals Immunologicals	**15** **14**	**29**	

Picture 5/6 Percentage of particular reasons for discarding of VMP from the register of authorised VMP



5.2 Antibiotic policy

During 2008 the active participation in meetings of Subcommittee for Antibiotic Policy of the Czech Medical Society of J. E. Purkyne (SCAP – CMS JEP) continued. The deputies of ISCVBM informed here about the usage and utilization of antimicrobial substances in veterinary medicine, about the changes in legislation relating to using of antimicrobial substances and about current course of events in veterinary sphere.

Periodic meetings of Coordination Group of National antibiotic program organised by the Ministry of Health with the participation of the director of the Institute as a member of Coordination Group also took place. The following issues were discussed: e.g. issues relating to constrained antibiotics, organisation of European antimicrobial day and antimicrobial resistance as a priority of EU Presidency.

Active participation in the seminar organised in conjunction with the SCAP deputies and human medicine deputies was ensured where the information relating to veterinary legislation were submitted, information relating to usage of antimicrobial substances and the joint participation in antimicrobial resistance was discussed.

In the end of the year the meetings of ISCVBM deputies took place which were aimed at the provision of actions prepared for the CZ PRES period.

Further the opinions for Ministry of Agriculture and Ministry of Health were elaborated which served as background papers for negotiations at level of European institutions and authorities. Opinions were aimed at the issues relating to usage of antimicrobial substances in veterinary medicine, eventually they were pronouncing to documents solving the issues of antimicrobial resistance (opinion to Draft DS 397/08). The review recording the number of authorised (fluoro)quinolones was elaborated for HMA and it was documented that the caution about "prudent use" was stated in SPC within CR.
From the perspective of international cooperation in the sphere of antimicrobial resistance the activities of Scientific Advisory Group on Antimicrobial (SAGAM) were monitored – namely the preparation of new document relating to 3rd and 4th generation cephalosporins. Also course of events in the new group which arose within the frame of Codex Alimentarius – Task Force on AMR was carefully recorded.

Professional public was informed about the events in the sphere of antimicrobial resistance also within the frame of accompanying program VETEX 2008. Deputies of ISCVBM also prepared the presentation for "Fourth International Conference on Antimicrobial Agents in Veterinary Medicine (AAVM)" devoted to use of antimicrobial substances in veterinary medicine in CR.
The active cooperation with the workplace of University of Veterinary and Pharmaceutical Sciences Brno was established which is aimed at the issues relating to monitoring of microorganism strains resistant to antimicrobial substances which are used in veterinary medicine.
Negotiations within the scope of Scientific Veterinary Committee were also devoted to the spheres of antibiotic policy where the following study was prepared: "Rational use of antimicrobial medicines in veterinary medicine."

5.3 Clinical evaluation of medicinal products during the year 2008

Total of 3 new applications for approval of clinical evaluation of medicinal products were submitted to the Department of clinical evaluation of VMP in the year 2008, namely from two submitters. After the fulfilment of suggestions or supplement requirements to submitted data the clinical evaluation was approved in all 3 products.
In connection with the approval of clinical evaluation of VMP the total of 14 inspection findings were carried out including the appropriate writing records evaluating the compliance with the valid legislation. The inspection findings were above all targeted on the field phase of the clinical evaluation, i.e. compliance with the principles of good clinical practice by the adherence of the approved protocols and accuracy and completeness of record forms related to product administration data, clinical conditions of animals and other actions associated with the laboratory examination of samples. Some of the inspection findings were performed also by the submitter, namely with a view to supplementation or specification of the submitted protocols and record forms and the results of laboratory examination provided by the submitter. There were no deficiencies at inspection findings which might influence the procedure of clinical evaluation or which would lead to its suspension. The clinical evaluation of three preparations was finished by the submission of appropriate clinical assessment report in 2008, field phase of the clinical evaluation was finished in 7 products, the clinical evaluation of 4 products will continue in 2009. The clinical evaluation of one product was suspended temporarily.
In 59 products the field check in terms of running marketing authorisation proceeding, monitoring of the side effects of VMP administration and market surveillance were carried out. No findings requiring subsequent precautions were found out.
In total 26 applications for the opinion relating to the unauthorised VMP and its approval of exception for importation or using in the CR were submitted to State Veterinary Administration in 2008 (18 pharmaceuticals, 8 immunologicals). In many cases there were repeated applications for the products with the positive opinion from previous years. The negative opinion was taken in 5 cases, in which the stated reasons were not found satisfactory. Under to given conditions the exception to manufacturing and distribution of Xylased 500 inj. (Bioveta a.s.) for the use in form of narcotising projectiles was renewed.
In terms of tasks associated with the market surveillance the compliance with the approved product literature (outer package, package leaflet, labelling) was checked in 169 products. From that in 4 cases there were major discrepancies, in 22 cases discrepancies with no effect on the safety and efficacy of the product.
There were 4 consultations were held in 2008 related to essential legislative data and requirements on clinical evaluation of several veterinary medicinal products.

5.4 Veterinary products, veterinary technical devices and biocides

The review of the activity of the Department of approval of veterinary products (VP), the register of veterinary technical devices (VTD) and biocides in the year 2008 (actual situation on the 31.12.2008)				
Sort of activities	**Transferred from the year 2007**	**Submitted in the year 2008**	**Executed**	**In proceeding**
Approval of VP	39	162	163	38
Variations to approved VP	0	24	24	
Renewal of approved VP	17	51	64	4
Discontinuation of VP approval proceeding			10	
Revocation of approved VP				142
Total	56	237	261	42
Evaluation whether it is VP or not, article 65, paragraph 1, letter i)		8	8	
Number of requirements on completion of application for approval, renewal and variation				
Discontinuation of the proceeding/transfer of approved VP/revocation of the approved VP	Revocated in total		157	
	by request			
	transferred → biocides		72	
	transferred → VTD			
	transferred → VMP		72	
	transferred → feeding stuff/feed additive			
Register of VTD				
Standpoints to biocides		84	84	
Standpoints to active ingredients		1	1	
Solving of adverse reactions of VP	1	1		2
Solving of adverse reactions of VTD				
Solving of adverse reactions of biocides				
Appeals against the decision				
Department of approval of VP and VTD (number of operations in total)	**57**	**323**	**346**	**44**

6. Activity of the Inspection Section

6.1. GMP Division

6.1.1. Department for GMP of Medicinal Products (MP), Autogenous Vaccines (AV) and Active Ingredients (AI)

The review of the activity:
The fulfilment of main projects and visions:

- ***fulfilment of the systemic inspection plan keeping the interval provided by the Decree on GMP and GDP(responsible Mr. Holý)***
  all planned inspections were performed
- ***further improving of qualification and proficiency of GMP inspectors***
  trainings were performed in required range
- ***evaluation of French Veterinary Authority within the scope of PIC/S and EMEA***
  fulfilled, final report was accepted by PIC/S and EMEA
- ***participation in implementation of Cross-Compliance programme in CR***
  main tasks were fulfilled, finalization of guidelines in 2009
- ***finalization of revision of the regulatory documentation and Quality Manual of Inspection Section***
  not completed, revision of Quality Manual and SOP was with regard to new Act on Pharmaceuticals and decrees postponed to 2009
- ***elaboration of SOP for control inspections***
  partially fulfilled, drafts prepared
- ***continuing to cooperation with Inspection Section of SIDC***
  joint GDP inspections with SIDC were carried out, no GMP inspections were carried out (revocation of manufacturing authorisation of VMP for IVAX company)
- ***cooperation withing EU – Slovakia, Lithuania***
  no joint inspections were carried out, only training for Croatian inspectors
- ***preparation and realization of special seminars in connection with new Act on Pharmaceuticals***
  the seminary for manufacturers and distributors was organised
- ***transfer of quality manager competencies to Mgr. Zubrová***
  handover of all background papers and transfer of competencies were not completed

Number of submitted applications in the GMP sphere of MP and AI: 16

Application for granting manufacturing authorisation of medicinal products – 2
Application for variation to a manufacturing authorisation of VMP
– 1 (variation affiliated with the inspection)
– 4 (variation without the inspection necessity)
Application for granting a license for control laboratories – 0
Application for granting GMP certificate – 5
Application for revocation of an AI manufacturer certificate – 1
Application for suspension/revocation of authorisation – 3

Number of issued decisions:

Manufacturing authorisation – 0 (2 applications from 2008 will be executed in 2009)
Manufacturing authorisation (variation of the decision) – 4 (1 application from 2008 will be executed in 2009)
Granting a licence for CL (variation) – 1
GMP Certificate pursuant to application – 5
GMP Certificate after inspection – 12 (according to obligation provided by the Directive 2004/28/EC)
Suspension of the authorisation – 1
Manufacturing authorisation revocation/suspension – 2
Revocation of AI manufacturer certificate – 1

Review of performed systemic inspections and comparison with the plan in 2008

Companies based on CoR (Company Register)	Plan	Executed	Remark
SPOFA a.s.	February	8.-9.1.2008	
SPOFA a.s.	February	-	Revocation of manufacturing
BIOVETA, a. s.	March	16.-17.4.2008	
TEKRO, spol. s r. o.	March	-	Revocation of joint inspection with Slovakian ISCVBM in Nitra
BIOVETA, a. s.	March	25.-26.6.2008	
SVÚ Olomouc	May	9.6.2008	
SVÚ Olomouc	May	23.6.2008	
Bioster, a.s.	May	21.8.2008	
Cymedica spol. s r. o.	May	23.-24.4.2008	
IVAX Pharmaceuticals s.r.o.	May	-	Revocation of manufacturing authorisation
BIOVETA, a. s.	June	22.-23.7.2008	
TAGREA, a.s.	June	26.8.2008	
BIOVETA, a. s.	June	4.12.2008	Opava
INTERVET, s.r.o.	August	10.9.2008	
DYNTEC s.r.o.	August	-	Postponed to March 2009
BIOPHARM, Research Institute of Biopharmacy and Veterinary Drugs a.s.	September	29.-30.10.2008	
MIKROP ČEBÍN a.s.	September	11.-12.12.2008	
KOMVET spol s r.o.	October	2.12.2008	
CONTIPRO C, a.s.	November	-	Postponed to January 2009

Further based on the application for manufacturing authorisation a control inspection was carried out at the manufacturer of medicinal products.

Within the frame of inspection of AI treatment there were 8 controls carried out in 8 subjects.

Number of inspections carried out in the sphere of GMP and treatment of AI: 16 (GMP) + 8 (treatment of AI)

Initial Systemic Inspection + variations	– 1
Periodical Systemic Inspections	– 14
Subsequent Inspections	– 0
Control Inspections	– 1
Manufacturers of AI	– 0
Manufacturers of MP	– 0
Controls of AI Treatment	– 8
GLP	– 0
Foreign Inspections	– 0

Number of processed protocols: 16 (GMP) + 5 (Treatment of AI) + 3 (Inspection findings – in the sphere of AI)
2 protocols from inspections carried out in 2007 were processed at the beginning of 2008

Summary of Inspection Activities
Estimated number of inspections was 24, scheduled number of inspections was 40, 15 controls were scheduled in the sphere of controls of AI treatment. Actually there were 16 inspections of GMP executed, the number of inspection days was 23, in the sphere of AI treatment there were 8 controls executed. The total number of inspection days in 2008 was 31. In 2007 the number of inspection days was 55 (in 2005 – 35, 2005 – 46, 2004 – 38).
The difference compared to plan is caused firstly by the failure of several scheduled inspections and by the postponement of inspections in companies Contipro C and Dyntec to the year 2009. A small number of inspections in the sphere of AI treatment was caused by the workload of employees in other fields of activities. Initially scheduled inspections within the frame of Cross-Compliance system were executed in limited extent and are being recorded within the frame of activity of Division for Market Control.

Training
The employees of Inspection Section – Division for GMP of MP, AV and AI took part in the training within the ranger of 76 days (Holý, Műllerová, Radošová, Kožíšek).
From the foreign trainings one GMP inspector took part in PIC/S seminary (May, 3 days), PICS/ISPE/PDA workshop (November, 2 days). Two inspectors took part in international PDA/EMEA conference and in related special workshops in Budapest (February, 4 days), two inspectors took part in training organised by TAIEX in Prague (March, 5 days).

Cooperation (SIDC, EMEA, PIC/S)
The employees of Inspection Section took part in Ad Hoc GMP Inspection Group meeting at EMEA in 2008 (4 periodical meetings, Mgr. Holý). Mgr. Holý acted as a ISCVBM deputy at the PIC/S conference (two committees in 2008).
Mgr. Holý acted as a chief auditor of the assessment of French veterinary agency (February) within the frame of PIC/S and EMEA JAP.

Within the frame of cooperation with SIDC there were no joint inspections executed in the area of GMP, inspection schedules and on-coming guidelines were mutually exchanged.
In 2008 the training for Croatian inspectors took place in ISCVBM aimed at quality assurance system, inspections, pharmacovigilance sphere and marketing authorisation.

Consultations, providing of information

Type of consultation	Personal	Telephone	E-mail	Total
Number	35	95	62	192

Personal consultations were carried out within the scope of submitted applications for granting of manufacturing authorisation of variation to a manufacturing authorisation.

The Assessment of Quality Indicators
The quality indicators appointed for the activities of this department were evaluated, no violations of procedures or limit exceeding were found out.

Quality Assurance, Internal Audits
For a year 2008 the revisions of regulation documentation and the quality manual were scheduled with regard to issuing of decrees and variations within the frame of EMEA regulations, but they were not executed, the revisions of SOP and Quality Reference Manual were postponed to the beginning of 2009. The revisions of all forms and guidelines published on the internet or used in the activity of Inspection Section were conducted.
The internal audit in the Division for GMP Inspection of MP, AV and AI and audit aimed at the sphere of quality assurance were scheduled in 2008. Internal audits were postponed again from the time reasons to 2009. Within the frame of quality assurance the annual activity evaluation was carried out including the deviations and divergences.

The review of activity in terms of Rapid Alert System (RAS) in 2007
In 2008 the total number of received information regarding quality defects of VMP in terms of RAS was 113. This number includes the information concerning all cases of quality defects from external authorities (from that most comprises of information concerning quality defects of human medicinal products) and separate organisational divisions of the Institute. Total of 31 quality defect reports were received in the sphere of VMP.

Reports from External Authorities	concerning human medicinal products	82
	concerning veterinary medicinal products	7
Internal Reports from Organisational Divisions of the Institute	Laboratory Control Section	16
	Section of Marketing Authorisation	3
	Inspection Section	3
Reports Received from MAH		2

Quality defects of VMP received by the Division of Laboratory Control Section concerned mainly:

- unsatisfactory pH - 1
- unsatisfactory density - 4
- unsatisfactory appearance - 2
- efficacy - 3
- assay of excipients - 1

extractable content - 1
mass uniformity - 1

Quality defects of VMP received by the division of MA Section and Inspection Sections were related to differences in labelling (immediate package, outer package, package leaflet). The most common shortcomings were the differences in withdrawal periods, storage temperatures of the products, different content of data on multilingual labelling.
Two reports concerning unsuitable results of continuous product stability monitoring were received from MAH, concerning 2 products.
In 2008 no information concerning quality defect were sent to external authorities within the frame of RAS.
Pursuant to RAS background papers there were 6 administrative proceedings opened with MAH of VMP for violation of Act 378/2007 Coll., on Pharmaceuticals and Act 166/1999 Coll., on Veterinary Care:

Specification of Violation of the Law	Number of Administrative Proceedings
Act on Pharmaceuticals § 33,article 3, section a)	4
Act on Veterinary Care § 72, article. 1, section o)	1
Act on Pharmaceuticals § 77, article.1, section g)	1

Summary of deviations
No significant deviations from the set procedures on main activities of the section were found out in 2008. But in the sphere of quality assurance the internal audit schedule and schedule of revision of regulation documentation were not fulfilled.

Precautions
The performance of internal audits and finalization of regulation documentation are the key tasks for the first half-year 2009.
Since there were no significant deviations from the set procedures found out during 2008, no corrective actions were taken in the sphere of inspection executing.

6.1.2. Activities of Department for GMP of Medicated Feedingstuffs

Review of activities:
The fulfilment of main tasks in 2008:

- ***fulfilment of inspection schedules stated in part A***
  fulfilled
- ***further trainings and education of inspectors***
  fulfilled
- ***clarification of conditions for farm manufacturers of medicated feedingstuffs (1st quarter of the year 2008), release of ISCVBM guideline administering this sphere of manufacturing of medicated feedinstuffs***
  fulfilled, the guideline was released in January 2009
- ***revisions of SOP in the sphere of medicated feedinstuffs manufacturing in connection with new Act on Pharmaceuticals***
  not fulfilled, continues in 2009

- ***cooperation with Regional Veterinary Administration – workshop on issues regarding new Act on Pharmaceuticals (1st quarter 2009).***
  fulfilled
- ***joint activity within EU – joint inspection with Slovakian ISCVBM – manufacturer of medicated feedingstuff in Slovakia or in Czech Republic (2nd to 4th quarter 2008), joint abroad inspection within the frame of arranged cooperation with Lithuania***
  not fulfilled, continues in 2009
- ***Central Institute for Supervision and Testing in Agriculture (CISTA) – periodic meetings of ISCVBM deputies with CISTA deputies (generally once to twice a year)***
  fulfilled
- ***ISCVBM seminary centred on issues regarding Act on Pharmaceuticals and manufacturing of medicated feedingstuffs (1st quarter 2008)***
  fulfilled
- ***aiming at the quality of medicated feedingstuffs in the form of sampling (1st to 4th quarter 2008)***
  fulfilled

Number of submitted applications in the sphere of Good Manufacturing Practice of medicated feedingstuffs:

Type of Application	Manufacturing Authorisation	Variation to a Manufacturing Authorisation with Inspection	Variation to a Manufacturing Authorisation without Inspection	Application for Revocation of Manufacturing Authorisation	Total
Number	2	6	8	3	19

Compliance of the administrative terms for replies to applications:
Administrative deadlines for reply to applications were complied (maximal limit is 30 days).

Number of issued decisions:

Type of Decision	Authorisation of New Manufacture	Variation to a Manufacturing Authorisation with Inspection	Variation to a Manufacturing Authorisation without Inspection	Revocation of Manufacturing Authorisation	Total
Number	2	7	8	3	20

Compliance of the terms for decision issuing:
Three applications from 2007 were executed at the beginning of the year 2008.The stated administrative proceedings were executed in given time – to the 90 days without inclusion of the suspension caused by the applicant. As far as the total time for suspension of administrative proceeding more than 90 days was tolerated, it was in the cases when the applicants made the alterations in technological equipment and simultaneously the transfer of authorisations done by CISTA was proceeded and as lately as they were finished and further technology engineering necessary for the granting a manufacturing authorisation for manufacture of medicated feedingstuffs was done, the proceeding at ISCVBM continued.

Number of incomplete applications transferred to 2009:

Type of Application	Variation to a Manufacturing Authorisation with Inspection	From that Inspected in 2008	Administrative Variation to a Manufacturing Authorisation	Applications of New Manufacturers - incomplete	Incomplete Applications - Total
Number	2	1	0	0	2

Rationale: incomplete applications are suspended and waiting for removal of shortcomings on the part of manufacturer. On this account the applications will be executed during the year 2009.

Number of inspection carried out in 2008:

Type of inspection	Initial Systemic	Systemic Variation	Periodical Systemic	Subsequent	Control	Total of Inspections	Total of Inspection Days	Total of Person/Day Units
Number	2	7	38	2	3	52	53	109

Compliance of the inspection procedures

The inspection procedures guidance described in appropriate SOP were complied. The letter with the announcement relating to inspection was sent to the manufacturer before the inspection. Inspections were carried out according to the set schedule, the inspection protocol was elaborated from each inspection following the records made into control sheet and then it was sent to the manufacturer.

Time schedule of periodical systemic inspections for the year 2008 was fulfilled excepting two periodical systemic inspections form the December 2008, which could not be carried out due to lack of time (reason: the necessity of inspection performance in applicants for variation to a manufacturing authorisation for veterinary medicinal products, increased number of control inspections and inspections in two new applicants) – hence they were included in inspection schedule to 1st half-year 2009. The number of subsequent and control inspections compared to schedule was exceeded.

Consultations, Providing of information

Type of Consultation	Personal	Telephone	E-mail	Total
Number	7	78	63	148

Personal consultations were carried out mainly within submitted applications for manufacturing authorisation or variation to a manufacturing authorisation.

Sampling in manufacturers of medicated feedingstuffs

During the inspections the sampling of granulated medicated feedingstuffs with the active ingredient CTC, doxycycline and amoxicillin was proceeded in 2008 – in total 24 samples were taken. The samples were investigated in the ISCVBM laboratory. The evaluation took its course continuously.

Within the frame of Market Surveillance programme all requested samples of medicated premixes in manufacturers of medicated feedingstuffs were taken (see records from Market Surveillance).

Cooperation (CISTA, Regional Veterinary Administration) and further activities

In 2008 the employees of Inspection Section took part in:

- a meeting with employees of SVA/RVA – the workshop took place at ISCVBM in Brno – themed Surveillance of VMP using, cross-compliance, manufacturing of medicated feedingstuffs for own use
- two meetings with CISTA employees (issues relating to coccidiostatics and its residues in feedingstuffs for non target animal species) – June, November 2008
- presentation of approval procedures and control of manufacturers of medicated feedingstuffs in CR for deputies of Veterinary Directorate of Croatian National Agency "Ministry of Agriculture, Fisheries and Rural Development" – organised via TAIEX (December 2008)
- training of inspectors – see training records, total time of trainings was 34 days in 2008

6.2. GDP Division – GDP Inspection and Market Surveillance

6.2.1. Department for GDP

Review of activities:
Fulfilment of main tasks and visions:

- ***fulfilment of systemic inspection schedule in course of interval compliance provided by the decree on GDP***
  fulfilled
- ***improving of qualification and proficiency of GDP inspectors***
  fulfilled
- ***within the frame of systemic inspections in distributors – implementation of control of MP supplies from abroad suppliers in connection with their possible parallel importation***
  fulfilled in large distributive companies, will be performed henceforth in 2009
- ***control of VMP distribution to breeders on the basis of veterinary receipt at distributors***
  will be executed in 2009
- ***control of MP labelling and control of MP compliance with its valid dossier (packaging, package leaflet)***
  fulfilled, will be performed henceforth in 2009
- ***cooperation with Inspection Section of SIDC***
  fulfilled, will be performed henceforth in 2009
- ***preparation and performance of special seminars in connection with new Act on Pharmaceuticals***
  fulfilled, will be performed henceforth in 2009
- ***comprehensive revision of SOP in the sphere of GDP***
  will be finished during 2009
- ***sampling in terms of Market Surveillance***
  fulfilled

On 31.12.2008 there were total of 78 distributors, which have authorisation for distribution, these distributors dispose of 109 supplies.

Number of submitted applications: total 24

Type of application	Distributing Authorisation	Variation to a Distributing Authorisation with Inspection	Variation to a Distributing Authorisation without Inspection	Extension to Distributing Authorisation for MF and AI	Suspension of Distributing Authorisation	Revocation of Distributing Authorisation
Number	6	8	7	1	-	2

Number of issued decisions: total 22

Type of Decision	Distributing Authorisation	Variation to a Distributing Authorisation with Inspection	Variation to a Distributing Authorisation without Inspection	Extension to Distributing Authorisation for MF and AI	Suspension of Distributing Authorisation	Revocation of Distributing Authorisation
Number	5	7	7	1	-	2

All administrative proceedings were finished within the given time of 90 days without inclusion of suspension caused by the applicant.

Number of incomplete applications transferred to year 2009: in total 2

Variation to a Distributing Authorisation with Inspection	Variation to a Distributing Authorisation without Inspection	Applications of new distributors - incomplete	Extension to Distributing Authorisation for MF and AI	Revocation of Distributing Authorisation
1	0	1	0	0

Inspection activity

Inspections carried out within the frame of periodical control of distribution and control of veterinary medicines in CR.

Companies based on CoR (Company Register)	Inspection plan	Number of Inspection Days	Execution date/Remark
Veterinární zásobování, spol. s.r.o.	January 2008	1	12.3.2008/sampling of MF
GS Partners s.r.o.	February 2008	1	subsequent/postponed to January 2009
VIDIE s. r. o.	February 2008	1	26.3.2008/sampling of MF
PHARMAGAL CZ, s.r.o.	February 2008	1	16.4.2008
SAMOHÝL, a.s.	March 2008	1	12.9.2008/ PD control
VELE, spol. s r. o.	March 2008	1	17.4.2008/along with SIDC/subsequent
Tekro, spol. s r.o.	April 2008	1	18.6.2008/sampling of MF
Jihlavská lékárnická s.r.o.	April 2008	1	10.4.2008
Alliance Healthcare s.r.o.	April 2008	1	30.4.2008
ZÁVOD BIOCHEMICKÝCH SLUŽEB, s.r.o.	May 2008	1	20.5.2008
UNIVIT s.r.o.	May 2008	1	postponed to 2009
PHRAMED, s. r. o.	May 2008	1	5.6.2008/subsequent
PHARMOS, a.s.	June 2008	1	13.5.2008
Alliance Healthcare s.r.o.	June 2008	1	5.8.2008
BAYCO ČR s. r. o.	June 2008	1	12.9.2008
PHARMOS, a.s.	June 2008	1	23.6.2008
Pražská lékárnická s.r.o.	June 2008	1	23.6.2008/along with SIDC
Vétoquinol s.r.o.	July 2008	1	21.10.2008/control of compliance with the dossier

NORDIC Pharma, s.r.o.	July 2008	1	4.11.2008
IDEKO, s.r.o.	August 2008	1	29.4.2008
Zelenka s.r.o.	August 2008	1	13.8.2008
SCHAUMANN ČR s.r.o.	October 2008	1	25.6.2008
SCHAUMANN ČR s.r.o.	October 2008	1	14.10.2008
Alliance Healthcare s.r.o.	October 2008	1	13.10.2008
MEDIVET MALEČ, s.r.o.	November 2008	1	23.9.2008

Schedule of periodical systemic inspections numbering 22 and 3 subsequent inspections, there was total of 25 inspections.

Number of executed systemic inspections: 21 (1 inspection postponed into 2009)
Schedule of control inspections in distributors: 25

Number of executed control inspections: 31 (recorded within activities of Division for Market Control)
Schedule of inspections aimed at parallel importation: 4
Executed inspections of parallel importation: 4
Systemic inspections aimed at control of compliance with the dossier: 2
Executed inspections: 2
Schedule of subsequent inspections: 3
Executed subsequent inspections: 4 (in total)

Schedule of joint inspections with SIDC: 4
Executed joint inspections: 4

Number of executed collections of VMP samples within the Market Surveillance: schedule – 191 samples, 138 samples were collected, 53 samples were not marketed in CR (the collection of 83 samples was solved by the individual action).

Parallel importation was carried out although no decision on parallel importation was issued. Inspections aimed specifically at this sphere were executed and two administrative proceedings were initiated.

The total of 62 inspections in the sphere of VMP distribution were carried out in 2008, 4 subsequent inspections, 2 inspections aimed at the sphere of VMP marking, 31 control inspections which are recorded as a activity of Division for Market Control.

Actual number of joint inspection days: 39 (control inspections excluded)

Actual number of persons per days: 78 (control inspections excluded)

Non Inspection Activities
Schedule of trainings: 20 working days outside the Institute
Executed trainings: 23 working days outside the Institute

The comprehensive revision of templates and guidelines in the sphere of distribution of veterinary medicinal products, active ingredients and excipients and medicated feedingstuffs was carried out, revision of SOP is still in progress.

ISCVBM seminary aimed at issues relating to amendment of act on pharmaceuticals in the sphere of distribution was carried out in first quarter of 2008.
Cooperation with SIDC in the sphere of GDP is in progress.

Consultation, providing of information

Type of Consultation	Personal	Telephone	E-mail	Total
Number	12	45	20	77

Personal consultations were executed within the scope of submitted applications for distributing authorisation or variation to a distributing authorisation.

Summary
The total number of primary work activity performed outside the Institute was 101 person/days in the year 2008 in the sphere of inspection and authorisation of MP distribution. No crucial discrepancies were found out, all time limits provided by the Act on Pharmaceuticals of in regulation documentation during the year 2008. Greater attention was given to sphere of parallel importation, the attention will be given to this sphere henceforth in 2009 and from now on the correct labelling of MP marketed in CR will be checked.

6.2.2. Division for Market Control and Market Surveillance in 2008

Inspections carried out in 2008 were aimed at:

1. manufacturing, importation, distribution and using of VMP with prudent use
2. manufacturing, importation, distribution and using of hormonal VMP in food animals with a view to prostaglandins, gonadotrophins and hypothalamic hormones
3. using of VMP which are not intended for food animals at veterinary surgeons and distribution of this VMP in pharmacies
4. distribution of VMP in pharmacies – POM, OTC and unpacking of original packaging
5. distribution of VMP at trade networks, exhibitions and auctions
6. preparation of new VMP register for reporting of import and distribution of VMP and for reporting of manufacturing of medicated intermediate products and medicated feedingstuffs and its adjustment in compliance with amendment to an Act on Pharmaceuticals
7. preparation of protocols of active ingredient usage
8. elaboration of reporting of narcotic drugs and psychotropic substances usage
9. sampling of VMP original packaging within the frame of Market Surveillance
10. sales of VMP to breeders pursuant to veterinary receipt at distributors
11. Regional Veterinary Administration and ISCVBM joint controls of VMP using by breeders
12. deficiencies ascertained in VMP usage reporting at distributors
13. distribution of authorised VMP in trade networks

The Activity Review of Division for Market Control and Market Surveillance and Comparison with the Schedule

Type of inspection	Schedule	Executed - Louny	Executed - Brno	TOTAL
Distributor	9	5	26	31
Pharmacy	40	18	10	28
Veterinary Surgeon	42	35	11	46
Seller of selected medicinal products	16	-	-	-
Zverimex	90	1	96	97
Distributor of VMP	-	-	5	5
Manufacturer of Medicated Feedingstuffs	4	3	3	6
Breeder	20	7	7	14
Exhibitions	9	4	4	8
Total	**230**	**73**	**162**	**235**

The total of 18 administrative proceedings was initiated.

Market Surveillance Programme

Scheduled sampling (pieces)	Number of samples	Not sampled (pieces)
191	**138**	**53**

Non Inspection Activity

Trainings: (Kurfürstová, Kučerová, Dorn, Dr. Koutecká)
3.6. Homeopathy, the basis for treatment
27.6. Medicinal Plants
16.10. Aktuální otázky ochrany zdraví zvířat - Dorn, Dr. Koutecká
9. – 10.4. 3. středoevropský veterinární kongres – Dr. Koutecká

Participations in ISCVBM seminars:
Kurfürstová, Kučerová, Dorn, Dr. Koutecká
Seminary for distributors and feed mixing plants
Kurfürstová,Kučerová – Seminary on Marketing Authorisation
Dorn, Dr. Koutecká – Seminary with the Regional Veterinary Administration Deputies

New list of VMP for manufacturers of proprietary medicinal products, distributors and manufacturers of medicated feedingstuffs was made. It is made for reporting of VMP usage.
The report on antimicrobial substance usage in CR was elaborated.
The usage of active ingredients based on the administration form, pharmaceutical form, target animals and by request of the director.
The report on usage of narcotic drugs and psychotropic substances in CR was elaborated in 2007 based on reporting of individual Regional Veterinary Administrations to the Inspectorate for Narcotic Drugs and Psychotropic Substances at Ministry of Health.

The revision of ATCvet codes in authorised products was in progress continuously during 2008.

Summary

The schedule of inspection plan was exceeded by 5 inspections. The changes in number of inspections resulted from VMP usage reporting during the year, from the monitoring results and from the survey of active ingredients importation and distribution.

Joint Regional Veterinary Administration and ISCVBM ispections of the breeders were executed pursuant to detection of residues. The following breeders were concerned: Úněšovský statek a.s. Pernatec farm, Agrolan Budětice, Agrochov Kasejovice – Smolivec a.s., Česká drůbež s.r.o. Velký Malakov. The joint inspection in these breeders was executed by RVA Plzeň. Further joint inspection of the breeder Probios a.s. Kounov was executed by the RVA for Střední Čechy Region. No gross violation of Act on Pharmaceuticals or Act on Veterinary Care was recorded at the breeders. Major attention will be paid to VMP usage by veterinary surgeons at breeders as well during 2009.

To the part of breeder inspection the control at the Research Institute for Cattle Breeding was scheduled for, which have been purchasing and using the Oestrophan VMP in terms of research project. We found out that the product was used by the veterinary surgeon for the preparation of donors and acceptors of embryos. During the usage control of VMP with prudent use the inspected veterinary surgeons had records of laboratory tests for causal agents and for sensitivity to antibiotics. The usage control of these products will continue even in 2009 respectively aimed at poultry breeding.

The illegal usage was not found either at the inspections of usage of VMP not intended for use in food animals. Also in this case the inspections will continue in 2009.

At the inspections of distribution of medicinal products subject to medical prescription at pharmacies it was found out that some of the pharmacies breach the original packaging namely in antiparasitic drugs for small animals. At the specific inspection aimed at dispensing of veterinary biologicals at pharmacies no serious deficiencies were found out.

At exhibitions and auctions no sale of VMP was found out. By the inspection of manufacturing, importation, distribution and usage of hormonal veterinary medicinal products in food animals the differences in usage records and in reviews of stock movement records were found out for the period from 1.1.2007 to 31.12. 2007 at the manufacturer and distributor Bioveta a.s. Ivanovice na Hané. Major disproportions were found out namely in the product Oestrophan inj. At the other distributors the purchase and sale of this product was consistent with the records of sale statement and at the veterinary surgeons the purchase, sale and mainly usage were in good order as well. From this reasons the control of manufacturing and sale of Oestrophan inj. will continue.

6.3. Department for Pharmacovigilance

The review of activities:

a)Fulfilment of main tasks and aims:

- ***Receiving, evidence, assessment, solving and handover of information concerning adverse effects of VMP***
  - 45 reports of adverse effects which have occurred in CR were received
- ***Evaluation of periodic safety update reports:***
  - ***Assessment of PSUR MRP/DCP products– CZ – RMS – Σ20/year***
    - CZ acted as a RMS in 4 VMP, 7 PSURs were assessed.
  - ***Assessment of PSURs within the frame of European programme for cooperation in the sphere of veterinary pharmacovigilance***

- Assessment of PSUR for active substantion prednisone within the frame of PSUR Worksharing project. Total of 10 assessment reports were commented within the frame of this project.

- ***Assessment of the other PSURs (MRP/DCP, NP)***

- Total of 10 PSURs for products authorised by NP were assessed.

- ***Assessment of pharmacovigilance systems within the documentation for MA***
  - there were 60 applications for MA assessed (DCP - 32, MRP – 23, NP – 13).
- ***Preparation of pharmacovigilance inspection system and inspection executing in 2008 – 4 inspections***
  - non-executed, postponed to 2009.
- ***Finishing of management documentation***
  - non-executed, postponed to 2009.
- ***Preparation of guidelines and presentation of pharmacovigilance supervision system on seminars for marketing authorisation holders.***
  - brief statement within the frame of marketing authorisation seminar on intention of department for pharmacovigilance to carry out the pharmacovigilance inspections in the year 2009 which held 11.9.2008 (scheduling of inspections, types of inspections, announcements of inspections). The elaboration of the guideline has been postponed to 2009.

b)Reporting of adverse effects (NÚ)

Table No 1 - Review of Adverse effect reporting – total number in 2008, distribution based on place of origin

Total number of reports	**970**
Reporting from 3rd countries	925
Reporting from CR	45 (from that 19 unauthorized VMP)

Table No 2 – Reporting from CR – divided according to type of the product

Total number of reports	**45**
Veterinary Products	3
Unauthorized Veterinary Medicinal Products – exception given by State Veterinary Administration of CR	19
Veterinary medicinal products - pharmaceuticals	7
Veterinary medicinal products – immunologicals	16

Table No 3 – Detailed review of selected reports of adverse effects from CR

	Preparation	Animal Category	Description of Adverse Effect	Investigation - Results (ABON system)
1.	VMP intended for active immunisation of dogs against distemper, infectious hepatitis caused by canine adenovirus type 1 (CAV 1), parvovirosis and laryngotracheitis caused by canine adenovirus type 2 (CAV 2)	dog	death	O
2.	VMP intended for early active immunisation of puppies against distemper (CDV) and canine parvovirosis (CPV)	dog	lethargy, vomiting, dyspnoea	N
3.	VMP intended for vaccination of healthy puppies and dogs against distemper, infectious hepatitis, infectious laryngotracheitis, parainfluenza, parvoviral enteritis and leptospirosis	dog	inflammation of iris, corneal swelling in both eyes	B
4.	VMP against distemper, infectious hepatitis, infectious laryngotracheitis, parvovirosis, parainfluenza and leptospirosis	dog	pruritus (especially ears), restlessness, aggression	B
5.	VMP intended for active immunisation of cattle for reduction of clinical symptoms of dermatophytosis caused by *Trichophyton verrucosum* for prophylactic vaccination and for therapeutical usage	cattle	premature labours, dead/stillbirth calves, retained secundines, occurrence of trichophytic foci on skin, local reactions (oedemas) in injection site, diarrhoeas, deaths	A – local reactions (oedemas) O - further
6.	VMP intended for prevention of ectoparasitic infections	dog	pruritus, local reaction in injection site - dark necrotic firm dermal tissue and necrosis	B
7.	VP – ectoparasiticide	cat	salivation, trembling, muscle convulsions, comatose state	A
8.	VMP intended for the therapy of nematodosis and cestodosis (toxocarosis, ancylostomatosis, uncinariosis and taeniosis)	dog	intense diarrhoea	A
9.	VMP against pleuropneumonias caused by *Actinobacillus pleuropneumoniae*	pigs over 6 weeks	vomiting, depression, death	B
10.	VMP against pleuropneumonias caused by *Actinobacillus pleuropneumoniae*	pigs over 6 weeks	vomiting, dyspnoea, congestion of skin, death	B
11.	VMP intended for treatment of diabetes mellitus	dog	hyperglycaemia	B, continues to be solved
12.	VMP intended for prophylaxis and therapy of canine dermal mycosis	dog	fevers, apathy, low food intake, foci of	continues to be solved

	caused by *Microsporum canis* (Dermatophytes)		abscesses in injection sites	
13.	VMP against distemper, hepatitis, parvovirosis, laryngotracheitis, parainfluenza and leptospirosis	dog	swelling of palm size in injection site	B
14.	VMP intended for preventive vaccination against myxomatosis	rabbits	suspected lack of efficacy	unconfirmed
15.	VMP against haemorrhagic disease and myxomatosis	rabbits	suspected lack of efficacy	unconfirmed
16.	VMP intended for the therapy and prophylaxis of reproductive disorders	cows	anaphylactic reaction, death	continues to be solved
17.	VMP intended for sedation of animals before investigation and treatment in combination with VMP for short-time narcosis	cat	arrest of breathing and heart activity	B
18.	VMP for prevention and therapy of primary and secondary anaemias	piglets	anaphylactic shock	A
19.	VP - shampoo	cats	intensive skin pruritus, which led to skin lesions	O
20.	VMP against distemper, hepatitis, parvovirosis, laryngotracheitis, parainfluenza and leptospirosis	dog	vomiting, diarrhoea, apathy, tachycardia	B

Glossary:

veterinary product – VP
veterinary medicinal product – VMP
unauthorised veterinary medicinal product – UVMP
ABON system for assessment of causal relationship from between product administration and adverse effects:
A = probable
B= possible
O = unclassified (it is not possible to draw the conclusion for lack of information)
N = unlikely

c) RAS and NUI systems for veterinary pharmacovigilance

Department for pharmacovigilance elaborated 8 replies by request of competent authorities of other EC member states for information within the scope of Non Urgent Information System. No reports via RAS system were received and no reports were sent via NUI and RAS by ISCVBM in 2008

d) Cooperation

Mgr. Zubrová attended the following meetings of EMEA working groups in 2008:

- CVMP Pharmacovigilance WG – 5 *meetings*
- Eudravigilance JIG – 3 *meetings*
- PhV Inspectors Working Group Meeting – *2 meetings*

Pharmacovigilance system of Czech Republic was presented to Croatian inspectors in 2008 (TAIEX training).

e) Consultation, providing of information

Type of Consultations	Personal	Telephone	E-mail	Total
Number	3	5	10	18

Personal consultations were provided within the frame of submitted applications for marketing authorisation of VMP – pharmacovigilance system or solving of adverse reactions. There were 5 statements provided from the adverse effects database.

f) Training

In 2008 Mgr. Zubrová, PhD attended the trainings ranging 11 days. From foreign trainings which were arranged by EMEA there were "Introduction to Veterinary Eudravigilance Database" (half day, April) and Training for Assessor of PSURs of VMP (1 day, November).

g) Further activity

The list of subjects responsible for pharmacovigilance in EEC (CR) was compiled.

Precautions:
The key activity in 2009 will be elaboration of SOP and guidelines for the sphere of veterinary pharmacovigilance. Further priority will be execution of pharmacovigilance inspections with a view to help MAH in effectiveness of his pharmacovigilance system.

7. Activity of the Laboratory Control Section

In 2008 the audit of Laboratory Control Section workplaces associated with laboratory reaccreditation was carried out by the Czech Institute for Accreditation personnel. This audit examined the compliance of accreditation criteria resulting from standard CSN EN/ISO 17025 and assessed the professional level of the laboratory related to activity both in the field of monitoring of extraneous substances residues (drug residues) in the food chain and in the field of VMP quality control.

At this supervision the application for accreditation of new methods was submitted. The following new methods were checked and approved by the Czech Institute for Accreditation personnel:

- myxomatosis virus titre assay (poxvirus myxomatosae attenuatum) by the microtitration method
- efficacy determination of inactivated rabies vaccine by NIH test
- carazolol, propionylpromazine and chlorpromazine assay by LC-MS/MS method
- nitroimidazoles assay by LC-MS/MS method

On the basis of audit outcome the Czech Institute for Accreditation issued to Laboratory Control Section an Accreditation Certificated with effect till 31 October 2012.

In the metrology sphere the metrological security system of measuring tools was maintained and evolved in the Institute. Metrological order and list of measuring tools and accessory equipment were updated continuously. Pursuant to requirements of Act on Metrology the defined measuring tool examination was carried out by the employees of Czech Metrology Institute, periodic maintenance checks and calibrations of relevant operational measuring tools and maintenance checks of accessory equipment were carried out as well according to requirements of individual measuring tool users.

7.1 Official Veterinary Medicines Control Laboratory and Laboratory for Control of VP

Also this year the professional workplaces personnel of Official Veterinary Medicines Control Laboratory participated in number of national and international aptitude tests for executing of existing trials. Especially the offer of tests organised by EDQM was accepted namely for the sphere of physical-chemical trials.

- Quality in microbiology scheme (QMS) QM 23D145, LGC Standards, Determination of mould and yeast count
- Identification of microorganisms and susceptibility specification to selected antibiotics (4 times a year)
- PTS 099 Assay by liquid chromatography, EDQM; oxacilin sodium
- PTS 101 Dissolution testing, EDQM; Acetylsalicylic acid

Henceforth the collaboration with EDQM is going further in the sphere of controlling VMP authorised by centralised procedure – in 2008 the laboratory of analytical chemistry was charged with analysis of Metacam 15mg/ml peroral suspension.

7.1.1 Market Surveillance

The main activity of the department is focused on the field of quality control of VMP placed on the market in the Czech Republic – this project was launched already in 2005.

The personnel of the Official Medicines Control Laboratory closely cooperated with the experts from the Inspection Section on the preparation of year schedules and on the evaluation of the surveillance. Inspection Section ensures qualified sampling from the distribution network for the laboratory and executes the further steps in the event that the laboratory find out the results non compliant with the approved specification of the product.

Market Surveillance Programme 2008 was aimed at namely the control of VMP containing the substances from the group of antiparasiticides respectively in all three pharmaceutical forms of authorised VMP available at the market. Within the fulfilment of Market Surveillance schedule there were 134 preparations from the VMP- pharmaceuticals group investigated, 33 medicated feedingstuffs samples, and 36 immunological VMP, the analyses of the 25 remaining samples of VMP- pharmaceuticals and 4 medicated feedingstuff samples will be carry out during the beginning of 2009.

7.1.2 Official Batch Release of Immunological VMP

In 2008 the Institute as a official control authority initiated the procedure of official batch release of selected immunological veterinary medicinal products so called OCABR and thereby implementation of provision of article 102 of the Act 378/2007 Coll., on Pharmaceuticals (resulting from article 82 of Directive 2001/82/EC as amended). Conditions and requirements of Official Batch Release procedure of immunological VMP are then in detail specified in the EDQM documentation. Preliminary and formal administrative steps were executed by the Institute already in 2007 and consequently practical assertion of particular batches of selected immunological VMP was proceeded in 2008 in compliance with the article 102 of the abovementioned act in the following time schedule:

- October 2007 – Swine erysipelas vaccine – live, inactivated
- January 2008 – Rabies vaccine for foxes - oral, live
- July 2008 – Equine Influenza Vaccine – inactivated

Two possible ways of official batch release were defined. The first assume that the applicant does not have the issued Certificate on official batch release for the objective batch and the relevant laboratory of the Institute will analyze the submitted samples and pursuant to compliant results the certificate will be issued. The second option assume that the applicant will submit the valid certificate issued by the official control laboratory of the other EU member state, to which the opinion of ISCVBM will be issued without repeating of sample testing. The reviews of numbers of released VMP batches are stated in tables 7/1 and 7/2.

Table 7/1 Reviews of Submitted Applications for Official Batch Release and Issued Certificates

Applications/Certificate / Type of vaccine	Number of applications for batch release without issued certificate	Number of Issued Certificates
Swine erysipelas vaccine- inactivated	15	14 (1 batch in analysis)
Swine erysipelas vaccine- live	4	3 (1 batch in analysis)
Rabies vaccine for foxes - oral, live	2	2
Influenza vaccine for horses - inactivated	0	0
Total	**21**	**19 (2 batches in analysis)**

Table 7/2 Review of batch marketing authorisation in CR based on certificate issued by the official laboratory of other EU member state

Applications/Approval / Type of vaccine	Number of applications for batch release with the certificate issued by the official laboratory of other EU member state	Number of granted marketing authorisations of immunological VMP in CR
Swine erysipelas vaccine- inactivated	2	2
Swine erysipelas vaccine- live	1	1
Rabies vaccine for foxes - oral, live	0	0
Rabies vaccine for foxes - oral, live	0	0
Total	**3**	**3**

Review of sample analysis sent to laboratory assay in 2008:

From January to December 2008 total of 289 samples were analysed (review see graph No 7.1, 7.2 and tables 7/3, 7/4, 7/5) which represented the execution of 867 analyses.

Graph 7/1 Review of number of executed analyses in the sphere of VMP quality control – based on laboratory department – type of analysis in a year 2008

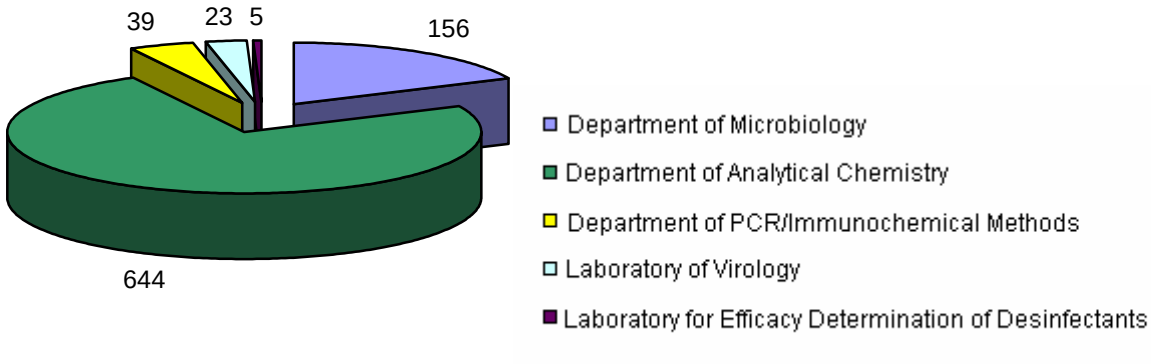


Table 7/3 Summary of samples analysed by Official Medicines Control Laboratory based on type of the applicant and sample nature in year 2008

Applicant	Sample	Quarter 2008				Total	
		I	II	III	IV		
Marketing Authorisation	VMP pharmaceuticals	1	1	-	-	2	2
	VMP immunologicals	-	-	-	-	-	
Approval	VP (desinfectants)	-	-	-	-	-	-
Inspection	VMP pharmaceuticals	37	38	26	23	124	193
	VMP immunologicals	8	10	8	10	36	
	medicated feedingstuffs	9	18	3	3	33	
Pharmacovigilance	VMP pharmaceuticals	-	-	-	2	2	9
	VMP immunologicals	-	3	1	3	7	
External Applicants	VMP	1	-	6	-	7	68
	Medicated feedingstuff	4	8	2	2	16	
	OCABR	3	5	5	8	21	
	Biological material	-	-	-	11	11	
	Other	6	3	-	4	13	
Management System Assurance	External (PTS, EHK)	2	5	1	2	10	17
	Internal (MK)	-	3	3	1	7	
Total	**Samples** /analyses/	**71** /196/	**94** /247/	**55** /219/	**83** /205/	**289** /867/	

Graph 7/2 Summary of Numbers of Samples based on the type of the applicant in 2008

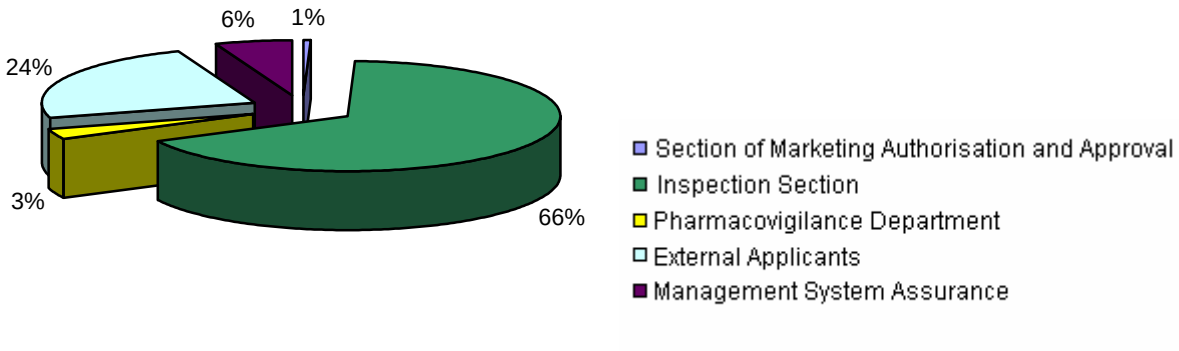


Table 7/4 Numbers of compliant and noncompliant samples in 2008

Samples	Compliant	Noncompliant	Nature of quality imperfection
Market Surveillance - Pharmaceuticals	117	7	1× extractable content 3× density 1× pH 2× appearance
Market Surveillance - Immunologicals	34	2	1× efficacy 1× germ count
Control of medicated feedingstuffs	33	-	not evaluated
Marketing Authorisation	2	0	-
Pharmacovigilance	7	2	1× germ count 1× pH
External applicants	68	0	-
Quality assurance system	17	0	-
Total	**278 [96,2 %]**	**11 [3,8%]**	

Table 7/5 Developmental summary of number of analysed samples and quantity of executed analyses during the period 2003 - 2008

Samples / Year	2003	2004	2005	2006	2007	2008
Number of analysed samples	395	234	238	300	306	289
Quantity of executed analyses	450	440	580	739	789	867

7.2. Laboratory Control - Residues

7.2.1. Monitoring

The essential activity of the Department for monitoring of extraneous substances residues is to carry out the monitoring according to the Decree 291/2003 Coll. Concerning prohibition of administration of some substances of animals whose products are designated for human consumption, and monitoring of presence of banned substances, residues and extraneous substances in animals and their products, due to the substances the animal products could be deleterious for human health. In June 2005 this Decree was amended by the Decree 232/2005 Coll., further in July 2006 by the Decree 357/2006 Coll.

According to Decree 291/2003 Coll. as amended the control of the following substances is appertained to ISCVBM laboratory: - Group A substances (substances with anabolic effect and banned substances) and Group B 2 section d.
Sample survey summary for 2008 is stated in Annex No 2 - Monitoring 2008.

The numbers of samples with non compliant results of ELISA and RIA screening methods were passed on for conformation by GC-MS and LC MS/MS and were as follows:

nortestosterone – 8, RALs – 26, chloramphenicol – 20, methyltestosterone – 10, trenbolone – 1, clenbuterole – 4, ethinylestradiol – 2, gestagens – 3, testosterone - 1

Non compliant samples in 2008

- chloramphenicol
  - Prot. No 1278 urine – cattle live, locality – Herbortice, land register No 63839, Ústí nad Orlicí Inspectorate - Pardubice Region
  - Prot. No 1490 muscle – turkey slaughtered, locality Kounov u Rakovníka, land register No 67115, Rakovník Inspectorate – Middle Bohemian Region
  - Prot. No 2479 muscle – layer on farm, locality - Velký Malahov, land register No 77966, Domažlice Inspectorate – Plzeň Region
- testosterone
  - Prot. No 543 serum – heifer live (6-18 months), locality - Chvalkovice na Hané, land register No 65518, Vyškov Inspectorate – South Moravian Region

In case of non compliant results the action proceeded according to Decree 291/2003 Coll. and "Sampling procedure and subsequent surveys in the event of over limit/non compliant determinations of biological active substances used in animals and unpermitted treatments in terms of Monitoring plan of banned substances and VMP residues" – "Monitoring plan of banned substances, residues and contaminants in food chain in 2008" Ref. No 153/2008.

7.2.2. Special Examinations

a) External Application

Invoicing – Applications for examinations sent by manufacturers, owners etc.
chloramphenicol – 8 (Prot. No 1, 476, 1089, 1090, 1091, 1095, 1096, 1718)

b) Special Actions of SVA
chloramphenicol – 2 (Prot. No 1702, 1736)
nitrofurans – 1 (Prot. No 1702)

c) Regular Controls of SVA
chloramphenicol – 1 (Prot. No 474)

d) Extraordinary Control Actions of SVA– chloramphenicol – HYG2
chloramphenicol – 26 (from that 1 non compliant) + 8 targeted

Special (circular) tests attendance in 2008:

Accredited HPLC testing laboratory

1) Thyreostatics in porcine urine
organised by RIVM, Bilthoven, Netherlands

2) Nitrofurans in porcine muscle
organised by AFSSA, Fougeres, France

Accredited GC-MS testing laboratory

Accredited ELISA testing laboratory

3) Nitrofurans in porcine muscle
organised by AFSSA, Fougeres, France

Extraordinary actions:

- Special workshops of SVA (June – Němčičky, December – Prague)
- Employees took part in special seminars (service, metrology, statistical methods trainings etc.) pursuant to official position and qualifications.
- Periodical annual workshop programmes of leaders EU CRL (BVG, RIVM) laboratiories were reported on meetings of regional coordinators for national monitoring of extraneous substances, leaders of National Veterinary Institute and ISCVBM Chemistry Department
- Euroresidues VI; 19-21.5.2008, Conference on Residues of Veterinary Drugs in Food, active attendance –Poster: 1/ Šťastný et al.; 2/ Rejtharová et al.

8. Legal Agenda

During 2008 there were in total 33 administrative proceedings were initiated for breaching of the Act on Pharmaceuticals 378/2007 Coll. as amended by the subsequent acts or for breaching of the Act on Veterinary care 166/1999 Coll. as amended by the subsequent acts, based on the ground works and requirements from the Inspection Section and other competent employees of the Institute (in total 34 administrative proceedings were initiated and administered in 2008, 49 in 2007, 48 in 2006, 29 in 2004). In 2008 there were 33 administrative proceedings finished (from that 4 started in 2007). The sum of inflicted fines was 214,500 CZK, which are the revenues of the state budget. The highest fine was 90,000 CZK, the lowest 1,000 CZK. Three administrative proceedings were accommodated due to reasoned disclaimer and these proceedings were stopped.
Three impose proceedings on market withdrawal were administered. Refunding of proceeding expenses in total high of 1,000 CZK was inflicted, the total charges were reimbursed amounting to 30,000 CZK.

9. Department of Informatics, ISCVBM Bulletin, Information Providing, Supervision of Advertising

Information technology

During 2008 the common activities of maintaining and innovation both servers and workstations took place. Simultaneously the consecutive renovation of computer equipment was made with regard to effectiveness of its use.
During the year the data connection to the internet from the existing wireless to new connection via optical fibre cable was changed. In the system of electronic document evidence the removing of small shortcomings in functionality which had appeared during the operating happened subsequently. In the second half-year the Cross Compliance system was launched. The changes in Labsystem database also took place where the recording and registration data library were divided. Labsystem was connected to SVA Information System via SVA VPN. Within the frame of EU Presidency and HMA meeting arranging the new system of accreditation was launched.

ISCVBM Bulletin

During 2008 ISCVBM via its Bulletin was regularly informing the public about issued decisions on marketing authorisation, their renewals, variations, transfers, terminations and revocations, about issued decisions of approved veterinary products, their renewal, variations, validity termination and revocation and about register of VTD. In ISCVBM Bulletin the further information were published – MA dispensations, issued ISCVBM guidelines, important information for holders of marketing authorisation decisions, updated lists of VMP and VP manufacturers, VMP distributors, manufacturers of medicated feedingstuffs, manufacturers of active ingredients, lists of over the counter VMP and reviews of validity of marketing authorisation decisions for VMP. The ISCVBM Bulletin was issued six times a year, every two months in the amount of 150 printed copies.

Public information about VMP, their approved SPC and PL were regularly provided to compiler of the Automated Information System of Medicinal Products (AISMP). These information including the information on VP, VTD and biocides were also provided for publication to the editors of the journal Veterinářství.

Information of the ISCVBM activities are also provided by ISCVBM web sites (www.uskvbl.cz).

Total of 23 personal consultations was carried out during the year 2008 relating to marketing authorisation. In the field of approved veterinary products, VTP and biocides the total of 45 personal consultations was carried out. In the field of manufacturing of VMP, medicated feedingstuffs, veterinary products, distribution and pharmacovigilance there were 57 personal consultations within the scope of submitted applications for manufacturing approval or variation to a manufacturing approval.

Information providing according to Act 106/1999 Coll.

Report on the activities of the Institute for the State Control of Veterinary Biologicals and Medicaments in the sphere of information providing submitted in accordance with paragraph 18 of the Act 106/1999 Coll., relating to the free information access, as amended by the subsequent acts

in the year 2008

Article 1 a)
During the year 2008 ISCVBM received in total 4384 applications for information provision which were made in accordance with the Act on Free Information Access.

Article 1 b)
All applications for information provision were granted according to aforementioned act, no appeal was brought.

Article 1 c)
In the matter of information providing according to aforementioned act no legal proceedings were conducted with ISCVBM, no court judgment was delivered.

Article. 1 d)
In the matter of information providing according to aforementioned act no administrative proceeding were conducted regarding sanctions for its breaching.

Article 1 e)

The sphere of provided information	**Number**
Marketing authorisation of VMP	2850
Approval of VP, biocides, and VTD	1320
Package Leaflet of VMP – revoked applications	5
Lists of VMP, VP and biocides	28
Pharmacovigilance	23
Manufacturing of VMP	192
Manufacturing of medicated feedingstuffs	148
Distribution	77
Total	**4643**

ISCVBM Library

The operating of registrar premises and ISCVBM library is provided by registration section of ISCVBM. The ISCVBM library manages the book stock and journal fund via the database. Total of 2731 books is registered on the 31.12.2008 (acquisition of the library fund were total 41 books compared to year 2007, from that 10 were Czech and 31 foreign).

Total of 34 journals were subscribed on the 31.12. 2008. From that amount 18 were Czech journals and 16 foreign. Acquisition was 1 Czech journal compared to year 2007, while number of foreign journals remained unchanged.

Total number of registration documentation items recorded in the database was 28,045 on the 31.12.2008 (annual acquisition 4,011 items).

Supervision in the sphere of VMP advertising

During the year 2008 the ISCVBM obtained 1 notice of unethical advertising manners regarding promotion of VMP on web pages for breeders. Further the Institute obtained the opinion of notice to advertising campaign – distribution of free samples of OTC VMP issued via a journal. The Institute advised the applicant of its opinion and suggested the solution which was not contrary to law.
In 2008 there was no administrative proceeding conducted and there were no penalties for violation of Act on Advertising Regulation.

10. Economical and Operating Sphere

The total amount of financial resources assigned to ISCVBM after adjustment was 51,867,000 CZK in 2008, from that investment resources were 2,500,000 CZK, uninvestment resources 49,367,000 CZK, from these 22,716,000 CZK fell on salaries.

Investment resources in total approved amount of 2,500,000 CZK were utilized for finalization of realization of conclusions resulting from energetic audit of the organization – heat insulation of the building, part B and C, amounting to 383,000 CZK, further for finalization of attic premises for Section of Marketing Authorisation above the part B and C of the building in amount of 10,619,000 CZK. Units and machinery, vehicles and reconstructions were provided in total amount of 2,922,000 CZK. Reserve fund (RF) resources amounting 3,270,000 CZK were used for realization of these investment projects. Simultaneously the resources from extra budget sources amounting to 9,029,000 CZK were used.

Uninvestment resources were utilized amounting to 49,367,000 CZK, from these the highest part were payroll costs and lawful contributions on health and social insurance of employees in total of 22,716,000 CZK. This year the RF resources were used on current expenses amounting to 5,500,000 CZK. Utilization of uninvestment resources for the other purposes was accomplished according to needs of the Institute during this year.

In the year 2008 the resources from cost refund were withdrawn in total amount of 17,892,000 CZK. On 27 February 2006 the Service Pricelist - cost payment of marketing authorisation applications, which have been drawn by the Institute on the basis of article No 112 of Act on Pharmaceuticals 378/2007 Coll. was published in the Ministry of Finance Bulletin. These financial resources are not part of the state budget and were drawn in compliance with the act 218/2000 Coll. as amended, in compliance with international regulations for drawing S-018/1000 and pursuant to Regulations for using the extra budget resources from Ministry of Agriculture from 7 November 2006, Ref. No 34386/2006-13012.

The regularity of resources drawing from the state budget is evident from the table No 1, interannual fluctuations occurred only in resources drawing from investment when the largest part of these costs are the resources used on building investments, and hence it is necessary to consider seasonal character of these operations.

The withdrawing of payroll costs was steady and corresponds to approved budget. In the Institute there were 84 recounted employees working in the year 2008.

In 2008 the Institute managed the property in total value of 142,778,000 CZK, from that 136,843,000 CZK was the corporeal property and 5,935,000 CZK incorporeal property.

The costs amounting to 792,000 CZK were drawn on official journeys abroad. These working journeys were undertaken by special employees from the Institute namely from the reason of participation on the EMEA meetings, scientific workshops and trainings.

The amount of short-term commitments to suppliers was 2,374,000 CZK and the amount of long-term commitments was 0 CZK and the amount of the outstanding debts were 538,000 CZK on the 31 December 2006.

The Institute is the permanent member of the following international organisations:

PIC/S
BfARM

The member fees in these organisations have been fully covered by the Ministry of Agriculture.

The Institute actively engaged in the preparation of CZ PRES of the Council, two experts were nominated to the special committees.

The Institute participates in the realization of the research and development project in cooperation with Veterinary Research Institute and the food safety project in cooperation with the University of Veterinary and Pharmaceutical Sciences Brno.

The Institute deputies takes part regularly in the EMEA meetings, but all costs of activities accompanying are covered or refunded from the EC (EMEA) resources.

11. Employees

Basic Personal Data

Table 11/1: Classification of employees according to age and sex – situation on the 31. 12. 2008

Age	Men	Women	Total	%
up to 20 years	0	0	0	0
21-30 years	1	3	4	4,6
31-40 years	7	23	30	34,5
41-50 years	3	19	22	25,3
51-60 years	2	18	20	23,0
61 years and more	5	6	11	12,6
Total	**18**	**69**	**87**	100
%	20,7	79,3	100	

Table 11/2: Classification of employees according to education and sex – situation on the 31. 12. 2008

Education	Men	Women	Total	%
Elementary	0	4	4	4,6
Craft	0	1	1	1,1
High School	2	2	4	4,6
High School with Graduation	0	0	0	0
Vocational Training with Graduation	4	29	33	37,9
Advanced Vocational Training	0	0	0	0
University Degree	12	33	45	51,7
Total	**18**	**69**	**87**	100
%	20,7	79,3	100	

Table 11/3:Total data of average salaries on the 31. 12. 2007

	Total
Average gross monthly salary	20 751,- CZK

Table 11/4: Total data concerning the beginning and ending of employment in 2008

	Total amount
Coming	15
Outgoing	17

Table 11/5: Length of employment – situation on the 31. 12. 2008

Length	Number	%
up to 5 years	27	31
up to 10 years	19	21,8
up to 15 years	20	23
up to 20 years	11	12,6
over 20 years	10	11,5
Total	**87**	**100**

12. Work Safety, Fire Prevention

The fire prevention inspections centred on electric appliances, patency of emergency exits, fire extinguishing equipment, condition of stand-by lighting and control of fire doors were carried out during the year 2008.
The education training of firewatchers and persons ensuring security guard besides working hours was carried out in February 2008.
The periodical revision of the fire main and fire extinguishers was carried out by TESPO Company in April 2008.
During the year the construction work took place, the fabrication of stairways to 4^{th} over ground floor was initiated.
New employees incorporated during the year were immediately taught in fire prevention and protection in the workplace.
No fires were recorded during 2008.

13. Conclusions and perspectives by the year 2009

First half of the year 2009 will be in token of activities associated with CZ PRES. The Institute expects already in January expert and logistic preparation of HMA meeting which will be followed by series of meetings of working groups of HMA – as is European Surveillance Strategy Group (ESS), EMACOLEX solving matters of law, Quality Manager Working Group, Working Group on VMP Testing or Enforcement Officers Working Group.

In April 2009 then the informal meeting of Committee for Veterinary Medicinal Products is scheduled, which will take place in Brno and in May the series of meetings will be finished by the second meeting of Head of Medicines Agencies in Mariánské Lázně.

During 2009 the Institute will also prepare new version of its website, which should better correspond to current scientific and legislative requirements including publishing of approved summaries of the product characteristics.

In the second half-year 2009 the moving of monitoring laboratory to modernized premises of former State Veterinary Institute Brno should realize.

The Institute will continue in modernization of information technologies and its information system so that it could respond to special and regulatory queries which should be solved.

Explanation of appplied abbreviations

Abbreviation		Explanation
Czech	**English**	
AISLP	AISMP	Automatic Information System of Medicinal Products
ATB	ATB	Antimicrobials
ATC	ATC	Anatomic Therapeutical Classification
ATM	ATS	Antimicrobial Substance
AV	AV	Autogenic Vaccine
AZL	ATL	Accredited testing laboratory
BOZ	HSP	Health Safety and Protection
CAVDRI		Collaboration Agreement between Veterinary Drug Regulatory Institutions
CVMP	CVMP	Comittee for Veterinary Medicinal Products
ČIA	CIA	Czech Institute for Accreditation
ČL	PhB	Pharmacopoeia Bohemica
ČLK	CPC	Czech Pharmacopoeia Committee
ČLS JEP	CMS JEP	Czech Medical Society of J. E. Purkyne
ČMI	CMI	Czech Metrology Institute
DIMDI	GIMDI	Deutsches Institut für Medizinische Dokumentation und Information
EDQM	EDQM	European Directorate for the Quality of Medicines
EEA	EEA	European Economy Area
EHK	EQA	External Quality Assessment
EHS	EEC	European Economic Community
EK	EC	European Committee
EL	EuPh	European Pharmacopoeia
ELK	EuPhC	European Pharmacopoeia Committee
EMEA	EMEA	European Medicinal Agency
ES	EC	European Community
EU	EU	European Union
FGV	PVG	Pharmacovigilance
GC	GC	Gas Chromatography
GC-MS	GC-MS	Gas Chromatography – Mass Spectrometry
SVP	GMP	Good Manufacturing Practice
HEVRA	HEVRA	Heads of European Veterinary Regulatiory Authorities
HPLC	HPLC	High performance Liquid Chromatography
HVLP	MPMP	Mass Produced Medicinal Product
IPVPN	IPVPN	Internet Protocol Virtual Private Net
LL	AI	Active Ingredient
KL	CL	Control Laboratory
MěVS	MVA	Municipal Veterinary Administration
MK	MF	Medicated Feedingstuff
MRA	MRA	Mutual Recognition Agreement
MF	ME	Ministry of Finance
MZ	MH	Ministry of Health
MZE	MA	Ministry of Agriculture
NCCLS	NCCLS	National Committee for Clinical Laboratory Standards

PECA	PECA	Protocol on European Conformity Assessment Agreement
PERF	PERF	Pan-European Regulatory Forum
PIC/S	PIC/S	Pharmaceutical Inspection Cooperation Scheme
PN	CS	Company Standard
PO	FP	Fire Protection
RHP	HFE	Hand Fire Extinguisher
SAGAM	SAGAM	Scientific Advisory Group on Antimicrobials
SDP	GDP	Good Distribution Practice
SKP	GCP	Good Clinical Practice
SLK	SLC	Laboratory Control Section
SOP	SOP	Standard Operating Procedure
SÚKL	SIDC	State Institute for Drug Control
SVS ČR	SVA CR	State Veterinary Administration of the Czech Republic
SZÚ	SHI	State Health Institute
TAIEX	TAIEX	Technical Assistance Information Exchange Office
ÚKZÚZ	CISTA	Central Institute for Supervising and Testing in Agriculture
ÚSKVBL	ISCVBM	Institute for State Control of Veterinary Biologicals and Medicaments
VAS	VAC	Veterinary Antibiotic Centres
VEDDRA	VEDDRA	Veterinary Dictionary for Drug Regulatory Activities
VICH	VICH	Veterinary International Conference on Harmonisation
VLP	VMP	Veterinary Medicinal Product
VPN	VPN	Virtual Private Network
VTP	VTD	Veterinary Technical Device

Annex No 1

Table A Organizational structure of the Institute for State Control of Veterinary Biologicals and Medicaments

Directorate			
Director			
	Secretariat		
	Legal Department		
	Department for Publicity, Information and Advertising Supervision		
	Quality Manager		
	International Harmonisation Department		
	Personnel Department		
	Economic Department		
		Department of Registrar Office and Dispatching Office	
		Department of Accountant and Material and Technical Support	
		Department of Labour and Wages	
		Department of Administration and Register Office	
		Department of Information Technology	
		Technical Operations Department	
			Maintenance Office
			Cleaning Office
	Laboratory Control Section		
		Quality Manager	
		Secretariat	
		Cleaning Office	

Continuing on further page

	Division of Laboratory for Monitoring of Veterinary Drug Residues	
		Office for Acceptance and Recording of Monitoring Samples
		HPLC Department **GC Department**
		Department of Screening Methods
	Division of Official Medicines Control Laboratory	
		Department of Analytical Chemistry
		Department of Microbiology
		Workplace for decontamination, washing and sterilisation of laboratory glassware and preparation of nutrient media
		Laboratory for bacterial endotoxines
		Laboratory of virology
		Department of PCR and Immunological Methods
		Department of "in vivo" Biological Methods and Experimental Plant for "in vivo" Experiments
	Control Laboratory of Veterinary Medicinal Products	
Inspection Section		
	Quality Manager	
	Secretariat	

Continuing on further page

		Division for GMP Inspection of Medicinal Products, Medicated Feedingstuffs, Autogenous Vaccines and Veterinary Products	
			Department for GMP of Medicinal Products, Active Ingredients and Autogenous Vaccines
			Department for GMP of Medicated Feedingstuffs
		Division for GDP	
			Department for GDP Inspection
		Division for Market Control, Dispensing and Usage of Medicinal Products	
			Department for Monitoring of Medicinal Product Usage
			Department for Control of Dispensing and Usage of Medicinal Products and Veterinary Products
		Pharmacovigilance Department	
		Field Office Louny	
	Section of Marketing Authorisation, Approval and Register of VTD		
		Quality Manager and Coordinator of Matters concerning EC Marketing Authorisations and CVMP	
		Division of Administrative Affairs – MA procedures and Approval	
		Division for Marketing Authorisation of Pharmaceuticals	
			Department for the Quality Assessment of VMP

Continuing on further page

		Department for the Safety Assessment of VMP
		Department for the Safety Assessment of Residues of VMP
		Department for Efficacy Assessment of VMP
	Division for Marketing Authorisation of Imunologicals	
		Department for the Assessment of Bacterial Vaccines and Hyperimmune Sera
		Department for the Assessment of Viral Vaccines for Poultry and Rabbits
		Department for the Assessment of Viral Vaccines for the Rest of Animal Species
	Department for Approval of Veterinary Products and the Register of Veterinary Technical Devices	
	Department for Clinical Evaluation	
	Department of Pharmacopoeia	

Annex
No. 2

MONITORING 2008

Group		Matrix - Group of Animals		Quantity
A1	stilbens	urine	cattle, pig, sheep, goat and horse	229
		muscle	poultry	38
		muscle	fish, rabbit and farm game	35
A2	thyreostatics	urine	cattle, pig, sheep, goat and horse	146
		muscle	poultry	37
		muscle	fish, rabbit and farm game	4
A3	boldenon	urine	cattle, pig, sheep, goat and horse	21
	estradiol	serum	cattle, pig, sheep, goat and horse	26
	etinylestradiol	urine	cattle, pig, sheep, goat and horse	58
		muscle	fish, rabbit and farm game	15
	gestagens	fat	cattle, pig, sheep, goat and horse	80
	corticosteroids	urine	cattle, pig, sheep, goat and horse	57
	methyltestosteron	urine	cattle, pig, sheep, goat and horse	58
		muscle	fish, rabbit and farm game	16
	nortestosteron	urine	cattle, pig, sheep, goat and horse	58
	stanozolol	urine	cattle, pig, sheep, goat and horse	24
	testosteron	serum	cattle, pig, sheep, goat and horse	26 *1
	trenbolone	urine	cattle, pig, sheep, goat and horse	58
		muscle	poultry	39
		muscle	fish, rabbit and farm game	3
A4	RALs	urine	cattle, pig, sheep, goat and horse	179
		muscle	poultry	39
		muscle	fish, rabbit and farm game	4
A5	beta-agonists	urine	cattle, pig, sheep, goat and horse	67
		liver	cattle, pig, sheep, goat and horse	132
		liver	poultry	39
		liver	fish, rabbit and farm game	8
	clenbuterol	water	feed water fo cattle	10
		feedingstuff	for cattle	10
A6	dapsone	muscle	cattle, pig, sheep, goat and horse	20
	chloramphenicol	urine	cattle, pig, sheep, goat and horse	140 *1
		muscle	cattle, pig, sheep, goat and horse	203
		muscle	poultry	208 *2
		muscle	fish, rabbit and farm game	30
		milk	cow, sheep and goat	90
		eggs	hen and quail	49
		honey	domestic	10
		water	feed water for poultry	11
		feedingstuff	for poultry	10
		farina	fish	5
	chlorpromazine	kidney	cattle, pig, sheep, goat and horse	28
	nitrofurans	muscle	cattle, pig, sheep, goat and horse	65
		muscle	poultry	52
		muscle	fish, rabbit and farm game	13
		milk	cow, sheep and goat	13
		eggs	hen and quail	11
		honey	domestic	10
	nitroimidazoles	muscle	cattle, pig, sheep, goat and horse	65
		serum	cattle, pig, sheep, goat and horse	10
		muscle	poultry	63
		muscle	fish, rabbit and farm game	8
		eggs	hen and quail	11
		feedingstuff	for poultry and rabbits	30

B2d	sedatives	kidney	cattle, pig, sheep, goat and horse	119
T o t a l			**2790**	

* the number behind the asterisk represents the number of noncompliant samples