CONCLUSIONS AND RECOMMENDATIONS

XXII Seminar on Harmonization of Registration and Control of Veterinary Medicines
Americas Committee for Veterinary Medicines (CAMEVET)
Riviera Maya, Quintana Roo, Mexico
October 10 to 14, 2016

Opening speeches

Dr. Rodolfo Rogelio Monter, District Chief, on behalf of Lic. César Armando Rosales Cancino, SAGARPA Delegate in Quintana Roo, welcomed all the participants, together with Dr. Joaquín B. Delgadillo Álvarez, Mexico Delegate and Member of the OIE Council, Dr. Guilherme H. Figuereido Marques, Brazil Delegate and President of the Regional Commission of the OIE for the Americas, Dr. Enrique Argento, Secretary of CAMEVET, Dr. Ofelia Flores, President of the Committee and OIE Focal Point for veterinary Product from Mexico, B.A. Alexandra Luna Orta, representative of INFARVET/CANIFARMA, and Dr. Jorge Padilla Sanchez, President of ALANAV.

Dr. Figuereido Marques, in his capacity as President of the OIE Regional Commission for the Americas, highlighted the value of the more than 20 years´ work carried out within the CAMEVET, a public-private initiative that is unique in its field.

Dr. Delgadillo Álvarez expressed a warm welcome to the participants, and noted the importance of the event for his country and for the entire region, and the efforts and dedication of the Organization Committee throughout the year.

Dr. Delgadillo went on to inaugurate the XXII CAMEVET Seminar.

President of CAMEVET takes office

Dr. Ofelia Flores took office as the President of CAMEVET Seminar up to the end of it.

Session I – CAMEVET Relations

Application of the documents harmonized by the Committee

Procedures for the participation of CAMEVET in the proposals for the creation and modification of OIE standards.
Rules currently under review.

Dr. Martín Minassian, Technical Assistant of the OIE Regional Representation for the Americas, made a distance presentation that included a description of the history and structure of the OIE, and of the functions of each of its specialized commissions, working groups and ad hoc groups.

He went on to present a summary of the 6th Strategic Plan of the OIE, whose main objectives comprise managing risks to health, the improvement of food safety, transparency and good governance.

He provided a detailed description of the steps required for the approval of standards and recommendations with a view to incorporating new standards to the Manuals and the Codes.

He also mentioned the most relevant events of the 84th. General Session, relating to

veterinary medicines, as CAMEVET competences. These include the following, among others:

The presentation of the Technical Topic N° 1 proposing the use of tools for the calculation of direct and indirect costs in animal health.

The Technical Topic N° 2, about the OIE activities relating to the Resistance to Antimicrobials (AMR), from the "One Health" concept and its importance for the OIE. He established that some of the objectives are to ensure the availability of antimicrobials that are critical to veterinary medicine.

To this end, the organism is working on the responsible use of antimicrobials and the collection of data relating to use in the various countries. In this regard, it was noted that the response obtained to date has been low, since only 19 of the 30 countries from the Americas Commission have answered the surveys on this topic. He clarified that they will ask for data again during this year and CAMEVET should encourage the provision of information.

He mentioned that modifications to 22 specific chapters of the Terrestrial Manual have been adopted, and chapters relating to vaccine manufacture and quality control have been added, taking in account that vaccination has a role to reduce the use of antimicrobials.

The project for the preparation of guidelines for the production of reference antigens and the virtual Biobank of the OIE was mentioned.

Lastly, Dr. Minassian presented the new diagnostic kits validated by the OIE, encouraging the industry representatives to participate in the procedure.

Status of the implementation of harmonized documents in the member countries.

Dr. Enrique Argento highlighted the difficulty in tracking the application of CAMEVET documents given that, as recommendations, they are not mandatory, and due to differences in legal mechanisms for their internalization.

He also recalled the concept presented in previous Seminars regarding the referential use of the approved documents.

He went on to enumerate the approved documents that were published more than ten years ago and are therefore up for revision. He pointed out that this revision does not necessarily imply that the documents will be modified.

Reviewing proposal of harmonized documents with more than 10 years since their approval.

A working group was created for reviewing the Rule for Good Manufacturing Practices for Veterinary Products, with the coordination of the Official Sector from Costa Rica and the participation of the Official Sectors from Argentina, Brazil, Chile, Colombia, Guatemala, Mexico and Panama and private sector representatives from ADIPRAVE (Uruguay), ALANAC (Brazil), ANALAV (Mexico) ALFA (El Salvador), ASIFAN (Costa Rica), ASOVET (Guatemala), CADIN (Nicaragua), CAPALVE (Paraguay), CAPROVE (Argentina), CEV (Uruguay), CIG (Guatemala), CLAMEVET (Argentina), INFARVET (México) and SINDAN (Brasil), FENALCO (Colombia), and FIVETCA.

It was noted that there is a draft underway concerning the rules for labeling and for

registration forms, which will be evaluated later on during this seminar.

Participation of CAMEVET in the VICH Outreach Forum

Dr. Enrique Argento made a presentation of his participation in representation of the Committee at the meeting held in Brussels in June 2016.

He highlighted the importance of the participation of the representatives from the different countries of the American continent in the meetings, and the participation of CAMEVET in the Working Group for the modification of the VICH Stability Guide for Active Ingredients and Veterinary Pharmaceuticals for climate zones 3 and 4.

Dr. Argento informed that a decision was made to hold the next meeting of the Steering Committee and the Outreach Forum in Buenos Aires in February 2017.

Dr. Rick Clayton, Technical Director of Health for Animals and member of the VICH Steering Committee, made a presentation to describe the operation, objectives and achievements of the organism referred to. Among these, he noted the application of the VICH Guides and the associated advantages.

He also mentioned the increased importance of the activities of the Outreach Forum, with the participation and contribution of a growing number of countries and regional organizations, including CAMEVET.

Dr. Eric De Rydder, a member of the regulatory affairs group of Health for Animals and member of the VICH Steering Committee, made a presentation on the convergence in regulatory affairs and the vision of industry with regard to regulation towards 2025.

In times of globalization, he emphasized the need for economy of resources that will lead to the use of a unique specimen dossier for all the countries. He highlighted that CAMEVET is making progress in this topic with the harmonized registration forms.

Conclusions of the Plenary Meeting of the official sector

Dr. Gloria Alarcón, OIE Focal Point for Veterinary Products from Paraguay, presented the conclusions of this meeting.

The final document of the meeting is included as an *Annex I*

Conclusions of the Plenary Meeting of the private sector.

Dr. Rodas Serrano, representative of FIVETCA, presented the conclusions of this meeting.

The final document of the meeting is included as an *Annex II*

Presentation of the 2016–2020 CAMEVET Strategic Plan

Dr. Carlos Francia, representative of CAPROVE and member of the working group, accompanied by Dr. Amani Desuque, representing the Official Sector in Argentina, presented the document and described the objectives selected by the member countries.

Having complied with the required distribution of the document and reached a consensus regarding the comments received, the document was put to the vote and approved. The document is included as an attachment.

Session I – Working Documents

Registry for Homeopathic Products

Dr. Mario Renck Real made a presentation explaining the technical answers to the comments received, such as those relating to the concepts of dilution and energization as a basis for assuring absence of toxicity.

Following its submission to the plenary meeting, the document was forwarded to Step III.

Bioequivalence Guide

Dr. Carlos Francia made a presentation of the document prepared, commending the high level of commitment of the Working Group, which allowed this complex topic to be addressed in the brief time span available.

The document was sent by the Office of the Secretary in the three languages last October 7, and is currently in Step III of the process, awaiting comments of the members of CAMEVET.

Instructions for Completing CAMEVET Forms for the Registration of Pharmacological and Biological Products

Due to the absence for personal motives of Dr. Federico Luna, Dr. Amani Desuque, representative of the Argentine official sector, and Dr. Carlos Francia presented a progress report on the instructions for the completion of registration forms for veterinary products.

They explained that the instructions constitute a guide, and therefore the contents recommended under each item are not mandatory.

The guides are available in the three languages of CAMEVET, and will be sent to the Secretariat for distribution and subsequent forwarding to Step III.

Labeling of Veterinary Products

Dr. Carlos Francia made a presentation on this topic on behalf of Dr. Niels Scherling, coordinator of the working group.

He informed of the progress made by the working group, which includes the completion of a survey that was answered by only 7 Member Countries. The aim of the survey was to determine the most common and best understood mandatory phrases in the region.

The results of the survey will lead to the proposal of a brief document called Agreement on Preferred Phrases. This draft will be distributed to the Spanish speaking countries, as they are the ones involved in the topic. Once the phrases have been harmonized by these countries, the document will be translated into the other languages and submitted to the consideration of all the countries.

On a separate note, Dr. Francia commented that the work group detected that the labeling rule currently in force is due for review. To this end, a work group was created, to be coordinated by CAPROVE (Argentina) with the participation of the Official Sectors from Argentina, Belize. Colombia, Guatemala, and Panama, and the private sectors of, ADIPRAVE (Uruguay); ALANAC (Brazil), ALFA (El Salvador), ANALAV (México); ANVET (Chile), APROVET (Colombia), ASIFAN (Costa Rica), ASOVET (Guatemala), CADIN (Nicaragua), CEV (Uruguay), CIA (Costa Rica), CIG (Guatemala), CLAMEVET (Argentina),

FENALCO (Colombia), INFARVET (México) and SINDAN (Brazil).

Policy governing generics

Dr. Ofelia Flores Hernández, Mexican Focal Point, presented a survey that was distributed to the Focal Points. The survey comprised 7 questions and was answered by 14 countries. She pointed out that intensive follow-up was needed to obtain this level of response which, however, is not sufficient. Consequently, the survey is not viewed as a complete success.

An analysis of the responses received indicates that the topic continues to elicit highly differing opinions, and reflects interest in the use of interchangeability, for which there is a draft guide on Bioequivalence. The countries may evaluate the enforcement of this guide.

Additionally, it was suggested to include the definitions of generics and innovators in the glossary. The definitions will be sent by the Work Group to the Secretariat for distribution and harmonization among the member countries.

Dr. Flores Hernández also indicated the need to revise the registration guides. This will be done simultaneously with the revision of the Guides for the Completion of Registration Forms.

Dr. Barabara Cordeiro, Focal Point from Brazil, commented that she had been unable to answer the survey due to the change in focal point. Dr. Catya Martínez, Focal Point from Panama, gave the same reason for not answering the survey. It was agreed that the survey will be distributed again to Brazil and Panama and other countries that did not answer it, and that the full data obtained would be processed at a later date. Once this has been done, a final report will be distributed to the countries.

The document will remain in the Work Group, in Step II status.

Guide for the Registration of Diagnostic Kits for Diseases

Dr. Byron Rippke, Focal Point from the United States of America and coordinator of the working group, presented the document prepared during the year.

He informed of the scope of the regulation in his country, and noted that it establishes the requirement for kits to be effective, for their specificity and sensitivity to be validated, and that they must be evaluated by three laboratories. They must include an indication of whether they are for screening or confirmation, and in some cases they may be reached by national regulations (as in the case of diseases included in a campaign).

Dr. Rippke expressed that the group has prepared a draft guide that has been translated into Spanish and Portuguese.

Dr. Emigdio Lemes Anaya, focal point from Cuba, mentioned that there may be some language problems which will be solved by the Work Group.

This document will remain in the Work Group, in Step II, and will follow the normal approval process subsequently.

Pharmacovigilance System

Dr. Camilo Giraldo, expert in Pharmacovigilance, explained the objectives and benefits of implementing a pharmacovigilance system. He noted that both companies and regulatory

authorities are under the obligation of keeping this system operative and up-to-date. However, it is necessary to make this known publicly so that society as a whole becomes aware of the benefits of reporting for human and animal health.

He noted the unfathomable importance of achieving harmonization in these topics and of the proper use of the data received. To this end, there must be a general legal basis, but the details must be contained in guidelines in order to avoid the difficulties of modifying existing legislation.

This presentation was made as part of the activity carried out by the working group.

Guide for the implementation of Pharmacovigilance Systems

Dr. Gabriel Ardiles, coordinator of the working group, presented a first agreed draft translated into English and Portuguese.

Dr. Emigdio Lemes Anaya asked about the costs relating to causes analysis, and the speaker answered that these must be borne by the holder of the registration.

Dr. Barbara Cordeiro commented that the term for reporting serious cases (15 days) seems too long. Dr. Ardiles answered that this is a maximum term and is necessary to carry out investigation. There is an exception that is applied when it is suspected that an event is related to product quality, in which case the term is 3 days. Dr. Fernando Zambrano Canelo, focal point from Chile, backed this explanation.

The document will be distributed by the Office of the Secretary, and is forwarded to Step III.

Resistance to Antiparasitics

In view of the absence of Dr. Berta Chelle, Focal Point from Uruguay, who was scheduled to make a presentation on this topic, Dr. Mercedes Etcheverry informed that Uruguay is willing to share its experience but that this topic is not considered for purposes of registration. Consequently, Uruguay is against the discussion of this topic for the creation of a guide.

Alexandra Luna Orta (B.A.), representative of INFARVET, informed that this Association has prepared a document on this topic, which will make available to CAMEVET, and offered to coordinate the corresponding working group. Once the subject has been evaluated, its scope will be defined. To this end, a working group was created, with the coordination of INFARVET, and comprising the Official Sectors of Colombia, Guatemala, México and Panama and the following chambers: ALFA (El Salvador), ANALAV (México), APROVET (Colombia), ASIFAN (Costa Rica), ASOVET (Guatemala), CADIN (Nicaragua), CAPROVE (Argentina), CEV (Uruguay), CIG (Guatemala), CLAMEVET (Argentina) and SINDAN (Brazil)

Proposal to review the stability guideline.

Dr. Amani Desuque, representative of the Argentine official sector, informed that she has been working on a proposal to modify the stability guide in response to comments presented by CLAMEVET and CAPROVE.

Drs. Milena Aguirre and Andrea Fraga explained the technical proposal, and provided the bibliographic background for it.

They explained that the problem lies with the use of lower temperature limits which cause difficulties relating to product storage and transport. Consequently, changes are proposed to the phrases used in product labeling to adjust them to the available international bibliography.

Dr. Fernando Zambrano Canelo expressed that these bibliographic references were considered at the time of the creation of the current standard, but it was deemed that the phrase contained in the document constituted a more suitable solution.

It was decided to create a working group to study this matter. The working group will be coordinated by CAPROVE, and made up by the official sectors of Argentina, Chile, Guatemala, Mexico, and Panama, and the following chambers: ALANAC (Brazil), ANALAV (Mexico), ANVET (Chile), APROVET (Colombia), ASOVET (Guatemala), CADIN (Nicaragua), CAPALVE (Paraguay), CEV (Uruguay) CIA (Costa Rica), CIG (Guatemala) CLAMEVET (Argentina), FENALCO (Colombia), INFARVET (Mexico).and SINDAN (Brazil).

Criteria for authorizing mixed plants

Dr. Carlos Rufrano, coordinator of the working group, made a presentation where he explained the concept of a mixed plant as one where veterinary and human products can be manufactured on the same premises. He said that, technically, this should be accepted because the cleaning validation and enforcement of GMP provide sufficient guarantees.

Some countries of the region authorize this type of plant and others do not.

A survey was carried out but only three countries answered: Argentina, Uruguay and Ecuador. Based on the lack of interest, a decision was made to drop the subject.

Distribution and transport guideline

Dr. Carlos Rufrano, Working group coordinator, explained the document was sent to all countries in the three languages. Comments was received only from some Spanish speaking countries.

The comments received were included in the Spanish version and it was sent again to all Spanish speaking countries on July 27th 2016 for comments.

No new comments were received, so it was proposed to translate and send this new version in the three languages.

Dr Benigno Alpízar, Focal Point from Costa Rica, proposed a new 60 days deadline for comments, and if there are none the document will be approved.

Training

Dr. Liliana Revolledo, author of the project, made an electronic presentation describing the scope and objectives of the project. She explained that the proposal involves distance training, and noted the possibility of using different software and web platforms, some of which are free and others have a cost.

The proposal includes theoretical activities, study groups and practical work. The courses will be divided into modules of increasing complexity.

The topics to be covered in the training include: basic principles relating to regulatory issues, good manufacturing practices for pharmaceuticals and for biologicals, common

protocols for product efficacy, pharmacovigilance principles, and safety studies. Issues will be included relating to the operation of the OIE, the use and scope of the OIE Manual and health Codes, and the activities carried out by the Regional Representation and CAMEVET.

This project will be submitted to the Regional Representation for evaluation.

Guide for potency test for vaccines containing in their formulation Bovine Viral Diarrhea Virus

Dr. Viviana Parreño, from the PROSAIA foundation, presented a technique for controlling the potency of vaccines that contain BVDV.

During the presentation, she showed the results of studies that determine the correlation between the serological responses of a bovine model and a Guinea pig model.

A working group was formed under the coordination of Dr. Parreño (Fundacion Prosaia INTA Argentina) the official sectors of Chile, Colombia and México and the Association CAPROVE (Argentina), CEV (Uruguay), INFARVET (Mexico) and Sindan (Brazil).

Veterinary Products for Aquaculture

Dr. Fernando Zambrano Canelo, new coordinator of the working group in replacement of Dr. Glen Gifford, gave a presentation on the progress made in the preparation of the related document.

He noted that this is an innovative document that includes concepts for regulating vaccines for aquaculture in the Americas.

He also noted that although the documents underway in English and in Spanish are currently in version 4, final draft stage, there is a delay with the incorporation of comments in Portuguese. Consequently, when the document has been completed, it will be submitted to the Secretariat to be forwarded.

New technical topics proposed

The official sector of Brazil proposed that work be carried out on the issue of **Stem Cells**. The plenary session requested that it prepare a concept document for the next Seminar presenting the proposed topic that will serve to evaluate the importance of this topic for the sector and the relevance of its harmonization.

The official sector of Brazil also proposed that work should continue on the subject of products that do not require registration. On this matter, Dr. Emigdio Lemes Anaya, of the official sector of Cuba, proposed that work on the subject should commence with a proper definition of terminology for incorporating to the Glossary. The coordinator of the group, Dr. Javier Carracedo, informed that, during a face-to-face meeting with the members of the working group, it was decided to propose a change to the name of the topic, to "Guide for the Classification and Registration of Veterinary Products without Therapeutic Indication". The proposal was accepted and, in view of the clarification this signifies, the official sectors of Costa Rica, Mexico and Panama, and the following Associations: ANALAV, CADIN and INFARVET, joined the Working Group that was formed during the XXI Seminar.

Election of new authorities to the Executive Committee

In accordance with the new regulation of the CAMEVET, official representatives and members were elected to cover the positions in the Executive Committee.

The Focal Points from Argentina, Dr. Federico Luna, from Brazil, Dr. Barbara Cordeiro, from Panama, Dr. Catya Martínez and from Paraguay, Dr. Gloria Alarcon, were elected in representation of the Official Sector.

The mandate of the representatives from the Official Sector will be for a term of three years, in line with the Regulation.

The Supporting Members elected to the Executive Board comprise the representative of the Associations from Argentina, Dr. Carlos Rufrano (CLAMEVET), from Costa Rica, Dr. Claudia Re-Huezo (ASIFAN), from Paraguay, Dr. Edith Gamarra (CAPALVE) and from Uruguay, Dr. Mercedes Etcheverry (CEV).

The representatives from Supporting Members will have a mandate of one year, according to the Regulation.

Invitations received

The Secretariat informed that an invitation was received from the OIE for one or more representatives of CAMEVET to attend the forthcoming 23rd Conference of the Regional Commission of the OIE for the Americas, to be held in Santa Cruz de la Sierra, Bolivia, from 14 to 18 November 2016 as observers. Dr Fernando Zambrano Canelo proposed that the CAMEVET representatives might be Executive Board members one from the oficial sector and one from the prívate sector. The designation will be done in the next Executive Board meeting.

Dr. Ofelia Flores Hernández expressed that she received instructions from Dr. Delgadillo Álvarez to invite all those present at the plenary to the 4th. World Conference of the OIE on Animal Welfare, to be held in Guadalajara, Jalisco, Mexico, from 6 to 8 December 2016.

Notifications

Dr. Ofelia Flores Hernández notified that Dr. Delgadillo Álvarez, Delegate for Mexico and Member of the Council of the OIE, signed a SENASICA – OIE Agreement which includes a Regional Seminar for the countries of the Americas on Antimicrobial Resistance, to be held in Mexico. Information on the venue and dates of this Seminar will be provided as soon as possible.

Approval of proposed venues for the following Seminars.

Through its Focal Point, Dr. Gloria Alarcón, Paraguay proposed to be the venue of the next Seminar, and presented a video to support this proposal.

The proposal was accepted unanimously.

CAMEVET Budget and Resources

Dr. Martin Minassian presented the balance sheet of CAMEVET for the budget at September 30, 2016, which was approved.

Conclusions and recommendations. Reading and approval of the final document.

The document containing the conclusions and recommendations was read and, following some suggested modifications, was approved.

List of acronyms used in the document

ADIPRAVE	Asociación de las Industrias de Productos Agroquímicos y Veterinarios (Uruguay)
ALANAC	Asociación de Laboratorios Farmacéuticos Nacionales / Associação dos Laboratórios Farmacêuticos Nacionais (Brasil)
ALFA	Asociación de Laboratorios Farmacéuticos de El Salvador
ANALAV	Asociación Nacional de Laboratorios Veterinarios
ANVET	Asociación Nacional de Laboratorios Veterinarios (Chile)
ASIFAN	Asociación Farmacéutica de la Industria Nacional
ASOVET	Asociación de Productos Veterinarios (Guatemala)
CADIN	Cámara de Industrias de Nicaragua
CAMEVET	Comité de las Américas de Medicamentos Veterinarios
CAPALVE	Cámara de Laboratorios Paraguayos de Productos Veterinarios
CAPROVE	Cámara Argentina de la Industria de Productos Veterinarios
CEV	Cámara de Especialidades Veterinarias (URUGUAY)
CIA	Cámara de Insumos Agropecuarios
CIG	Cámara de la Industria de Guatemala
CLAMEVET	Cámara de Laboratorios Argentinos Medicinales Veterinarios
FDA	U S Food and Drug Administration Administración de Medicamentos y Alimentos
FENALCO	Federación Nacional de Comerciantes
FIVETCA	Federación de Industria Veterinaria Centroamericana
INFARVET / CANIFARMA	Industria Farmacéutica Veterinaria (México)
OIE	Organización Mundial de Sanidad Animal
OIRSA	Organismo Internacional Regional de Sanidad Agropecuaria
SENASA	Servicio Nacional de Sanidad y Calidad Agroalimentaria (Argentina)
SINDAN	Sindicato Nacional da Industria de Produtos para Saúde Animal
VICH	International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products

List Annexes:

Annex I: Minute Plenary meeting of the official sector
Annex II: Minute Plenary meeting of the private sector.
Annex III: Strategic Plan 2016-2020
Annex IV: Balance 2015-2016

Annex I

MINUTES OF MEETING OF THE OFFICIAL SECTOR

1.- Dr. Ofelia Flores thanked Dr. Guillerme Marques, Regional President of the OIE for the Americas, for his participation and involvement in the CAMEVET Seminar, and welcomed all the participants.

2.- The topics discussed at the meeting of the Executive Committee held previously were listed, as follows:

1. Technical issues proposed for the official sector.
2. Functioning of Work Groups.
3. Training.
4. Participation of Focal Points at future CAMEVET Seminars.

3.- Presentation of the Officers attending the meeting.

The proposed topics were then described in greater detail:

1. The following technical issues were proposed:
   a) Review of the Good Manufacturing Practices Guide, proposed by Costa Rica.
   b) Resume work on "Products exempted from Registration", with a request to begin by drawing up a Glossary for the definition of concepts.
   c) Registry of Stem Cells, proposed by Brazil.
2. Concern is expressed over the lack of participation of the people registered in the Work Groups. Work in these groups is generally carried out by the Coordinator. A request is made to encourage participation.
3. Dr. Revolledo will make a presentation on the Training blueprint.
4. The participation of Focal Points in CAMEVET Seminars has become increasingly difficult, and most often this is due to late reception of the invitation by the countries, making it difficult to obtain the necessary permits. Another important matter is the budget of the national organisms to cover expenses relating to participation in Seminars. Previously, the OIE used to conduct a Workshop every two years directed at the Focal Points. However, due to budgetary constraints, these have been suspended.

A special request is made for the organizing country of subsequent Seminars to establish and communicate the date of the event with greater anticipation, as this also has an impact on the hiring of services, leases, and all the logistics surrounding the event. It is also requested that the invitations be distributed and the agenda be defined

and communicated well in advance to allow sufficient time for the countries to arrange the participation of their focal points.

There being no further business to discuss, the meeting was concluded.

Annex II

Monday, October 10, 2016
Riviera Maya – Quintana Roo – Mexico

Plenary Meeting of the Industry Sector

Minutes of the meeting
The representatives from Industry of the CAMEVET gathered in a plenary meeting coordinated by the members of the Executive Committee, Dr. Mercedes Etcheverry (CEV – Uruguay), Dr. Carlos Francia (CAPROVE – Argentina), Dr. Guillermo Leonel Rodas Serrano (FIVETCA – Federation of the Veterinary Industry of Central America) and Dr. Carlos Rufrano (CLAMEVET – Argentina), and reached the following conclusions:

a. The objective of the industry is to make CAMEVET a strong entity with decision-making power, to accelerate harmonization and ensure that the agreements reached are applied within each country.
b. As a sign of this commitment, a proposal will be made to the Plenary meeting to use CAMEVET funds to guarantee the participation of the Heads of Veterinary Product Registries.
c. With regard to the objective proposed in item (a) above, concern was expressed over the manner in which the new regulation was approved, without giving the industry the right to a say, a right guaranteed by the previous regulation.
d. Having detecting various flaws in the substance and the form of the new regulation referred to, a commitment was made to present proposed modifications to it for their discussion at the following meeting of the Commission for the Americas of the OIE to be held next November 14.
e. To facilitate the preparation of proposals, the repealed regulation and the draft prepared by the Executive Committee will be distributed.
f. Proposals will be focused on:
    a. Returning the former powers to the plenary meeting made up by the official sectors (with authority to a say and a right to vote) and industry (with authority to a say but no right to vote).
    b. The mechanism for electing representatives from industry.
    c. The use of CAMEVET resources.
    d. Making the CAMEVET an annual event to be held on the same date every year, to facilitate the organization, and comply with the requirements of the OIE in order to issue invitations to the official sectors in a timely manner.
    e. Description of the functions and autonomy of the Office of the Secretary of CAMEVET.
g. Based on the outcome of the meeting, a decision will be made regarding whether to choose the representatives from Industry to serve on the Executive Committee or to leave these posts vacant.

Annex III

CAMEVET STRATEGIC PLAN 2015-2020

Contents

Introduction

The COMMITTEE OF THE AMERICAS FOR VETERINARY MEDICINAL PRODUCTS, work group for the harmonization of the registration and control of veterinary medicines under the framework of the World Organization for Animal Health (OIE), has been working uninterruptedly since 1992, when the first Seminar for the Harmonization of Rules governing the Registration and Control of Veterinary Medicines was held in the city of Buenos Aires, Argentina. The Committee has a unique nature, as it brings together government and private sector efforts in a framework of open and true discussion. This committee has an annual meeting since 1998.

Its objectives, as indicated in the name of the opening seminars, have at all times been the harmonization of the rules governing the registration and control of veterinary medicines to ensure that products marketed in the region are manufactured, registered and controlled using equivalent systems in order to facilitate their trade between the different countries.

This process has brought significant progress in registration procedures for veterinary medicines, as it has permitted each player to have a better knowledge of the needs and obligations of the other players, generating an alignment among authorities in the sector that has served to encourage permanent updating and equalization of technical requirements. Additionally, it has led to a significant improvement in the work carried out by the veterinary services in the region. The discussion and efforts to harmonize essential requirements for the sector have led to new levels of requirements relating to the registration and control of veterinary medicines.

The deliverables from the group, in the form of rules applicable to the sphere of reference, constitute a set of documents that adapt the essential technical requirements for achieving effective, safe, innocuous and in compliance with quality standards veterinary products to the actual circumstances of each member country, while keeping them equivalent to those recommended internationally.

The first strategic plan was prepared in 2010, and envisaged work on a few objectives to

focus activities and achieve results in the medium term. The objectives selected at that time were:

- Prepare technical rules that enable the adaptation of international regulations to veterinary medicine registration and control in the countries of the region.
- Promote the full internalization of the regulations proposed by CAMEVET.
- Give visibility to the importance of veterinary medicines registration and control activities as a primary link in the animal origin food production chain.
- Encourage the participation of representatives from the region at forums for generating rules that pertain to the activity of the veterinary industry.
- Divulge the documents prepared by CAMEVET to the OIE member countries.
- Promote the incorporation of the technical rules prepared to the OIE Standards Manual.

These objectives have been achieved in varying degrees, as analyzed below.

Analysis of Results from the Strategic Plan 2010 -2015

- Prepare technical rules that enable the adaptation of international regulations to veterinary medicine registration and control in the countries of the region.

The results under this objective have been very fruitful. A very significant set of technical rules has been drawn up and approved that facilitate registration processes. Additionally, since these rules are equivalent to those issued by international organisms, work is being carried out to reduce the need for local trials when prior trials that are in line with the regional regulation are available. These rules include the following:

- BOV 001 Guide for Potency and Efficacy Trials for Bovine Vaccines whose formulation contains Bovine Herpes Virus (BOHV-1), the Causal Agent of Infectious Bovine Rhinotracheitis (IBR)
- BPM 004 Inspection Guide for Pharmacological Products (Including Ectoparasitics)
- ECT 001 Manufacture of Ectoparasitic Veterinary Products
- EST 001 Guide for the Preparation of Stability Studies of Veterinary Pharmaceuticals
- FORM 003 Registration Form for Subunit Immunogens Obtained Via Biotechnology
- GLO 001 Glossary of Terms
- RES 001 Technical Guide for conducting residue metabolism and kinetic studies of pharmacological agents for veterinary use in food-producing animals
- RES 002 Guide for calculating the withdrawal period in edible tissues
- RES 003 Guide for validating analytical methods for determining residues in animal origin biological matrixes
- ROT 002 Synonymity Agreement

In addition to these new documents, the following was reviewed and updated:

- AI 001 Efficacy Trials for Registration of Internal Antiparasitics for Ruminants and Swine

Despite having been a very productive period, communication difficulties came to light inside the work groups, which extended the time required to produce each document unnecessarily. Work is underway to solve this situation.

- Promote the full internalization of the regulations proposed by CAMEVET

Following intense debates, it has become evident that full internalization is very difficult –if not impossible- to achieve. This is because, in many cases, the generation of new rules entails complex legal processes that are different in each country. It has also been understood that the incorporation of the regulations to a legal framework can constitute a hindrance, since the process would have to be reinitiated every time an update is required. Consequently, the criterion currently promoted consists in applying the regulations of CAMEVET as referential guidelines accepted at a regional level, both in industry and in the government sector, thus avoiding the problems referred to.
Nevertheless, the enforcement criteria that have arisen are uneven in many cases, leading to confusion and difficulties in the industry. It is considered that, despite the significant progress achieved, this objective must be redrafted for the following period.

- Give visibility to the importance of veterinary medicines registration and control activities as a primary link in the animal origin food production chain

Although certain specific actions have been carried out, including the submission of memos by the secretariat of CAMAVET to the heads of services, it cannot be said that progress has been made in the understanding of the importance of registration and control of veterinary medicines in relation to the production of food of animal origin.
This is because, in every case, activities relating to the registration of veterinary medicines are linked to other activities that are quantitatively more burdensome. In every country of the region, registration comes either under the sphere of the Ministry of Agriculture – which also controls foodstuffs, or under the Ministry of Health – which also controls human medicines.
It is important to note that, at present, worldwide concern over the emergence of multi-resistant strains of microorganisms has become a global problem for public health. This is evidenced by the fact that three international agencies such as the FAO, WHO and OIE have included work to mitigate the effect of these multi-resistant strains at the top of their agenda. Consequently, the registration, rational use and control of veterinary and human medicines are currently the focus of action to improve the situation.
It is clear that CAMEVET must take advantage of this opportunity to grow stronger.

- Encourage the participation of representatives from the region at forums for generating rules that pertain to the activity of the veterinary industry

The participation of CAMEVET in different international forums, such as VICH Outreach Forum, has been an all-round success. The continued presence of CAMEVET representatives and their participation in discussions led to their integration into various work groups focused on the creation and modification of current regulations.
Although the CAMEVET has not been represented officially in the Codex, the countries of the region have begun to interact and take common stands toward issues that might affect their interests. A clear example of this is the joint intervention of Argentina, Brazil, Uruguay and Costa Rica to request the review of the MRL proposed for ivermectin in muscle by the JECFA.

- Divulge the documents prepared by CAMEVET to the OIE member countries.

The dissemination of the activities of CAMEVET was severely hindered by problems relating to the updating of the OIE web page. As an agency that operates under the umbrella of the OIE , the only means to make known the results of its work is via this web page. For various reasons, web contents have not been updated since 2010. Updating will be done during 2015.

- Promote the incorporation of the technical rules prepared to the OIE Standards Manual

Communication flaws and difficulties arose. The need for the heads of service to endorse the projects proposed by CAMEVET posed an obstacle difficult to overcome. Solutions are being sought to make this type of effort materialize. Between these activities, the continued CAMEVET presence as an observer in VICH Outreach Forum meetings can be mentioned.

Methodology for Preparing the Plan

A survey was conducted among the member countries, requesting each country to indicate the top three issues that, in their opinion, the CAMEVET should focus on during the period 2015 - 2020.

The survey was sent to all the member countries by the CAMEVET SECRETARIAT on 19 December 2013, with 19 February 2014 as the due date for delivery, and with a reminder of the due date made on 27 January 2014. As this cycle did not achieve significant results, the request was reiterated during the XX Seminar, on 20 November 2014, with 20 February 2015 as the new due date.

The following countries answered the survey (in alphabetical order):

- Argentina
- Canada
- Cuba
- Colombia
- Ecuador
- Guatemala
- Jamaica
- Paraguay
- Uruguay

Responses to the survey led to a set of topics the member countries wish to see included in the objectives of the organization for the next five year period. These topics are listed below:

- Internalization of CAMEVET Rules
- Harmonization of labelling
- Resistance to antimicrobials and antiparasitics and their impact on public health
- Pharmacovigilance
- Monitoring and control of residues in edible tissues and by products of animal origin (like milk, eggs, honey and meat
- Unification of criteria for standardizing withdrawal periods
- Updating of good manufacturing practices for veterinary medicines
- Informal practices in trade and manufacture of veterinary medicines. Contraband.
- Strengthening of the National Veterinary Service in relation to sanitary surveillance
- Continuous Training
- Assessment of the proper use of veterinary medicines. Good Prescription Practices.
- Improved communication.

Following an initial analysis, it was considered that, in terms of the generation of national plans, the monitoring and control of residues in milk, eggs and meat is an issue that in most cases is outside the scope of the Registration of Veterinary Medicines. Consequently, it was decided to exclude this issue as an objective but to include it in the training programs.

The unification of criteria for standardizing withdrawal periods has been worked on previously, through the preparation of the Guide for Calculation of Withdrawal Periods in Edible Tissues. However, it continues to pose certain aspects that remain unsolved at world level. For example, under the sphere of the VICH, the criterion applied is the risk analysis, and each country applies it differently, leading to the establishment of disparate withdrawal periods. This generates confusion. However, solving this issue does not seem the competence of the CAMEVET, but its treatment in other international forums could be proposed.

The internalization of CAMEVET Rues is an issue that has been worked on since the creation of the Committee, and –as mentioned- was included in the Strategic Plan for 2010-2015, with the outcome indicated above. Issues continue to emerge that need to be solved.

On another matter, the enforcement of the "One Health" concept to reduce the risk of diseases with a major impact on the interface between animals, man and ecosystems requires focusing on the work carried out in certain non-traditional areas, such as infectious diseases of wild animals, work animals, competition animals, and companion animals, in addition to food-producing animals (included the aquatic species).

It is also vital to continue collaborating toward the strengthening of technical capabilities, management, legislation and good governance relating to member country veterinary services, an activity the OIE pursues through the World Animal Health and Welfare Fund, and in collaboration with partners around the world such as the FAO, the WHO, and regional partners, as well as through national, regional and international donors. Attention will be paid to issues relating to the "One Health" concept, the development and strengthening of capacities, and strengthening of communication skills and the supply of information relating to veterinary medicines to the Delegates to the OIE and to national focal points.

Within this framework, work is needed in the strengthening of communication tools and their interface with veterinary professionals, the public at large, and the media. It is worth noting the worldwide improvement and harmonization of veterinary legislation, the use of veterinary medicines, and continued veterinary education. The CAMEVET will also work with academic institutions, professional associations and organizations to improve training in the regulatory aspects relating to veterinary medicine – an issue not included in the agenda for professional training in the sector.

Following this analysis, the objectives listed below were selected from the topics proposed by the member countries.

Objectives

a. Prepare science-based rules and guidelines applicable to the countries of the region and in line with international guidelines relating to the following topics, applying animal health, veterinary public health, and animal welfare principles:
    a. Good Use Practices
    b. Labeling
    c. Resistance to veterinary antimicrobials and antiparasitics
    d. Pharmacovigilance
b. Review and update the full set of rules applicable to Good Manufacturing Practices relating to Veterinary Products, to continue the process of improving the installed

capacity in the region and guaranteeing the continued production of safe, effective and in compliance with quality standards veterinary medicines.

c. Design a training system that will strengthen the capacity of the government authorities of the member countries relative to the registration and control of veterinary medicines, with the aim of improving animal health, veterinary public health and animal welfare, as well as their capacity for participating in the preparation of international rules and guidelines relating to these topics, and strengthening their ability to apply these rules and guidelines.
d. Communicate, in a timely and accurate manner, information on the progress made in the harmonization of rules governing the registration and control of veterinary medicines in the regional and international sphere, availing itself of modern information technology, unofficial information and tracking systems.
e. Promote activities that facilitate the internalization of approved work guides and the enforcement of common regional criteria in all matters relating to the registration and control of veterinary medicines.
f. Continue and strengthen the participation of CAMEVET and its member countries in international forums where work is carried out in the design of policies and governance that relate to veterinary medicines, animal health, veterinary public health and animal welfare decision-making.

The Strategic Plan must be followed-up by an initial Work Program that puts in practice the objectives, and that will be put to the approval of the 2015 Assembly, with an estimate of the resources necessary for its implementation to be prepared by the Executive Committee. A Work Program will be submitted each year during the planning period, and a progress report on these objectives will be prepared during the third year of the Plan (2018) with a view to making the necessary adjustments to the Work Program in order to achieve the objectives by the year 2020.

Detailed Strategic Objective

Prepare science-based rules and guidelines applicable in the countries of the region and aligned with the international guidelines relating to the following issues, applying animal health, veterinary public health and animal welfare principles: ➢ Good Use Practices ➢ Labeling ➢ Resistance to internal antimicrobials and antiparasitics ➢ Pharmacovigilance

It should be taken into account that the preparation of work guides is an essential activity for the harmonization of requirements for product registration. This activity has been carried out by CAMEVET since its commencement and is one of the reasons for its existence.
The issues selected to work on come under the sphere of the control of veterinary products, and are a core responsibility of the Public Health sector. They are also included in the international policy agenda, which will contribute to project the CAMEVET to other forums and regions.
Some of these issues have already been covered, although without achieving an effective solution. For example, labelling is a very important issue because it represents the link between the authority and the consumer. The lack of harmonization results in high costs which are transferred to the price of products, leading to a drop in accessibility to veterinary medicines and, consequently, to losing the battle against more inclusive veterinary health. Solving this issue would represent a huge success for all the parts involved in the system.
Another example has been the issues around the lack of compliance of product withdrawals. This caused residues above the approved tolerances, commercial sanctions and banning of correctly registered drugs. The Good Practices of use of veterinary drugs are the key to avoid these issues.

The importance of veterinary products in food animal production and public health need to be well communicated to people in decision levels to get adequate resources for the operation of the registry of veterinary medicines, pharmacovigilance and medicated food control programs. The incidence of infections caused by resistant strains is an emerging important issue to bear in mind in this regard.

Review and update the full set of rules applicable to Good Manufacturing Practices relating to Veterinary Products to continue the process for improving the installed capacity in the region and guaranteeing the continued production of safe, effective and in compliance with quality standards veterinary medicines.

The current version of Good Manufacturing Practices for Veterinary Products dates back to 2002, and is based on the 1991 recommendations of the WHO. The enforcement criteria for these rules, however, are more recent because the guides for inspection of the different types of facilities were revised and updated in 2010.
Nevertheless, production technologies, the control methods available, and priority in control types currently used have changed substantially in recent years. Consequently, in order to keep veterinary medicines manufacturing standards updated, it is imperative to conduct an integral review of the current regulations.
This review will require a discussion of the priorities for expanding or reforming facilities, and changes in the procedures applied, as medium-term objectives. Therefore, the new regulations should be viewed as a guide for investments made by industry in the gradual

and progressive modernization of facilities and processes.

Design a training system that will strengthen the capacity of the official authorities and the industry regulatory affairs representatives of the member countries relative to the registration and control of veterinary medicines, with the aim of improving animal health, veterinary public health and animal welfare, as well as their capacity for participating in the preparation of international rules and guidelines relating to these topics, and strengthening their ability to apply these rules and guidelines.

It has been noted that the regulatory aspects involved in the registration of veterinary medicines are not included in any of the graduate study programs related to the sector. There are only a few isolated postgraduate programs that include these aspects, although without covering all the requirements.

Therefore, there is an essential and urgent need to prepare and organize a specific training program that covers these aspects, offering continued training for new professionals. This would increase the availability of trained professionals for the government sector and industry, and enhance the quality of the service provided by these professionals.

Additionally, training is an essential tool for developing consensus among the parties (in industry and in government organisms) and countries of the region in terms of the criteria applied. Starting this process will only benefit all those involved.

Considering the numerous members in the region and its significant extension, this training offering should be organized through information systems that provide flexible distance education modes.

Communicate, in a timely and accurate manner, information on the progress made in the harmonization of rules governing the registration and control of veterinary medicines in the regional and international sphere, availing itself of modern information technology, unofficial information and tracking systems.

Effective communication is necessary in every organization. Without it, it is impossible to carry out any process or activity. Within CAMEVET this has been an issue that has presented significant difficulties that are not the responsibility of the organizers or of the member countries.

The steps taken to date, which include an improvement in the functioning of the Secretariat, have overcome this issue in part, but this is not enough. The CAMEVET must have suitable and up-to-date IT support.

Solving the problems with the official web page of the CAMEVET is an absolute priority. Although work is underway, efforts should not be used sparingly to guarantee effective and updated communication between the member countries, and from the CAMEVET to the world.

Promote activities that facilitate the referential use of approved work guides and the enforcement of common regional criteria in all matters relating to the registration and control of veterinary medicines.

Although harmonized documents and approved guides that establish clear procedures for filing and registering veterinary medicines are available, the difficulty described in internalizing them has led to a disparity of criteria in applying these documents.

These disparities do not occur when there is deep discussion and fluent communication. One clear example is the rule governing stability, which was discussed extensively with significant participation of all the member countries. At present, when it is applied, there are no differences in the requirements of the various authorities.

Consequently, it is essential to generate mechanisms that contribute to create common criteria to avoid duplication of trials and disparity in the approvals granted. Specific

workshops or discussion seminars on properly identified issues would be very useful. Encouraging bilateral communication between the government sectors of each country could also constitute a path for solving specific differences.
This should spark the beginning of mutually recognized registration procedures – a path some countries of the region and of other regions around the world have already commenced.

Continue and strengthen the participation of CAMEVET and its member countries in international forums where work is carried out in the design of policies and governance relating to veterinary medicines, animal health, veterinary public health and animal welfare decision-making.

The participation of CAMEVET in international forums has been very successful and has developed communication channels that are mutually beneficial. This continued presence has been appreciated and is reflected in the protagonist role of CAMEVET in the discussions with other regional organizations. In fact, CAMEVET has been summoned to participate in different work groups with its experts, contributing important regional criteria for the creation of rules applicable to the region.
It has also successfully requested the updating of certain rules, such as the stability rule of the VICH, which were not applicable in the region due to the predominant temperatures.
The importance of avoiding duplicate efforts when trials carried out in line with suitable protocols exist is undeniable. In addition to the evident economic benefit, aspects relating to animal wellbeing, the avoidance of unnecessary deaths or suffering, are highly important for the professional ethics involved in the development of veterinary medicines.
Making CAMEVET known in international forums will not only strengthen the committee, but also bring greater recognition of the veterinary medicines industry as a cornerstone of animal origin food production and Public Health.

Institutional Arrangements

Members

The CAMEVET is made up by representatives from 24 countries in America. The annual assembly, which has been held for almost 20 years, usually gathers representatives from 20 countries.
The industry segment is represented through chambers of local or international veterinary medicines producers, which have a voice in every discussion. Around 150 representatives from the various industries gathered under the chambers of the region attend each annual assembly.

Resources

The activities of CAMEVET are funded through the registration fee charged at each annual assembly and paid exclusively by industry representatives. To date, this has enabled the entity to maintain its regular activities, including participation in international forums, hiring the permanent staff of the Secretariat, and service fees paid to the OIE for the use of the facilities of the Regional Representation.
Consideration must be given to explore new sources of incomes and avoid if it's possible, new increases in the inscription fee.. Training activities could constitute a source of funding. Additionally, the possibility of obtaining funds from multilateral organisms such as the World Bank must be evaluated. These could be used to fund projects of regional interest.

Basic Texts

The Regulation of the CAMEVET, which is currently being reviewed and renewed, must

be a suitable and useful instrument to clearly establish the proper functioning of the Committee. The updated version of this regulation must be available on the official web page of the organization.

Work Groups

The mechanism for creating technical recommendations is based on the detection of one or more topics of interest for the countries of the region and the creation of technical work groups that will study these topics and prepare documented proposals.
It is essential to ensure that the work groups established fulfill the proposed assignments. Once a commitment to coordinate a work group has been assumed, the responsible person must organize the work and ensure that the requested documents are prepared and submitted in the established time spans.
The functioning of these work groups must be strengthened, since their task is essential to the successful attainment of the purpose of the CAMEVET.

Annex IV

Anexo I – Contabilidad en Dólares

Ingresos	01/01/2016 - 30/09/2016
Recursos disponibles al 31 de diciembre de año 2015	USD 85.180,00
Inscripción al Seminario CAMEVET 2016	USD 3.500,00
Subtotal de Ingresos	**USD 88.680,00**
Egresos	
Gastos fijos (Salarios)	
Secretario CAMEVET (Dr. Enrique Argento)	USD 3.600,00
Asistente Administrativa (Srta. Ana Maria Sgammini)	USD 2.700,00
Gastos Admin. Por uso de las Oficinas de la OIE (150/mes)	USD 1.350,00
Subtotal Gastos Fijos	**USD 7.650,00**
Gastos para la Reunión Anual de CAMEVET	
Financiación a Puntos Focales para Reunión Anual de CAMEVET	USD 0,00
Financiación para Oradores Reunión Anual de CAMEVET	USD 0,00
Gastos Staff CAMEVET (Viáticos)	USD 0,00
Compras de Materiales para la Reunión Anual de CAMEVET	USD 0,00
Subtotal	**USD 0,00**
Gastos de Participación en Otros Eventos	
Participación en reuniones del VICH Outbreach Meetings Dr. Enrique Argento to attend 7th Vich Outreach Forum Meeting From June 20-22 in Brussel - Belgium	USD 1.196,00
OIE Conference Regional Commission for the Americas	USD 0,00
Subtotal	**USD 1.196,00**
Otros Gastos	
Internet (Dominio de CAMEVET)	USD 0,00
Pago de confección de recibos CAMEVET	USD 39,00
Subtotal	**USD 39,00**
Gastos Variables	
Cambio de Dólares a Pesos Argentinos	USD 3.600,00
Subtotal	**USD 3.600,00**
Subtotal de Gastos	**USD 12.485,00**

Total de Ingresos menos Egresos hasta September 2016	**USD 76.195,00**

Anexo II – Contabilidad en pesos argentinos

Ingresos	**01/01/2016 - 31/09/2016**
Recursos disponibles al 31 de diciembre de año 2015	ARS 48.806,30
Cambio dólares americanos a pesos argentinos	ARS 34.930,00
Inscripción al Seminario CAMEVET 2016	ARS 0,00
Subtotal	**ARS 83.736,30**

Egresos	
Gastos para la Reunión Anual de CAMEVET	
Gastos por compra de tiquetes aéreos (Dr. Argento – Sta. Ana Sgammini)	ARS 28.898,42
Gastos por compra de tiquete aéreo (Dr. Lemes)	ARS 4.280,00
Subtotal	ARS 33.178,42
Gastos de Participación en Otros Eventos	
Gastos por compra de tiquetes aéreos -Dr. Argento – Vich	ARS 35.581,26
Subtotal	ARS 35.581,26
Otros Gastos	
Varios (Clases de Ingles Secretaria)	ARS 8.500,00
Miscelaneos (Traduccion ESP/ENG de Conclusiones Seminario CAMEVET 2015)	ARS 1.600,00
Subtotal	ARS 10.100,00
Subtotal de Gastos	ARS 78.859,68

Total de Ingresos menos Egresos hasta Septiembre 2016	**ARS 4.876,62**