Ústav pro státní kontrolu veterinárních biopreparátů a léčiv
Institute for State Control of Veterinary Biologicals and Medicaments
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ANNUAL REPORT

ON ACTIVITIES OF ISCVBM BRNO

2013

Basic information on the Institute, position of the Institute

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1 Introduction

Let me introduce the annual report on activities of the Institute for State Control of Veterinary Biologicals and Medicines, which summarizes results of activities achieved in 2013.

In my opinion, with respect to data presented in the report, it can be stated that the Institute succeeds in fulfilment of its responsibility given in legal instructions of the Czech Republic as well as responsibility resulting from international obligations of the Czech Republic within the frame of the EU.

During the course of previous years the Institute incorporated into the system of international marketing authorisation procedures with active role in position of so-called „Reference Member State“ in international authorisation procedures of mutual recognition and in decentralised procedure, actively incorporated in activities of European Medicines Agency and its professional Committee for Veterinary Medicinal Products (CVMP) and relevant working groups where the representatives of the Institute actively act as raporteurs or co-raporteurs both within the scope of preparation of guidelines of CVMP and within the scope of assessment of applications for maximum residual limits and marketing authorisation of veterinary medicinal products.

In terms of the area of veterinary medicinal products authorisation, despite the relatively unfavourable trend in number of food animals breeded in the Czech Republic during the last period, the Institute did not register drop down in authorised veterinary medicinal products. To the contrary, the number of authorised veterinary medicinal products has been permanently increasing. Ratio of products authorised by the European Commission based on assessment by CVMP by means of so called centralised procedure of authorisation has been increasing and in case of new authorisations the major part represents authorisations by the MRP/DCP procedures.

Increased interest of pharmaceutical companies is noticeable namely in medicines for small animals, where new antiparasitic medical substances or new combinations of medical substances have been introduced to market. There is perceptible development of products in the cathegory of „innovative“ or „advanced“ therapeutic procedures represented by products based on monoclonal antibodies, immunomodulators, stem cells etc.

Interest of pharmaceutical companies in development of new products in the field of large animals is limited and except for few exceptions (for instance introduction of monepanthel) number of new therapeutical substances in this field is very low.

Current discussion on antimicrobial policy implies, that with respect to social interest it is necessary for the CR both to create conditions to maintain the „old“ products on the CR market and to create conditions to innovations and development of new molecules for veterinary medicine.

Pressure from the side of human medicine as well as pressure to food safety from the side of consumers results in necessity to search for solutions over the all-society in the field of antimicrobial policy and use of antimicrobial products, which will lead to adjustment of a long-term sustainable and economically effective system. From this point of view, the Institute acknowledges establishment of Working group for antimicrobials at the Ministry of Agriculture of te CR. The aim of this Group is to search for consensual solution taking into account needs of wide range of parties concerned.

In connection with these complex concerns it is necessary to take into account future revision of terms for authorisation of many products, which are currently on the market and in which data on efficiency or safety no longer correspond to terms in practice. From the view

both of pharmaceutical companies and the Institute as well as practice the best approach is to search all-European solution and solve the problems of dosage, indications or other terms of authorisation by means of review on the level of the European Medicines Agency with follow up implementation of results from reviewing in the conditions of the CR with incorporation of both original products and generics. However, this approach is not applicable in all cases, thus it will be necessary to revaluate some older products on the CR level by means of national activity, which conditions for use may not correspond to current level of expert knowledge.

The Institute also perceives simillar progress in the field of antiparasitic resistance. Despite the situation in the CR is not so serious compared to other countries – for instance in the Great Britain – it is possible to notice significant occurence of antiparasitic resistence in selected parasites namely in small ruminants. For future it will be necessary to take systematic approach and search convenient solutions also in this field.

Another field which is becoming more significant represents questions related to environmental protection. These are risks connected with antimicrobial resistence, usage of medicinal products which might be cumulating in the enviroment or recent problems of so called PBT compounds (perzistent, bioaccumulative, toxic), involving many substances with significant importance for veterinary medicine. It will be necessary to search complex solution also in this field.

In terms of inspection activities it is necessary to state that manufacture of veterinary medicinal products and inspection of good manufacturing practice is stabilized and we believe that international activities of the Institute within the frame of PIC/S and JAP (Joint Audit Programme) in coordination with European Medicines Agency contribute not only to international reputation of the Czech Republic in this field but also assist to domestic manufacturers to market its products within the EU countries as well as in the third countries. In the field of good manufacturing practice there is noticeable shift to the concept of so called „consistent manufacture“ and the Institute has been monitoring the development in this field and preparing in cooperation with domestic manufacturers on its implementation in practice.

A specific consolidation can be seen in the field of medicated feed also, where we noticed a decrease in number of manufacturers during the last period, which was caused by changes in market in the conditions of the Czech Republic..

Distribution of veterinary medicinal products and sales of selected medicinal products are stabilized as well. I am convinced that introducing of the system of sales of selected medicinal products into the veterinary sphere has brought revival of veterinary market, introduced veterinary medicinal products to breeders result in benefit for all involved participants – breeders, veterinary surgeons and pharmaceutical companies.

From an inspection regard, the most problematic is an internet market and illegal import of medicinal products into the Czech Republic, where the Institute has been preparing draft of legislation amendment, which would lead to limitation of any illegal practice with veterinary medicinal products.

In terms of laboratory control there is a system of market surevillance in place, which is based on assessment of risk for veterinary medicinal products as a main tool of quality control of veterinary medicinal product over the Czech market. Importance of official control is well-founded in regular findings of results out of range of authorised specifications. There are similar experiences in other countries, for instance in France there are reports on trend of increase in results of OMCL laboratory analyses out of the authorised specifications.

In relation with official batch release the situation is also stabilized and in the OCABR system there remain life vaccine against erysipelas, innactivated vaccine against horse flu and life rabies vaccine for foxes.

In terms of monitoring sphere the range of analytical methods (analytes, matrixes) is determined by specification from the State Veterinary Administration resulting from communication with relevant european reference laboratories.

In conclusion of this introduction I would like to express my thanks for excellent cooperation and support from the Ministry of Agriculture, State Veterinary Administration and other partners of the Institute in the field of state administration as well as to regulated subjects – marketing authorisation holders, manufacturers and other entities.

My endeavour is that Institute for State Control of Veterinary Biologicals and Medicines fulfils its mission in full and in a way to contribute to maximum development of professional activity, with minimalization of administrative impacts, thus bringing the maximum effect for those using the results of Institutes activities.

Prof. Alfred Hera, D.V.M., PhD.

2 Quality assurance system

In the field of quality assurance system several important measures were adopted during the last year.

In relation with change in organisational structure introduced in Provision of Director No. 006/2012/1000, which came into force on November 1, 2012 and in relation with initiations from customers, amendments to legislation and need to update various procedures used within the Institute, there was carried out revision of Organisational Order of the Institute and other system controlled documents – regulations for terms of declaration of interests, terms of travel refunds, regulation for shortcomings in quality and rapid allert system, order of samples procedure as well as new instructions reflecting the IT development – description of systems and applications in the intranet of the ISCVBM and safety and backup of data.

In 2013 internal auditors were reassessed and new internal auditors were appointed.

Regular review of quality system was carried out taking into account results from audits, initiations from customers and other inputs in correspondence with requirements of quality standards in place and concrete tasks in the field of quality management were specified by means of aims of quality for the year 2014.

In the second half of 2013 preparation for the third stage of comparison of agencies was launched in terms of implementation level of quality assurance system and capability of the Institute to fulfill tasks within the frame of EU (Benchmarking Excercise – BEMA).

3 Activitiy and cooperation with national, European and other international institutions

3.1 Preparation and comments on legislation

In 2013 the Institute participated on preparation and comments to amendments of the Act No. 378/2007, with relation namely to implementation of the new EU legislation in the field of pharmacovigilance and counterfeits of medicines. Although both EU rules refered to human medicines, the national modification lead to amendments to veterinary medicines as well, thus with regard to formal amendments to the Act, re-arrangement of individual articles, new articles or modification of article wording, which regulated human and veterinary problems commonly (for instance field of medical substances). Concurrently with implementation of new EU regulations modifications were made in those parts of the Act, which had become problematic during use of the Act in practice.
Another significant change implemented within the frame of amendments to the Act on Pharmaceuticals there was modification of conditions of procedure for variations of authorisation, in which the Act directly incroporated a link to the directly applicable regulation of the Commonwealth – Regulation No. 1234/2008, which regulates changes both in subject and procedural aspect. National regulation in the field of veterinary medicinal procucts is applied only to conditions on which it is possible to market the products corresponding to conditions prior to changes in authorisation and further solution of changes which do not relate to SPC.
In relation with amendments to the Act also modification of implementation decrees was made with participation of the Institute during preparation and comments.

3.2 Ministry of Agriculture, State Veterinary Administration and other partners of the Institute in the Czech Republic

3.2.1 Ministry of Agriculture

MZe and ISCVBM – establishment of Working group for antimicrobials
With regard to increase of both international and national importance of antimicrobial resistance issue first meeting of a core coordinating group (June 2013) and further meeting of Working group for antimicrobials at MZe (September 25, 2013). In the meeting in June the **Core coordinating group of Working group for antimicrobials** (PSA at Mze) drafted the statutes and the most serious issues were discussed in the field of AMR - antimicrobials usage and laboratory diagnostics in CR. Statutory meeting of the complete **Working group for antimicrobials** took place in September 25, 2013 in Mze. One of the task of this group apart from setting of exact rules and priorities of antimicrobial policy within Mze is cooperation with CKS NAP and thus with human field to create update of Action plan targeted to antimicrobials for the Czech Republic. The group should deal with the antimicrobials problem in resort of agriculture for a long term period on a conceptually basis, therefore discussions of the group were focused on priorities to solution and progressive definition of specific tasks and responsibilities. Further meeting is supposed to be held in January 2014.

Cross-Compliance Inspection

Checks of obligations of farm animal breeders producing animal products for human consumption, which comprise also requirement of Cross-Compliance Inspection – SMR 10: prohibition of use of some substances with hormonal and thyreostatic effect and betasympathomimetics in animal farms (Directive 96/22/EC) are managed based on risk analysis by SVA CR. The inspections are carried out by Regional veterinary administrations, the inspectors from the Institute take part in selected inspection within the frame of methodical cooperation. No requirement for cross-compliance inspection was applied from SVA CR.

Committee for GMO at Mze CR

Also in 2013 the Institute appointed one employee for work in the Committee. The work consisted in advisory activity of Committee for the Ministry of Agriculture of CR, namely during composition of expert positions to submitted applications and granting of approvals resulting from articles of the Act No. 78/2004 Coll., as amended, on handling with genetically modified organisms and genetic products.

As of November 22, 2013 there have been approved 49 species of genetically modified organisms within the EU. In the territory of CR there was approved to grow only GMO corn, which was grown mostly in the Plzeň region.

In 2013 several important amendments to legislation were solved:

- *Commission Regulation which establishes implementation rules* for applications on genetically modified food and feeds corresponding to Regulation (EC) No. 1829/2003 EP and EC, ammending the Commission Regulation (EC) No. 641/2004 and (ES) No. 1981/2006.
- Commission implementing Decision amending implementing Decision No. 2011/844/EU concerning emergency measures relating to unauthorised GM rice in rice products from China

Following legislation being solved:

- Implementing Decision of Commission dealing with implementing rules for the Article No. 32 of Regulation of EP and EC No. 1829/2003 relating to reference laboratory of EU for genetically modified organisms according to Committee Regulation No. 1981/2006.
- In March 2014 the Commission plans to submit draft modificating the zero tolerance of admixture of unatuhorised GM materiál in food (analogy to 619/2011 for feed is already in use)
- Regulation No. 882/204 relating to official inspections.

According to information from the Ministry of Environment the Act on the Central Institute for Supervising and Testing in Agriculture has been amended (newly Act No. 279/2013 b.), with cancel of duplicity for announcement of areas for growing of GM crops. Also the Act No. 78/2004 Coll., will be amended to relieve the administrative burden namely during laboratory use of GMO in the lowest cathegory of risk.

At the same time the issues of GM pollen in honey was solved. It was decided that honey is a unary product and its pollen is a natural compound not an ingredient (definition according to Regulation No. 1829/2003).
In 2013 a positive findings of GM was detected in papaya imported from Thailand. Discussions have been made regarding enlisting of GM in papaya to the Annex No. I of Commission Regulation No. 669/2009 (EU), regarding feeds and food that are subject to increased level of official controls in place of its import to the EU countries.
Also there was found unauthorised growing of GM wheat in USA. One of the most frequently used importing place might have been in Spain, however, according to findings from USDA the wheat should not be on EU market. (methods for testing obtained on borders).

Quality, safety and efficacy of genetically modified veterinary medicinal products has further been assessed by EMA in a procedure of so called centralised authorisation procedure.
For possible need of identification of genetic modification in medicines it could be further used SVI in Jihlava.
The Committee meeting took place in November 26, 2013.

3.2.2 State Veterinary Administration and Regional Veterinary Administrations

Cooperation with State Veterinary Administration and Regional Veterinary Administrations continued in 2013 in the field of planning and providing of monitoring of extraneous substances. Results are presented in Chapter 7.2.1 Planned monitoring.
Further activities continued in the field of cooperation among inspectors in solving of above limits findings, medicated feeds, antimicrobial policy and in other fields.
Representatives of the Institute took active part in meetings of the State Veterinary Administration – epizootology, monitoring.
The Institute actively took part in preparation of opinions (positions) for the State Veterinary Administration to be presented in discussions on the EU level (e.g. CVO or working groups of the European Commission) in the Institute´s sphere of action (e.g. field of antimicrobial resistance).

3.2.3 State Institute for Drug Control

Close cooperation continued with State Institute for Drug Control in all levels. Joint inspections were carried out – see details in the Chapter 6. Activities of the Inspection Section. Representatives of the Institute took part in meetings held by SIDC, information has been interchanged between the institutes and cooperation has been carried out in laboratory analyses.

3.2.4 CISTA

Testing of one feed mixture (chlortetracycylin) was carried out in laboratories of the ISCVBM based on agreement between ISCVBM and CISTA in the field of inspection of cross contamination of feed mixtures.

Cooperation between CISTA and Institute proceeded during inspection of follow-up contamination of FM (feed mixture) after production of medicated feed – sample withdrawal by CISTA, laboratory analyses in CISTA and ISCVBM, hand-over of results from analysis, mututal consultations on resulsts from analyses, consultations concerning evaluation of cross contamination of FM with medicines.

3.2.5 Ministry of Health

Pharmacopoeia Committee – activity of the Institute for Pharmacopoeia in 2013

In 2013 the Institute further participated on activities of Pharmacopoeia Committee according to tasks determined by the Act on Pharmaceuticals.
Among these main activities it was participation on activity of Pharmacopoeia Committee of the Ministry of Health of CR (prof.MVDr. A.Hera, CSc. – vice-chairman, MVDr. Jana Jeřábková - member), activity of Section for veterinary immunologicals and pharmaceuticals and activity in groups of experts of European Pharmacopoeia Commission (MVDr.Jana Jeřábková and Jaroslav Maxa, PharmDr., PhD).
In 2013 employees of ISCVBM participated similarly to previous years in the work on preparation of the Pharmacopoeia Bohemica 2009 - Appendix 2014. This work consisted mainly of translations of revised articles and sections of pharmacopoeia for the european part (this part will include texts corresponding to European Pharmacopoeia - Appendices 8.0. to 8.2.) and of preparation of national part, which includes updated list of doses for animals of some of the medical substances used in veterinary practice.
Pharmacopoeia activity was arranged and coordinated at ISCVBM by the Section of veterinary immunologicals and medicines of the Pharmacopoeia Commission of MZ CR, whose official administration place is in ISCVBM. The Institute ensured its work through the Department of Pharmacopoeia lead by Dr. Jana Jeřábková. In 2013 there were eleven employees of ISCVBM working in the Department of veterinary immunologicals and medicines of the Pharmacopoeia Committee at MZ CR and five other members from other work places, which was 16 members in total within this Committee.
MVDr. Jana Jeřábková, PhD. and Jaroslav Maxa, PharmDr., PhD. actively took part in this Committee as a members of groups of experts of the Pharmacopoeia Commission, including participation on meetings in Strasbourg.

3.2.6 Expert Committee for Experimental Animals Protection

Activity determined by the Act related to protection of animals against torture No. 246/1992 Coll. as amended in the ISCVBM experimental facility was ensured by the Expert Committee according to needs and tasks of the Institute to ensure quality, safety and efficacy of veterinary medicines. The Committee had five members and in addition to supervisory obligation they ensured agenda relating to discussion, approval and inspection of all experiment projects.
By the end of 2013 with relation to new expert tasks there was submitted one project for approval. The approval process continued in the next year.
Fulfilment of specified requests for animal welfare is supported as well by trained employees of the Institute. There are 10 employees of the Institute qualified according to § 17 of the Act No. 246/1992 Coll. and 4 employees completed special course for laboratory assistants, technicians and tenders with re-examination of professional qualifications.

Process of approved experiment projects was continualy monitored by the Committee so that welfare of experimental animals and objectivity of results were ensured. Necessary data records on commencement, progress and termination of experiments were ensured as well. Summary Report for Calendar Year 2013 for the Ministry of Agriculture CR was elaborated including registery and analysis of animals used for experimental purposes by the Institute. Request to ensure welfare of animals during extra-work time (holidays etc.) was fulfilled by trained employees of the Institute.
Similarly to previous years, disposal of cadavers and contaminated materials after termination of the experiment by the contracts with the companies Agris s.r.o. Medlov and SITA Brno.
To have the full picture we present numbers of experimental animals used during 2013 within the scope of terminated experiment projects, that are comparable to numbers used during the year 2011 and 2012, which is also listed in the following table.

Numbers of laboratory animals used in the animal testing facility of the ISCVBM

Year Animal	2011	2012	2013
Mouse	760	700	872
Guinea pig	30	40	42
Poultry	4	4	4
Total	**794**	**744**	**918**

3.2.7 Other national cooperating institutions

Cooperation continued with the Veterinary Research Institute (**VÚVeL**) within the scope of joint grant project of both workplaces, which is focused to determine sensitivity and resistence profiles by means of micro dilution method at pathogenes insulated from the clinic of diseased animals „Development and production of veterinary sets for determination of MIC antimicrobial substances by a standardized micro dilution method and a new concept of evaluation of effectivity of antimicrobial substances by MPC determination“.
Highly active previous cooperation with workplaces in **VFU** slightly stagnated in 2013**.** Nevertheless, workers from ISCVBM (Dr. Bureš and Dr. Pokludová) visited laboratory which analysed profiles of AMR using molecular biological methods (Dr. Dolejská, prof. Literák) and CEITEC workshop dedicated to present situation in the field of AMR analysis with molecular biological methods, with presentations both by representatives from foreign university (DE) and colleagues from VFU. It would be efficient to follow-up this cooperation in 2014.
Cooperation with **KVL** was again strengthened in 2013. Representatives from ISCVBM met the representatives from KVL at meeting in march, where they discussed problems on use of antimicrobials. Several articles were published in periodical Zvěrokruh by KVL rrrelating to use of medicines (e.g. *Prescriptioning of antimicrobials – questionnaire among veterinary surgeons of CR* , Pokludová L., Bureš J., Hera A.)
Zvěrokruh 2013, 5: 16-18, Translation of poster of questionnaire FVE/HMA Zvěrokruh 2013, 5; Problems on off label usage of human LP (Dr. Koutecká, Prof. Hera).

3.3 Institutions of the EU and other foreign partners

3.3.1 European Medicines Agency (EMA)

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

Committee for Veterinary Medicinal Products

In 2013 representative of ISCVBM participated in 11 regular meetings of Committee for Veterinary Medicinal Products (CVMP).

Institute for State Contriol of Veterinary Buiologicals and Medicines actively participated in preparation of opinions/reports on centralised authorisation procedures, revision procedures, postauthorisation measures, maximum residual limits, scientific advisory and proposals for new expert guidelines.

Within the scope of Committee activity namely following agenda was discussed (partial list of the most important items with impact on regulation of VMP and potential impact on CR):

Launch of revision procedure (referal) for products containing medical substance lidocaine, based on request from Netherland and with regard to information on potential genotoxic cancerogenous substances that could occure during metabolism of this substance (2,6 xylidin).

Among other referals there was reassessment of efficacy for injection products with base of florfenicole, assessment of environmental impact for detamethrin, altrenogest and other mackrocyclic lactones, reassessment of safety of residues for products containing barium selenite, reassessment of efficacy and dosage for peroral and injection products with base of enrofloxacine. Results from procedure of revision adopted in statements from CVMP become obligatory through decision of European Commission and further implemented in terms for authorisation procedure of products, where authorisation decision is issued by ISCVBM.

Within the centralised procedure there were adopted statements from CVMP for several innovative products, e.g. generic alternation to original products with base of meloxicam, vaccine against edema disease, vaccine against equine West Nile fever, insuline product for pets, vaccine against hoof and mouth disease, where it was first case of authorisation using concept of „multistrain dossier“, product with base of oclacitinib maleate for treatment of pruritis connected with athopic dermatitis in pets, antiparazitic product with base of combination of spinosad / milbemycine oxim for treatment and prevention of flea infestation in dogs and at the same time for prevention of heartworms and treatment of listed gastrointestine infections with nemathelmintes.

As far as residues and maximum residual limits are concerned, CVMP adopted positive statements for MRL in diclazuril for use in rabbits, there was assessed triptorelin acetate for use in pigs.

Following the findings of illegal treatment of equine CVMP prepared statement to presence of fenylbutazone residues in horse meat, which was elaborated in cooperation with EFSA and published in April 2013.

Another important step with assumed future impact to evaluation of food safety is in form of conceptual measure by means of introducing a value of „injection site reference value“, thus a reference value for amount of residues in place of injection application. This value introduces special limit for place of injection administration of substances, where

protective period is determined with regard to tissue distribution by other tissue than muscle and where amount of residues in place of injection administration of substance may lead to toxicologically causeless extension of withdrawal period. This period uses unconsumed part of specified acceptable daily intake – ADI and value is mentioned in public assessment report for relevant MRL.
Presented concept was used in 2013 for evaluation of two substances – tildipirosine and further for ivermectin.

As far as new rules are concerned / guidelines approved by CVMP, CVMP discussed and adopted in various stages for instance rules for evaluation of contents of genotoxic impurities, evaluation of risk of antimicrobial resistance for human health, revision of guideline for evaluation of efficacy of antimicrobial veterinary medicinal products, revision of guideline for efficacy of intramammar products, evaluation of antiparasitic products and various other guidelines.

CVMP further actively participated in the field of international harmonization within the frame of VICH process, where CVMP presented statement in various stages of preparation to following guidelines: e.g. GL 23(R) study on evaluation of safety of residues in food of animal origin – evaluation of genotoxicity, GL 34 tests of presentce of contamination with *Mycoplasma spp.*, GL 35 elektronical standards for data transmission, GL 50 harmonization of criterions for relief from testing of safety of inactivated veterinary vaccines for target species, GL 51 statistical evaluation of data on stability within the scope of quality evaluation of VMP.

Further important agenda solved by CVMP was a problemas on availability of VMP for minor species of animals and minor indications (Minor Use / Minor Species - MU/MS). Several applications for classification to MU/MS cathegory was assessed and applications for financial relief related to MU/MS. These were for instance following products – oncological product for treatment of horses, vaccines determined for ferrets, anti inflammatory products determined for treatment of small animals and other combinations of indications and target species.

Important agenda was also in the field of protection of testing animals where CVMP worked on statement based on Decision of European Pharmacopoeia Committee in April 2012 regarding restraint from testing of safety of all veterinary vaccines on target species coming into force from April 1st 2013. On the CVMP level (centralised products) measures were introduced to implement these new rules which significantly contribute to fulfilment of 3R principle.

Last but not least CVMP participated in solution of antimicrobial resistence problem, where in 2013 preparation of common statement of CVMP, CHMP (human MP), EFSA and ECDC continued regarding impact on animal health and human health as a result of antimicrobial use in veterinary sphere. Prepared statement consists of four parts:

- Use of antimicrobials with potenatial to influence efficiency of antimicrobials used in human for treatment of multiresistant microorganisms, namely with regard to colistin and tigecyclin,
- Appropriateness of classification of veterinary antimicrobials with regard to choice of its usage – first, second etc.);
- Whether there is an importance to consider a public form of support for development of new antimicrobials for veterinary use,
- Whether it is necessary or not to restrict use of currently authorised antimicrobials in veterinary medicine.

Joint working party for quality of human and veterinary medicinal products
Joint CHMP/CVMP Quality working party (QWP)

Joint CHMP/CVMP working party dealing with quality of human and veterinary medicines (QWP) met four times in 2013 (from that one meeting was shared with GMDP IWG working party and one meeting with representatives of industry). Within the scope of the party there were discussed revisions of current guidelines relating to quality of medicines, elaboration of new guidelines, questions and answers for industry. At the same time QWP collaborates with EDQM (within the scope of elaboration and revisions of European Pharmacopoeia (Ph. Eur.) monographies, general texts and certification procedure of manufacturers of medical substances QWP group also actively participates in elaboration and revisions of guidelines ICH and VICH. The agenda also contains solving of questions relating to quality of particular human and veterinary medical products authorised by all kinds of procedures (MRP, DCP, CP, NP).

Namely following points from the field of veterinary medicines were subject of QWP agenda:

- New form of declaration of QP concerning implementation of principles of GMP for manufacturers of medical substances (together with GMDP IWG, which is a rapporteur)
- Project of harmonisation of assessment ASMF within EU
- Harmonisation of principles for definition of income drugs within the scope of medical substance synthesis
- Development of guideline for inspection of genotoxic impurities in veterinary medicines
- VICH GL3 – stability of medical substances and products – incorporation of climate zones III and IV
- Revision of guideline for stability study within the scope of control of variations in authorisation
- Microbiological quality of premixes for medication fo feed
- Choice of sterilization procedures (decision scheme, standard vs. Nonstandard procedures)
- Stability of generics vs. Original products
- Concept of monographs of Ph. Eur. For final medicinal product forms
- Revision of guideline for manufacture of medicinal products

Safety Working Party
Safety Working Party CVMP

Following the agenda from the previous period there were 3 meetings of the working group carried out during 2013. The meetings were focused on safety issues of VMP from the perspective of user, from the perspective of safety for target species of animals as well as for safety of residues. Working group has continued in the field of preparation of guidelines for VMP marketing authorisation, prepared opinions for CVMP and discussed the professional topics of given issue.
The group worked on preparation on proceedings to following assessment:

- Evaluation and determination of withdrawal period for milk (preparation of model and consideration of statistical approaches)

- Approach to residue values that are below the quantification limits
- Clarification of safety requirements for generic anf hybrid applications
- Evaluation of residual studies in honey (VICH guideline)
- Evaluation of genotoxicity according to VICH guideline GL23(R)
- Risks for underground water (together with ERA WP)
- Procedure for evaluation of safety of usage and safety of user on using of medicated collars

Other discussed issues were:

- Clarification of used guidelines and approaches for CVMP
- EMA – EFSA common evaluation of phenylbutazone residues in horse meat
- Implementation of 3R principles
- Alternative reference linits and evaluation of exposition (TTC, ArfD)
- Acute risk for determination of safety for consumer and residue in place of VMP application
- Guideline for determination of withdrawal period for milk in DC products
- Draft of VICH guideline for specification of depletion studies of residues in aqua species.

With regard to validity start of VICH guidelines GL 46 – 49 harmonisation has been commenced on wording and requirements of other valid guidelines for evaluation of residues established earlier.
At the same time details for meeting of CCRVDF were prepared including data for EU position at mentioned meeting.
Issues of VICH guidelines drafts regarding testing of genotoxicity of impurities were commented.

Working group for efficacy of veterinary medicines
Efficacy Working Party

The party works on establishment of new guidelines for evidence of efficacy, its comments and implementation. The party cooperates with other parties on common topics. EWP met four times during 2013 on two-days meetings, where the following actual issues were solved:
Revised guidelines:
- Guideline for evaluation of products with fixed combination (EMEA/CVMP/83804/2005) draft of document of questions and answers
- Management of efficacy studies for intramammar products in cattle, multi proffessional guideline (EWP, SAGAM): has not been finished, multi professional guideline (EWP, AMWP), public consulting till April 30, 2014
- Management of efficacy studies on non steroid antiinflammable products: has not been finished yet, public consulting till May 31, 2013, new draft of post-consultation guideline XII/2013
- Documented efficacy of veterinary medicinal products containing antimicrobial substances
Multi proffessional guideline (EWP, SAGAM): has not been finished yet
- Evaluation of better taste of peroral products: has not been finished yet, public consulting till May 31, 2013, new draft of post-consulting guideline XII/2013
- testing and evaluation of efficacy of antiparasitic substances for treatment and prevention of tick and flea infestation in dogs and cats: has not been finished, public consulting till January 31, 2013

- VICH – guideline on requirements for evidencing of bioequivalence – multi- professional guideline (EWP, QWP, SWP) – has not been finished yet
- SPC for anthelmintic products (EMEA/CVMP/EWP/170208/2005), Anthelmintic resistence, draft of position paper XII/2013 EWP

Revision of following guidelines was suggested:

- Efficacy evaluation of anthelmintics: general requirements
- Efficacy evaluation of anthelmintics: specific recommendation for pigs
- Efficacy evaluation of anthelmintics: specific recommendation for cattle
- Efficacy evaluation of anthelmintics: specific recommendation for sheeps
- Efficacy evaluation of anthelmintics: specific recommendation for goats
- Efficacy evaluation of anthelmintics: specific recommendation for horses
- Efficacy evaluation of anthelmintics: specific recommendation for dogs
- Efficacy evaluation of anthelmintics: specific recommendation for cats
- Efficacy evaluation of anthelmintics: specific recommendation for poultry
- Efficacy evidence of ectoparasitics

Working group for Immunological veterinary medicinal products
Immunological Working Party (IWP)

Immunological working party met three times in 2013. The main task of this working party was namely preparation of several guidelines for evaluation and marketing authorisation of immunological veterinary medicinal products and preparation of statements with relation to current issues, for instance evaluation of risk of occurence of RD 114 virus in veterinary medicinal products or wide use of autogenous vaccines.
The following current issues were solved at IWP meetings:

- Work proceeded on guideline „Table of foreign agens, on which testing shall be made with regard to manufacture and inspection of bacterial and viral vaccines for veterinary use“,
- „Guideline on requirements for combination vaccines and associations of immunological veterinary medicinal products“ was finished and submitted for public comments,
- Work proceeded on „Guideline on indications of veterinary vaccines“,
- Guideline specifying change or addition of strains in vaccines against horse flu was reviewed and finished,
- „General strategy for risk handling of contamination with RD 114 virus in veterinary products“ was elaborated
- Work proceeded on guideline on „replacement of cell lines used for manufacture of immunological veterinary medicinal products“,
- In the meeting in October 2013 there was discussed and highlited need of all-European regulation of preparation and usage of autogenous vaccines.

Pharmacovigilance working party - CVMP

During 2013 there were 6 meetings of working group for pharmacovigilance.

New procedure for products approved in centralised procedure was implemented during the previous year and in 2013 the procedure was stabilized – continuous inspection of centrally approved products, namely evaluation of new reports and current knowledge. Activity is supported with SOP on safety monitoring of centrally authorised products – SOP/V/4032 and is considered as initiation with possible modifications in future, namely with respect to possible recommendation and findings. During the course of the year the documents EMA/672075/2013 and EMA/721194/2013 were updated – dokuments specifying time schedule for evaluation of products for assessors of centrally authorised products (in-time sending of e-mails, concurrent evaluation of several products etc.).

All the year the working group focused on the question on „signal detection". Prior to adoption of the document „PhV surveillance and signal detection of veterinary medicinal products" (EMA/CVMP/PhVWP/901279/2011) several open discussion have been made. Signal detection is considered to be an up-to-date instrument in the field of monitoring of adverse effects, however it requires relevant tools and for instance only some of the member states use some of the targeted databases (United Kingdom, France, Spain, Sweden). During the year the questionnaire „Review of approches to signal detection across member states" (EXT/318506/2013) had been sent to member states, which was evaluated. An effort is appreciated to support „signal detection" with cooperation in this field as well as convenient education and training. Creation of Best Practice Guide for Signal Detection is not out of the question in future .

During the year, an „Updated recommendation on harmonising the approach to causality assessment for adverse events to veterinary medicinal products" (EMA/CVMP/PhVWP/552/2003) guideline was discussed and adopted, concerning evaluation of causality of adverse effects. The guideline was prepared for pharmacological products, vaccines were excluded.

Within its meetings or in form of so called Non-Urgent Information (NUI) the party solved several individual cases of adverse effects, e.g. effect in Sphynx cats after administration of some types of anesthetics, adverse effects after administration of VMP for treatment and prevention of ectoparasitoses in cats (in relation with kidney insufficiency) .

There are 6 meetings of pharmacovigilance working group planned for 2013.

In 2013 EMA organised several short-term trainings, e.g. VEDDRA Workshop (Veterinary Dictionary for Drug Related Affairs). The aim of this three-hours workshop was harmonisation of position of attendees for selection and use of convenient terminology included in VEDDRA Coding (within the frame of evaluation of cases of adrverse effect after administration of veterinary medicines).

At the end of the year 2012 the member states obtained questionnaire, which was evaluated, concerning the activity of national authorities in relation to WorkSharing Initiative (cooperation and synchronization of management and assessment of Periodically revised reports on product safety). Results from questionnaire become basis for discussion of HMA in

this field and proposal of Action plan and written agreement on participation in programme including involving of individual member states. At present, 25 member states aprticipate in the programme, 3 member states do not participate (Cyprus, Greece and Romania did not undertake the role of assessor for any active substance).

Working group for pharmacovigilance inspections

In 2013 there were 4 meetings of working group for pharmacovigilance inspections, with focus mainly on human sphere. EC however works also on revision of veterinary part of legislation with assumed finalisation in 2014. The effort is to create similar legislation both for human and veterinary sphere, although the sphere of e.g. animal infection is significantly different.

From November 11 to 13, 2013 there was training organised in EMA premises in London, focused on pharmacovigilůance inspections. Approx. 100 participants were presented from 25 member states both from human and veterinary sphere of PhV inspections and it was designed as a complex of common presentations and discussions followed with separate workshops for human and veterinary sphere. The training obtained positive assessment both from participants and lecturers.

There are 4 meetings of pharmacovigilance inspections working party planned for 2014.

EudraVigilance Veterinary Joint Implementation Group (JIG)

In 2013 there were 4 meetings (teleconferences) of above mentioned working group. The meetings are organised in two parts (with and without presence of IFAH-Europe representatives).

By the end of 2013 the EVVeT database contained 67 thousand reports on adverse effects occured in EHP and 40 thousand reports of adverse effects outside EHP (reports from third countries). 7 400 reports out of the total number of reports relate to adverse effects in human after administration of VMP in animal.

EVVET 3 project was stopped in January 2013 by financial reason (project conducted from 2010). The aim of this project was to conform the EVVeT databese with VICH guidelines on pharmacovigilance (GL42, GL30, GL24, GL35) and obtain convenient tools for supervision and management of pharmacovigilance data.

In 2014 there are 4 meetings planned of EVVeT JIG.

Working Group of inspectors of GMP and GDP

(Good Manufacuring and Distribution Practice Inspectors Working Group – GMDP IWG)

Withing the frame of harmonisation of procedures and approaches in the field of inspections in manufacturers of medicines the GMP and GDP inspectors working group is organized by (GMDP IWG). During the year 2013 four meetings of this group took place.

The members of this group are representatives of inspectorates from the EU/EEA countries, the observers are representatives from EDQM, countries acceding EU and third countries with concluded agrrement 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, with additional new part from 2009 concerning guidelines and inspection procedures in the sphere of good distribution practice. In 2013 these meetings were attended by MVDr. Műllerová. In 2013 there were discussed namely revisions of chapters 2, 3, 5, 6, 8 of Guidelines for GMP, Supplements 15, 16, 17 of Guidelines for GMP, common interpretation of Supplement 19. During 2013 there were also implemented changes in approval for manufacture of medicines and GMP certificate concerning types of manufacturing processes.

Working group for evaluation of environmental impact assessment

Enviromental risk assesment working group

Working group for assessment of environmental risks (Environmental risk assessment working group, ERA WP) is involved in negative influences of veterinary products and medicines to nontargeted organisms in environment and other environmental risks represented by persistence etc. The group prepares documents for CVMP (guidelines implementation documents, expertises etc.), supporting legislation and contributing to rational evaluation of veterinary medicines impact to living environment. In addition to acitivities for EMA the group endeavours to harmonize approaches both to other groups with simmilar specializations within the scope of multinational organizations namely DG SANCO, ECHA (legislative REACH), OECD, SETAC and others.

In 2013 ERA WG met three times (January, June, October). Current issues mentioned below were solved on these meetings (meantime also email communication and negotiations with work on texts editation were carried out).

- Guideline for evaluation of PBT characters of VMPs – comments proceeded and final draft for CVMP was prepared

- Ivermectin and its environmental risks – work on REVIEW for evaluation of risk-benefits on the CVMP level. Vermectin compound of antiparasitic generaly represents significant issue (many negative characters, high bioacumulation and persistency) and in future a final assessment and decision on risk management should be finalized.

- Testing of ecotoxicity of medicinal products in invertebrates living in excrements (dung fauna). Harmonised procedure was prepared according to requirements of current EMA and OECD guidelines, which, however, takes into account new findings and issues (extractability of residues etc).

- Risks of medicines for underground waters – represent generaly and formaly a complex issue, which needs to be solved not only from the view of ERA WP, but also from safety view for human (in competence of CVMP Safety WP). After previous discussions with CVMP specific partial steps were discussed for finalisation.

- Antimicrobial resistance – preparation of document continued, which would present sufficient material for CVMP to assess relevant regulatory steps in future.

- Other activities – harmonisation was initiated to use some of the gOECD guidelines in legislation of VMPs (e.g. Fish Embryotoxicity Test), there were discussed and prepared opinions to several referal procedures pending, to problems of risk evaluation with regard to metabolites and to the problem of toxic impacts of mixtures of medicines. In the course of the year ERAWP organized practical workshop for assessors focused on obtaining of experience withm assessment of environmental risks according to current recommendation and obligatory procedures.

Other activities of the Institute within the frame of medical agency

QRD

Working group of the Quality Review of Documents (QRD) consists of representatives of the national agencies of EU member states, representatives of European Commission and representatives of European Medicines Agency. The main aim of this group is to ensure comprehensibility, conformity and accuracy of information on medicinal products (summary of product characteristics - SPC, package leaflet and labelling) and its translation, that are enclosed to opinions of the committees and decision of European Commission. Furthermore the group controls conformity of all information presented on medicinal products with requirements of EU legislation.

In 2013 all SPC, PL and labelling translations for VMP whose marketing authorisation or extensions of marketing authorisation expired during this year were revised. Also in cases of

approved variations and renewals of registration (also IB – texts reviewed ad hoc) where changes have been made in texts the accuracy was checked.

During the first half a year there were revised texts to 6 new marketing authorisations, to 4 extensions of marketing authorisation, to 7 marketing authorisation renewals, to 5 variations of type II, to 2 variations of type IB and to 5 year revaluations of marketing authorisation. In the second half of 2013 texts to 6 new marketing authorisations were checked, 4 marketing authorisation were extended, 7 marketing authorisations were renewed, text to 1 referal was checked, 7 variations of type II, 2 variations of type IB and 2 year revaluations were carried out.

ESVAC (European Surveillance on Veterinary Antimicrobial Consumption)

ESVAC project coordinated by European Medicines Agency which was launched in 2009 was continuing in 2013. The Czech Republic through the representative of ISCVBM, further participated on further proceeding and development of project. In March 2013 an annual meeting took place which was attended by all EU member states, Norway and Switzerland. Above all the questions connected to submission of data from 2011 and its harmonized evaluation and publishing were discussed. CR represented Dr. L. Pokludová with presentation of information on targeted inspections focused on veterinary surgeons with the highest number of prescriptions of antimicrobials with limited indication (Use of sales data at national level.

Public discussions were also attended by representatives of EC, FVE, pharmaceutical industry and other bodies, for whom information on consumptions of veterinary antimicrobials are substantial. During 2013 elaboration of report analysing development of consumptions of veterinary antimicrobials was carried out (resp. veterinary antimicrobials sale) in connection with analysis of population condition of livestock in 25 EU states including EEA states (+ Switzerland) whose requested data were available. Publication is available on EMA website: Sales of veterinary antimicrobial agents in 25 EU/EEA countries in 2011 (third ESVAC report). The report informs on sale territories and trends in relation with population of farma animals, with evidence of analyses for individual member states, groups of antimicrobials with comments on critically important molecules. There is also bried specification of consumption condition in pills for animals as pets (dogs and cats). Project is designed on uniform templates for data collection so that this information could be further analysed in details, which would result in obtaining the most credible and comparable data within the frame of EU member states, so that a long term trend could be evaluated in future and risk analysis conducted with relation to antimicrobial substances usage in animals, namely with impact on occurrence and development of resistance. In 2013 also work of two restricted working groups continued „*Ad hoc* WG on unit of measurement“ and „*Ad hoc* WG on collecting data by species“, CR was not a member of these subgroups (it was not addressed for nomination – number of members was limited). Nevertheless, CR has become a member of „*Ad-hoc* ESVAC expert group to provide advice on surveillance on sales of veterinary

antimicrobial agents“ (*Ad hoc* expert subgroup focused on harmonisation of primary data collection, which meets (mostly in form of Adobe meetings and 1 per year personally) to discuss future aims of project, data publication and targeting of analyses. Documents from these meetings were circulated internally via electronic mail and commented in meeting in February 2014.

Also request for filling of templates on data on sales in 2012 was announced. ÚSKVBL provided this data for validation by EMA. Further meeting of the group was announced (February 2014). Similarly to previous year, Dr. Pokludová was charged with coordination of cooperation within the ESVAC project, filling of data to standard ESVAC templates and communication with EMA team in the field of antimicrobial consumption surveillance, who at the same time presents the data on consumption on national and international levels. Input data on consumption, its collection, presentation to public through ÚSKVBL Bulletin and other compilation in ESVAC are ensured similarly to previous years by experts from Inspection section MVDr. L. Koutecká CSc. and D. Dorn.

3.3.2 European Commission

Standing Committee on veterinary Medicinal Products

In 2013 one meeting of Standing Committee for Veterinary Medicinal Products was convened (December 2013). On this meeting the Committee discussed implementing decission of Commission by which the Annex to Directive (EU) No. 37/2010 on pharmacologically active substaces and its classification according to maximum residual limits in food of animal origin regarding chloroform. Chloroform as a banned medical substace is listed in Annex No. II to the above mentioned Directive. Chloroform was used in vaccine approved according to special conditions against foot and mouth disease, thus as an adjuvant necessary for stability of this specific product. The Committee assessed safety of chloforom residues for consumer and concluded that according to submitted scientific documents chloroform can be accepted for limited usage as adjuvant in veterinary vaccines provided, that amount of substance which can be administered is limited. The Committee discussion also resulted in listing of chloroform in the Table No. 1 of the Directive No. 37/2010 with following limitation: Usage only as adjuvant in inoculants and only in concentrations not exceeding 1 % wght./vol. and total dosage not exceeding 20 mg in one animal and erasure of chlorofomr from Table No. 2 of mentioned Directive.

Working group for resistence on antimicrobials
(Working group on AMR)
In 2013 this working group arranged one meeting (February 2013). On February meeting of this group there was presented information on EC plan to fulfilment of EC Action plan published in November 2011, information on proceeding in ESVAC project, inormation on monitoring in zoonotic and indicator bacterias – finalisation of new Decision 2013/652/EU on harmonised monitoring of AMR (in force from January 1, 2014) and technical information on AMR monitoring, new moitoring of ESBL, AmpC and carbapenemases, collecting and elaboration of data (EFSA). Further there was presented information from projects within the human medicine (ECDC, EARS- net and ESAC-net) and information on international

projects. Similarly to 2012, there were two meetings of „Prudent use of antimicrobials group“, where Mgr. Pokludova as a representative of ISCVBM presented and defended statements **RESTRICTED WORKING GROUP ON ANTIMICROBIAL RESISTANCE (PRUDENT USE OF ANTIMICROBIALS) – SANCO/G4** „Guidelines on the prudent use of antimicrobials in veterinary medicine. The group met in two workshops in Brussels to discuss repeatedly modified versions of document concerning particular steps and measures leading to maximum prudent use of antimicrobials within the scope of the EU member states (see above). At the end of 2013 (11.12.2013) there was hold a „**Joint Conference on Antimicrobial Resistance: State of play of the 5 year action plan“**, organized by DG SANCO, with participation of Mgr. L. Pokludová Dr. (presentation of statement „Chalenges in research and risk assessment field – within the panel discussion „Risk Assessment Panel“), KVL CR was represented by Dr. Bernardy and human medicine sphere was represented by Doc. Hrabák.
Further meeting of Working group on AMR and restricted working group to discuss above mentioned guideline is expected to be held in February 2013, where another version of guideline is supposed to be presented with assumed finalization by the end of 2014.

3.3.3 Institutions ensuring cooperation of member states

Veterinary Coordination Group for Mutual Recognition and Decentralized Procedures (CMDv)

The Veterinary Coordination Group for Mutual Recognition and Decentralized Procedures (CMDv) holds regular monthly meetings in the facilities of European Medicines Agency (EMA) in London. The meetings are attended by appointed members of competent national medicines agencies of the EU member states, representatives of the European medicines Agency (EMA) and a representative of the European Commission (EC).

CMDv group is formed from EEC countries and its activity is focused on following themes at international level of the EU:

- Individual VMP authorised by procedures MRP/DCP
- Negotiation on applications according to relevant legislation
- Elaboration and revision of relevant SOP of marketing authorisation procedures
- Harmonization of conditions, instructions and requirements in EU member states
- Reduction of national requirements
- Current questions and reminders from national agencies
- Current questions and reminders from pharmaceutical industry

According to needs to solve relevant business matters there are „ad-hoc“ working subgroups established and terminated as a part of the CMDv group.

CMDv group cooperates with oter working institutions and groups:
EMA,EK, HMA,CVMP,CMDh,QRD,QWP,SWP,EWP,PhVWP-V,IWP,
IFAH-EUROPE,EGGVP,AVC,TIGes Vet.

Among the main questions solved and discussed at CMDv group meetings in 2013 were:

- Improvement of proceedings of DCP/revision of VET legislation
- Issue on packaging of VMP/revision of VET legislation
- Guideline for Transparency/Access to documents in veterinary sphere
- Directive 1234/2008 on registration variations/revisions 712/20
- Update of conditions for „Worksharing procedure "
- Standard validation checklist / simplification of validation procedure
- Reduction of national requirements to authorisation procedures
- VNeeS form of marketing authorisation documents
- CESP Platform /Electronic applications
- ASMF Worksharing/Pilot stage
- Requirements for Mock-ups
- Update of requirements for el. applications
- VET Clinical trials survay update
- Improving of DDPS system
- Update of webpage of CMDv
- Updating of relevant guidelines of CMDv
- Updating of CTS system

In 2013 the EU presidency countries were member states Irland and Lithuania. These countrie ensured tasks connected with position of presidency country according to work content of CMDv group incuding Presidential working meetings.

HMA

Within the EU there are regular meetings held of heads of medicine agencies both human and veterinary in the relevant country hosting the presidency. There were 4 meetings in 2013 (2 x Ireland, 1 x Lithuania, 1 x Slovenia) on which recommendations were dscussed for the whole scope of medicine policy on common meetings with representatives of European Commission and European Medicines Agency. During 2013 there were discussed following areas, the fulfilment of which is regularly surveyed at individual meetings:

- Area of veterinary pharmacovigilance
- Antibiotic policy – common conclusions for human and veterinary area
- Procedures for simplification of medicinal legislation
- Harmonization of relevant area – in summary: safety of medicines, indication area, dosing, withdrawal periods, area of packaging and limitation of some of medicinal (namely antibiotics), autogennous vaccines, area of telematics
- On every meeting there is presented a report of Steering Committee of European Medicines Agency covering all activities in the field of quality of medicines, similarly iformation from EuropeanCommission are presented on prepared legislation. Every half a year there is meeting with stakeholders held (representatives of manufacturers of medicines IFAH, representatives of generic medicines manufacturers) and other interested organizations, on which common issues are solved to reach simplification of medicines availability and minimalization of risks resulting from usage of medicines.

HMA – V – Work group for resistance to antimicrobials

In 2010 working group was established for antimicrobial resistence, with a leadership by United Kingdom. Other countries entered to activity of the group - France, Spain, Ireland, Sweden, Deutschland and Czech Republic. At the beginning of 2011 the document was published: „HMA-V Action plan of the antimicrobial issues". The group started working on particular tasks to fulfill action plan of HMA for antimicrobial resistance. Thus the Czech Republic become a referee for one of the items of the action plan focused on finding of prescription customs of veterinary practicioners. Consecutively an electronic version of questionnaire was elaborated, which was prepared for translation in cooperation with FVE and significant support from UK. At the beginning of 2012 it was accessible in 5 languages for release to be filled by veterinary practicioners in the member states. More than 3000 answers were obtained from veterinary practicioners within the EU member states. The answers were elaborated by the central office of FVE (European Federation of Veterinary Practicioners) in cooperation with colleagues from Agencies in UK and CR. In cooperation with FVE, UK and CR two publications were prepared on resuts from questionnaire among veterinary surgeons in selected EU countries (including CR) in professional journal „Veterinary Records". The first one has been published: „N. De Briyne, J. Atkinson, L. Pokludová, S. P. Borriello, S. Price: *Factors influencing antibiotic prescribing habits and use of sensitivity testing amongst veterinarians in Europe***,** Veterinary Record, Vet Rec. 2013 Sep 25 doi:10.1136/vr.101454. The second publication (*Survey on antibiotics most commonly used to treat animals in Europe* De Briyne, Atkinson, Pokludová, Borriello) is expected to be released to print in the first quarter of 2014. The results were also presented in form of posters (one of the co-authors is Dr. Pokludová) at the meeting of OIE in Paris (March 2013) and at WVC (World Veterinary Congres) In Prague (September 2013). Czech translation of the poster HMA/FVE was published in the journal of KVL Zvěrokruh 5/2013

Working group for law enforcement
Working Group of Enforcement Officers

The Institute was continuing in activity within the mentioned working group under HMA, within the scope of which there is also a specific veterinary group with the aim to exchange experiences and information on illegal activities relating to veterinary medicines. In 2013 the working group met two times, within the scope Irish (Dublin) and Lithuanian (Oslo, Norway) presidency.

3.3.3 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 2013. With respect to its profession MVDr. Jana Jeřábková, Ph.D. ensures namely agenda relating to immunological vaterinary medicinal products. Jaroslav Maxa, PharmDr., PhD, ensures activities relating to work on monographs of antibiotics and synthetical chemical medicines.

Within the scope of activity of European Pharmacopoeia Dr. Jeřábková, PhD. as a member of Group 15V (group of experts for veterinary vaccines and immune serum) took part in two workshops in 2012, also Dr. Radka Smítalová, PhD. ,who had been appointed to the 15V group for further š-years period, took part in one meeting as a specialist for diseases in pigs and mloeculary-biological methods. Workshops of 15V group discussed current issue on elaboration of new articles and revisions of current articles of the European Pharmacopoeia. Following articles were elaborated in 2013:

- Revision of article „Life vaccine against brucelosis“
- Revision of general article „Vaccines for veterinary use“
- Revision of article „Avian viruse vaccines: tests of foreign agens in inoculum“
- Revision of article „Avian life virus vaccines: tests of foreign agens in final product batches“
- New chapter „Healthy chicken flocks for manufacture of inactivated vaccines for poultry“

On behalf of the Expert Group 7 (Group of antimicrobials) of the European Pharmacopoeia Committee Dr. Maxa took part in three meetings in 2013. During the year 2013 the group continued in work on revisions of monographs of penicilin and tetracycline antibiotics, erythomycines etc. Revised monography on demeclocycline HCl, with participation of laboratory from our Institute, was proposed to approval by the Commission. Based on the results of analysis of batches the revisions of monographs of tylosine, tylosine tarttrate and new monography of tylosine phosphate, which were published in Pharmaeuropa. Further Dr. Maxa and the laboratory under his management participated in colaborative studies of standards: ampicilin, azithromycin, cefalotin sodium salt, cefatrizin propylenglycol, erythromycin, lincomycin HCl, piperacilin, tetracyclin HCl.

Within the scope of Expert Group 10A (chemical substances) Dr. Maxa took part in three meetings in 2013. Elaboration of monography of indometacine was approved and published, on which the ISCVBM laboratory participated. Method on adjacent substances for monography of albendazole was verified. From the new monographs the group worked for instance on zolmitriptane, bupivakaine, naratriptane HCl, dexamfetamin sulphate, ropivakainu HCl etc. Revisions of several other monographs were carried out, e.g. flupentixole chloride, desloratidine, hydroxycarbamide, xylazine etc.

Pharmaceutical Inspection Convention/Scheme (PIC/S)

The Institute has been PIC/S member since 2005. The contribution of membership is partly access to seminars and trainings for inspectors on required level and partly increase of the international reputation of Institute and recognition of results of its inspections also by the authorities outside EU/EEA (Australia, New Zealand, Israel, Íran, Egypt and others) and thus simplification of the Czech industry access to these markets. In terms of PIC/S membership the Institute has been participating in preparation of guidelines within the PIC/S and in the harmonisation of inspection procedures. Inconsiderable contribution is the possibility to take part in highly professional seminars and obtaining of many contacts to GMP inspectors. In 2013 Dr. Műllerova took part in two metings of PIC/S committees + PIC/S seminary (May – Geneva, October – Ottawa). In 2013 the new structure within the frame of PIC/S was implemented. Dr. Műllerova is a member of working group - Compliance Sub – Committee, dealing with coordination and survey of evaluation proceeding in acceding agencies,

reviewing of reports and recommendations from evaluation, monitoring of correctional measures. This group will commence its activity on January 1, 2014.
Within the scope of JVP (Joint Visit Programme) in 2013 Dr. Müllerova also entered the veterinary group consisting of French and Belgian authority. During the years 2014 and 2015 three joint inspections are scheduled – In France, Belgium and Czech Republic.

3.4 Activity of the Institute in Relation to Regulated Subjects

Seminars

By means of its affiliate at Czech Association for medical technique the Institute in 2013 organized two seminars for marketing authorisation holders and manufacturers of veterinary medicinal products and testing laboratories. On the seminars there were negotiated current issues in the sphere of VMP regulation in CR and EU, information on amendment to the law on medicines, general rules for submission of aaplications and documents for authorisation, information on common european platform for electronic submission of applications, validation of electronic applications, information on variations of authorisation, information on clinical evaluation of veterinary medicines, new products in the field of antimicrobials, information on new guidelines in the field of immunological VMP, information on usage of autologous stem cells. Seminar concerning good laboratory practice was prepared for manufacturers of VMP with a lecturers Ing. Eva Niklíčková, representative of inspectorate SLP – SÚKL and Ing. Petr Finger representative of ASLAB (Center for assessment of proficiency of laboratories, National inspection authority SLP).

Guidelines

During 2013 the Institute issued/revised according to needs and provisions of the law on medicines 7 guidelines.

Generaly valid guidelines

Number	Name	Valid from	Substitutes	Ammends
UST – 4/2008/Rev. 3	Administration fees and reimbursement costs for expert activities	15.10.2013		UST – 4/2008/Rev. 2

Guidelines on marketing authorisation of veterinary medicinal products

Number	Name	Valid from	Substitutes	Ammends
REG – 1/2010 Rev. 1	Detail information on draft of texts on inner one-dose packages of immunological veterinary medicinal products in other than Czech language	28.10.2013		REG-3/2009

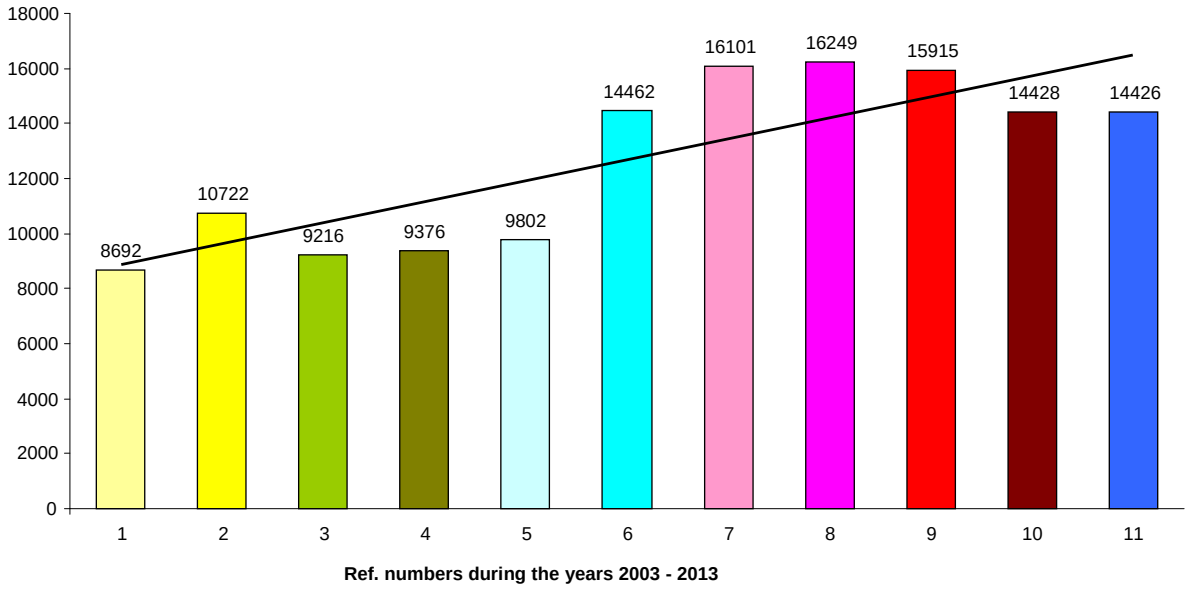
REG-3/2013	Detail information on variations of marketing authorisation of veterinary medicinal products	4.8.2013	REG – 4/2008	
REG-2/2013	Harmonization of texts of veterinary medicinal products between the Czech Republic and Slovac Republic	22.7.2013	-	-
REG – 1/2013	Specification of conditions for submission of aplicationa and marketing authorisaton documents	15.3.2013	REG – 4/2009	

GMP Guidelines

Number	Name	Valid from	Substitutes	Ammends
INS/VYR – 01/2013	Supplement to Guidelines for GMP – Part I, Chapter 1 and 7 ……..	31. 1. 2013	-	Guidelines for GMP
INS/VYR-MK-01/2012	Way of filling of instruction for manufacture of medicated feed and contact adresses of relevant RVA SVA for mailing	1.1.2013	USKVBL/INS/VYR-MK-01/2010	

4. Agenda of the Institute

Similarly to previous years, in 2013 the registry and forwarding office of the Institute registered documents by means of Magion records system software with interconnection to the Documentum system software. In total of 14426 ref. numbers evidenced.



Ref. numbers during the years 2003 - 2013

5. Activity of Section of marketing authorisation, registery of VTD and clinical evaluation

5.1 Marketing authorisation of VMP

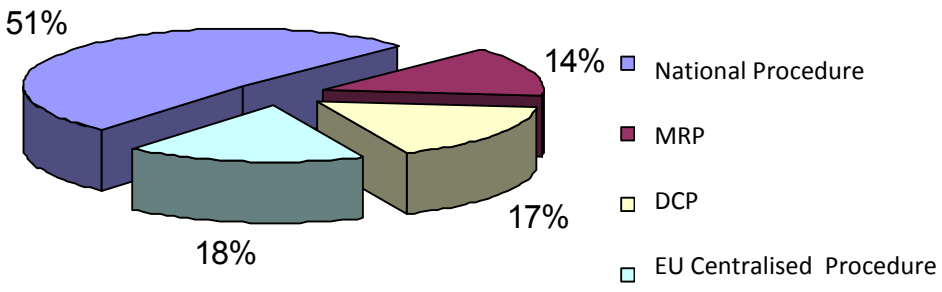
Incorporation of the CR to European Procedures of Marketing Authorisation, authorisation through national procedure, authorisation agenda

For authorisation purposes of veterinary medicinal products the Czech Republic implemented authorisation procedures in relation to its character and taking into account relevant legislative standards.
In 2013 veterinary medicinal products were approved by four basic types of authorisation procedures – national procedure, mutual recognization procedure, decentralized procedure and centralized procedure. National procedure, mutual recognisation procedure and decentralized procedure were carried out in compliance with requirements of consolidated Directive of European Parliament and Board No. 2001/82/ES, as amended by the Directive 2004/28/ES and in case of centralised procedure of the Commonwealth in compliance with Regulation No. 726/2004.

TYPE OF PROCEDURE	TOTAL
NATIONAL PROCEDURE	890
MUTUAL RECOGNITION PROCEDURE BY EU MEMBER STATES / DECENTRALISED PROCEDURE	226 263
CENTRALISED PROCEDURE	285
TOTAL NUMBER OF AUTHORISED VMP IN CR	**1664**

Tab. 5/1: Number of authorised VMP based on procedure type on the 31.12.2013

Obr. 5/1: Percentual representation of marketing authorisation procedures in 2013



Tab. 5.2: : Summary of total number of submitted applications and cases when MAwas granted in 2013– Mutual Recognition Procedure and Decentralised Procedure 2013

Type of marketing authorisation	Cathegory of VMP	Number of Applications			
		CR concerned member state (CMS)		CR reference member state (RMS)	
		Submitted Applications	Granted MA	Submitted Applications	Granted MA
Mutual Recognition Procedure – First Use	Pharmaceuticals	7	9	2	5
	Immunologicals	0	3	2	0
Mutual Recognition Procedure – Repeated Use	Pharmaceuticals	5	5	0	0
	Immunologicals	0	0	0	0
Mutual Recognition Procedure - decentralised procedure	Pharmaceuticals	70	52	6	5
	Immunologicals	1	2	4	0
Renewal of marketing authorisation	Pharmaceuticals	58	24	1	2
	Immunologicals	5	5	1	0
		At variations to marketing authorisations, the numbers represent real number of submitted applications, not the real number of evaluated changes in application			
Variation Type IA	Pharmaceuticals	197	189	14	3
	Immunologicals	61	61	2	2
Variation Type IB	Pharmaceuticals	52	38	3	3

	Immunologicals	**12**	**5**	**0**	**0**
Variation Type II	**Pharmaceuticals**	**63**	**53**	**0**	**0**
	Immunologicals	**27**	**34**	**0**	**0**

* In compliance with regulation of Directive No. (ES) 1234/2008 and ammendment No. (ES) 712/2012 it is possible to aggregate variations to marketing autorisation into one application – so called formo f aggregation of Variations and distribution of work. The number mentioned in table for 2013 thus represents number of applications submitted, not the number of real variations of marketing authorisation processed. Due to this fact, the number of variations to marketing authorisation is lower compared with last years.

VMP marketing authorisation with mutual recognition procedure and decentralized procedure

Marketing authorisation procedures MRP and DCP fall within the international authorisation procedures of the EU and have become during the last years the most utilized procedures for authorisation of new pharmaceutical and immunological veterinary medicinal products (MRP: Mutual recognition procedure - veterinary medicinal product primarily authorised in CR is authorised to other EU member states, DCP: Decentralised procedure – veterinary medicinal product is for the first time authorised in selected EU member states at the same time). MRP and DCP are applied also in other types of authorisation procedures – procedure of renewal of marketing authorisation and variations to marketing authorisation of veterinary medicinal product.
In 2013 the Czech Republic was in both positions regarding MRP and DCP authorisation procedures:
a) role of referece member state (RMS – Reference member state i.e. country, which had been selected by an applicant for regulatory, professional and general coordinating position)
b) role of concerned member state (CMS – Concerned member state i.e. country which had been selected by an applicant as a target member state for marketing authorisation of given product).

CR/RMS:

During the last year CR was in position of RMS in the field of **new marketing authorisations** in ten DCP procedures and in four MRP procedures, in which pharmaceutical products prevailed compared with immunological products. In the field of **marketing authorisation renewal** CR was in position of RMS both in pharmaceutical and immunological products, where the number remained on the same level. In the field of **variations to marketing authorisation** CR took part in RMS role both at pharmaceutical and immunological products at variation type IA and IB, thus with higher number of products than in previous year. At variations type II there was the same situation as in previous year, there was no application for CR in the position of RMS.

In 2013 CR was for the role of RMS both in MRP and DCP procedures by foreign and Czech companies. Though the number of applications for new MRP and DCP marketing authorisations has significantly increased from the side of the czech companies, by which our „domestic“ companies obtain experience from international process of marketing authorisations of veterinary medicinal products.
In 2013 the number of applications for new marketing authorisation with DCP procedure several times increased. Generaly, in CR the DCP process has been applied in higher rate than MRP process.
With the numbers of applications proceeded the CR with its role of RMS ranks among the active EU member states and reaches front positions among the so called „eastern EU counrties. This contributes to enhance and improvement of CR position both in regulatory and professional field of marketing authorisation of veterinary medicinal products.

CR/CMS:

Numbers of applications for **new marketing authorisation by MRP**, where the Czech Republic was in position of CMS have decreased both in case of received and granted applications at pharmaceutical products, at immunological products the figures of received and granted applications range at the same level similarly to last year.
Number of applications for **new marketing authorisation by DCP** at pharmaceutical products in case of received and granted applications has decreased compared to last year, in case of immunological products the numbers of received and granted applications range at the approximately same minimum number as in the last year.
Also in 2013 the situation is similar to previous years when number of applications received for marketing authorisation of pharmaceutical products is several times higher than number of applications received for marketing authorisation of immunologicals and when marketing authorisation through DCP procedure prevail the authorisations by MRP.

Number of applications for **marketing authorisation renewal** at pharmaceutical products has significantly increased both in case of received and granted applications, concerning immunological products the number of applications both received and granted has decreased.

Number of applications for **marketing authorisation variations type II** remained for pharmaceutical products on the same level, in case of immunological products it has significantly increased.

Number of applications for **marketing authorisation variations type IA** at pharmaceutical and immunological products both in received and granted applications increased compared with previous years. At **variations type IB** the number of received applications has significantly decreased and a certain decrease was also in number of granted applications.

Marketing authorisation of veterinary medicinal products by national procedure

The national procedure represents another applied procedure for marketing authorisation of veterinary medicinal products in the Czech Republic. This procedure was applied at most of the authorised products. In total 1664 authorisation proceeded, of which 890 products are authorised by means of national procedure. The number of products

authorised by this procedure remains stable for several years long. Although in the course of the year some of the national authorisations became withdrawn, the number is compensated with new received applications for authorisation. In 2013 the number of 13 applications for marketing authorisation was received of which 8 assessments were completed and remaining assessments will be finished in 2014, due to the necessary interruption of administrative procedure to obtain supplementary documentation from applicant.

Validity of authorisation according to the Act No. 378/2007 Coll., on Pharmaceuticals, as ammended, may be extended based on risk/benefit ratio. Once the authorisation has been extended it becomes valid for unlimited period. Only by pharmacovigilance reasons the Institute can issue decision on extension of authorisation validity for 5 more years, however, the decision can be issued only once. Due to this fact ten number of autorised products according to the Act for unlimited period increases. In 2013 the number of 36 applications were received, though the number of 56 granted applications significantly number of received applications due to the completed procedures from previous years, which were time demanding, since in many cases those products were authorised in past according to different rules compared with current valid ones.

The highest number of received applications for products authorised by national procedure in 2013 represents similarly to last year the applications for marketing authorisation variation. In this year there was legislative break through in the field relating to applications for variations to marketing authorisation. The Act on medicines was ammended in its provision relating to variations, where with validity from August 4, 2013 there is a link to procedure for assessment of variations according to directly applied EU legislation. This legislative act is Commission Regulation No. 1234/2008 as ammended, the current version contains since August 4, 2013 separate chapter for variations by solely national procedure. Commission Regulation enables more simple and flexible system on assessment of variations to mareting authorisation. Amon others, it enables to aggregate variations, when authorisation holder is allowed to announce more variations in one application, in certain cases also for more authorisation numbers.

In connection with changes, the Veterinary Institute during determining number of applications for variation to marketing authorisation in 2013, due to the administrative burden, figured out number of applications received, not the number of real assessed variations that are incorporated in each application. By this fact, the number of variations in tables may appear as decreased in comparison with previous years (figure represented number of variations assessed within the scope of each received applicaton). However, actually it has increased. The highest number of announced application for variation in the last year related to variation type IA -298, further variation type IB -97 and lowest number related to variations type II – 57.

National procedure is applied also in case of transfer of authorisation holder, both for products with national authorisatin and products with MRP/DCP procedure. This relates to transfer of authrisation from original holder to the new authorisation holder. There were 118 applications of this type.

Parallel import, which is determined in the Act on medicines as distribution of medicinal product from other member state to the CR, provided it has been authorised in a member state

and distribution is not provided by marketing authorisation holder in the CR or in cooperation with him, falls under the national applications. In 2013 there were submitted and granted 2 applications for parallel import for immunological products.

Tab. 5/3 : Summary of number of submitted applications and granted applications in 2013 by national procedure

Type of marketing authorisation	Cathegory of VMP	Number of applications	
		Submitted applications	Granted applications*
Marketing authorisation	Pharmaceuticals	11	6
	Immunologicals	2	2
Renewal of marketing authorisation	Pharmaceuticals	27	43
	Immunologicals	9	8
Marketing authorisation transfer	Pharmaceuticals	75	78
	Immunologicals	43	43
Marketing authorisation withdrawal	Pharmaceuticals	27	29
	Immunologicals	12	12
Parallel import	Pharmaceuticals	0	0
	Immunologicals	2	2
	At variations to marketing authorisations, the numbers represent real number of submitted applications, not the real number of evaluated changes in application [1]		
Authorisation variation type IA	Pharmaceuticals	169	154
	Immunologicals	129	85
Authorisation variation type IB	Pharmaceuticals	73	63
	Immunologicals	24	19
Authorisation variation type II	Pharmaceuticals	31	57
	Immunologicals	26	30

* Higher number of granted applications than number of applications submitted means, that in given year there were completed also applications submitted at the end of previous year.

[1] In compliance with regulation of Directive No. (ES) 1234/2008 and ammendment No. (ES) 712/2012 it is possible to aggregate variations to marketing autorisation into one application – so called form of aggregation of Variations and

distribution of work. The number mentioned in table for 2013 thus represents number of applications submitted, not the number of real variations of marketing authorisation processed. Due to this fact, the number of variations to marketing authorisation is lower compared with last year.

Tab. 5/4: Number of submitted and granted applications in 2013 in comparison with previous years

Type	Year	Submitted Applications	Granted Applications
Application for new marketing authorisation	2013	110	89
	2012	136	126
	2011	104	101
	2010	111	72
	2009	116	106
	2008	148	77
	2007	87	58
	2006	60	46
Application for renewal of marketing authorisation	2013	101	82
	2012	64	92
	2011	80	218
	2010	126	189
	2009	171	178
	2008	282	145
	2007	201	133
	2006	198	92
Application for marketing authorisation variation **(in 2013, number of variations to marketing authorisation represents number of applications submitted, not the real number of assessed variations incorporated in application,appart from previous years, thus the figure is lower)**	2013*	883	796
	2012	1057	1022
	2011	976	1104
	2010	893	869
	2009	688	642
	2008	590	679
	2007	543	462
	2006	453	449
Application for marketing authorisation transfer	2013	78	81
	2012	26	24
	2011	32	72
	2010	62	22
	2009	8	3
	2008	45	45
	2007	13	10
	2006	13	13
Application for marketing authorisation withdrawal	2013	39	41
	2012	27	28
	2011	22	33
	2010	48	43
	2009	43	43
	2008	17	17
	2007	12	11
	2006	25	25
Application for discontinuance of administrative proceeding	2013	10	10
	2012	7	7
	2011	5	5
	2010	35	35
	2009	24	24
	2008	29	29
	2007	21	21
	2006	11	11

Appeal against the MA decision	2013	0	0
	2012	0	0
	2011	1	1
	2010	2	2
	2009	0	0
	2008	2	2
	2007	2	8
	2006	12	6
Administrative corrections in the MA decisions	2013	6	6
	2012	8	8
	2011	15	15
	2010	29	29
	2009	30	30
	2008	25	25
	2007	20	20
	2006	15	15
Total	2013	1227	1105
	2012	1325	1307
	2011	1235	1549
	2010	1306	1261
	2009	1080	1026
	2008	1138	1019
	2007	899	723
	2006	788	657

[*] In compliance with regulation of Directive No. (ES) 1234/2008 and ammendment No. (ES) 712/2012 it is possible to aggregate variations to marketing autorisation into one application – so called form of aggregation of Variations and distribution of work. The number mentioned in table for 2013 thus represents number of applications submitted, not the number of real variations of marketing authorisation processed. Due to this fact, the number of variations to marketing authorisation is lower compared with last year.

In 2013 the Section of marketing authorisation, approval, registery and clinical trials received 1227 applications. Compared with 2012, as regards received applications, it is possible to state, that in all types of administrative proceedings the number of applications increased, including the applications for variations, where formulation was changed in this year and therefore the number in table cannot be compared with numbers from previous years. In only one case of marketing authorisation application received the number was lower by 26 applications compared with 2012. However, in total we can state that administrative load in the Section of marketing authorisation has again icreased compared with 2012.

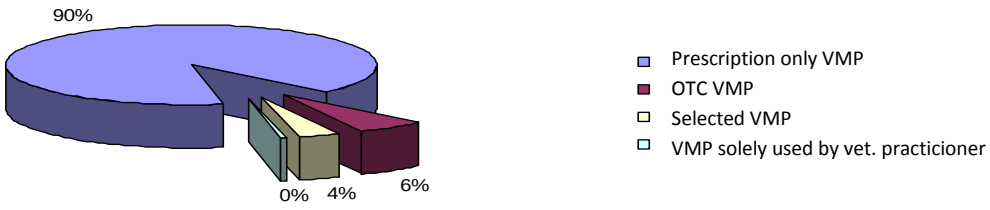
Summary of VMP authorised according to its character and way of dispensing

On the date of Dec 31, 2013 in the Czech Republic were authorised 1664 products in total, from which there were 1269 pharmaceutical products and 395 immunological products. According to the way of dispensing we select them to veterinary medicinal products on prescription representing nearly 90% of total number of VMP, less amount these are OTC veterinary products and so called selected medicinal products without limitation to dispensing on prescription similarly to OTC medicines, which can be sold also by retailers of selected medicinal products. The last cathegory in terms of dispensing are veterinary products solely used by veterinary practicioner.

Tab. 5/5: Summary of authorised VMP according to its character and way of dispensing and usage

Type of VMP	Total	Prescription only VMP (RP)	OTC VMP (VP)	Selected VMP (VY)	Solely used by veterinary practicioner (OV)
Pharmaceutical products	1269	1096	96	70	7
Immunological products	395	395	0	0	0
Total	1664	1491	96	70	7

Obr. 5/5-2: Percentual representation of authorised VMP according to way of dispensing and usage



5.2 Antibiotic policy

Sphere of antimicrobial policy is distinguished with enormously high international activity namely in international context during the past 2 years period. ISCVBM and its experts actively participate in number of actions and projects within this sphere both at national and at international level.

During 2013 active participation continued on meetings of Central coordination Group of National Antibiotic Program **CKS NAP**. Representative of ISCVBM (Prof. A. Hera) informed on consumption and usage of antimicrobial substances in veterinary medicine, on changes in legislation implied on usage of antimicrobials and on current situation in veterinary medicine. ISCVBM in cooperation with MA and CKS NAP prepared poster for Antibiotic Day , which was presented on this Day at MA.

One of the significant actions where statements regarding usage of antimicrobials were presented was **Central European Veterinary Congress - WVC (World Veterinary Congres) in Praze** (September 2013), where ISCVBM was asked to present two statements (use of antimicrobials in pigs and poultry breeds) *Use of Antimicrobials in Poultry in CZ - Current Status and Perspective of Possible Approaches for the Future* (ID 355)L.Pokludova, J. Bureš, A. Hera ; *Trends in Use of Antimicrobials in Pigs in the Czech Republic (ID 373)* L.Pokludova, J. Bureš, A. Hera .

AMEG
Antimicrobial Advice ad hoc Expert Group
From the view of international cooperation in the AMR field the activities of AMEG were monitored at European medicinea Agency as well as documents that had been published and were accessible on website of EMA.
Professional employees from ISCVBM participated on comments to prepared EMA guidelines (in relation to antimicrobials and AMR):

- Guideline for ATM efficiency evaluation
- Guideline for assessment of efficiency of intramammar products

Documenta EMA / CVMP/ CHMP point out that antimicrobial resistence in veterinary medicine needs to be solved, solution shall include whole complex of follow-up measures and prior to adoption of premature !simple! solutions i tis necessary to obtain dteailed information on risk and range of resistence transfer from animals (food) to human.
Opinion on colistin EMA/755938/2012,
http://www.ema.europa.eu/docs/en_GB/document_library/Report/2013/07/WC500146813.pdf

- It is a first document from the row of scientific documents, which were elaborated by European Medicines Agency – CVMP and its scientific groups on request from European Commission

(see doc: EMA/363834/2013,
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/07/WC500146812.pdf
Second opinion of CVMP is on tigecyclin: EMA/291760/2013
http://www.ema.europa.eu/docs/en_GB/document_library/Report/2013/07/WC500146814.pdf

Further documents and summarization are to be submitted in the first half of 2014

ESVAC

In 2013 Mgr. Pokludova took part in meeting of ESVAC working group and participated in preparation of international report on consumptions of antimicrobials in 2011 (mainly by means of so called Adobe conferences). According to valid Act on medicines ISCVBM collects data on consumptions of antimicrobials in veerinary medicine. Data are available in consolidated form since 2003 on the website of ISCVBM (www.uskvbl.cz) as well as published in ISCVBM Bulletin.

WG AMR at DG SANCO

Representative of ISCVBM – Mgr. Pokludová took part also in meeting of Working group for antimicrobial resistance (DG SANCO) and in meeting of restricted working subgroup for responsible use of antimicrobials (EK SANCO G4)

Participation and active participation in international conferences (selected presentations and publications with relation to antibiotic policy):

International publications:

N. De Briyne, J. Atkinson, **L. Pokludová**, S. P. Borriello, S. Price:

Factors influencing antibiotic prescribing habits and use of sensitivity testing amongst veterinarians in Europe, Veterinary Record, Vet Rec. 2013 Sep 25 doi:10.1136/vr.101454

Ivan Literak, Tomas Reitschmied, Dobroslava Bujnakova, Monika Dolejska, Alois Cizek, Jan Bardon, **Lucie Pokludova**, Pavel Alexa, Dana Halova, and Ivana Jamborova.
Broilers as a Source of Quinolone-Resistant and Extraintestinal Pathogenic Escherichia coli in the Czech Republic Microbial Drug Resistance. February 2013, 19(1): 57-63.

Publications in CR:

L. Pokludová, J. Bureš, A. Hera, L. Koutecká
Aspekty používání antimikrobik ve veterinární praxi malých zvířat
Veterinární klinika 2013; 10:19-31

Předepisování antimikrobik - anketa mezi veterinárními lékaři ČR
Pokludová L., Bureš J., Hera A.
Zvěrokruh 2013, 5: 16-18

Posters:

Conference on Antimicrobial Resistance ARAE 2013 , Ghent, BE
ANALYSIS OF THE TRENDS OF SALES AND PRESCRIPTIONS OF CEPHALOSPORINS OF THE 3rd AND 4th GENERATION IN VETERINARY MEDICINE – AN EXPERIENCE FROM THE CZECH REPUBLIC
Pokludová L., Bureš J., Koutecká L. , Kučerová Z. , Hera A.

5.3 Clinical evaluation of medicinal products and granting of import and use of medicinal products without marketing authorisation

In 2013, total of 7 applications for approval of clinical evaluation of medicinal products were submitted to department of clinical evaluation (KH). Regarding application for approval of clinical evaluation of Canine Periodontal Gel product, having assessed the documentation which had been sent the product was evaluated as a borderline product, which falls into the cathegory of veterinary product or veterinary technical product, thus, to assess the product it was sufficient to obtain approval from departmental commission in compliance with the Act on protection of animals against torture.

Following KH were approved:

1) Hyobac APP 6 veterinary emulsion for piglets
2) Ornivac ND inj. Emulsion for poultry

At previously aproved KH of the product Bio Bos Respi 2 intranasal, based on assessment of announcement on changes in conditions of KH it was extended due to the need of completion of data for authorisation procedure being processed.

Due to the submission at the end of the year 2013 and required completion of data and recommendation from ISCVBM the applications for KH were not finished at Lineomam 330 mg/100 mg intramammar solution, Biosuis PRRS Live, Biosuis Parvo Ery, all products from applicant Bioveta a.s. Ivanovice na Hané. Similar situation was at applications from VÚV s.r.o. Dol on approval of KH for medicinal products Vaderis 5 g/l solution for treatment of bees and Gabon Flum 4 mg strips to beehives.

3 KH were completed with summary report:

1) Hyobac APP 2+5+6
2) Ornivac ND+IB2+EDS
3) Hyobac APP 6 veterinary emulsion for piglets

With respect to granted approvals and followed up clinical evaluations the inspections were carried out with evaluation of compliance of field phase with approved clinical protocol specified in application, filling of records on health condition of test animals during testing and observace of good clinical practice. Consecutive results relating to safety after administration of evaluated products were assessed. Some findings were carried out also at applicant with focus on completing or specification of results from laboratory part of clinical evaluation.

As a conclusion it can be stated, that during carried out inspections there were no findings which could negatively influence evaluation being processed or lead to suspension of evaluation. In total there were 6 control findings carried out.

Within the scope of carried out market surveillance on medicinal products, at 3 immunological products out of 5 planned there was commenced and finished field verification of safety after administration to target animals.
Verification was carried out and evaluated at these products: Bio Bos Respi 4 inj., Moraxebin Neo inj. and Bio Bos Respi 3 inj. Also verification in field conditions was finished at product Rotavec corona that was processed in 2012.

No adverse effects after administration, which would require follow-up measures, were found in any case.

By reason of ensurance of complex veterinary care by private surgeons, 15 expert opinions in total there were worked out on requirement of SVA CR for applications for import on unauthorised medicinal products according to § 46 of the Act No. 378/2007 Sb., on Pharmaceuticals, which were a basis to issuance of Decision on approval for exception to applying veterinary practicioners.

Applications for import of veterinary medicinal product authorised in other member state according to § 48 of the Act No. 378/2007 Coll., on Pharmaceuticals, were 268 in total. Two of them were not processed due to the formal imperfections (not completed). All other applications were approved with positive opinion to import and use in a form of Decision.
The most frequent application was a request for import of the veterinary medicinal product Levitape susp. (antiparazitics for sheep) due to the increase of resistence to a long-term application of benzimidazole products as an antiparasitic product of the first choice. There were in total 138 applications submitted. At products for diagnosis of Cushing syndrom in dogs (Synacthen amp. 250 mg) there were approved 41 applications in total. By reason of elimination of economic losses in sheep farming caused by higher occurrence of pathogenes – Mannheimia haemolytica a Pasteurella multocida there were applications for exception to import of product authorised in other member state – Heptavac P Plus – 31 applicants.

5.4 Veterinary non-medicinal products, veterinary technical devices and biocides

5.4.1 VP and VTP

Summary of approvals of veterinary non-medicinal products (VP), registery of veterinary technical devices (VTD) and evaluation of biocides in 2013 (current situation on Dec 31, 2013)				
Type of activity	**Transfered from the year 2012**	**Submitted/ Approved in the year 2013**	**Executed**	**In proceeding**
Approval of VP	8	135	135	16
Variations of approved VP		88	87	1
Discontinuation of VP approval proceeding			4	
Withdrawal of approved VP				
Total VP	8	227	231	17
Evaluation whether it is VP, § 65 article 1, i)				
VTD registery		8	8	
Solving of adverse effects of				

- **VP**				
- **VTP**				
- **biocides**				
Appeals against Decision				
Dept. of approval of VP, VTD and biocides – total number of operations in 2013	**8**	**235**	**239**	**17**

	Submitted/approved in 2013	**All approvals on the Dec 31, 2013**
Total number of Evidenced products	**135**	**1360**
VP – KP cosmetics	**37**	**594**
VP – DI dietetics	**70**	**471**
VP – DG diagnostics	**17**	**216**
VP – AR aquarium fish	**1**	**22**
VP – VA varia	**10**	**57**
Number of registered VTD	**8**	**97**

5.4.2 Biocides

Summary on evaluation of biocides in 2013 (current situation on Dec 31, 2013)				
Type of activity	**Transfered from the year 2012**	**Submitted/ Approved in the year 2013**	**Executed**	**In proceeding**
Evaluation whether it is biocide or product from other cathegory § 65 article 1, i)		12	12	
Authorisation of biocidal active substances (opinion of MA CR)				
Authorisation of biocidal products (committal opinion of MA CR)	3	37	38	2
Assessment of application for marketing authorisation, § 7 article 5 of the Act No. 120/2002 Coll.		26	24	2
Assessment of application for MRP for marketing authorisation, § 10 article 7 of the Act No. 120/2002 Coll.		11	11	
Opinion to biocides-announced		70	68	1

according to §35 of the Act on biocides				
Changes of opinions		7	7	
Cancellation of decisions/Cancellation of opinions			1	
Biocides in total	3	113	113	3
Solving of adverse effects of biocides				
Appeals against Decisions				
Total number of operations in 2013	**3**	**113**	**113**	**3**

	Submitted/approved in 2013	**All approvals on the Dec 31, 2013**
Number of cancelled biocides	**123**	
Number of approved biocides	**57**	**1098**
Total number of approved biocides from the beginning of the approval process		**1685**
Total umber of cancelled iocides frm the beginning of approval process		**652**

6 Activity of the Inspection Section in 2013

6.1 GMP Inspections

6.1.1 Report on evaluation of activity in Department of GMP including field of quality assurance and RAS

1) Evaluation of fulfilment of the main tasks and visions in 2013:

- ***Fulfilment of the systemic inspection plan on keeping the interval provided by the Decree on GMP and GDP (responsible Radošová)***
  ☺ All planned inspections were performed.
  Two more inspections compared to plan were carried out with relation to new applications for granting of manufacturing authorisations for veterinary medicinal products, thus at EponaCell, s.r.o. company and control laboratory Lunaria spol. s.r.o.. furthermore there was performed 1 systematic inspection concurrently with variation to manufacturing authorisation (new manufacuring site) – Orifarm Supply s.r.o with regard to approaching term of systematic inspection. Further there was performed 1 control inspection above the plana t bodies manufacturing veterinary medicinal products with connection to use of bovine foetal serum PAA Linz and 1 special inspection of National Reference Laboratory SLAK at SVI Praha. With connection to a two-days visit of australian competent authority the visitors became acquaianted in two days with manufacture of veterinary medicines in the Bioveta a.s. company.
- ***Further increasing of qualification and knowledge level of DMP inspectors (Műllerová, Radošová)***
  ☺ Trainings were performed in necessary and planned range.
- ***Finishing and execution of revision of the regulatory documentation and finishing of revision of Quality Manual of the Inspection Section (responsible Zubrová)***
- 😐 Partially fulfilled – revision of some of the SOP, forms and questionnaire for VMP manufacturers. Furthermore the templates were updated for guidance of regulatory process by authority. Revision of Quality Manual of the Inspection Section has not been finished.
- ***Revision of regulatory documets in the field of RAS, MP LP, MS, updating in the field of regulatory documentation on handling MS*** *(responsible Műllerová, Radošová)*
  😐 partially fulfilled – forms were prepared in the field of VP, SOP were updated for inspection performance at manufacturers and revision of RAS guidelines was approved, which came into force from on March 1, 2013. Translation of Chapter 4 of GMP Guidelines and Supplement 11 of GMP Guidelines was published as well as Questionnaire for manufacturers of medicinal products in compliance with requirements of regulatory documentation. In 2013 Guideline No. 2013-VYR-01 Supplementation of guidelines for GMP Chapter 1 and Chapter 7 were published. Furthermore the templates were updated for range of activities according to the Compilation of Community Procedures on Inspection and Exchange of Information with validity from January 2, 2013.
  Updates in the field of regulátory documentation of handling LL will be a task for 2014.
- ***Finishing of revision of register database on VMP manufacturers (responsible Radošová)***

☺ fulfilled – marketing authorisation database was completed with manufacturers of VMP and further concurrent completing of information is processing with regard to assessment of marketing authorisation documents.

- ***Continuing of cooperation with inspection sections at SIDC and ÚŠKVBL (responsible Műllerová)***
  ☺ Joint GMP inspection was performed at company Contipro Pharma a.s. Further joint inspection with employees from SIDC was performed at company Glenmark Pharmaceuticals s.r.o. Employees from ISCVBM took part in seminars arranged by SIDC.
- ***International cooperation – (responsible Műllerová)***
  ☺ fulfilled – In 2013 a representative from Australian national authority visited ISCVBM, including an inspection of ISCVBM activity namely in inspection section. The participants also visited manufacturing site of veterinary medicinal products in Bioveta a.s. company.
- ***Preparation and performance of special seminars in the field of manufacture (responsible Műllerová)***
  ☺ fulfilled - Seminar for manufacturers of veterinary medicinal products was organised on June 6,2013. Further, lectures were ensured for sudents from VFU in the field of GMP on November 15, 2013, lecture on GLP in the field of animals protection at IPVZ on November 5, 2013 and lecture for qualified persons of manufacturers of medicinal products regarding legislation on pharmaceutical manufacture of veterinary medicinal products on October 12, 2013.
- ***Execution of audits in the field of pharmacovigilance and distribution (responsible Zubrová)***
  ☹ not fulfilled – Programme of internal audits was prepared and adopted in te Inspection section for the year 2013 comprising inspected area of good distribution practice and pharmacovigilance, which was submitted to quality manager of ISVBM. However, internal audits of GDP and pharmacovigilance have not been carried out yet and will be postponed to 2014.
- ***Other international cooperation (responsible Műllerová)***
  ☺ participation in Inspectors working group at EMA – GMDP IWG (69.-72. meeting) - fulfilled
  Activities in the field of PIC/S – participation in PIC/S Committee + PIC/S seminary (May – Geneve, Octoer – Ottawa) – fulfilled
  New structure implemented within the frame of PIC/S. MVDr. Műllerová is a member of Compliance Sub – Committee working group, involving in coordination and surveillance of evaluation of agencies from accessing countries, revision of reports and recommendation from evaluation, surveillance of remedial measures. This group will commence its activity from January 1, 2014. Assumed range of participation in teleconferences and meeting is 12 days.
  Within the scope of JVP (Joint Visit Programme) Dr. Müllerova entered the veterinary group in 2013 formed by French and Belgian authorities. Three joint inspections are planned for the period 2014 and 2015 – in France, Belgium and Czech Republic.

2) Summary of ativities in the GMP field

Number of submitted applications in the field of GMP of VP and AI: 14
Application for granting of manufacturing authorisation of AI – 0

Application for variation to manufacturing authorisation of AI – 1 (variation affiliated with inspection)
– 9 (variation without the need of inspection)
Application for granting a license of control laboratory – 1
Application for variation to license of control laboratory – 1
Application for granting GMP certificate – 3
Application for withdrawal of AI manufacturer certificate – 0
Application for suspension/withdrawal of authorisation – 2
Application for renewal of authorisation – 0 (with inspection)

Number of issued Decisions: 14
Manufacturing authorisation – 1 (application from 2012)
Manufacturing authorisation (variation to Decision) – 10
Granting a license for CL (+ variation) – 0
Withdrawal/suspension of manufacturing authorisation – 2
Withdrawal of certificate for manufature of AI – 1 (termination of activity of company)

Number of issued certificates: 24
GMP certificated on application – 3
GMP certificated on inspection – 21 (according to requirements of Directive 2004/28/EC)

At the beginning of 2014 one application for granting a license of control laboratory was executed, 3 applications for variation to manufacturing authorisation and 4 certificates of GMP were issued after inspection.

Review of preformed system inspections and comparison with the plan for 2013
I. Inspection activity

Part A – inspections carried out within the scope of regular surveillance on manufacture and control of veterinary medicines

Company based on CoR (Company Register)	**Schedule**	**Executed on**	**Approval/ Note**
Bioster a.s.	January	23.1.2013	Radiative capture
Bioveta a.s. Opava	February	19.2.2013	Sterile, viral antigens
KOMVET spol.s.r.o.	February	29.1.2013	Unsterile manufacture
Alliance Healthcare s.r.o.	March	29.4.2013	Unsterile manufacture
PURUS-MEDA, s.r.o.	March	3.4.2013	Unsterile manufacture
Contipro Pharma a.s.	April	21-22.3.2013	AI manufacture – joint SIDC
Contipro Pharma a.s.	April	14.-15.5.2013	Sterie manufacture
Cayman Pharma s.r.o.	April	12.-13.3.2013	AI manufacture
Movianto Česká republika a.s.	May	19.4.2013	Unsterile manufacture
Noviko a.s.	May	29.5.2013	Unsterile manufacture
Nordic Pharma s.r.o.	June	30.4.2013	Batch certification
Výzkumný ústav včelařský	June	11.7.2013	Unsterile manufacture

Company based on CoR (Company Register)	Schedule	Executed on	Approval/ Note
s.r.o.			
Aveflor a.s.	July	26.-27.8.2013	Unsterile manufacture, selected MP
Favea, spol.s.r.o.	August	21.-22.8.2013	Unsterile manufacture
Bureau Veritas Czech Republic, spol.s.r.o.	September		Control laboratory – authorisation withdrawn on request
Stachema Kolín spol.s.r.o.	September	30.-31.10.2013	Unsterile manufacture
Glenmark Pharmaceuticals s.r.o. s.r.o. s.r.o.	October	16.-17.9.2013	Unsterile manufacture – joint with SIDC
ALS Czech Republic, s.r.o.	October	10.12.2013	Control laboratory
Trow Nutrition Biofaktory s.r.o.	November	13.11.2013	Unsterile manufacture
SVÚ Jihlava	November	20.11.2013	Control laboratory
Chemopharma a.s.	December		AI manufacture – company terminated its activity

Joint inspections with SIDC: Joint inspection with SIDC was performed at – Glenmark Pharmaceuticals s.r.o. in period 16.-17.9.2013 and inspection focused on AI manufacture in Contipro Pharma a.s. in period 20.-21.3.2013.
In cooperation with SIDC and ASLAB there were **4** GLP inspections performed – Tekro a.s., Bioveta a.s., Meditox s.r.o., Biopharm VÚVBL a.s..
Within the scope of supervision on AI treatment there were **4** inspections performed. Based on import controls of AI in cooperation with Customs office there were no findings of new or risk subjects. Regular inspections of registered bodies were set internally with frequency of 3-4 years.

Compared to plan there were another **2** inspections performed based on application for granting of manufacturing authorisation and for granting of activity of control laboratory, **1** control inspection at manufacturer of veterinary medicinal products relating to bovine serum. Further there was **1** inspection carried out based on application for variation of manufacturing authorisation at company ORIFARM SUPPLY s.r.o. Due to the near date of system inspection the periodic system inspection was shifted from the beginning of 2014 to the end of 2013. On April 18, 2013 there was extraordinary inspection of SLAK national reference laboratory performed in cooperation with Marketing authorisation section, SVI Jihlava and State Office for Nuclear Safety.

Part B – inspections performed based on application submission:

Epona Cell s.r.o.	15.1.2013	Application for manufacturing authorisation
Lunaria spol.s.r.o.	11.12.2013	Application for granting of activity

Bioveta, a.s.	28.5.2013	Focused on usage of bovine sera
ORIFARM SUPPLY s.r.o.	3.12.2013	Variation to manufacturing authorisation + sysem inspection
SVÚ Praha(NRL SLAK)	18.4.2013	Extraordinary control

Part C: Field of import and distribution of active ingredients (treatment with medicinal substances) is area still a point of interest of SI. Number of inspections performed – **4**

Number of inspections performed in the field of GDP: 25 (GMP) + 1 GLP

Systematic initial + variations – 3 (1 performed concurrently as a periodic system one and included also in this number)
Systematic periodical – 17
Follow-up – 0
Control – 2
OCABR control – 0
AI manufacturers – 2
VP manufacturers – 1
Inspections on treatment with AI – 4
GLP – 4
Foreign – 0

Number of elaborated protocols: 23 (GMP) + 1 (protocol on inspection findings) + 4 (protocol on GLP inspection) + 4 inspection on treatment with AI+ 1 (report on official control NRL SLAK)

Summary of inspection activities:

Estimated number of inspections: **29 inspections + 5 controls** in the field of treatment with AI
Estimated number of inspection days: **38 (A+B) + 5 (C) = 43**
Total number of man-days (number of inspection days x assumed number of inspectors per inspection): **102**

Actually there were **23** GMP inspections + **4** GLP inspections, **2** control inspections and in the field of AI treatment surveillance there were **4** inspections performed. Number of inspection days was **44**. Total man-days **78.**
During 2013 the activity was suspended on request at **2** subjects – Bureau Veritas Czech Republic – control laboratory and company MIKA a.s.
Activity of Chemopharma a.s. company was terminated and authorisation for maufacture of AI was withdrawn.
In 2013 a representative from Australian national authority visited ISCVBM, including an inspection of ISCVBM activity namely in inspection section. The participants also visited manufacturing site of veterinary medicinal products in Bioveta a.s. company.
Data were evaluated from the Customs office on movement of medicinal substances on the territory of the CR and inspections were performed at main suppliers of medicinal substances and persons hadnling medicinal substances. This area will be further in focus of Inspections section during 2014.
Compared to programme there were **2** inspections performed with relation to new application for manufacturing authorisation for veterinary medicinal products – EPONA CELL s.r.o. and

with application for authorisatio of activity of control laboratory LUNARIA spol.s.r.o. At Orifarm Supply s.r.o. company there was carried out inspection focused on application for variation to manufacturing authorisation and concurrently periodic system inspection.
On April 18, 2013 an extraordinary inspection at SLAK national reference laboratory in cooperation with Marketing Authorisation Section, SVI Jihlava and State office for Nuclear Safety.

Training
The employees of Inspection Section – Department of GMP in 2013 took part in training in the range of **20,5 dní** (Műllerová – 7 days, Radošová 6,5 days, Kožíšek – 7 days).
From the trainings abroad one employee took part in training organised by PIC/S – Canadian authority – with theme „Global Supply Chains and GMP Compliance"

Cooperation (SIDC, EMA, PIC/S…)
The employees of Inspection Section in 2013 took part in meeting GMDP Inspectors working group at EMA (4 meetins, MVDr. Műllerová).
MVDr. Műllerová represented ISCVBM at meeting of PIC/S Committee (two meetings in 2013: May - Geneve; October - Canada), and took part in training with themec„Global Supply Chains and GMP Compliance".
Within the scope of HMA working group WGEO the ISCVBM was represented by Mgr. Zubrová at meeting in Irland (April).

Within cooperation with SIDC there was joint inspection performed in the GMP field at manufacturer of medicines Glenmark Pharmaceuticals and AI manufacturer Contipro Pharma a.s., te cooperation also continues in the field of GLP. Protocols from GMP and GLP inspections were jointly elaborated.

Consultations, providing of information

Type of consultation	**Personal**	**Phone**	**E-mail**	**Total**
Počet	10	135	145	290

Two personal consultations were carried out within the scope of submitted applications for granting of manufacturing authorisaton or variation to manufacturing authorisation.

Assessment of documentation for marketing authorisation
During 2013 all marketing authorisation documents on requests from Marketing authorisation section were assessed. In total with regard to GMP requirements there were **246 applications assessed**. Data on VMP manufacturers were evidenced in register database.

3) Quality indicators evaluation:

No.	**Description**	**Limit**	**Evaluation**
002-01	Periods of administrative proceeding for application for granting manufacture authorisation for VMP	Max. 90 days	Periods were met, **in one case the period was exceeded due to postponement of inspection on request of manufacturer**.
002-02	Periods of administrative proceeding for applications for variation to manufacturing authorisation for \vmp with inspection	Max. 90 days	Periods were met.

002-03	Periods of administrative proceeding for variation to manufacturing authorisation of VMP without inspection	Max. 30 days (resp. 60 days)	Periods were met**,** average period of elaboration was **12,3 dnů, in one case request for completing of application.**
002-04	Confirmation of application receipt	Max. 30 days	Periods were met.
005-01	Periods of administrative proceeding for application for issuing of certificate	30, resp. 60 days	Periods were met, average period for elaboration **was 3 days.**
009-01	Period for elaboration of protocol	30 working days	In most case the periods were met, average period of elaboration **was 18,4 working days. Period was not met only in one case.**
009-02	Basic content of system protocol of GMP inspection – initial	Acc. to DP GMP	All protocols consist of description of all necessary chapters
013-01	Good classification of deficiencies in GMP protocol on inspection	Acc. to legisl.and DP GMP	All nonconformities in GMP inspection protcols were classified in compliance with risk
023-01	Minimum intervals of inspections at manufacturers of veterinary medicinal products	Min. 1x in 2 years	In most of inspections the period set was met. Some GMP inspections were in 2013 postponed within the range of the year 2013, only the inspection at Orifarm Supply s.r.o., planned to 2014 was rescheduled to 2013. Period between inspections longer than three years has never been ovrereached
023-04	Minimum intervals of inspections at control laboratories	Min. 1x in 2 years	Interval was met.
023-05	Minimum intervals of inspections at manufacturers of veterinary AI	Min. 1x in 3 years	In 2013 there were planned and carried out 2 inspections at manufacturers of AI. Interval was met.
024-01	Periods of administrative proceeding at application for granting of approval for activity as control laboratory	Max. 90 days	One application had been submitted which was executed in requested term.
024-02	Periods of administrative proceeding at applications for variation to approval for control laboratory with inspection	Max. 90 days	One application had been submitted which was executed in requested term.
024-03	Periods of administrative proceeding at application for variation to approval for control laboratory without inspection	Max. 30 days (resp. 60 days)	Application was not submitted
024-04	Confirmation of application receipt	Max. 30 days	Periods were met.
025-01	Periods of adminitrative proceedings at application for issuing of certificate for manufacturer of AI	Max. 60 days	In 2013 no application for certificate for manufacturer of AI submitted.
025-02	Confirmation of application receipt	Max. 30 days	In 2013 no application for certificate for manufacturer of AI submitted.

026-01	Period for elaboration of protocol of control laboratory	30 working days	Periods were met, average period of elaboration **was 21 days.**
026-02	Basic content of system protocol on GMP inspection – initial	Acc. to DP GMP	All protocols consist of description of all necessary chapters.

4) Quality assurance, internal audits

Within the scope of quality assurance finishing of Quality manual revision and finishing of individual SOP were planned. At most of the documents revision has been further continuting. Revision has been finished at SOP 002/3000 – Procedure for authorisation of manufacture and approval of variations and at SOP 025/3000 Procedure for granting of AI manufacturer certificate (revision incorporates all relevant forms and templates). Further priciples of risk management were included to Checklist of manufacturer ans Questionnaire for manufacturer of medicines, which was updated according to document of European Commission – Explanatory Notes on the preparation of a Site Master File and with document PIC/S for preparation of Site Master File document.
In 2013, guideline 2013-VYR-01 Ammendment to GMP Guidelines Chapter 1 and Chapter 7 was published. Further the templates for range of activities according to Compilation of Community Procedures on Inspection and Exchange of Information was published with validity from January 2, 2013.
Updating of documents was fulfilled in the field of RAS – Directive 009/1000 - Quality defects in veterinary medicines, rapid allert system in ISCVBM., which came into force from March 1, 2013.
Internal audits in areas of GDP nad pharmacovigilance were not carried out, they will be postponed to 2014.

5) Summary of activities within the scope of rapid allert system (RAS) in 2013

In 2013 the total number of received information regarding quality defects in VMP within RAS (Rapid Alert System) was 227. This number includes information concerning all cases of quality defects from external authorities, most of which is information on quality defects of human medicinal products, updating of RAS database, reports on manufacturing places non-conforming to GMP requirements and reports from individual organisational sections of ISCVBM on quality defects. In total there were 155 external reports on quality defects of veterinary and human medicinal products, 38 reports concerning manufacturing places non-conforming to GMP requirements and 13 reports concerning revision of database.

Reports from external authorities	Concerning human medicinal products	145
	Concerning veterinary products	10
	Updating of RAS database	13
	GMP non-compliance	38
Retailer, breeder	Veterinary non-medicinal product	1
Internal reports from organisational sections of ISCVBM	Section of laboratory control	10
	Section of marketing authorisation, FVG	2
	Inspection section	5

Reports received from marketing authorisation holder		3

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

- Unsatisfactory size of particles – 4
- Unsatisfactory content of active or preserving agent, pH - 3
- Unsatisfactory determination of microbiological quality – 3

Quality defects of veterinary medicinal products received by the department of Marketing authorisation section and Inspection section were related to non-conformities with packaging (inner packaging, external packaging, PI) and differencies in data specified in marketing authorisation dossier. Most often non-conformities were incomplete or valid data on packaging in comparison with marketing authorisation documentation, different data on withdrawal periods and foreign language wording on packaging.

- Non-conformities in packaging – 7
- Non-conformity of data specified on packaging of authorised products - 1

In 2013 there were 2 pcs of information sent on noncompliance with GMP conditions during manufacture of medicinal products, further one announcement on possible falsification was sent to distributors.
In 2013 2 pcs of informaction were sent to external authorities within the scope of Rapid Allert System (RAS)

In 2013 based on RAS data there were commenced 3 administration proceedings with marketing authorisation holders of veterinary medicinal products for violation of Act No. 378/2007 Coll., on Pharmaceuticals:

Specification on violation of the Law	Number of administrative proceedings
Act on Pharmaceuticals § 33,Article.3, a)	3

6) Summary of deviations:

No significant deviations from the set procedures on main activities of the section were found out in 2013. In the field of quality assurance there was performed partial revision of regulatory documentation.

7) Corrective measures:

Finalization of regulatory documentation is a target task for the first half of the year 2014.
Since there were no significant deviations from set procedures found in 2013 , no corrective measures were taken in the field of inspection performing.

6.1.2 Activity of GMP MF Department

Specifications of targets in 2013 and evaluation of its fulfilment:

- fulfilment of inspection plans mentioned in inpsection part - I.A
  Fulfilled - three premises, where insections planned were cancelled in 2013 and in Tekro, spol. s r.o., company, plant in Nová Dědina, the inspection was postponed to 2014 based on request of manufacturer, which has been carrying out total renovation of plant.
- proceeding of revision of SOP in the field of manufacture of medicated feed with relation to the Act No.378/2007 Coll., on Pharmaceuticals and relevant Decree – *fulfilled.*
- Inspection at applicants for manufacture of medicated feed for self-consumption (so called farmer manufacturers – primary manufacture) – *no application submitted.*
- Follow-up inspections of new authorised manufacturing (handed-over) premises (převzatých) from the year 2012 – fulfilled (AFEED CZ a.s., Dibaq a.s.).
- CISTA – regular meetings of ISCVBM representatives with CISTA representatives (usually 1-2x a year), possibility of common inspections and exchange of information, particular cooperation in inspection of follow-up contamination of KS after manufacture of medicated feedingstuff, including collecting of samples and analysis of feed samples started in 2010 still continues.
  Fulfilled, samples collecting of follow-up KS and medicated feedingstuffs – four mutual meetings were carried out between ISCVBM and CISTA regarding solution of cross-compliance problems.
- Collecting of samples of medicated feedingstuffs at manufacturers of medicated feedingstuffs – *fulfilled, during 2013 there were collected and analysed five samples of medicated feed in total.*
- Complex elaboration of results from analyses of medicated feedingstuffs samples and follow-up KS, carried out in ISCVBM during the year 2013 - *fulfilled.*
- Cooperation with department of market control at inspections in veterinary practicioners prescribing medicated feed with assumption of 15 – 20 inspections – *fulfilled, see „Other inspection activity".*
- Collecting of samples of medicated feed within the market surveillance plan for 2013 – *fulfilled.*
- Cooperation with ČMSOZZN in the sphere of expert information providing within the frame of surveillance of manufacture of feedingstuffs to complete documents from the EU, etc. – *fulfilled, further participation in joint meetings of representatives from ČMSOZZN, ISCVBM and CISTA arranged by MA with theme of cross-contamination of KS with medicines.*
- Joint activity within the EU frame – joint inspection with ÚŠKVBL at manufacturer of medicated feedingstuffs in Slovakia or in CR . *Not carried out.*
- Training for qualified persons and managers of quality control in manufature of medicated feedingstuffs – *Not carried out, postponed to next year.*

Summary of activities:

Number of applications supplied in the field of GMP MF:

Type of application	New manufature authorisation	New manufature authorisation - farm manufacturer	Variation to authorisation with inspection	Variation to authorisation without inspection	Application for suspension of authorisation for manufacture	Application for withdrawal of authorisation validity	Total
Number	0	0	2	3	0	1	6

Compliance with administrative terms to reply to application:

Administrative terms to reply to application were complied (max. limit is 30 days)

Number of decisions issued:

Type of decision	Authorisation of new manufacture	Authorisation of new manufature-farm maufacturer	Variation to authorisation with inspection	Variation to authorisation without inspection	Suspension of authorisation validity	Withdrawal of authorisation validity	Total
Počet	0	0	2	1	0	1	4

Compliance with terms for decision issuing:
Mentioned administrative proceedings were executed in given time of 90 days in maximum without inclusion of the suspension oeriod caused by applicant. As far as the total time for suspension of proceeding of more than 90 days was tolerated, it was in the cases, when the applicant had been carrying out a merger with another company which called for longer period due to administrative and legal acts connected with a merge, or the applicant had been carrying out changes on the technology and when it had been completed the administrative proceeding at ISCVBM continued

Number of incomplete applications transfered to the year 2014:

Type of application	Applications from new manufacturers - not finished	Variations to authorisation for manufature with inspection	Variation to authorisation without inspection	Withdrawal of authorisation	Applications not finished in total
Počet	0	1	2	0	3

Justification: *application transfered to the year 2014 had been submitted by manufaturer at the end of 2013. In one case the inspection of GMP MF was carried out and submission of requested documents has been expected from manufacturer, in second case the manufaturer was asked in due term to supply documentation and in third case the variation was finied in January 2014.*

Certificates of GMP MF:

Number of applications for issuing of certificated on GMP MF	Number of GDP MF certificates issued
0	0

Number of inspection carried out at manufacturers of MF in 2013

Type of inspection	Systematic initial	Systematic variation	Systematic periodical	Follow-up	Control	Total		
						inspections	Inspection days	Man/days
Number	0	3	25	2	4	34	35	70

Time schedule of inspections, that were to be carried out in 2013 was met.
Time schedule of follow-up and control inspections was met.

Compliance with proceedings of inspections:

Proceedings during conducting of inspections complied with those specified in relevant SOP. Prior to any periodic systematic inspection the manufacturer had been sent a letter informing on inspection to be carried out. The inspections were executed always according to time schedule specified in advanceč. Inspection protocol had been elaborated from every inspection (based on records made in control sheet) and this protocol was sent to manufacturer.

Other inspection activity

Inspection in veterinary practicioners related to veterinary dicines prescriptions, participation in GDP inspections (medicated feedingstuffs), inspections in wholesaler stores with pet shop products (veterinary non-medicinal products and selected veterinary medicinal products), pharmacies – these **controls (inspection) are included in reports from department of market control and departmend of distribution** (**28 inspections carried out in total**).

Type of inspection	Control - pharmacies	Control veterinary practicioners	Control breeders	Control exhibitions	GDP inspections	Total		
						inspections	Inspection days	man/days
Number	5	11	2	2	8	28	28	56

In 2013 there was carried out in total
62 inspections (63 inspection days) in the field of medicated feedingstuffs manufacture, market and distribution control, i.e. **126 man/days.**

Consultation, providing of information

Type of consultation	personal	telephone	e-mail	Total
Number	10	200	30	235

Personal consultations were carried out mostly within the frame of questions of potential applicants for manufacture of medicated feeds or variation in authorisation for manufacture.

Sampling at manufacturers of medicated feedingstuffs

During inspections in 2013 samples of granulated medicating feedingstuffs were withdrawn with active substances CTC, Doxycyclin, Amoxicilin – in total 5 samples of granulated form of medicated feedingstuff were withdrawn. The samples were analysed in the ISCVBM laboratory. Analyses were performed continually.

Collaboration with state administration bodies (CISTA, SVA, RVA etc.) and other activities

Employees of GMP MF duringn 2013 took part in:

- ČMSOZZN – conference – Brno (lecture with theme of manufacture of feedingstuffs)
- 4x meeting of employees of CISTA and ISCVBM – cross-contamination theme, determination of limit of contamination with medicines,
- 1x active participation in traiing of inspectors at CISTA (two lectures with theme of manufacture and distribution of medicated feedingstuffs),
- 1x meeting with representatives from ČMSOZZN and CISTA and MA with theme of cross-contamination after manufacture wit medicines (MA Praha),
- Cooperation with SVA (monitoring) on elaboration of on-line form for information transfer regarding medication of feedingstuffs, 1x participation in meeting on monitoring, 1x workshop with presence of representatives from SVA and RVA from two regions,
- Training of inspectors – see reports on trainings.

Collaboration between CISTA and ISCVBM was in course during inspection of follow-up contamination of medicated premixes after manufacture of medicated feedingstuff – withdrawal of samples by CISTA, laboratory analyses in ISCVBM, handing-over of results from analyses, consultations regarding evaluation of cross-contamination of KS by medicines.

6.2 GDP inspections

Fulfilment of main aims and targets specified for the year 2013:

- Fulfilment of plan of systematic inspections in compliance with time schedule determined in Decree on GDP
  fulfilled
- Inspection of sales of selected veterinary medicinal products to authorised customers, inspection of occurence of medicines not authorised on the market

fulfilled, to be further carried out in 2014

- Enhancement of qualification and level of knowledge of GDP inspectors
  fulfilled
- Within the scope of systematic inspections at distributors – implementation of inspection of supplies of medicines from foreign suppliers with relation to its potential parallel importation
  fulfilled, to be further carried out in 2014
- Inspection of labelling of LP and inspection of LP compliance with its valid authorisation documents (packaging, PI)
  fulfilled, to be further carried out in 2014
- Inspection of gradual recalls of VMP and inspection of occurence of VMP with expired marketing authorisation validity on the market
  fulfilled, to be further carried out in 2014
- Cooperation with inspection section of SID
  fulfilled
- Preparation and performance of scientific seminars with relation to amendments to legislation and new guidelines
  Will be carried out in 2014
- Comprehensive revision of SOP
  Will be further continuing in 2014
- Withdrawal of samples within the scope of market surveillance
  fulfilled

I. Summary of inspection activities:

In 2013 there were registered **100 distributors with 130 stores**.

Number of submitted applications: total 25

Type of application	Authorisation of distribution	Variation to authorisation of distribution with inspection	Variation to authorisation of distribution without inspection	Extension of distribution authorisation for MF a AI	Suspension of validity	Withdrawal of authorisation validity	GDP certificate
Number	6	4	10	-	-	3	2

Number of issued decisions: total 25

Type of application	Authorisation of distribution	Variation to authorisation of distribution with inspection	Variation to authorisation of distribution without inspection	Extension of distribution authorisation for MF a AI	Suspension of validity	Withdrawal of authorisation validity	GDP Certificate
Number	6	4	10	-	-	3	2

All administrative proceedings were executed in determined time of 90 days without inclusion of suspension caused by applicant. Two applications were submitted in 2012 (variation without inspection and new distributor).

Number of incomplete applications transfered to the year 2014: 2 in total

Variation to authorisation with inspection	Variation to authorisation without inspection	Applications of new distributors - incomplete	Extension of authorisation for distribution of MF and MS	Suspension of authorisation validity
0	1	1	0	0

part A – planned inspections carried out within the scope of periodic control of distribution and control of veterinary medicines in CR (systematic – periodic and follow-up inspections)

Company according to Company Register	Inspection plan for 2013	Date of inspection execution/Remark	Number of days
Ecolab Hygiene s.r.o.	February	10.4.2013	1
NOVIKO s.r.o. Praha	February	25.4.2013	1
Dr. BUBENÍČEK, spol. s r.o.	February	12.3.2013	1
Boehringer Ingelheim, spol. s r.o.	February	24.6.2013	1
Plaček s. r. o.	March	26.2.2013	1
DOMI, v.o.s.	March	20.2.2013	1
Tekro, spol. s r.o. Osek	March	16.10.2013	1
GATCO, spol. s r.o.	March	25.4.2013	1
Proviservis s.r.o.	April	10.1.2013	1
MEVET spol. s r.o.	April	3.12.2013	1
Josef Kvapil - JK ANIMALS	April	22.3.2013	1
Vetmedical s.r.o.	May	18.4.2013	1
Europak s.r.o.	May	30.7.2013	1
Alliance Healthcare s.r.o. Ostrava	May	27.3.2013	1
BAYCO ČR s. r. o.	May	Transfer to 2014	-
Jiřina Dudová - DUSLE	May	11.6.2013	1
MVDr. Luboš Soukup	May	12.6.2013	1
CETUS CZ s.r.o.	June	3.9.2013	1
Veterinární centrum s.r.o.	June	15.5.2013	1
Vitakraft CHOVEX s.r.o.	June	19.6.2013	1
BIOPHARM, spol. s r.o. Králův Dvůr	June	16.10.2013	1
BIOPHARM, spol. s r.o. Roudnice nad Labem	June	17.10.2013	1
"D.D.D." spol. s r.o.	July	Authorisation withdrawn by June 4, 2013	-
NOVIKO s.r.o. Hudcova	July	18.9.2013	1
NOVIKO s.r.o. Palackého tř.	July	18.9.2013	1
PHARMACY - distribuce léčiv s.r.o.	July	7.6.2013	1
PROFIVIT spol. s r.o.	July	27.11.2013	1
Pfizer Animal Health Czech s.r.o.	August	Transfer to 2014	-
B.H.K.V. s.r.o.	August	14.5.2013	1
ELI LILLY ČR, s. r. o. Hudcova	August	21.11.2013	1
ELI LILLY ČR, s. r. o. Palackého tř.	August	21.11.2013	1
MVDr. Petr Lehnert	August	21.8.2013	1

GLON c.e. s.r.o.	August	12.6.2013	1
Ing. Petr Gregorovič	September	15.11.2013	1
FIDES AGRO, spol. s r.o.	October	3.10.2013	1
Trouw Nutrition Biofaktory s.r.o.	October	25.9.2013	1
PANDA PLUS s. r. o.	October	30.5.2013	1
Alliance Healthcare s.r.o.	December	24.6.2013	1

Plan of periodic systematic inspections for 2013 was 38 inspections **in total.**
Number of executed inspections was 35 systematic periodic **inspections.** (2 inspections were transfered to further period, 1 inspection was not executed due to the cancellation of authorisation).

Number of executed inspections in total: 46
In 2013 GDP department carried out 46 inspections in total, in the range of 46 inspection days. Summary of inspections carried out is listed in table below:

Type of inspection	Systematic initial + II. part	Systematic periodical	Inspection changed	Follow-up inspections
Number	6+1 (7)	35	4	-

Number of elaborated protocols in 2013: 46. Average time for elaboration of protocol was 5 days.

Plan of systematic inspections extended for control of compliance to authorisation documentation**: 2**
Executed inspection: 1

Plan of inspections focused on parallel import: **at every systematic and control inspection**
Plan of joint inspections with SIDC: 2 joint inspections planned in the field of GDP.
Executed inspections: 3 joint inspections.

Part B – control activity carried out by GDP department (including inspections carried out by department of market control and surveillance)

Type of inspection	**Control inspections**						**Total**
	Distributors	**- Pharmacies**	**Veterinary surgeons**	**Breeders**	**Zverimex** (VVLP) + e-shop	**- Exhibitions**	
Number	12	5	29	15	25	2	**88**

Plan of estimated rate of employees of GDP on ensuring of control inspections at distributors, veterinary surgeons, breeders and pharmacies, in estimated number of 80 inspection days (included in plan of activities of Department for market control).
Actual executed control inspections: 88. **Number of elaborated control protocols: 88**.
These are also evidenced within the scope of activities of department for market control.

In total during 2013 the GDP deaprtment executed 134 inspections in the field of distribution of MP, out of which it was 46 inspections of GDP (systematic, variational, focused on sphere of medicines labelling) and 88 control inspections, which are evidenced in activities of Market control department.

Estimated number of inspection days: 48 (without control inspections)
Actual number of inspection days: 46 (+88 control inspections)

Estimated number of man/days (number of inspection days x assumed number of inspectors on inspection): 96
Actual number of man/days: 92 (+176 control inspections)

II. Non inspectional activity

Plan of training: 20 working days out of Institute
Executed trainings: 20 working days out of Institute

Complex revision of SOP
Revision of SOP will be further carried out in 2014

Seminar of ISCVBM focused on questions of new decrees and guidelines in the sphere of distribution was not carried out, it was transfered to 1-2. Quarter of the year 2014.

Cooperation with SIDC in the field of GDP:
Being executed, 3 joint inspections were carried out in 2013.

Withdrawal of samples for EDQM in 2013:
2 veterinary medicinal products were withdrawn.

III. Consultation, providing of information

Type of consultation	personal	telephone	e-mail	Total
Number	14	120	45	179

Personal consultations were carried out with relation to submitted applications for granting of authorisation for distribution or variation to authorisation for distribution and to information relating to sale of selected VMP

Summary

Plan of general inspection activity in the field of GDP was 116 man/days.
Actual number of general work activity executed outside of Institute was **112 man/days in 2013** in the field of surveillance and approvals of distribution of medicines, however, without **control inspections (176).**
No substantial shortcomings were found, during 2013 all time periods determined in the Act on Pharmaceuticals or in regulation documentation were met.
Attention was given to the field of parralel import which will be continuing also during 2014, furthermore the control of labelling of medicines on the market in CR will be carried out.

Great attention was given to controls of wholesaler stores with pet shop products focused on distribution of selected veterinary medicinal products.

6.3 Department of market control, dispensing and usage

1) <u>Inspection activity</u> – specified targets

1. Control of usage of human medicines by veterinary surgeons with focuse on keeping of cascade rule.
2. Analysis of usage of human medicines for the EU needs.
3. Control of dispensing of veterinary medicinal products on prescription in the form of inj., sol., pulvis and biopreparates in pharmacies per 2012 with focus on food animals. Inspection on usage of these products at final breeders. At the same time a joint inspection of veterinary medicinal products on prescription dispensing without prescription and unpacking of original packaging.
4. Control of keeping of conditions on usage of veterinary medicinal products authorised for exception at veterinary surgeons and final breeders. Namely it is inspection on number of batches imported, keeping of period for applicability and usage in target animals.
6. Inspection of sales of veterinary medicinal products in market, exhibitions and auctions.
8. Inspection of VMP sales through internet.
9. Inspection of distribution and sales of selected veterinary medicinal products.
10. Preparation of new list for reports on import and distribution of veterinary medicinal products and reports on manufacture of medicated intermediate products and medicated feedingstuffs.
11. Elaboration of protocols on consumption of active antimicrobial substances for ESVAC and ISCVBM.
12. Elaboration of reports on consumption of OPL by veterinary surgeons in CR per 2012.
13. Sample withdrawals of original packagings of veterinary medicinal products within the programme of market surveillance.
14. Inspection of accurracy of import and sales evidence of veterinary medicinal products at distributors.
15. Inspection of accuracy of manufacture evidence of medicated feedinstuffs and manufacturing instructions for medicated feedingstuffs.
16. Inspection of usage of VMP with limited indication.

Summary of activities of Department of market control and surveillance and comparison with plan.

Type of inspection	Plan	Executed - Louny	Executed - Brno	Total
Distributor	**14**	2	15	**17**
Pharmacy	**43**	15	6	**21**
Veterinary surgeon	**43**	38	29	**67**

ZOO shops	**172**	0	174	**174**
Manufacturer of medicated feedingstuffs	**6**	0	5	**5**
Breeder	**30**	6	15	**21**
Exhibitions, exchanges	**10**	0	3	**3**
Manufacture of VM	**-**	0	1	**1**
Manufacturer of VP	**-**	0	1	**1**
TOTAL	**318**	**61**	**248**	**310**

In connection with market surveillance 21 administration proceedings were launched in 2013

Market surveillance

Plan of withdrawn samples pcs.	**Number of withdrawn samples pcs.**	**Number of samples not withdrawn pcs.**
235	**136**	**99**

2) <u>Non-inspectional activity</u>

Training : Kurfürstová, Kučerová, Dorn, Koutecká

7.2. Interdepartmental seminary on zoonoses: Koutecká
25.7. Seminary on Act on Control – Dorn, Koutecká
22.2. training on „most often shortcomings during elaboration of protocol on control findings“ – Dorn, Koutecká, Kučerová, Kurfűrstová
27.2. Handling OPL: Dorn, Koutecká
4.11. Anticorruption training : Koutecká, Dorn, Kučerová, Kurfűrstová
27.11. Seminary on ammendments to act on addictive drugs and precursors: Koutecká, Dorn.

New list of veterinary medicinal products for manufacturers and distributors of VMP, distributora and medicated feedingstuffs manufacturers was elaborated, which serves to reporting on consumption of veterinary medicated product.

Protocol on consumption of antimicrobial substances, antiparasitics and biopreparates in CR had been elaborated according to requirements of the Director of ISCVBM.

Statement on consumption of active substances according to ESVAC requirements had been elaborated
Report on consumption of OPL in CR in 2013 has been elaborated according to reports from idnividual RVAs for the Inspectorate of Narcotic Drugs and Psychotropic Substances at the Ministry of Health of CR has been elaborated.

Statement on sales of human medicines to veterinary surgeons has been elaborated.

Tables were ealborated for annual report on withdrawal of medical products containing additive substances listed in Annexes 1 and 5 of the Act on addictive substaces, for

distributors and pharmacies. These tables have been sent to all distributors and pharaciies have been informed via Chamber of Pharmacists. According to Ammendment of the Act No. 273/2013, which ammends the Act No. 167/1998 on addicitve substances this report will be sent by distributors and pharmacies directly to ISCVBM, dept. in Louny.

3) Summary.

Plan on the number of inspections to be carried out was not fulfilled by 8 inspections. This was caused by more time spent on data elaboration for ESVAC. All antimicrobial active substances were re-calculated from salts to bases and matrix modified for reports on distribution of VMP and manufacture of MF.

Based on cooperation with SIDC a summary on distribution of human medicinal products to veterinary surgeons was obtained. Selected medicinal products for inspections were listed in following groups:

1. Prohibited substances for food animals,
2. Products containig addictive substances,
3. Products containing antimicrobial substances.

At veterinary surgeons the inspections were focused on usage of human medicinal products from above mentioned groups. Further inspections of human medicinal products planned for 2014 will be carried out in simillary way. During inspection it has been found, that human medicinal products from above mentioned three groups, have been used namely in veterinary ambulances and clinics in pets and sport animals (dogs, cats, pidgeons, etc.). In some cases there has been found usage for self consumption of veterinary surgeons. Considering these reasons the inspections in 2014 will be extended by usage of human medicinal products from other groups. At human medicinal products containing medicinal substances prohibited in food animals the inspections of dispensing of these products in pharmacies were carried out. No unauthorised dispension was found. Summary on human medicinal products used in veterinary practice has been elaborated for internal use.

Joint inspections at breeders and veterinary surgeons with inspectors from RVAs were executed in cases where residual substances had been found in products from food animals. RVAs were adressed by ISCVBM with offer for common participation in some of the inspections.

In 2013 an analysis was carried out in cooperation with marketing authorisation section of distribution of veterinary medicinal products with limited indication to veterinary surgeons and breeders. Insections were executed at veterinary surgeons with the highest consumption of these products. During these inspections we were focused on protocols on laboratory analyses, reasons for usage of VMP with limited indication and a questionnaire prepared from marketing authorisation section was filled with every veterinary surgeon. Results from inspections were handed over to marketing authorisation section for further outputs.

In 2013 the inspections in pharmacies were also focused on dispensing of VMP on prescription without prescription, thus namely for usage in food animals and unpacking of original package.

Chamber of veterinary surgeons in 5 cases adressed ISCVBM with request for seeking of purchaser at VMP – biopreparates with suspicion on unauthorised purchaser. Products were seeked in cooperation with distributors, some cases were solved in cooperation with relevant Regional veterinary administrations. Based on findings of distribution the inspection of usage was carried out. In one case it was impossible to find final consumer, this case was solved in cooperation with Regional Veterinary Administration and Police of CR. Chamber of veterinary surgeons has been informed on our procedure.

6.4 Pharmacovigilance department

1) Summary of acitivities:

a) Fulfilment of main tasks and aims:

- Receiving, registery, assessment, solving and handover of information on adverse effects of VMPs (assumption: 50 reported adverse effects, which have occurred in CR).
  - *55 reports on adverse effects which had occurred in CR were received*
- Evaluation of periodic reports on safety of veterinary medicinal products (PSUR):
  - PSUR assessment of VMP authorised via MRP/DCP (elaboration of AR) – CR in role of RMS – Σ 3/year
    - ☺ fulfilled - *13 PSUR assessed in total (for 11 VLP), at which CR is RMS*
  - PSUR assessment for VLP authorised via NP - Σ 70/year
    - 😐 partially fulfilled – *24 PSUR assessed within the application for extension of authorisation of VMP via NP*
  - Elaboration of statement to assessment reports (AR) PSUR for VMP authorised via MRP/DCP (CR as CMS) - Σ 30/year
    - ☹ task revaluated – *capacity transfered to the area of PSUR worksharing and assessment of PSUR for VMP authorised via MRP/DCP (CR in role of RMS)*
  - PSUR assessment within the frame of PSUR Worksharing project (HMA)
    - ☺ fulfilled - *during 2013 there was carried out PSUR assessment for combination of active substances tetracycline+neomycine+bacitracine+prednisolon (holder Intervet International B.V.) and PSUR for benzoyl peroxid (holder Virbac) within the project PSUR Worksharing (HMA)*
  - *Other PSUR assessment*

    - ☺ *fulfilled* – 61 PSUR evaluated tat were submitted within the scope of application for authorisation extension via MRP (85 PSUR assessed in total)
- Assessment of pharmacovigilance systems within the authorisation documents scope –Σ 200 applications/year assumed - ☺ fulfilled - *243 applications assessed in total*
  - *Carried out assessments: 111 applications for VMP authorisation:*

    NP: 10 VMP

DCP: 85 VMP, out of which in 10 VMP where CR in RMS role
MRP: 16 VMP out of which in 4 VMP where CR in role of RMS

5 applications for variation to authorisation of VMP

127 applications for transfer of VMP authorisation (main item was common transfer of several tens of VMP from Pfizer, spol. s r.o., to Zoetis Česká republika)

- Pharmacovigilance inspections execution – 2 inspections planned
  - ☺ fulfilled – *2 inspections executed of local representatives of marketing authorisation holders, who are responsible based on contracts for pharmacovigilance activities on the territory of CR. These were MEVET spol. s r.o. company – representative of Merial and Sogeval companies and company Samohýl a.s. (MVDr. Petráš) – representative of Norbrook Ltd company.*
- Completing of control documentation.
  - Modification and completing of SOP 004/3000 „Evaluation of completeness and assessment of marketing authorisation documentation in terms of pharmacovigilance“ on extension of authorisation, transfers and variations - 😐 partially fulfilled – *being carried out due to the ammendments to the Act on Pharmaceuticals and new guideline of EC to Reulation No. 1234/2008 (variations to authorisation)*
  - Update of SOP 029/3000 „Planning, preparation and management of pharmacovigilance inspections“
    - 😐 partially fulfilled – *being carried out due to the new control order (template of protocol)*
  - Preparation of SOP for evaluation of Periodically updated reports on product safety (PSUR) and SOP for handling reports on suspicion to adverse effects of VP and VMP and reports on suspicion for adverse efects of VTP
    - 😐 partially fulfilled – *being carried out*

b) Reports on adverse effects (NÚ)

Table No. 1 – Reports from the Czech Republic

Total number of reports	**55**
Veterinary medicinal products - pharmaceuticals (in total)	22 (out of which 5 MCL*)
Veterinary medicinal products – immunologicals (in total)	33

Notice: Compared with previous period the numbers are cathegorized in different way.

** In 5 cases in total of nonconforming findings of residues from medicines there was investigated concrete veterinary medicinal product (in 3 cases by employees from ISCVBM, in 2 cases (group B1)by employees from RVA).*

In 2013 employees from Pharmacovigilance department investigated in collaboration with relevant RVAs or other employees from ISCVBM Market surveillance department total of 14 nonconforming findings of prohibited substances and residues of medicines within the frame of monitoring of extraneous substances in food and materials of animal origin. Particularly these were:

1 nonconforming finding of substance from group A3: 17-β-19- nortestosteron

6 nonconforming findings of substances from group A6 (2x metronidazol, 3x chloramphenicol, 1x dimetridazol and ipronidazol)

7 nonoconforming findings of substances from group B1 (5x dihydrostreptomycin, from which in 2 cases concrete VMP was investigated, 1x neomycine, 1x enrofloxacine incl. Ciprofloxacine with investigated concrete VMP)

Table No. 2 – Reports from the Czech Republic – distribution according to type of product

Product	Animal cathegory	Description of NÚ	Result - evaluation (ABON system)
VMP for active immunisation against canine adenovirus Type 2, prevention of mortality and clinical symptoms caused by canince parvovirus (type 2a, 2b and 2c), prevention of clinical symptoms caused by canine distemper and canine adenovirus Type 1, reduction of pathological symptoms of disease caused by parainfluenzae virus and reduction of infection risk caused by *Leptospira canicola* and *Leptospira icterohaemorrhagiae*.	dog/yorkshire terrier	After administration of medicine anaphylactic shock and death of animal by next day.	B
VMP for active immunisation of dogs against distemper, infectious hepatitis of dogs caused by canine adenovirus type 1 (CAV 1), canine parvovirosis, respirátory disease caused by canine adenovirus type 2 (CAV 2) and canine parainfuenzae (CPi); for active immunisation against leptospirosis caused by germs *Leptospira interrogans*, ,	dog/yorkshire terrier	After administration the dog was not able to stand up; due to paraplegis an euthanasia was done.	O

serogroups *Canicola* and *Icterohaemorrhagiae*; for active immunisation against rabbies.			
VMP for active immunisation of dogs against distemper, hepatitis, parvovirsis, laryngotracheitis, parainfluenzae and leptospirosis.	dog/yorkshire terrier	After administration, head shaking and slight edema, vomiting, diarrhea lethargy of puppy. Further, health condition recovered.	A
VMP for treatment and prevention of ectoparasitosis – namely against fleas, ticks, lice, running lice, mites, and its evolution cycles	dog/Bernese Mountain Dog	Sucking ticks found, bitting of fleas after administration of product.	O1 (SLEE)
VMP for active immunization of pigs to moderate virus infestation in blood and lymph tissue and decreasing of mortality and weight loos connected with infection of porcine circovirus type 2 ORF2.	pig	After preventive administration, less ingestion monitored, temperature increased, weakened condition of animala and occurence of neurological symptoms (ataxia).	A
VMP for active immunization of dogs from 6 weeks age against distemper, infectious hepatitis, infectious laryngotracheitis of dogs, parvovirosis of dogs, parainfluenzae of dogs and leptospirosis caused by serotypes *L.icterohaemorrhagiae, L.grippotyphosa* a *L.sejroe*.	dog/French Bulldog	After administration occurence of facial edema, whole-body nettle rash, pruritis and vomiting; symptoms disappeared by the next day.	A
VMP for treatment and prevention of flea infestation (*Ctenocephalides felis*) for period from 7 to 8 months, prevention of development of larvae stadium.	dog	After administration, lethargy, slackness, bouncing to subjects, turbidity. After clinical examination bilateral blindness and myridiasis confirmed on. Euthanasia.	O
VMP for active immunization of cats against infectious feline peritonitis from 16 week age.	cat	After administration of product hyper sneezing and hypersalivation, later breathlessness	O1

		(open chops). Due to neurolgical symptoms euthanasia in one animal (out of 4 animals) .	
VMP for active immunization of horses against equine influenza.	horse	Warm edema in administration place, local edema of neck 15-20cm, painful warm edema, recovery after administration of cool gel.	A
VMP for active immunization of cats against virus rhinotracheitis of cats, calicivirus infection, infection with germ *Chlamydophila felis*, infectious panleucopenia and 2 weeks after against component of leukemia of cats.	cat	After administration suspicion of infectious panleucopaenia of cats followed by dead. (Preventive administration in animal with disease).	O1 (SLEE)
VMP for active immunization of pigs against infection with *Mycoplasma hyopneumoniae* to reduce occurence of pulmonic lesion and reduction and occurence of pneumonic lesion and clinical symptoms caused by *Haemophilus parasuis*, serotype 4 and 5.	pig (piglets)	After administration of product dose, notice of rapid breathing, hyperaemia of mucosae and breathing difficulties (anaphylactic reaction). Some animals also suffered from decubitus, heart failure and abnormal motion of limbs or death.	B
VMP for active immunization of poultry against Newcastle virus to reduce clinical symptoms and mortality.	poultry – laying hens of consumable eggs	Analysis of low titre of antibodies in poultryafter administration of vaccine – administration found noncomforming with authorisation decision, unsuitable combination with oter products and unsuitable vaccination scheme.	Use of product Použití beyond conditions of authorisation (off label use)
VMP for active immunization of	Cat (male)	Death of animal by 15	A

cats against panleucopaenia, herpesvirus and calicivirus infection and rabbies.		minutes after administration of drug with symptoms of breathlessness and pulmonary oedema (acute failrue of circulatory and pulmonary system).	
VMP for active immunization of cats agains virus rhinotracheitis, calicivirosis and panleucopaenia.	cat	After administration of drug, bloody diarhea occured, hypothermis, neurological symptoms followed by death.	B
VMP for treatment of infestation with imagos and immature stages of nematodes of gastro-intestinal and respiratory a respiratorního tract of animals.	hedgehog	After preventive admiistartion animals were languid, weak, not able to stay on legs; followed by collapse of organism and death of one of the two animals.	Case is not evaluated since orimary source (veterinary surgeon or breeder) is not known
VMP for treatment of existing intramammary infections in torridity to receive protection against new infections during torridity.	cattle	After administration of product, lay down of animals, decreased activity (lassitude). Febris and diarhea occured in one animal During 24 hours erythema of udder, animal was not able to stand up. Follown with change to purple colour and death of animal.	B

Comments:

SLEE – suspicion of insufficient expected efficacy

VLP – veterinary medicinal product

ABON system for evaluation of causation between administration of VMP and NÚ:

A = probable

B = possible

O = not classified (conclusion cannot be determined for insufficiont information)

O1 = insubstantial (cases in which oter factors forestalled to draw a conclusion, however, causation wit product cannot be omitted)

N = improbable

c) RAS and NUI systems for veterinary pharmacovigilance

Pharmacovigilance department elaborated 7 statements on requests for information from competent authorities of other EU member states within the NUI (Non-Urgent Information) system and sent 1 request for information (NUI).
In 2013 one report in RAS system was received (pharmacovigilance).

d) Cooperation

MVDr. Brychta **took part in following EMA workshops** in 2013:
CVMP Pharmacovigilance Working Party meeting
29.-30.1., 26.-27.3., 28.-29.5., 9.-10.7., 24.-25.9., 26.-27.11.2013
PhV Inspectors Working Group meeting
21.3., 13.6., 19.9., 5.12.2013
Out of the office in 26 days + 10 days of preparation for meetings.

Mgr. Eva Zubrová, PhD., took part in following meetings in 2013:
Eudravigilance Veterinary Joint Implementation Group (EMA): 17.7.2013 (teleconference), 16.10.2013 (teleconference)
Working Group of Enforcement Officers (WGEO, HMA): 17. – 19.4.2013 (Irland)
ESS meeting in Brussesls: 21.6.2013 (teleconference)
Meeting on extraneous substances monitoring (ÚVS SVS ČR): 24.10.2013
Meeting of lawyers from SVA – 20.2., 10.4., 9.10.2013
Working groups for revision of Regulation (ES) No. 882/2004 – 27.5.2013
Out of the office in 13 days + 6 days for preparation to meeting

e) Consultation, providing of information

Type of consultation	*Personal*	*Telephone*	*E-mail*	*Total*
Number	5	20	14	**39**

Personal consultations were performed within the frame of submitted applications for VMP marketing authorisation – pharamcovigilance system or solving of adverse effects.

f) Training

MVDr. Brychta took part in following trainings during 2013 in te range of 9 days in total:

- Conference on food quality „Ingrovy dny“ – Mendel University, 27.2.2013 Brno
- Handling narcotics and psychotropic drugs – 28.2.2013 Brno (seminary of Vetoquinol company)
- News in EU and Czech legislation, Good Vigilance Practice - SIDC, 23.5.2013 Prague

- Control Residues Training – seminary of European Commission, 12.-15.3.2013 Riga (Latvia)
- Training to Act No.255/2012 Coll., on control (Control order) – MA, 6.8.2013 Prague
- VEDDRA Workshop (Veterinary Dictionary for Drug Related Affairs) – training 27.11.2013, EMA (London, UK)

Mgr. Eva Zubrová, PhD., took part in following meetings during 2013 in the rage of 12 days in total:

- BTSF – Training course on control on residues of veterinary medicinal products in food of animal origin (European Commision): 26.2. – 1.3.2013
- Remedy of failure decission in administrative proceedings: 22.3.2013
- PhV IWG training on PhV data analysis: 7.5.2013
- Seminary by SIDC „Pharmacovigilance and amendment to the Act on Pharmaceuticals“: 23.5.2013
- Seminary by ISVBM for marketing authorisation holders: 22.5.2013
- Seminary ba MA – acceptance of the Act No. 255/2012 Sb., on control (control order): 25.7.2013
- Seminary Kočka není pes (disease of cats, behaviour of cats): 11.9.2013
- Pharmacovigilance Inspectors Working Group Training Course (EMA): 11.-13.11.2013

g) Other activity

Lecture on meeting of CVMP Pharmacovigilance Working Party (EMA), concerning experience in the area of PhV investigation of animal smell after administration of product for immunological castration.
Lecture on meeting of WGEO to „Recent cases – VMPs in the Czech Republic“ theme.
Lecture activity, resp. providing of expert basis (e-learning), within the frame of training of selected veterinyr medicinal products retailers.
MVDr. Brychta further participated in other activity of Inspection section:

- 7 inspections of veterinary practicioners (6 inspections focused on use of MP with limited indication and 1 inspection – MP containing pseudoefedrine)
- 2 inspections of pet shops (selected veterinary medicinal products)

Apart from pharmacovigilance activity Mgr. Zubrová, Ph.D. further participated in other activity of Inspection section:

- Administrative proceeding managed by SI
  - as an administrative body authorised for all acts as an official authority (see Chapter 8. Legal agenda of Annual Report on Activity of ISCVBM),
  - updating of templates for administrative proceeding in official authority,
  - participation in meetings of SVA lawyers (see above),
- Updating of document „Jednotný integrovaný víceletý vnitrostátní plán kontrol ČR 2013 – 2015“ – chapters on control activity of ISCVBM
- Elaboration of document „Výroční zpráva z úředních kontrol ČR za rok 2012“ – chapter on results from controls of ISCVBM
- 1 SDP inspection

2) Conclusion:

In 2013 there was recorded 55 reports in total on suspicion for adverse effect of veterinary medicinal product on the territory of CR. Compared to previous years, collaboration was highly increased among relevant RVAs of SVA during finalization of investigations of prohibited substances and residues findigs in food and raw materials of animal origin within the scope of monitoring of extraneous substances in food and raw materials of animal origin (in 2013 total of 14, in 2012 total of 5 cases).
Compared to 2012, there was wider engagement in PSUR assessment during 2013 in products authorised within MRP/DCP procedures in which CR is in the role of reference member state (in 2013 total of 13 PSUR, in 2012 total of 3 PSUR). Further there was evaluated higher number of PSUR submitted within the application for extension of marketing authorisation (in 2013 total of 85, in 2012 total of 55).
For several years there is high number of evaluated pharmacovigilance systems connected with submitted applications for authorisation, including transfer of authorisations or variations of authorisation (in 2013 total of 243, in 2012 total of 191).
Evaluation activity of pharmacovigilance systems and namely PSUR still represent one of the main activities of Pharmacovigilance department and in given range including investigation of individual cases of adverse effects this activity will remain on priorit position for the future.

In connection with veterinary products in 2013, awareness of authorisation decision holders was also deepen on their obligation to report adverse effects of veterinary products according to the Act. No. 166/1999 Sb., on veterinary care, Coll.

In 2014 attention of employees of Pharmacovigliance department will be focused on finalisation of SOP on evaluation of Periodically updated reports on safety of product (PSUR) and SOP on handling reports on suspicion to adverse effects of VP and VMP and with reports on suspicion to adverse effects of VTP. Considering new Act.No.255/2012 Coll., on control (Control order), amendment of the Act on Pharmaceuticals and new guideline of EC to Regulation No. 1234/2008 (assessment of marketing authorisation variations) it will be necessary to carry out revision of both existing valid control documentation.
In connection with „veterinary pharmacovigilance“ there is still convenient and well-established information and „tutorial“ activity – therefore „veterinary pharmacovigilance“ will be included, where possible, to lectures provided by ISCVBM.
With regard to written agreement within the frame of PSUR Worksharing Initiative (HMA) and namely to approval of several new active substances (and other assumed to be approved in the future) we expect continual increase of activity in this area.

7 Activity of the ISCVBM testing laboratory

In 2013, due to expired validity of certificated of accreditation the laboratory succesfully passed regular audit performed by employees of the Czech Institute for Accreditation continually in October, namely in department: Laboratory for Residues Monitoring of Extranesous Substances. In the field of extraneous substances monitoring there was extended range of analytes in test No. 122 determination of corticosteroids in urine by LC-MS/MS method by eight new substances .
New Certification on Accreditaion was issued both in Czech and English language.
This Certification is valid till September 27, 2017.

Education of employees of Testing laboratory was carried out according to preliminary plan and 26 employees took part in 30 seminars and conferences held in the Czech Republic. Foreign business trips see individual departments of Testing laboratory

In the field of metrology the system of metrological assurance of instruments in ISCVBM was maintained and developed. Metrological instructions and list of auxiliary instruments were continually revised. Based on requirements of the Act on metrology determined instruments were verified by authorised worker of Czech Institute for Metrology, as well as regular service checks and calibrations of relevant working instruments and service checks of auxiliary equipment were carried out according to requirements of individual users of instruments.

7.1 Official Control Laboratory of veterinary medicines

Employees of workplaces in the department of official medicines control laboratory took part in several national and international tests in 2013 of capability to execute relevant tests.
Namely the offer for tests organised by EDQM was utilised namely for the sphere of physically-chemical tests.
Tests for checking of laboratory capability of organised by EDQM:

PTS 139 potentiometric determination of pH
PTS 140 water: semi-micro determination
PTS 141 LC – related substances

Other organisations:
- - Bacteriological diagnostics, EHK SZÚ – AP CEM, Identification of microorganisms and determination of sensitivity to selected ATB 4 x per year
- LGC Standards – sterility; determination of number of germs

7.1.1 International cooperation

European Directorate for the Quality of Medicines & HealthCare (EDQM):

A/ Cooperation was further continuing in the field of control of veterinary medicines with centralised authorisation (CAP Programmes), which has been carried out since the year 2000 – in 2013 no analysis was carried out of veterinary medicinal product within thei programme:

B/ Within the scope of new international standards analyses of chemical substances we participated in determination of following substances:

Azithromycin CRS
Cefatrizine propylene glycol CRS 2
Calcium folinate
Tetracycline HCl CRS 3
Diacerein
Prednisolone CRS 8
Erythromycin C CRS 5 – determination of efficacy by microbiological method
Piperacillin CRS 4
Progesterone CRS 3
Lincomycin HCl CRS 4
Rifaximin CRS 2
Bacitracin Zinc CRS 3 - determination of efficacy by microbiological method
Marbofloxacin

European Pharmocopoeia

Dr. Maxa continued in expert work in group 7 for antibiotics and group 10A for chemical substances, which acts at European Pharmacopoeia Committee.

Within the scope of work in the groups of experts (Group 7 a 10 A) at European Pharmacopoeia Committee the employees of the analytical chemistry department participated in verification, development and validation of methods for determination of associated substances for monography of demeclocycline HCl, tylosine and tylosine tartrate, tylosine phosphate, albendazole.

Irish medicinal agency

Based on agency request there was carried out analysis of microbiological quality in 5 veterinary medicinal products –sterility in 3 products for intramammar administration, 2x mikrobiological testing of non-sterile products (capsules and solution for peroral administration)

7.1.2 Cooperation with CISTA

Based on agreement concluded between the Institute and CISTA the laboratories of the Official Medicines Control Laboratory department analysed within the frame of cross-contamination of 1 feedingstuff (chlortetracycline)

7.1.3 Market surveillance

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

The employees of the official Medicines Control Laboratory closely cooperated with the experts from the Inspection Section onm the preparation of year schedules and evaluation of the surveillance. Inspection Section ensures qualified withdrawal of the samples from the distribution network, which are handed-over to laboratory to analysis and executes further steps in case when the laboratory finds out the results non-compliant with the approved specification of the product.

Market Surveillance Programme 2013 was focused namely on the control of authorised VMP containing substances of various pharmacological groups, namely antibiotics (tetracyclines, macrolides, sulphonamides, amphenicoles, penicilines) in dosage forms available on the market. Market control of immunological veterinary medicinal products related to control of elimination of contamination with mycoplasmas in selected life vaccines, further to verification of efficacy of inactivated vaccines against rabies and verification of virus titre in vaccines against Newcastle disease in poultry, vaccines against myxomatosis of rabbits and poultry bursitis, further efficacy control of vaccines against tetanus and efficacy of inacivated vaccines against erysipelas .

Within the fulfilment of Market Surveillance Programme there were 107 products analysed from the VMP-pharmaceuticals, 7 samples of medicated feedingstuffs and 24 immunological veterinary medicinal products, i.e. 138 products in total .

7.1.4 Official Batch Release of Immunological VMP

Since 2008 the Institute in the position of official control authority has been using the official batch release procedure to selected immunological veterinary medicinal products, so called OCABR thus fulfilling the 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 specified in details in the documents of EDQM. Preliminary and formal administrative steps of the Institute were executed in 2007, consequently in the year 2008 practical application of the particular batches of selected immunological VMP was executed in compliance with Article § 102 of above mentioned Act in 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 oficial release have been defined. The first assumes, that an applicant does not have the issued Certificate on official batch release for the given batch and competent laboratory of the Institute will analyse submitted samples and based on the compliant results the certificate is issued. The second option assumes, that the applicant submits valida certificate issued by the official control laboratory from the other EU member state, to which the ISCVBM issues its opinion without repeating the testing of samples. The reviews of current numbers of released batches of immunological VMP are listed in tables T 7/1 and T 7/2.

Based on evaluation of results obtained from repeated testing of products included in the system of official batch release the decision was taken to terminate application of this procedure by December 31, 2012 in immunological veterinary medicinal products (IVMP) from the group of Swine erysipelas vaccine – inactivated, which will be further monitored only within the regular market surveillance.

In the OCABR system further remain Swine erysipelas vaccine - live, Equine Influenza Vaccine – inactivated, Rabies vaccine for foxes - oral, live.
In other products the Institute does not require submission of documents on manufacture and samples of batches of IVMP prior to its release on market in the Czech Republic. Evaluation of documentation and possible analyses in these IVMP for issuance of OCABR/OBPR is carried out by the Institute only on application of the marketing authorisation holder.

Tab.7/1 Review of Submitted Applications for Official Batch Release and Issued certificates in the period 2008-2013

Applications/ certificate / Type of vaccine	Number of applications for release without issued certificate						Number of issued certificates					
Period	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**
Swine erysipelas vaccine inact.	15	17	16	16	15	**8**	15	17	16	16	15	**8**
Swine erysipelas vaccine live	4	2	2	2	4	**2**	3	2	2	2	3*	**2**
Rabies vaccine for foxes oral, live	2	10	16	25	21	**29**	2	10	16	25	21	**29**
Equine Influenza Vaccine inact.	0	1	3	0	4	**5**	0	1	3	0	4	**5**
Total	**21**	**30**	**37**	**43**	**44**	**44**	**20**	**30**	**37**	**43**	**43**	**44**

*1 batch was not compliant, 1 subbatch suspended by applicant during analysis

Based on request of marketing authorisation older 2 batches of inactivated vaccines against rabies were released by OCABR system

Tab. 7/2 Review of the batch marketing authorisation with release on the CR market based on certificate issued by official control laboratory from other EU member state in period 2008-2013

Applications/ approval / Type of vaccine	Number of applications to release with certificate issued by the laboratory of other EU member state						Number of marketing authorisations with IVMP batch release on the CR market					
Period	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**
Swine erysipelas vaccine inact.	2	10	8	14	6	1	2	10	8	14	6	**1**
Swine erysipelas vaccine live	1	1	1	0	0	0	1	1	1	0	0	**0**
Rabies vaccine for foxes oral, live	0	0	0	0	0	0	0	0	0	0	0	**0**
Equine Influenza Vaccine inact.	0	17	7	5	12	10	0	17	7	5	12	**10**
Total	**3**	**28**	**16**	**19**	**18**	**11**	**3**	**28**	**16**	**19**	**18**	**11**

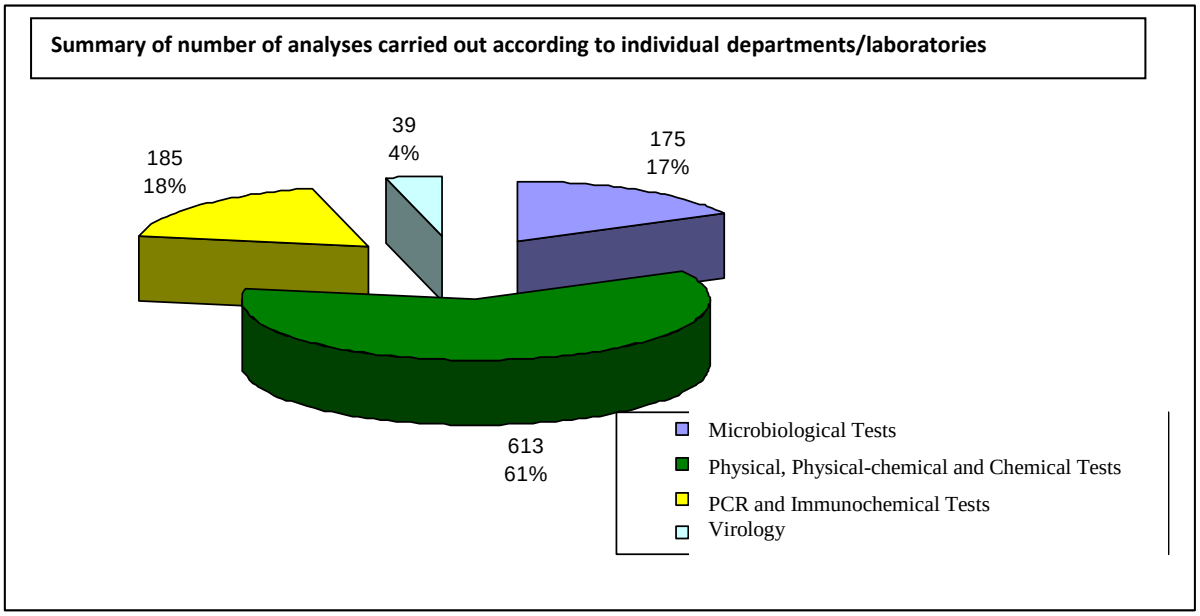
OBPR:

Based on request of marketing authorisation holder there were released 2 batches of vaccine against eimeria.

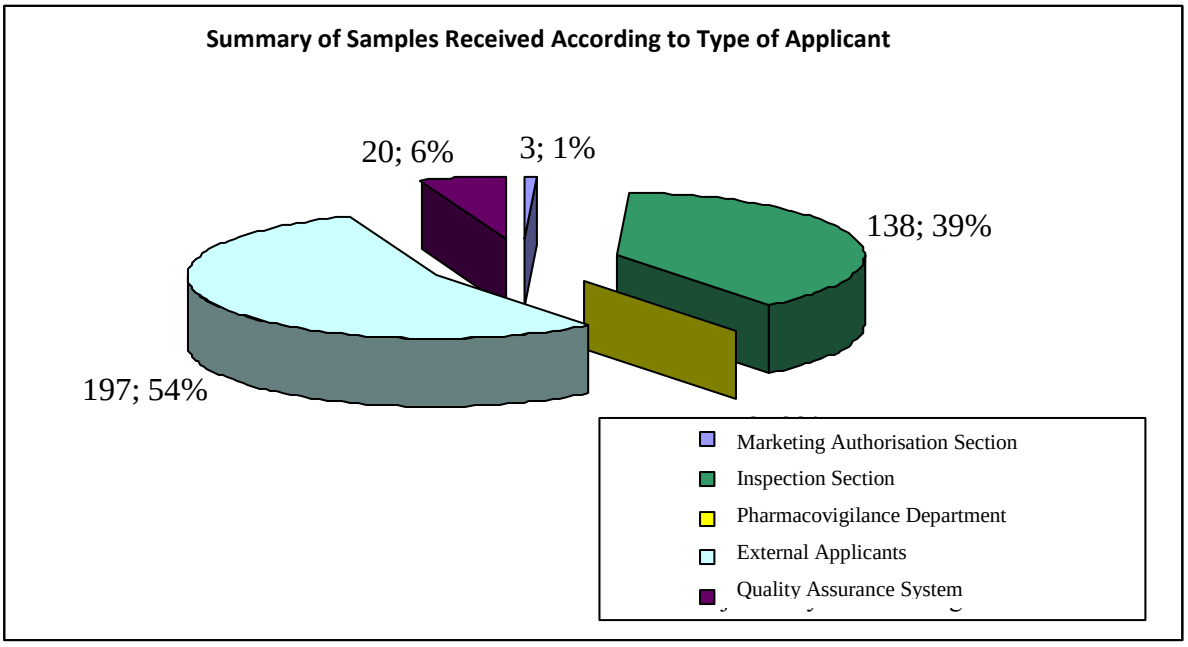
Summary of analysis of samples submitted for laboratory testing in 2013:

In the period January - December 2013 there were analysed **358 samples**), which represented to carry out **1012 analyses**. (review see charts 7.1, 7.2 and tables 7/3, 7/4, 7/5)

Graph 7.1 Summary of number of analyses carried out in the field of quality control of medicines
According to laboratory departments – in the year 2013



Graph. 7.2 Summary in graph of number of samples according to type of applicant in 2013



Tab. 7/3 Summary of samples analysed in the official medicines control laboratory according to applicant and character of sample in 2013

Applicant	Sample	Quarter 2013				Total	
		I	II	III	IV		
Marketing authorisation	VLP pharmaceuticals	-	1	-	2	3	3
	VLP immunologicals	-	-	-	-	-	
Approval	VP	-	-	-	-	-	-
Inspection	VLP pharmaceuticals	13	28	37	29	107	138
	VLP immunologicals	1	5	9	9	24	
	MeKS	-	6	-	1	7	
Pharmacovigilance	VLP pharmaceuticals	-	-	-	-	-	-
	VLP immunologicals	-	-	-	-	-	
External applicants	VLP	3	10	3	9	22	197
	MeKS	-	-	-	4	4	
	OCABR	2	11	18	13	44	
	Biological material and Others	3	9	15	97	124	
Quality assurance management	External (PTS, EHK)	2	4	4	2	12	20
	Internal (MK)	4	1	-	3	8	
Total	**Samples /analyses /**	**28** /144/	**75** /246/	**86** /292/	**169** /330/	**358** **/1012/**	

Tab. 7/4 Numbers of compliant and non-compliant samples in 2013

Samples	Compliant	Non-compliant	Character of defect in quality
Market surveillance of VMP pharmaceuticals *	91	16	6× size of particles 5× mikrobiological quality 3× active substance 2× relative density 1× water content 1× appearance 1× solubility 1× pH
Market surveillance of VMP immunologicals	24	-	-
Authorisation/ Approval	3	-	-
Pharmacovigilance	-	-	-
External applicants (only OCABR)	44	-	-
Total	**162 (91%)**	**16 (9%)**	

* *only pharmaceuticals – compliant* 85,05% , *non-compliant* 14,95%

Tab. 7/5 Summary of development of number of analysed samples and analyses carried out in period 2003 –2013

Samples / year	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Number of analysed samples	395	234	238	300	306	289	278	257	263	294	**358**
Number of analyses carried out	450	440	580	739	789	867	810	812	903	979	**1012**

7.1.5 Other activities – foreign seminars and conferences

Participation in Annual OMCL Meeting including sumbission of reports on analyses of pharmaceuticals and immunopreparates – including official batch release. Helsinki, Finland.

Meeting of WG for elaboration of GL on qualification of pH meters Štrasburk, Francie

Work at AdG GEON, Strasbourg, France

Participation in regular meetings of groups of experts held at EDQM, France
(Group 7 Antibiotics and Group 10A Chemical substances)

CAP Annual Meeting, Praha, ČR – meeting on questions of testing of products authorised with centralised procedure and MRP/DCP procedure.

7.2 Laboratory control - rezidues

7.2.1. Monitoring programme

Fundamental activity of the Laboratory for monitoring of residues of extraneous substances Department is carrying out of monitoring in compliance with Decree No. 291/2003 Coll., *on prohibition of administering some substances to animals, the products of which are intended for human consumption, and on monitoring of the presence of unauthorised substances, residues and contaminants in live animals and animal products which could make the products of animal origin harmful to human health,* as amended by Decree No. 232/2005 Coll., No. 357/2006 Coll. and No. 129/2009 Coll.

According to Decree No. 291/2003 Coll., as amended, in the competence of the ISCVBM laboratory is to monitore substances of the groups A1 – A6 (substances with anabolic effect and prohibited substances - specified in detailes in the Annex No. 1 to Decree No. 291/2003 Coll.) and group B2, Article d (sedatives). For these areas of residues monitoring the laboratory is called National reference laboratory (Decree No. 298/2003 Sb.).

The total number of **2723 samples were analysed in 2013**. The samples were analysed with analytical methods GC-MS(/MS) or LC-MS/MS.

From the total number, there were **2474 samples from planned monitoring programme**. Summary of analysed samples according to regular Monitoring Programme on presence of prohibited substances, residues and contaminationg substances in food chain for the year 2013 is listed in Table ***„Monitoring Programme 2013 at ISCVBM“***.

2467 samples from the total number were evaluated as **compliant**. Remaining **7 samples** were evaluated as **noncompliant**, due to determined contamination with following prohibited substances:

Analyte:	**Animal:**	**Matrix:**	**Region**
chloramphenicole	**calf**	muscle	Liberecký
	deer		Plzeňský
	chicken		Plzeňský
nitroimidazoles (metronidazole)	**goose**	muscle	Jihočeský
	chicken		Zlínský
nitroimidazoles (dimetridazole ipronidazole)	**pig**	Blood serum	Ústecký
17β-19-nortestosterone	**pig**	urine	Olomoucký

Proceeding of follow-up inspection in case of **non-compliant** samples was carried out in compliance with instructions specified in Decree No. 291/2003 Coll. and „Proceeding for withdrawal of samples and further inspection in cases of overlimit /non-compliant findings of biological active substances used in animals and prohibitive treatment within the scope of programme for monitoring of presence of unlimited substances and residues in veterinary medicines“ specified in Regular monitoring Programme of presence of prohibited substances, residues and contaminating substances in food chain for the year 2013.

During follow-up inspections there were analysed 58 samples from place of animal origin with non-compliant results. All these targeted samples were then evaluated as compliant:

Analyte:	Animal:	Matrix:	Number of samples:	Region:
chloramphenicole	calf, cow	Blood serum, urine, muscle, milk	14	Liberecký
	deer	muscle, feedingstuff, water	7	Plzeňský
	chicken	muscle, feedingstuff, water	10	Plzeňský
nitroimidazoles	goose	blood serum, feedingstuff, water	4	Jihočeský
	chicken	blood serum, muscle, feedingstuff, water	15	Zlínský
	pig	blood serum	5	Ústecký
17β-19-nortestosteron	pig	urine	3	Olomoucký

7.2.2. Other analyses (external applications)

a) Applications for analysis from food producers and other institutions (86 samples in total)

Analyte:	Matrix:	Number of samples:
nitroimidazoles	muscle	35
nitroimidazoles, nitrofurans	honey, eggs	3
nitrofurans	milk, cheese	19
thyreostatics	milk	22
chloramphenicole	milk, feedingstuff	7

b) Extraordinary actions of SVA

1) Extraordinary control action of SVA – KMU DRŮBEŽ 2013
Determination of nitroimidazoles
- 60 samples of poultry muscle

2) Extraordinary control action of SVA – KMU DRŮBEŽ 2013/2
Determination of chloramphenicole and dapsone
- 36 samples of poultry muscle
Determination of beta-agonists
- 8 samples of poultry liver

3) Other samples requested by SVA
Determination of chloramphenicole
- 1 sample of pork gut

7.2.3. Participation in interlaboratory proficiency tests

Date of execution :	Analytical method :	Performing organisation
May 2013	Determination of thiouracile in urine of cattle	RIKILT, EU-RL Wageningen, Netherlands
October 2013	Nitroimidazoles in poultry muscle	BVL, EU-RL Berlin, BRD
October 2013	Chloramphenicole in honey	SVI Olomouc

Results from participation in three proficiency tests were evaluated as excellent.

7.2.4. Other activity

- Active participation in meetings of SVA CR, regional coordinators for national monitoring of extraneous substances, managers of department of chemistry in SVA Praha, Jihlava, Olomouc, ISCVBM Brno and representatives of IC SVA Liberec regarding questions on monitoring of extraneous substances.

- Participation of employees according to profession in professional workshops (analytical, company, metrological, training on statistic methods etc.).

- Active participation (Mgr. Rejtharova in position of a trainer) in six one-week trainings „Better training for safer food“ provided by European Commission with topic of residues monitoring (presentation „Accreditation of residue monitoring laboratories“) and practical training „Follow up after non-compliant finding in residue monitoirng“).

- Active participation in seminary provided by Labicom on preparation of samples (presentation by Rejtharová, Rejthar: Preparation of samples of biological material for determination of residues of veterinary medicines).

- Participation in regular workshops and seminars by EU-RL RIKILT, Neterland and BVL, Germany

- **Publications:** in scientific journal **Food Additives & Contaminants: Part A,** Volume 50, No. 6 (published by Taylor & Francis) were in 2013 published following articles:

Rejtharová, Rejthar: *Development and validation of an LC MS/MS method for the determination of six gestagens in kidney fats*

Zelníčková, Rejtharová: *Determination of 5-nitroimidazoles in various types of matrices using molecular imprinted polymer purification*

Církva, Šťastný: *Method for the determination of thyreostats in milk samples using LC-MS/MS*

8 Legal Agenda

During 2013 there were initiated **22 administrative proceedings in total** for breaching of the Act No. 378/2007 Coll., on Pharmaceuticals or Act No. 40/1995 Coll., on Advertising Regulation and on amendment on the Act No. 468/1991 Coll. on Operation of Radio and Television Broadcasts.
Based on the suggestions from inspections or results from analyses of withdrawn samples there were initiated **21 administrative proceedings** in total during 2013 (in 2012 there were initiated 33 administrative proceedings in total, in 2011 there were 23 administrative proceedings, , in 2010 there were 29 procedures in total, and 30 administrative procedures in total in 2009). Furthermore, there was **1 administrative proceeding ex offo**, which was closed by varation to marketing autorisation of veterinary medicinal product based on amendment to the Act No. 167/1998 Sb., on addictive substances.

Total amount of penalties during 2013 reached **CZK 58.000,- .** The penalties represent an income of the state budget. The highest amount of penalty was CZK 14.000,-, the lowest one was CZK 1.000,- Kč.
Within the scope of administrative procedures in compliance with article § 79 section 5 of Administrative Procedure Code an obligation was imposed to cover the costs of procedure in a lump sum of CZK 1.000,- , **in total the covered costs amounted to CZK 10.000.-**

9 Department of informatics, ISCVBM Bulletin, providing of information, Supervision of Advertising

Information technology

During 2013 common activities in maintenance of computer technique both servers and computer machinery on userś side were made. Computer technique was gradually innovated with regard to efficiency of its utilization.
An important upgrade of Documentum SW was made and new Documerntum was completely implemented in virtual environment. During the year a disc array was also extended, which is necessary for digitalization of archive documentation. For this reason a SW modification was made and new workplace with necessary equipment for scanning and storage of archive documentation was arranged.
In a half of the year a new web presentation of the Institute was launched on the websites of the Ministry of Agriculture, which was thus included in the other web presentations of all subsidiary authorities of MA on the e-agri webpages. All information from the government department of the MA is enabled for public from one point www.eagri.cz.

Bulletin

During 2013 ISCVBM via its ISCVBM Bulletin regularly informed cooperative bodies and public about issued decisions on marketing authorisation of veterinary medicinal products, its renewals, variations, transfers, expiration of validity and withdrawals, on issued decisions on approval of veterinary non-medicinal products, its renewals, variations, expiration of validity and withdrawals and registering of VTD. Further the ISCVBM Bulleting informed on approvals on exceptions from authorisation, issued ISCVBM guidelines, importnat information for marketing authorisation holders. There are no more published updated lists of manufacturers of VMP and VP, distributors of VMP, manufacturers of MF, manufaturers of active substances, these lists are presented on the ISCVBM website (www.uskvbl.cz). In 2013 ISCVBM Bulleting was published in two months period in amount of 150 pcs.

AISLP, Veterinářství journal

Public information on VMP, its approved SPC and PI were regularly provided to compiler of Computerized information system of medicinal products (AISLP). Information on new authorised veterinary medicinal products, renewal, variation, expiration of authoristaion validity, suspension of authorisation and withdrawal of VMP, including basic information on VP, VTD and biocides were provided to editors of Veterinářství periodical.

Authorised veterinary medicinal products 2014

During the last quarter of 2013 works on Authorised veterinary medicinal products 2014 publication were commenced. The publication will consist of information regarding authorised veterinary medicinal products till January 31, 2014 by means of scientific texts,

including 3 registers and accompanying texts. 24 scientific employees of the Institute aprticipated in preparation of this publication.

Personal consultations

A total of 47 personal consultations were provided during 2013 regarding marketing authorisations of VMP, out of which 31 consultations were covered by the applicant for consultation. In the field of VP, VTD and biocides approvals there were provided 50 personal consultations. In the field of VLM, MF, VP manufacture, distribution and pharmacovigilance a total of 39 personal consultations were privede within the scope of submitted applications for granting of approval for manufacture or approval for variation to approval for manufacture, distribution and pharmacovigilance.

Library

Service of library of the Institute is provided by the Marketing Authorisation Department of ISCVBM. The library manages the book and periodicals stock by means of database. A total of 2972 books were evidenced by December 31, 2013.
A total of 34 periodicals were subscribed by December 31, 2012. From this amount 18 periodicals were Czech and 16 periodicals were foreign.

Total number of items of registration documents recorded in the database were 44522 by December 31, 2013 (annual increase 2034 items).

Supervision in the sphere of VMP advertising

During 2013 the Institute received one reuqest for inspection of advertising in the Jezdectví journal with suspicion to breach rules for advertising aimed to non-professional public.
Further the Institute inspected 2 advertisements for feed formic acid. In one case an administration proceeding was commenced, the other case was handed-over to inspection by CISTA.

Providing of information according to Act No. 106/1999 Coll.

Report on the activitied of the Institute for State Control of Veterinary Biologicals and Medicines in the sphere of providing of information submitted according to paragraph 18 of the Act No. 106/1999 Coll., on free access to information, as amended.

In the year 2013

Article 1 a)
During the year 2012 ISCVBM received a total of **8048 applications** for information according to the Act on free access to information.

Article 1 b)
All applications for information according to above mentioned Act were granted, no appeal was filed.

Article 1 c)
In the matter of information providing according to above mentioned Act no legal proveedings were conducted with ISCVBM, no court judgement was delivered.

Article 1 d)
In the matter of information providing according to above mentioned Act no administrative proceeding were conducted with ISCVBM regarding sanctions for its breaching.

odst.1 e)

Spheres of provided information	**Number**
Marketing authorisation of VMP	5800
Approval of VP, biocides, VTD	1500
Advertisement of VMP	5
Pharmacovigilance	39
Manufacture of VMP	290
Manufacture of MF	235
Distribution	179
Total	**8048**

10 Economic and operating sphere

10.1 Report on activities and economy

The total amount of financial resources assigned to ISCVBM after adjustment was 43 590,000 CZK in 2013, from which the investment resources were 217,000 CZK, noninvestment resources were 43, 373,000 CZK, from which 20,801,000 CZK were assigned to salaries of employees. According to the Article 112, of the Act No. 378/2007 Coll. as amended and Decree No. 427/2008 Coll., on determination of amount of costs for expert activities conducted upon request, provided by the State Institute for Drug Control and Institute for State Control of Veterinary Biologicals and Medicaments. These financial means are not part of state budget and were drawn by the Institute in compliance with terms of the Act No. 218/2000 Coll. as amended, according to internal rules No. S-018/1000 for drawdown and based on Regulations for using the extra budget resources of the Ministry of agriculture from November 7, 2006, Ref.No. 34386/2006-13012. In 2013 the amount of 25,240,000 CZK were included to incomes of the organisation and drawn.

10.2 Incomes

Prescribed incomes in total amount of 1,650,000 CZK were succesfully fulfilled and exceeded. From the total incomes of 3,751,000 CZK the tax incomes were 2,681,000 CZK.

10.3 Balance of resources drawn

Balance of resources drawn which is evident from table in Annex No.1, was kept in annual. Distortion, which deflected percentage of resource drawn upwards was caused by including of both extra-budget resources – approved exceeding.

10.4 Employement

Resource drawn of payrolls in the amount of 20,801,000 CZK was balanced and corresponded to approved budget. A part of these resources amounting to 8, 673,000 CZK, was covered from extra-budget resources. In the year 2013 there were 75 full-time-equivalent employees.

10.5 Financing of capital reproduction

Capital expenditures in total assigned amount of 217,000 CZK were drawn to purchase of part of SW for ISCVBM within the ICT programme in the amount of 100,000 CZK and purchase of air-conditioner unit in the amount of 117,000 CZK. An amount of 3,343,000 CZK from extra-budget resources was use for development of Documentum SW and upgrade of SW systems Kofax Expres, Okinfo, Attendance system. Scanner, disc array and paper cutter were purchased to ensure digitalilsation of archive documents. A total amount of 4,689,000 CZK was used to cover capital expenditures, from which an amount of 4,474,000 CZK was used from extra-budget resources above the scope.

10.6 Cofinancing of EU programmes

The Institute does not draw resources from EU programmes.

10.7 Extra-budget resources

Noncapital expenditures were drawn in the amount of 62,221,000 CZK, consisted of payroll part amounting to 27,621,000 CZK and mandatory social and health insurance of employees in the amount of 9,366,000 CZK. Current expenses in amount of 24,963,000 CZK were drawn on the main activities of the Institute.
In the tracked period, the Institute transfered to incomes financial resources in the amount of 25,241,000 CZK. These resources were drawn according to above mentioned rules and internal regulation, thus in the amount of 9,145,000 CZK on current expenditures, in the amount of 11,622,000 CZK to payrolls with and 4,474,000 CZK to ivestments.

10.8 Budgetary resources not expended

In 2013 the Institute did not account on budgetary resources not expended.

10.9. Research and development projects

In 2013 the organization does not keep records on resources for reserach and development.

10.10 Foreign and domestic business trips

The amount of 803,000 CZK was drawn on the costs of foreign and domestic business trips These trips were undertaken by the specialists of the Institute namely for participation in EMEA Committees, seinars and trainings and trips within te scope of inspection activities.

10.11 Liabilities and receivables

Shrot-term and long-term liabilities to suppliers are not evidenced by December 31, 2013.
Short-term receivables by December 31, 2012 are 56,000 CZK, consisting of advance payments (pre-payment of printed publications, fuels, water-rate….) and outstanding invoices for expert activities – laboratory analyses of products ordered by private applicants .
Long-term receivables are ot evidenced.

10.12 Advance payments for investment supplies and works

In 2013 the organization does not keep records on amount of above mentioned advance payments.

10.13 Remedial measures from controls

In 2013 one public control was carried out by the Section of audit and supervision from the Ministry of the Agriculture which resulted in following remedial measures:
Remedial measure to the item 8.1.2 Check of accounting evidence:
Fill-in the signature of Mr. Marek Nováček to list of signature specimens
Remedial measure to the item 8.1.4. Overdue receivables
According to the item 5.2.15 of the Regulation No. S-21/1000 on accounting to carry out check of invoices issued and possibly account for penalty late interest, in case where effective, as well as in

case of settlement after due date, thus for the period from 01/2011 – up to now..

Remedial mesure to item 8.1.8. Travelling allowances
Inform employees on obligation to keep internal rules and submit requests for business trip accounting within the period specified in the internal regulation, thus till 10 days after finishing of business trip.

10.14 Assets

In 2013 the tangible assets of the Institute was in a book value of 66,908,000 CZK, depreciacion was 21,552,000 CZK, further intangible assets was 441,000 CZK in a book value and low-value assets in acquisition value was 21,100,000 CZK. Depreciacion of long-term assets started in the accounting period of 2011. Procedure was taken according to ČÚS 708. In 2013 we proceed with monthly balanced depreciacions in terms specified in depreciocion schedule to individual character of assets according to internal Regulation S-021/1000 on accounting. Evaluation of assets is in acquisition price, net value or appraisal and corresponds to internal Regulation S-021/1000 on accounting.

10.15 Membership in international organizations

The Institute is a permanent member of following organizations:

PIC/S
BfARM
EDQM
EMEA

The member fees in these organisations have been fully covered by the Institute.

11 Employees

Basic personal data

1. Classification of employees according to age and sex – situation by December 31, 2013

Age	Men	Women	Total	%
Up to 20 years	0	0	0	0
21 – 30 years	1	3	4	4,9
31 – 40 years	5	13	18	22,3
41 – 50 years	6	19	25	30,9
51 – 60 years	3	21	24	29,6
61 years and more	4	6	10	12,3
Total	**19**	**62**	**81**	100
%	23,5	76,5	100	x

2. Classification of employees according to education and sex – situation by December 31, 2013

Education	Men	Women	Total	%
Primary	0	3	3	3,8
Craft	0	1	1	1,2
Secondary school	2	3	5	6,2
Secondary school with graduation	0	0	0	0
Complete secondary vocational	4	24	28	33,8
Upper secondary	0	0	0	0
University degree	13	31	44	55
Total	**19**	**62**	**81**	100,0

3. Total data on average salaries on December 31, 2013

	Total CZK
Average gross monthly salary from state budget	22 888,-

4. Total data on commencing and termination of employment and service relationships in 2013

	Number
Commencements	0
Commencement – substitute for Maternity leave	1
Terminations	0

5. Length of employment and service relationships of employees – situation on December 31, 2013

Period	**Number**	%
Up to 5 years	15	18,5
Up to 10 years	20	24,7
Up to 15 years	14	17,3
Up to 20 years	16	23,5
Over 20 years	15	16,0
Total	**81**	100

12 Fire prevention and safety of work

During the year 2013 fire prevention inspections were carried out on both workplaces (Hudcova 56a, Palackého174), focused on electric appliances, capacity of emergency exits, extinguishers, emergency lights condition, checks of condition of fire doors and hand extinguishers.

Regular revision of fire water mains, extinguishers, portable extinguishers and fire doors was carried out in April 2013 by the TESPO company.

Professional training of fire guard staff and persons ensuring fire protection tasks was carried out in May 2013 in extra-work time arranged by the TESPO company.

The new employee was trained on fire protection immediately after his first entrance to workplace. No occurence of fire was recorded in 2013.

Employees took part in regular obligatory training on Safety and protection of work and fire protection including training of management. The trainings are provided according to valid legislation by the external engineer and fire-prevention officer (qualified persons for the branch of BP and PO).

13 Conclusion

I believe, that submitted Report on activities of ISCVBM represents evidence on range and intensity of tasks, that are provided by the Institute.

According to notification, in 2014 the Institue is expecting submission of two drafts which would represent an essential shift in conditions applied on regulation of veterinary medicinal products (revision of code for veterinary muedicinal products – Directive 2001/82/ES as amended) and conditions for manufacture and distribution of medicated feeds (revision of Directive 90/197/EHS).

In addition, the European Commission is obliged to present a report on application of Regulation (EC) No. 470/2009, on coditions for evaluation of pharmacologicaly active substances with regard to MRL determination and several other areas concerning residuals of veterinary medicinal products.

Considering notificated changes it can be assumed, that legislation beig revised will bring higher demands on expert capacities of the Institute and demand on higher rate of coordination and intensity of cooperation among individual medicinal agencies within the territory of the EU.

Despite the limited sources the Intitute makes effort to develop in maximum possible range its expert capacities and utilize it in maximum possible effectivity. Therefore an agreement was prepared during 2013 between the Institute and the Austrian medicinal authority (AGES medicinal agency) on cooperation on assessment of applications for marketing authorisation of veterinary medicinal products within the frame of international authorisation procedures, with the main aim for Institute to actively participate on centralized procedure of authorisations. As a result of cooperation in 2013 the Institute was a co-raporteur in two authorisations by centralized procedure.

Existing form of financing remains essential for the Institute. I can definitely state that existing form of financing is highly effective both from the view of budgetary resources control and needs of the Institute and enables the Institute to fulfill obligations resulting from legislation and international obligations in necessary extent and quality.

Further task in 2014 will be preparation of conditions for consecutive implementation of rules for consistent manufacture of veterinary medicinal products and other measures reflecting the general trend to leave off the control of final medicinal products and implement inspection procedures in individual steps during manufacture of medicinal products. These changes result both from legislation for protection of experimental animals and implementation of 3R principles followed by changes in technical regulation for terms on veterinary medicinal products – i.e. omission of requets for safety testing of veterinary immunological products batches on target species. Mentioned trend is obvious and it is a common responsibility of the Institute and pharmaceutical industry to realize these changes and implement them according to procedure with maximum gain from positives given by these changes.

In the forthcoming period the Institute will develop a maximum effort to fulfill its task within the frame of international atuhorisation procedures, where acceptance of results from evaluations provided by the Institute in th position of a reference member state is a need for successful position of products on the markets within the other member states.

Other significant role will be fulfilment of task which will result from working group for antimicrobilas at the Ministry of Agriculture. Searching for corresponding solutions in the field of antimicrobial policy, which will reflect interests of the Czech Reublic, will be another priority.

Other areas, which are considered as priorities by the Institute are as follows:

- Surveillance of antiparasitical resistance problem,
- Support of availability of veterinary medicinal products for minor animal species namely for bees ans fish; concerning the diseases of bees to survey availability of medicines for treatment of varroasis with regard to occurence of resistance to available medicinal products,
- Strengthening of expert capacity of the Institute in evaluation of „new“ veterinary therapies, thus on products based on stem cells, monoclonal antibodies, immunomodulators, phages and other „biological products“, where the most intensive development can be expected followed by the widest share of newly authorised original products, also with regard to its potential of usage as alternatives to antimicrobial products,
- High quality of communication with regulated subjects with aim to ensure effective rate of regulation and limitation of relevant administrative burden,
- Development of cooperation with other state authorities also within the network of medicines agencies in the EU (in connection with HMA activities).

Let me express thanks to all of you, who are using services from the Institute of State Control of Veterinary Biologicals and Medicines and for cooperation up to now and it is my wishes that Institute is able to fulfill its role over the Czech Republic and the EU to your satisfaction.

Prof. MVDr. Alfred Hera, CSc.

Abbreviations

AISLP	AISMP	Automatic Information System of Medicinal Products
ATB	ATB	Antibiotics
ATC	ATC	Anatomic Therapeutic 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 from 1.5.2004
CMDv		Veterinary Coordination Group for Mutual Recongition Procedure and Decentralised Procedure
CCRVDF		Committee for Residues in Veterinary Medicines in Food
CVMP	CVMP	Committee for Veterinary Medicinal Products
ČIA	CAI	Czech Accreditation Institute
ČL	PhB	Pharmacopoeia Bohemica
ČLK	CPC	Czech Pharmacopoeia Committee
ČLS JEP	CMS JEP	Czech Medical Society of J.E.Purkyně
ČMI	CMI	Czech Metrology Institute
CVO	CVO	Chief Veterinary Officer
DIMDI	DIMDI	Deutsches Institut für Medizinische Dokumentation und Information
EDQM	EDQM	European Directorate for the Quality of Medicines
EEA	EEA	Evropský Economiy Area
EHK	EQA	External Quality Assessment
EHS	EEC	European Economic Community
EK	EC	European Commission
EL	EuPh	European Pharmacopoeia
ELK	EUPhC	European Pharmacopoeia Committee
EMA	EMA	European Medicinal Agency
ES	EC	European Community
EU	EU	European Union
EWP	EWP	Efficacy Working Party of medicinal products
FTP, WWW		Internet website
FVG	PVG	Pharmacovigilance
GC	GC	Gas Chromatography
GC – MS	GC-MS	Gas Chromatography – Mass Spectrometry
GMO	GMO	Genetically Modified Organisms
GMP	GMP	Good Manufacturing Practice
GRD	QRD	Quality Review of Documents
HEVRA	HEVRA	Heads of European Veterinary Regulation Authorities
HMA	HMA	Heads of Medicines Agencies
HPLC	HPLC	High Performance Liquid Chromatography
HVLP	MPMP	Mas Produced Medicinal Product
IPVPN	IPVPN	Internet Protocol Virtual Private Net
IWP	IWP	Immunological medicinal products Working Party
LL	AI	Active ingredient
KL	CL	Control Laboratory
MěVS	MVA	Municipal Veterinary Administration
MK	MF	Medicated Feed

MRA	MRA	Mutual Recognition Agreement
MRP	MRP	Mutual Recognition Procedure of VMP in EU member states
MF	MF	Ministery of Finance
MZ	MH	Ministery of Health
Mze	MA	Ministery of Agriculture
NCCL	NCCLS	National Committee for Clinical Laboratory Standards
OVS	RVA	Regional Veterinary Administration
PECA	PECA	Protocol on European Conformity Assesment Agreement
PERF	PERF	Pan-European Regulatory Forum
PCR	PCR	Polymerázová řetězová reakce, Polymerase Chain Reaction
PIC/S	PIC/S	Pharmaceutical Inspection Co-operation Scheme
PN	CS	Company Standard
PO	FP	Fire Protection
QWP	QWP	Quality Working Party of medicinal products
RHP	HFE	Hand Fire Extinguisher
SAGAM	SAGAM	Scientific Advisory Group on Antimicrobials
SDP	GDP	Good Distribution Practice
SKP	GCP	Good Clinical Practice
SLK	SLC	Section of Laboratory Control
SOP	SOP	Standard Operating Procedure
SÚKL	SIDC	Státní ústav pro kontrolu léčiv, State Institute for Drug Control
SVP	GMP	Good Manufacturing Practice
SVS ČR	SVA CR	State Veterinary Administration of the Czech Republic
SWP		Pracovní skupina pro bezpečnost léčivých přípravků/Safety Working Party
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 Medicines
VAS	VAC	Veterinary Antibiotic Centers
VEDDRA	VEDDRA	Veterinary Dictionary for Drug Regulatory Activities
VICH	VICH	Veterinary International Conference on Harmonisation
VLP	VMP	Veterinary Medicinal Product
VMRFG		Veterinární koordinační skupina pro postup registrace vzájemným uznáním členskými státy EU , Veterinary Mutual Recognition Facilitation Group
VP	VP	Veterinary non-medicinal Product
VPN	VPN	Virtual Private Network
VTP	VTD	Veterinary Technical Device

Přehled o plnění základních ukazatelů rozpočtu

za rok 2013

ORGANIZAČNÍ SLOŽKY STÁTU

Organizace (OSS):

rozpočtové funkční zařazení (paragraf)

	v Kč			*%*	*v Kč*	*%*	*v Kč*	*%*	*v Kč na 2 des.místa*	*%*	*v Kč na 2 des.místa*	*v Kč na 2 des.místa*
Závazné ukazatele	**Schválený rozpočet 2013**	**Upravený rozpočet k 31.12.2013**	**Skutečnost k 31.3.2013**	**Čerpání na UR 2013**	**Skutečnost k 30.6.2013**	**Čerpání na UR 2013**	**Skutečnost k 30.9.2013**	**Čerpání na UR 2013**	**Skutečnost za rok 2013 celkem vč. použití povolených nároků a mimorozp.zdrojů**	**Plnění/čerpání na UR 2013 v %**	**ze sl.9: použití povolených nároků z nespotř.výdajů**	**ze sl.9: použití mimorozp. prostředků - jiné zdroje**
a	**1**	**2**	**3**	**4 (sl.3/sl.2)**	**5**	**6 (sl.5/sl.2)**	**7**	**8 (sl.7/sl.2)**	**9**	**10 (sl.9/sl.2)**	**11**	**12**
Rozpočet příjmů												
P ř í j m y OSS celkem	**1 650 000**	1 650 000	865 076	52	1 874 916	114	2 834 357	172	3 751 211,46	227		
(vč. doplňkových, nahodilých a ost. příjmů)												
z toho: daňové příjmy	**1 450 000**	1 450 000	526 896	36	1 491 646	103	2 141 060	148	2 680 636,46	185		
Rozpočet výdajů												
1. Běžné výdaje OSS celkem	**43 373 000**	43 373 000	12 665 440	29	28 785 415	66	43 755 241	101	64 136 867,21	148		20 766 572,00
v tom: platy zaměstnanců a ostatní platby za proved.práci (podsesk. pol. 501,2)	**20 801 000**	20 801 000	4 911 948	24	12 704 220	61	20 046 670	96	29 473 847,00	142		8 672 847,00
z toho: státní správa (rozp.odv,106)	**20 801 000**	20 801 000	4 911 948	24	12 704 220	61	20 046 670	96	29 473 847,00	142		8 672 847,00
platy zaměstnanců (pol. 5011)	**20 599 000**	20 599 000	4 898 148	24	12 677 420	62	20 004 470	97	29 271 847,00	142		8 672 847,00
povinné pojistné placené zaměstnavatelem * (podsesk.pol. 503)	**7 072 000**	7 072 000	1 933 707	27	4 300 703	61	6 780 601	96	10 020 766,00	142		2 948 766,00
převod fondu kult. a soc. potřeb (pol. 5342)	**206 000**	206 000	71 238	35	146 906	71	146 906	71	292 730,00	142		86 730,00
účelové a ostatní běžné výdaje	**15 294 000**	15 294 000	5 748 547	38	11 633 586	76	16 783 064	110	24 349 524,21	159		9 058 229,00
2. Kapitálové výdaje OSS celkem (čerpání z rozp. výd.účtu 916-)	**217 000**	217 000	118 943	55	3 558 386	1 640	3 558 386	1 640	4 689 272,57	2 161		4 474 000,00
z toho :												
systémově určené výdaje-SMVS P 129 010	**217 000**	217 000	118 943	55	3 558 386	1 640	3 558 386	1 640	4 689 272,57	2 161		4 474 000,00
z toho:												
společné projekty EU a ČR												
Úhrn výdajů (1 a 2)	**43 590 000**	43 590 000	12 784 383	29	32 343 801	74	47 313 627	109	68 826 139,78	157,89433		25 240 572,00

MONITORING PROGRAMME 2013 ON ISCVBM

Group	Analyt	Animal	Matrix	2013
A (1)	STILBENS	Cattle (bovine,cow, calf)	Urine, liver	54
		Sheep, goat	Urine, liver	5
		Pig	Urine, liver	38
		Horse	Urine, liver	2
		Poultry (chicken, hen, turkey, aqua)	Muscle	21
		Fish	Muscle	18
		Rabbit	Muscle	1
		Pharm animals	Muscle, liver	2
		Total		**141**
A (2)	THYREOSTATICS	Cattle (bovine, cow, calf)	Urine	87
		Sheep, goat	Urine	3
		Pig	Urine	54
		Horse	Urine	1
		Poultry (chicken, hen, turkey, aqua)	Muscle	21
		Rabbit	Muscle	1
		Pharm animals	Muscle	2
		Milk	milk	22
		Total		**191**
A (3)	TRENBOLONE	Cattle (bovine, cow, calf)	Urine	12
		Pig	Urine	23
		Poultry (chicken, hen, turkey, aqua)	Muscle	21
		Rabbit	Muscle	1
		Pharm animals	Muscle	2
		Total		**59**
A (3)	ANDROGENNOUS STEROIDES	Cattle (bovine, cow,calf))	Urine, muscle	58
		Sheep, goat	Urine	2
		Pig	Urine	67
		Poultry (chicken, hen, turkey, aqua)	Muscle	19
		Fish	Muscle	10
		Pharm animals	Muscle	2
		Total		**158**
A (3)	METHYLTESTOSTERONE	Cattle (bovine, cow, calf)	Urine, muslce	13
		Sheep, cow	Urine	0
		Pig	Urine	11
		Poultry (chicken, hen,turkey,aqua)	Muscle	8
		Fish	Muslce	5
		Total		**37**
A (3)	ETHINYLESTRADIOLE	Cattle	Urine	25
		Sheep, cow	Urine	0
		Pig	Urine	28

		Fish	Muscle	15
		Total		**68**
A (3)	STANOZOLOL	Cattle (bovine, cow, calf)	Urine	14
		Pig	Urine	11
		Horse	Urine	1
		Total		**26**
A (3)	CORTICOSTEROIDES	Cattle (bovine, cow, calf)	Urine	34
		Sheep, goat	Urine	0
		Pig	Urine	51
		Horse	Urine	1
		Total		**86**
A (3)	GESTAGENS	Cattle (bovine, cow, calf)	Fat	22
		Sheep, goat	Fat	2
		Prase	Fat	50
		Horse	Fat	1
		Total		**75**
A (3)	ESTRADIOL	Cattle alive	Serum	14
		Cattle slaughtered	Serum	11
		Total		**25**
A (3)	TESTOSTERONE	*Cattle alive*	Serum	15
		Cattle slaughtered	Serum	11
		Total		**26**
A (4)	RESORCYL ACID LACTONES	Cattle (bovine, cow, calf)	Urine	57
		Sheep, goat	Urine	3
		Pig	Urine	55
		Horse	Urine	1
		Poultry (chicken, hen, turkey, aqua)	Muscle	25
		Rabbit	Muscle	1
		Pharm animals	Muscle	1
		Total		**143**
A (5)	BETA-AGONISTS	Cattle (bovine, cow, calf)	Urine, liver, hair	107
		Sheep, goat	Urine, liver	2
		Pig	Urine, liver	79
		Horse	Liver	1
		Poultry (chicken, hen, turkey, aqua)	Liver	37
		Rabbit	Liver	1
		Pharm animals	Liver	8
		Milk	Milk	10
		Feeding mixture for cattle	Feed	10
		Feed water for cattle	Water	5
		Total		**260**
A (6)	CHLORAMPHENICOL	Cattle (bovine, cow, calf)	Urine, muscle	164
		Pig	Urine, muscle	145
		Sheep, goat	Muscle	2
		Horse	Muscle	2
		Poultry (chicken, hen, turkey, aqua)	Muscle	149

		Fish	Muscle	14
		Rabbit	Muscle	4
		Pharm animals	Muscle	3
		Milk	Milk	63
		Egg	Egg	49
		Honey domestic	Honey	5
		Total		**600**
A (6)	NITROIMIDAZOLES	Cattle (bovine, cow, calf)	Muscle, serum	28
		Sheep, goat	Muscle	0
		Pig	Muscle, serum	46
		Poultry (chicken, hen, turkey, aqua)	Muscle, serum	53
		Fish	Muscle	5
		Rabbit	Muscle	2
		Pharm animals	Muscle	1
		Egg	Egg	11
		Feed mixture for poultry and pigs	Feed	30
		Feeding water for poultry	Water	5
		Total		**181**
A (6)	NITROFURANS	Cattle (bovine, cow, calf)	Muscle	24
		Seep, goat	Muscle	0
		Pig	Muscle	40
		Poultry (chicken, hen, turkey, aqua)	Muscle	40
		Fish	Muscle	9
		Rabbit	Muscle	2
		Pharm animals	Muscle	1
		Milk	Milk	12
		Egg	Egg	11
		Honey domestic	Honey	5
		Total		**144**
A (6)	DAPSONE	Cattle (bovine, cow, calf)	Muscle	26
		Pig	Muscle	50
		Poultry (chicken, hen, turkey, aqua)	Muscle	23
		Milk	Milk	12
		Total		**111**
A (6) B (2d)	CHLORPROMAZINE SEDATIVES	Cattle (bovine, cow, calf)	Kidneys	45
		Sheep, goat	Kidneys	2
		Pig	Kidneys	95
		Horse	Kidneys	1
		Total		**143**
T O T A L				**2474**