anmat
Administración Nacional de Medicamentos, Alimentos y Tecnología Médica

Ministerio de Salud
Presidencia de la Nación

HSI Symposium on Global Harmonization of Vaccine Testing Requirements. Making the elimination of ATT and TABST a concrete global achievement.

Patricia Aprea
Director
Evaluation and Control of Biologicals and Radiopharmaceuticals
NATIONAL ADMINISTRATION OF MEDICINES, FOOD AND MEDICAL TECHNOLOGY
REPUBLICA ARGENTINA

ANMAT

NATIONAL ADMINISTRATION OF MEDICINES, FOOD AND MEDICAL TECHNOLOGY

NATIONAL REGULATORY AUTHORITY OF MEDICINES OF ARGENTINA

ANMAT is an agency decentralized from the National Public Administration that was created by decree 1490/92.

Having a nationwide jurisdiction, it cooperates in the protection of human health by assuring the quality of the products it regulates: drugs, foodstuff, medicinal products, in vitro diagnostic devices, cosmetic products, dietary supplements and household cleaning products.

Granted with an economic and financial autarky, in the technical and scientific field it is under the authority of the Ministry of Health- Secretariat of Policies, Regulation and Institutes

Main responsibilities

- To fulfill the process of authorization, registration, standardization, control, vigilance and monitoring of the products used in the human medicine, and authorization and inspection manufacturers, importers and distribution establishment
- to establish regulation framework to fulfill regulatory functions
- to coordinate regulatory actions with Jurisdictional (provincial) health authorities.
- to bring capacitating and training in regulatory actions

ANMAT

NATIONAL ADMINISTRATION OF MEDICINES, FOOD AND MEDICAL TECHNOLOGY

NATIONAL REGULATORY AUTHORITY OF MEDICINES OF ARGENTINA

DIRECTORATE OF EVALUATION AND CONTROL OF BIOLOGICAL AND RADIOPHARMACEUTICAL PRODUCTS

- MARKETING AUTHORIZATION OF BIOLOGICALS AND RADIOPHARMACEUTICALS
- POST MARKETING SURVEILLANCE
- LICENSE OF MANUFACTURING AND IMPORTING ESTABLISMENT
- GMP INSPECTIONS
- LOT RELEASE
- LNC

THE USE OF ANIMALS FOR MEDICAL OR PHARMACEUTICAL NEEDS
ANMAT COMMITMENT

ANMAT is a strongly committed Agency with a more humane use of animals in the medical or pharmaceutical practices and then in the implementation of 3R principles as it is expressed in its Code of Ethics, in its Quality Policy on Social Responsibility and in the Regulation in force.

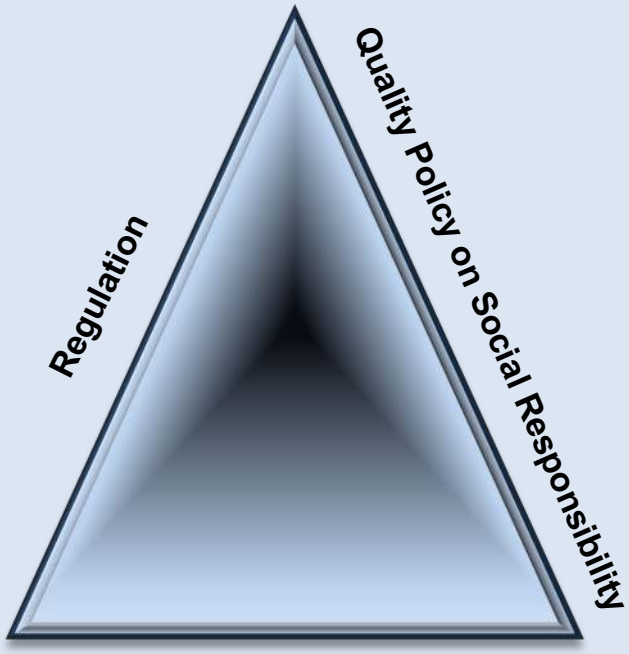
- The use of animal models in assays that result in benefits for public health, carries the responsibility of complying with strict standards of conduct in the ethical treatment of them.

- Those assays that involve the use of animal models should be replaced by those that do not require them or by those that have been adapted to minimize the number of animals needed per assay, or to improve animal welfare as well prevent unnecessary suffering.

THE USE OF ANIMALS FOR MEDICAL OR PHARMACEUTICAL NEEDS
ANMAT COMMITMENT

BASE DOCUMENTS AND PRINCIPAL ASPECTS TO BE CONSIDERED

Animal Life Conditions



Design of assays.

Human Resources

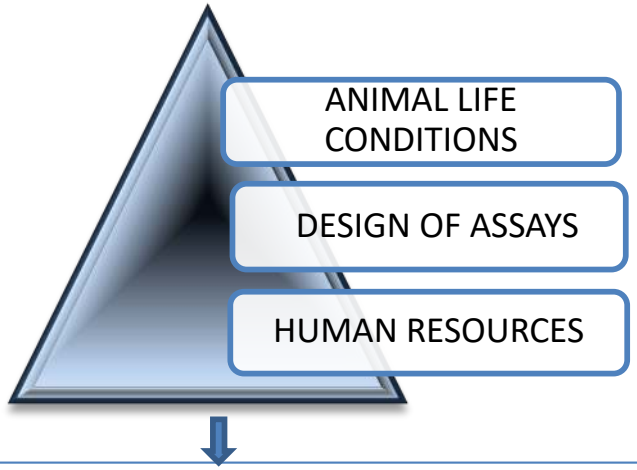
Code of Ethics

ANMAT
DR. CARLOS CHIALE

CODE OF ETHICS

QUALITY POLICY ON SOCIAL RESPONSABILITY

REGULATION



DIRECTORATE OF EVALUATION AND CONTROL OF BIOLOGICALS AND RADIOPHARMACEUTICALS
DR. PATRICIA APREA

CICUAL (IACUC) ⟺ 3R PROGRAM ⟺ INNOVATION SUPPORT PROGRAM ⟺ I + D PROGRAM

Veterinary Sciece Lab-Dr. Eduardo Catturini
Inmunobiologicals Lab- Analytical lot release- Dr. Paola Cassano
Biologicals Lab- Bioq. Ma. Veronica Lopez Cepero

Marketing Authorization,, GMP compliance and Documental Lot Release
Bioq. Marina Rossi
Bioq. and Pharmacist Ma. Cecilia Copello
Bioq. Karina Mouriño

Trainging and collaborative work

Collaboration with Bioterium technicians Career Internships
Development of Auxiliary of Bioteries
Participation to ECUAFyB (

3 D printed Rat: used for training of new Auxiliaries and Technicians of the Laboratory of Veterinary Sciences. Goals: to Implement an alternative resource as a didactic tool, inanimate object (3D printing), for the teaching of practical maneuvers prior to contact with live animals. Minimize the use of laboratory animals. and avoid suffering

Alternative methods

VETERINARY SCIENCE LAB

INTRARECTAL ANESTHESIA IN RATS USING COMBINED CYCLEHEXAMINE AND BENZODIAZEPINE (TILETAMINA/ZOLAZEPAN)
Lattanzio, L* 1; Caturini, E.D.2 y Gullace, F.A.2

USE OF THE INTRARECTAL ROUTE IN MICE FOR ADMINISTRATION OF A COMBINATION OF ACEPROMACIN AND MIDAZOLAM AS ANESTHESIA PREMEDICATION
Caturini, E.D. ; Bergerou, C.C. ; Godoy, M. L. ; Pucheta, N.C. ; Ribet, M.E. y Aprea, P. I.

ANESTHESIA INTRARECTAL IN GUINEA PIGS USING A COMBINATION OF DISSOCIATIVE ANESTHESIC AND UNA BENZODIAZEPIN (KETAMINA/DIAZEPAM)
Caturini, E.D. ; Bergerou, C.C. ; Pucheta, N.C. ; Julin, H.C. y Gullace, F.A.

HISTOPATOLOGICAL EVALUATION OF STRAIGHT AND COLON IN GUINEA PIGS BY THE INTRA RECTAL ROUTE WITH KETAMIN/DIAZEPAM
Caturini, E.D.1; Blanco Crivelli, X.2; Bergerou, C.C.1; Pucheta, N.C.1; Julin, H.C.1; Gullace, G.F.1 y Gullace, F.A.1

BIOLOGICALS LAB

Erythropoietin: feasibility of replacement in vivo potency assay for n vitro assay in some production stages.

ACTh. In vitro assay for potency proposed by a manufacturer

Pyrogen assay in rabbit:: feasibility of replacement pyrogen assay for endotoxin assay in some production stages of antivenoms

Biodistribution assay in radiopharmaceuticals: elimination for lot release

IMMUNOBIOLOGICALS LAB

Hepatitis B In vitro assay for the determination of hepatitis B content by the ELISA. (Replacement of in vivo assay in which the titer of the response is determined in mice is determined . Only animals are used for the validation of the in vitro method, responding to the reduction and replacement of animals

Tetanus vaccine: Use of assay. in guinea pigs for determination of potency by determining the titer of the response (replacement challenge test in mice , which includes mice vaccination and subsequent exposure to the tetanus toxin and its effects. (animal suffering is reduced and the number of animals is reduced as well complying with the refinement and the reduction principles

Argentine Pharmacopeia
745 Vaccines for human use

For the protection of vertebrate animals the tests must be carried out by using the minimum number of animals and the least suffering, anguish or terminal damage. The criteria for judging the essays in the monographs should be on the basis for of these aspects. For example, if it is indicated that an animal is the parameter to show positivity, infection, etc. As soon as typical clinical signs or death occur and sufficient indication is obtained of the positive results, the animal in question it must be treated humanely or given adequate treatment to prevent unnecessary suffering. Alternative test methods can be used to demonstrate compliance with the monograph and the use of such tests is particularly estimated and promoted when it leads to replacement or reduction of animals used or reduction of suffering, provided that it has been carried out a validation of these methods.

- Update of Good Practices in Bioteries Regulation
- Authorization and surveillance of bioteries regulated by the ANMAT Program
- Accreditation of Bioteries not regulated by the ANMAT – Verification of Good Practices in Bioteries
- Accreditation program for third-party laboratories for biological tests (GBP+GLP)
- Guide on good practices for biological testing laboratories
- Review of general chapters and monographs of Pharmacopoeia Argentina
- Introduction in the Argentine Pharmacopoeia a General Chapter on Alternative Methods (we have created an Ad hoc working group)
- Articulation and collaborative Program with organizations and institutions that are working in the development of alternative methods in our Country

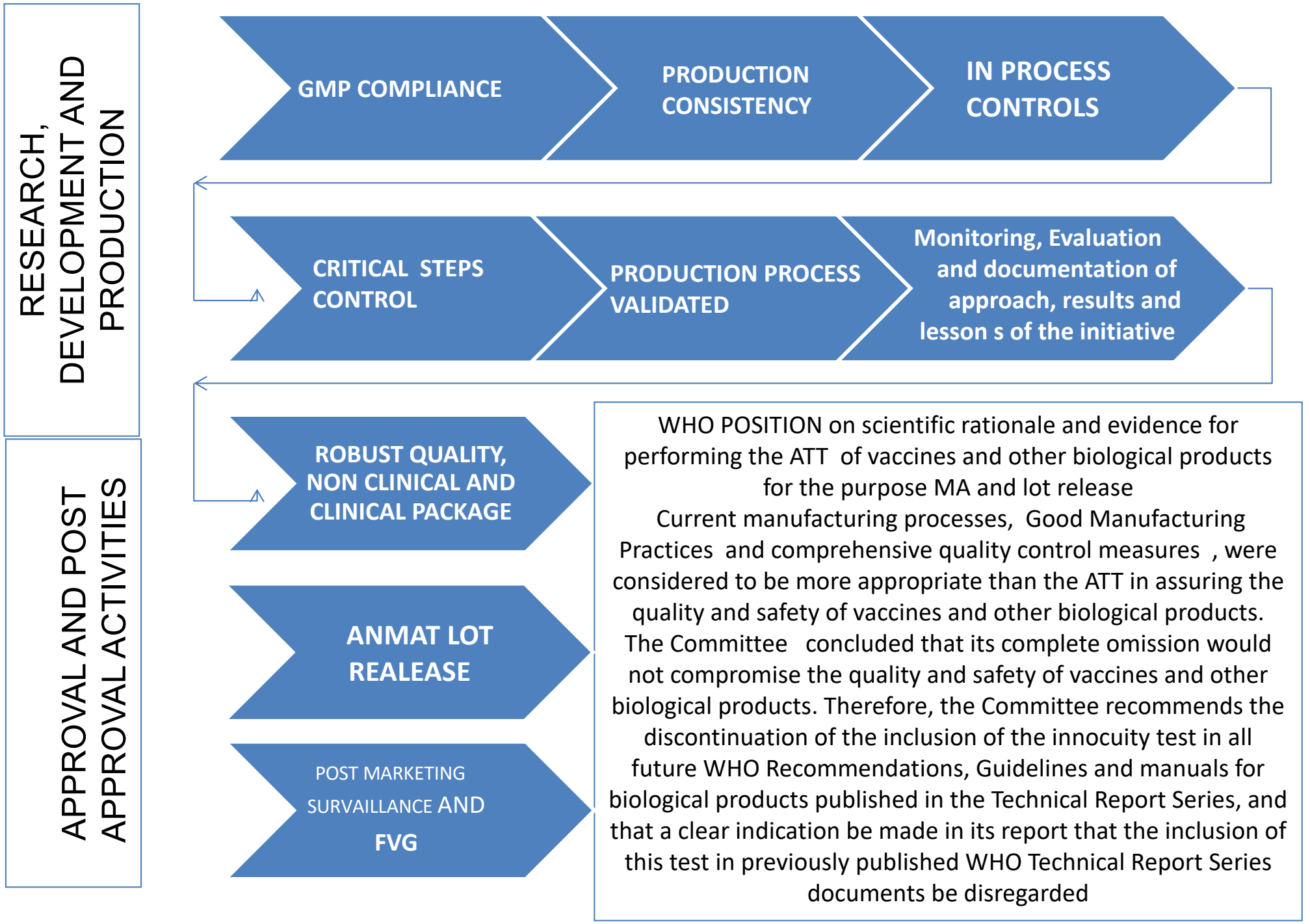
ABNORMAL TOXICITY TEST IN ARGENTINA

ATT REGULATORY REQUIREMENT?

ATT IN VACCINES

- **IT IS NOT REQUIRED IN THE MARKETING AUTHORIZATION**
- **IT IS NOT REQUIRED FOR LOT REALESE**

Argentine Pharmacopeia has eliminated the ATT form vaccines monographs (only one exception aPertussis. This monographs in revission)


RESEARCH, DEVELOPMENT AND PRODUCTION
APPROVAL AND POST APPROVAL ACTIVITIES
GMP COMPLIANCE
PRODUCTION CONSISTENCY
IN PROCESS CONTROLS
CRITICAL STEPS CONTROL
PRODUCTION PROCESS VALIDATED
Monitoring, Evaluation and documentation of approach, results and lesson s of the initiative
ROBUST QUALITY, NON CLINICAL AND CLINICAL PACKAGE
ANMAT LOT REALEASE
POST MARKETING SURVAILLANCE AND FVG
WHO POSITION on scientific rationale and evidence for performing the ATT of vaccines and other biological products for the purpose MA and lot release
Current manufacturing processes, Good Manufacturing Practices and comprehensive quality control measures , were considered to be more appropriate than the ATT in assuring the quality and safety of vaccines and other biological products.
The Committee concluded that its complete omission would not compromise the quality and safety of vaccines and other biological products. Therefore, the Committee recommends the discontinuation of the inclusion of the innocuity test in all future WHO Recommendations, Guidelines and manuals for biological products published in the Technical Report Series, and that a clear indication be made in its report that the inclusion of this test in previously published WHO Technical Report Series documents be disregarded

Elimination of ATT

Elimination of ATT is a the correct decision but ….

- Some ARNs still required ATT both during the marketing authorization as well as for lot release
- MA submissions received by ANMAT included the test even it is not required for us
- National Companies must comply that requirement for exporting their products
- ANMAT is required as ARN of the exporting country to certified the ATT is fulfilled, even it is not required for us.
-

Elimination of ATT

"Individually, we are one drop. Together, we are an ocean."

Efforts should be done globally

anmat
Administración Nacional de Medicamentos, Alimentos y Tecnología Médica

Ministerio de Salud
Presidencia de la Nación

Thank you!

¡Muchas Gracias!

Av. de Mayo 869
(C1084AAD), Buenos Aires - Argentina
(+54-11) 4340-0800 / 5252-8200