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ONLINE FORUM

“Cuba and Germany: Cooperation Opportunities in the Biotechnology and Biopharmaceutical Sector”

14.04.2021

REGULATORY FUNCTIONS FOR PRODUCTS TO BE INTRODUCED IN CUBA

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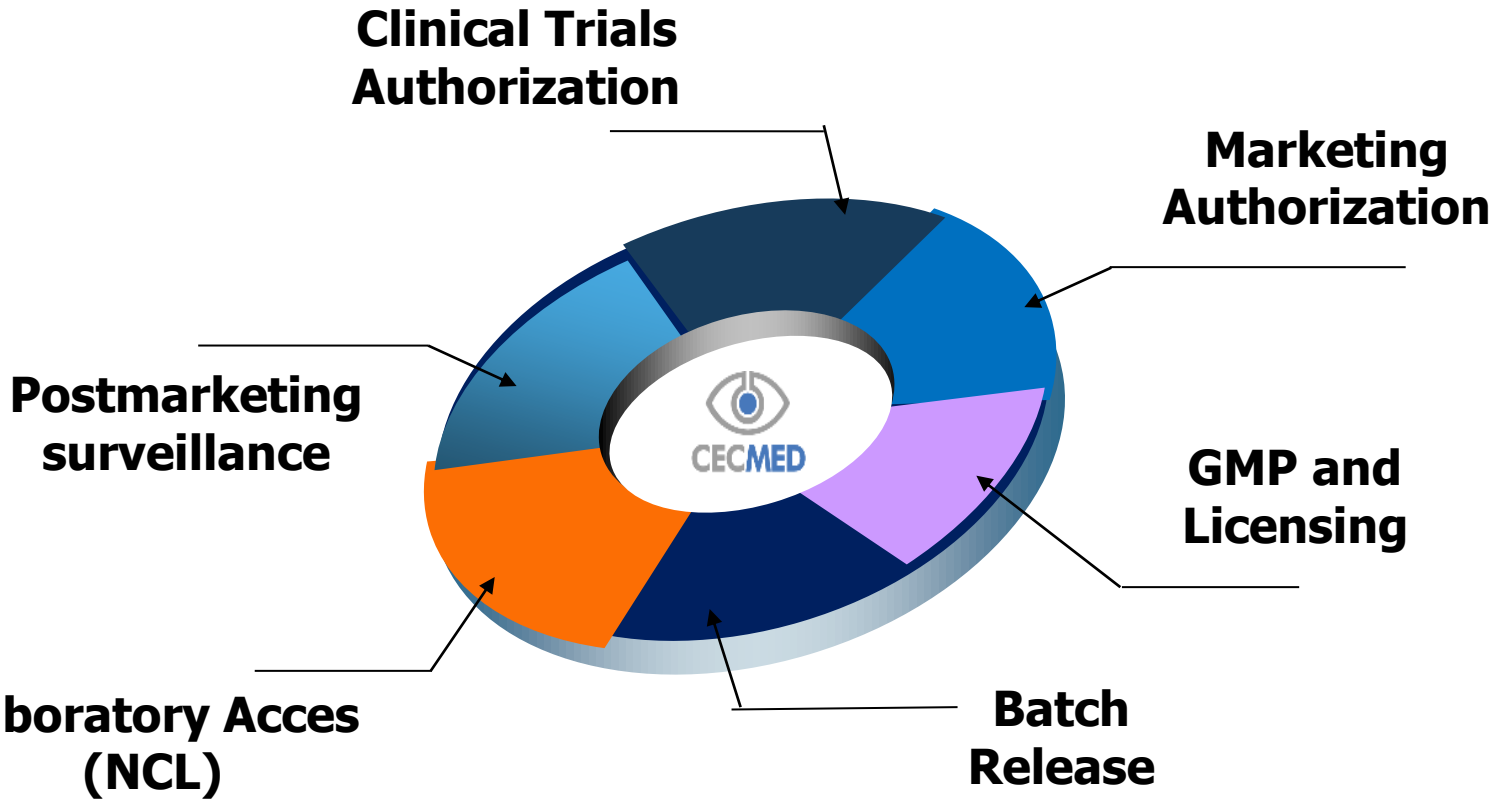
NATIONAL REGULATORY AUTHORITY

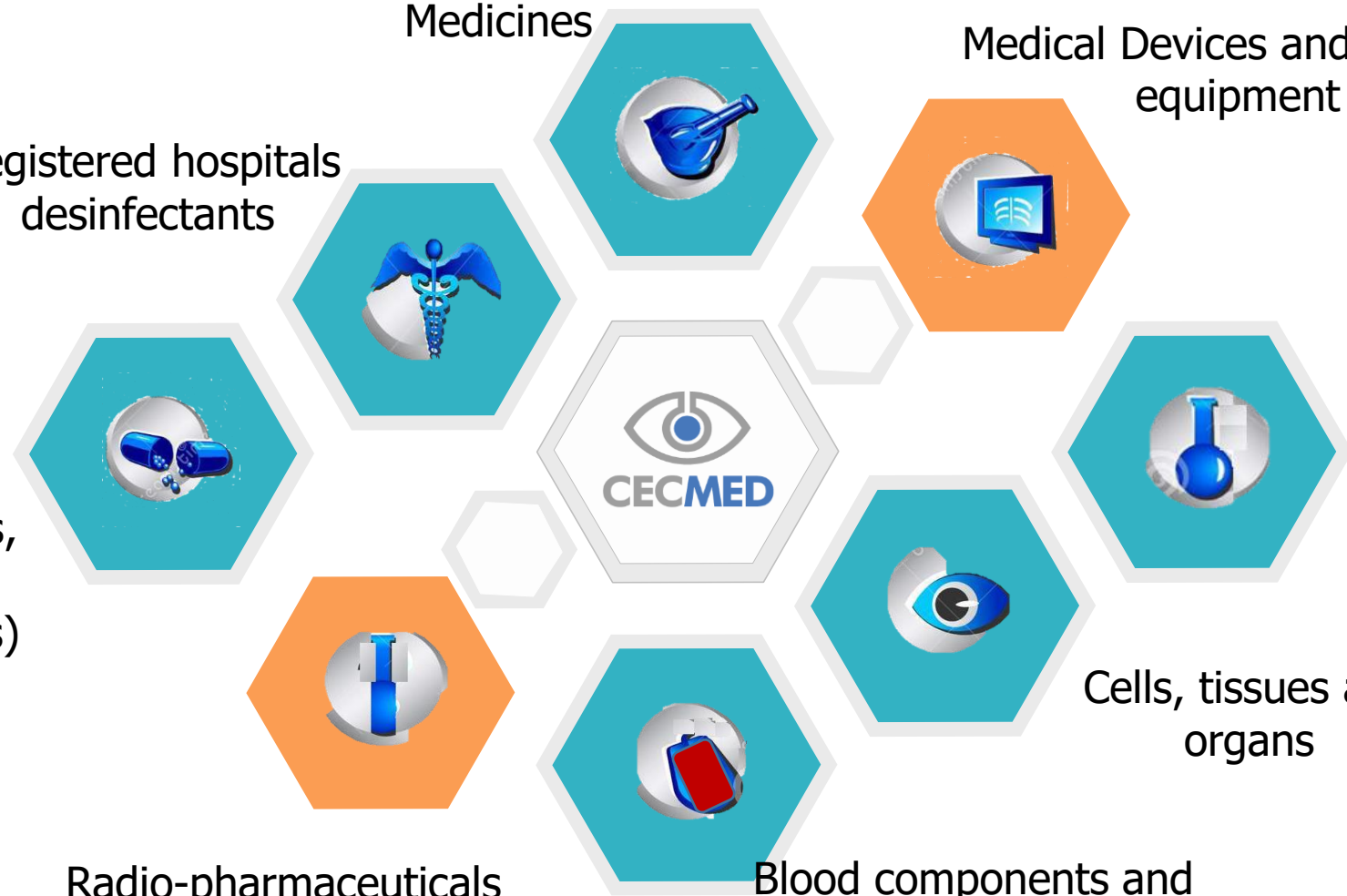
Created in 1989, subordinated to the Ministry of Health, empowered by the Cuban State to implement and conduct regulation, control and monitoring/vigilance of medicines, equipment and medical devices for human use.

Regulatory process implemented thought the recommended WHO

6 basic regulatory function



REGULATION SCOPE. PRODUCTS



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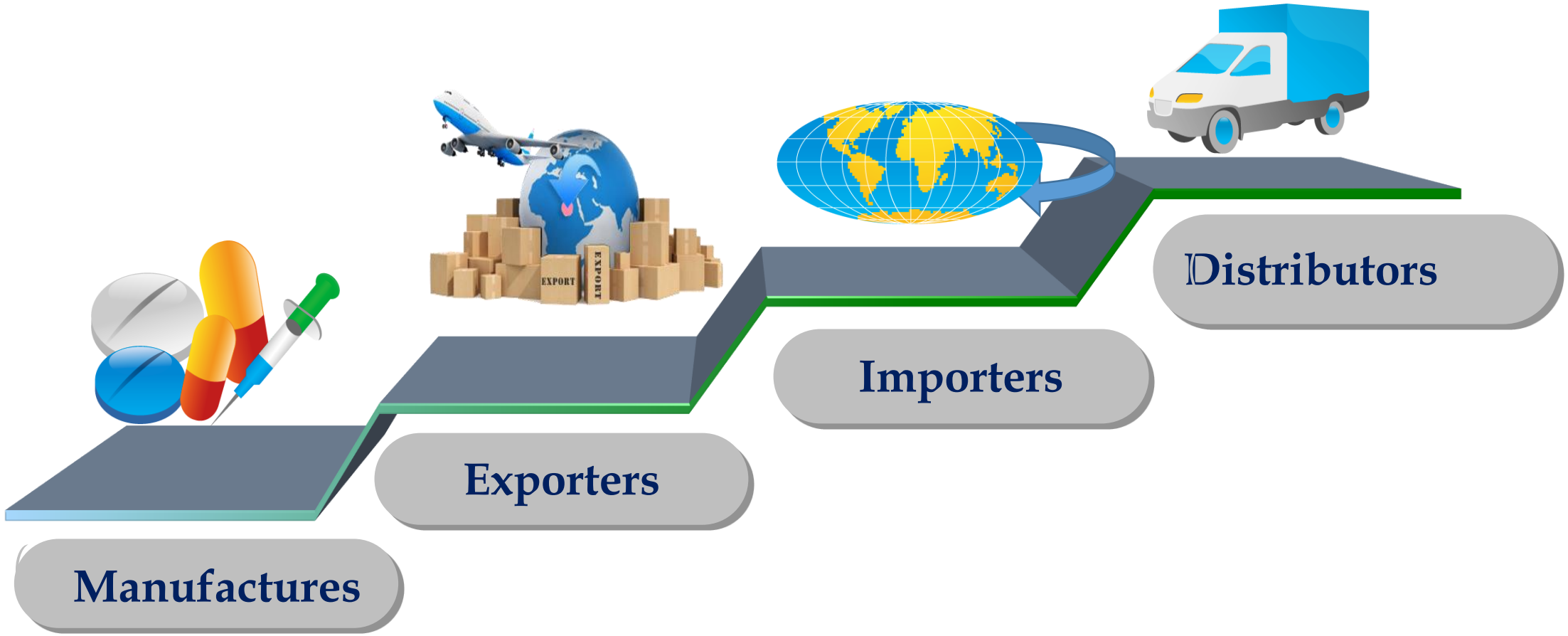
REGULATED SECTOR



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DRUGS, BIOLOGICS AND BIOTECHNOLOGICS

PRE-LICENCE FUNCTIONS OVERVIEW

- **MARKETING AUTORIZATION**
- **GMP AND LICENSING**
- **CLINICAL TRIAL AUTHORIZATION**

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MARKETING AUTHORIZATION (MA)

Official authorization for ***the commercialization of medicines (whether locally produced or imported) in the National territory, approved once evaluated as satisfactory its quality, security and efficacy***, as well as the characteristics of its manufacturer.

- There are specific procedures for MA application (MAA) of Drugs and Biological products.
- MA Renewable every 5 years and subject to Modifications/Variation approval or notification.
- Requirements for MAA are aligned with CTD format recommended by the ICH
- Imported medicines to be authorized in Cuba do not need to have clinical trials conducted in National territory but should comply with the clinical development accordingly to international guidelines and prove GCP compliance during development of clinical studies.

MARKETING AUTHORIZATION APPLICATION (MAA)

- **Marketing Authorization (Conventional, standard):** Authorization granted by CECMED, to commercialize a drug product in the National territory, once evaluated as satisfactory its safety, quality and efficacy, as well as the characteristics of its manufacturer.

- **Conditional Marketing Authorization:** Authorization granted by CECMED for specific type of products, subject to specific restrictions and conditioned to the completeness of the clinical information by the applicant.
  - Medicines that have substantial advantages over others available and that will be used in the therapy of life-threatening or fatal diseases which have efficacy markers.
  - Drugs products intended for the treatment, prevention or diagnostics of rare diseases.

- **Temporary Marketing Authorization:** Authorization granted by CECMED approving the commercialization of the product in a limited period of time o for an specific amount. **Not applicable to biologics**

MARKETING AUTHORIZATION ESPECIFIC GUIDELINES

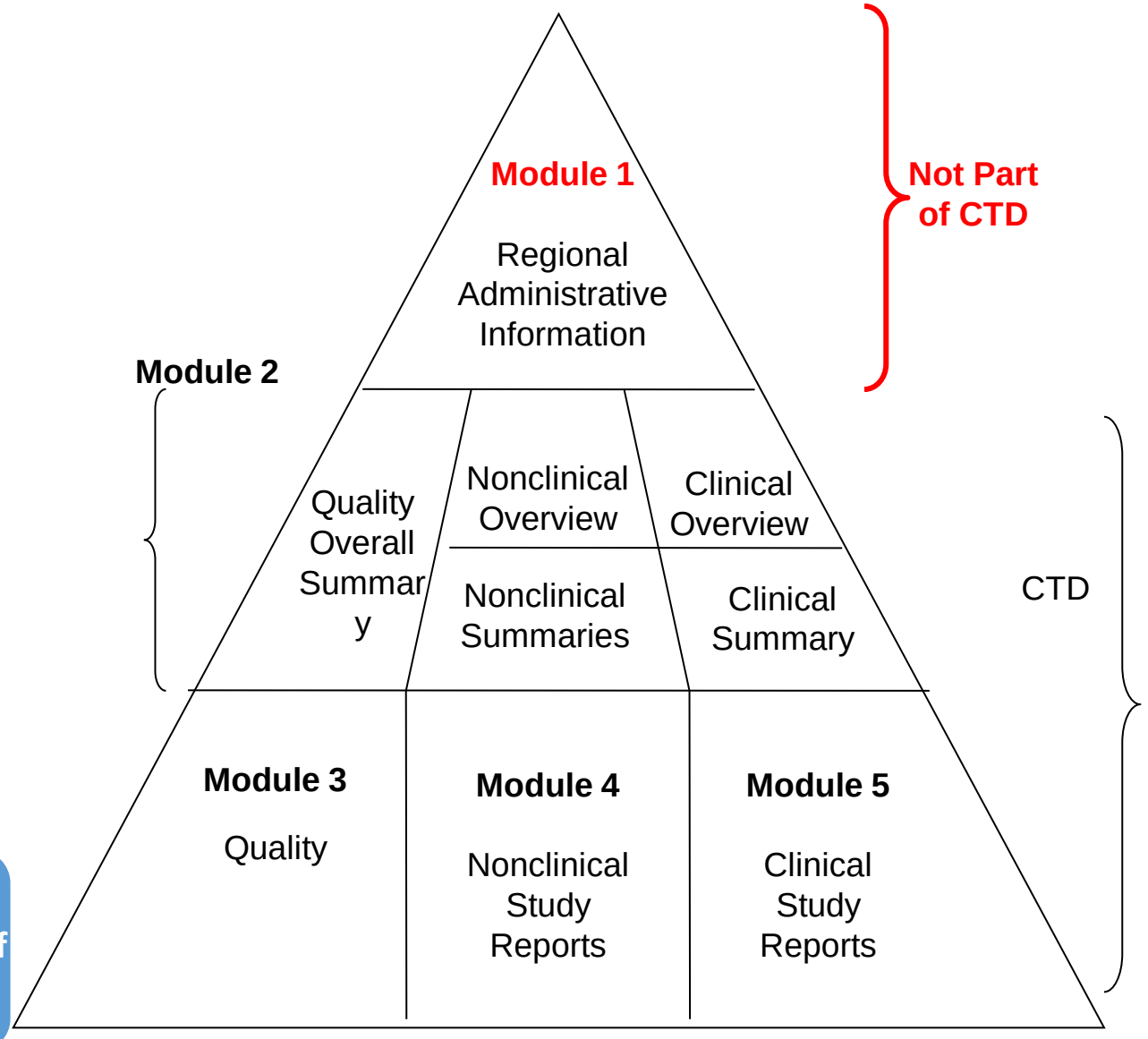
Resolution CECMED 64/2012, approves and enforces the Regulation of CECMED 61/2012. Requirements for the Sanitary Registry of medicines for human use.

The Drugs Products marketing authorization information are aligned with the requirements of ICH but they not exactly follow CTD structure, there is no correspondence between modules

Resolution CECMED 221/2015: Approves the Regulation 83-15 "Requirements for the Sanitary Registration of biological products for human use".

The Biological Products marketing authorization information must comply with the **CTD format of ICH**, according to the regulation of CECMED No. M-83-15.

Resolution No. 70/2011. *Approves and enforces* **Regulation No. 56-2011 Requirements for the registration of known biological products (Biosimilars).**



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DRUGS PRODUCT CATEGORY FOR MAA

Class I. New Product

- Products that have been **less than 5 years in the market.**

  the are divided in two categories (A y B).

Class II. Known Product

- Products that have **more than 5 years in the market.**

  Is grouped in one category (C).

CLASS I CATEGORY A.

- Pharmaceuticals, including biologicals, whose API is a new molecular entity.

CLASS I CATEGORY B.

- Pharmaceuticals, including biologicals, whose API is of known use, and it is presented as association of APIs or as a new salt, ester, isomer, complex, derivative, pharmaceutical form, administration route, strength or concentration.

CLASS II CATEGORY C.

- Pharmaceuticals, including biologicals, from different sources or not, which are presented with the same API, pharmaceutical form, strenght, indications of another product or other products registered in Cuba or abroad.

TIMELINES AND FEES (MEDICINES)

	Marketing Authorization	RENEWAL	VARIATIONS	CD*
Calendar days	180	150	150	120
Fees	https://www.cecmed.cu/sites/default/files/adjuntos/Reglamentacion/Res.%20No.%209%20ListadoRedconcu%C3%B1o_0.pdf			

**** CD: Request for completion of information (regulatory requirement)***

The applicant has up to 120 calendar days to complete the requested information

GOOD MANUFACTURING PRACTICES (GMP) AND LICENSING

A licensing system and GMP certification process that includes:

- procedures for inspections
- training and evaluation of auditors
- classification of non-conformities and
- analysis of granting certification based on risk.

CUBA: www.cecmed.cu/reglamentacion/aprobadas
http://www.cecmed.sld.cu/Pages/Public.htm
OMS: www.who.int/medicines/publications/pharmprep/en/
PICS: www.picscheme.org

DESCRIPCIÓN	CUBA	WHO	PIC/S
Buenas Prácticas de Fabricación, principios generales	**Reg.16-2012**	Anexo 2, SIT 986	PE 009-14
• Aerosoles de dosis metradas para inhalación	**Anexo 1** (2014)	-	Anexo 10
• Formas sólidas	**Anexo 2** (2014)	-	-
• Productos medicinales herbarios	**Anexo 3** (2003)	Anexo 3, SIT 937	Anexo 7
• Productos estériles	**Anexo 4** (2011)	Anexo 6, SIT 961	Anexo 1
• Radiofármacos	**Anexo 5** (2015)	Anexo 3, SIT 908	Anexo 3
• Agua de uso farmacéutico y vapor limpio	**Anexo 6** (2014)	Anexo 2 , SIT 970	-
• Productos en investigación para ensayos clínicos	**Anexo 7** (2004)	Anexo 7, SIT 863	Anexo 13
• Semisólidos	**Anexo 8** (2006)	-	Anexo 9
• Ingredientes farmacéuticos activos	**Anexo 9** (2006)	Anexo 2, SIT 957	PE 009-14
• Productos biológicos	**Anexo 10** (2012)	Anexo 3, SIT 996 Anexo 2, SIT 999	Anexo 2
• Limpieza	**Anexo 11** (2013)	-	-
Productos derivados del plasma humano	**Reg. No. 36-2003**	Anexo 4, SIT 961	Anexo 14
Buenas Prácticas de Laboratorio	**Reg. No. 37-2012**	Anexo 1, SIT 957	-
• Validación de técnicas analíticas	**Anexo 1** (2014)	-	-
Guía de Administración de Riesgo a la Calidad	**Resolución No. 155/2012**	Anexo 2, SIT 981	-

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GOOD MANUFACTURING PRACTICES (GMP) AND LICENSING

- **Scope:** Pharmaceutical products for human use, active pharmaceutical ingredients and raw materials for the manufacture of Biologics and others.

- **Timelines:** 180 days

- **Validity:** Licensing (apply only for local pharmaceutical operations). 5 years

  GMP certification. 30 month

- **Types of inspections:** Full inspection for Certification process.)

  (Others: Follow-up inspection, Concise inspection and Special inspection)

CLINICAL TRIAL AUTHORIZATION PROCESS IN CUBA

(Function established in CECMED by Ministerial Resolution 178/1991)

- Regulations and procedures implemented for the development of the following activities:
  - Authorization and Modification of Clinical Trials (CT)
  - Early access to research products, based on specific conditions.
  - Management of adverse events during the execution of Clinical Trials
  - Inspection of Clinical Trials.
  - Certification Program for clinical sites or services.

CLINICAL TRIAL AUTHORIZATION LEGAL BASES

- Reg. 26-2000 Requirements for management and use of investigational products during clinical trials and the responsibilities of parts.

- Reg. 27-2002. Requirements for Phase I and Phase II Trials for local investigational products for treatment cancer and HIV/AIDS.

- Reg.45-07. Requirements for notification and report of serious and unexpected adverse events in the clinical trials.

- Reg. 21-08 Requirements for Authorization of Clinical Trials and Modifications.

- Reg. 58-2008 Requirements for Certification of Good Clinical Practices.

- Reg. 63-2012 Compassionate Use of investigational products

CLINICAL TRIALS AUTHORIZATION

ESSENTIAL DOCUMENTS

- Clinical Trial Authorization Dossier:
  - Quality Information (CMC)
  - Non Clinical information
  - Clinical Trial Protocol
- Approval Letter from the Ministry of Health.
- Approval letter from the Ethics Committee of Trial Site(s)
- Clinical trial Registration code from the Cuban Public Register of Clinical Trials (*https://rpcec.sld.cu*)

TIMELINES

Clinical Trials	Days
Clinical Trials Authorization	90
mod/CT type 1Mayor	60
MOD/CT type 1menor	40
Response to queries by the applicant	75

SUPPORT OF PROJECTS OF NATIONAL HEALTH INTEREST

- Prioritize and accelerated regulatory process.

- Regulatory scientific advise and technical regulatory meetings discussion on projects proposal and approaches for development and/or approval.

Innovation Office: Under implementation for the regulatory advise of innovative products that represent an impact on public health systems.

- Regulatory technical committees between agencies or differentiate regulatory channels that allow assist, advise and monitor agreements for the technologies transfer between companies, products development strategies and/or introduction of products in both countries.

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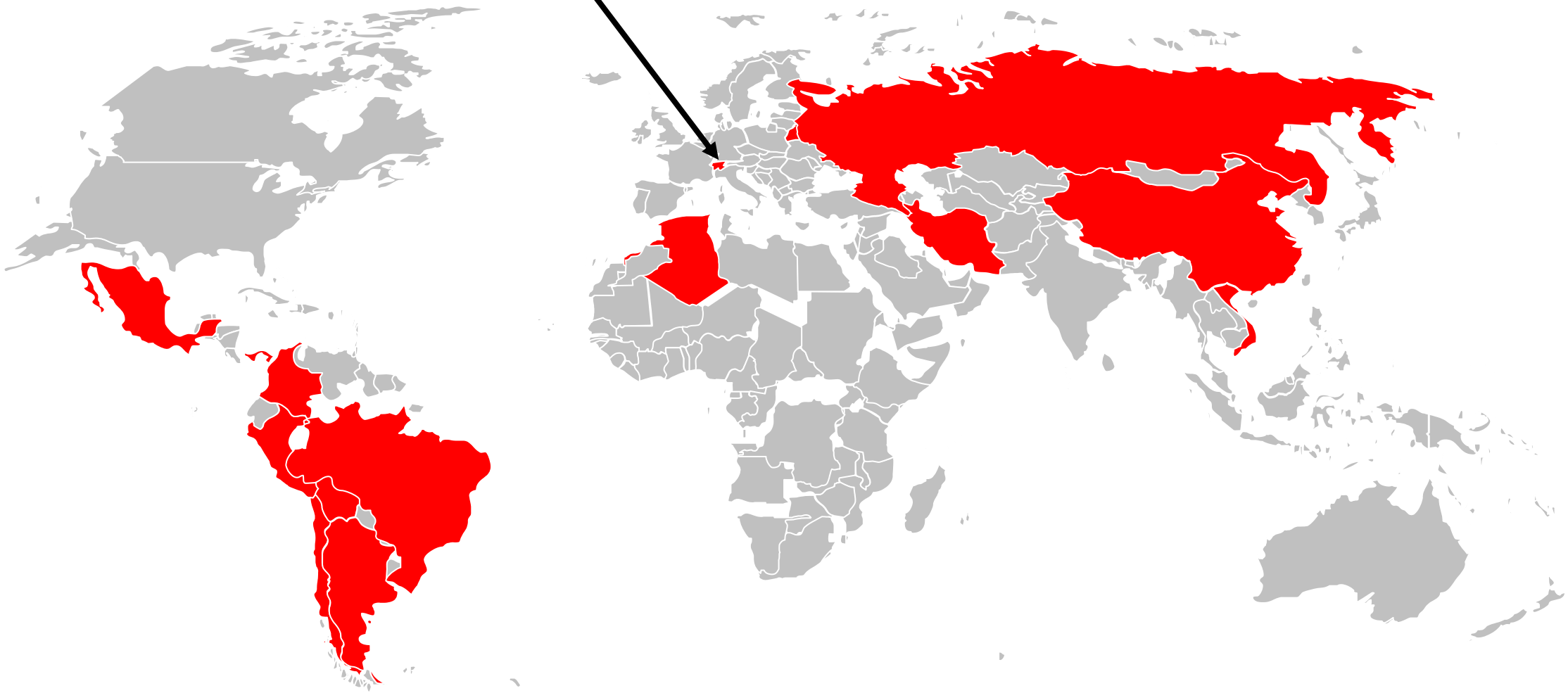
COOPERATION AGREEMENTS

CONFIDENCIALITY AGGREMENT
WHO/FCH/IVB/QSSWHO/FCH/IVB/QSS - CECMED



Achievements as National Regulatory Authority

List of Regional Reference Authorities for medicines in the Americas Regional Reference Authorities for medicines in the Americas (AMRO/PAHO)

The National Regulatory Authorities (NRAs) in the listed countries were assessed against WHO Regional Office for the Americas (AMRO)/Pan American Health Organization (PAHO) standardized evaluation procedure and AMRO/PAHO data collection tool.

1. Argentina
2. Brazil
3. Canada
4. Chile
5. Colombia
6. Cuba
7. Mexico
8. United States of America

List of vaccine producing countries with functional NRAs

The National Regulatory Authorities (NRAs) in the listed vaccine producing countries were assessed against the WHO vaccine assessment tool and announced as "functional NRAs" before introduction of the Global Benchmarking Tool (GBT) in 2016.

The list will be updated regularly as new information becomes available.

Country	Is the country producing one or more WHO prequalified vaccine?
1. Australia	producing WHO prequalified vaccine(s)
2. Belgium	producing WHO prequalified vaccine(s)
3. Brazil	producing WHO prequalified vaccine(s)
4. Bulgaria	producing WHO prequalified vaccine(s)
5. Canada	producing WHO prequalified vaccine(s)
6. China (People's Republic of)	producing WHO prequalified vaccine(s)
7. Cuba	producing WHO prequalified vaccine(s)
8. Denmark	producing WHO prequalified vaccine(s)
9. France	producing WHO prequalified vaccine(s)
10. Germany	producing WHO prequalified vaccine(s)
11. India	producing WHO prequalified vaccine(s)
12. Indonesia	producing WHO prequalified vaccine(s)
13. Islamic Republic of Iran	not producing WHO prequalified vaccine
14. Italy	producing WHO prequalified vaccine(s)
15. Japan	producing WHO prequalified vaccine(s)
16. Mexico	not producing WHO prequalified vaccine
17. Netherlands	producing WHO prequalified vaccine(s)

- **Quality Management System Certified by AENOR, ONN (ISO 9001-2015) since 2008**

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MEMBERSHIPS AND WORKING GROUPS

- Observer of The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)
- Member of the International Medical Device Regulators Forum, IMDRF
- WHO / PAHO Collaborating Center on Health Technology Assessment
- Member of the WHO International Regulatory Cooperation for Herbal Medicines (IRCH)
- Member of the Network of Drug Authorities from Ibero-America, EAMI
- Joint work with The Centre for Innovation in Regulatory Science, CIRS
- ICMRA Associate Member

World Health Organization

Pan American Health Organization
Regional Office of the World Health Organization

IMDRF International Medical Device Regulators Forum

Red eAMI Red de Autoridades en Medicamentos de Iberoamérica

ICH

CIRS Centre for Innovation in Regulatory Science

ICMRA

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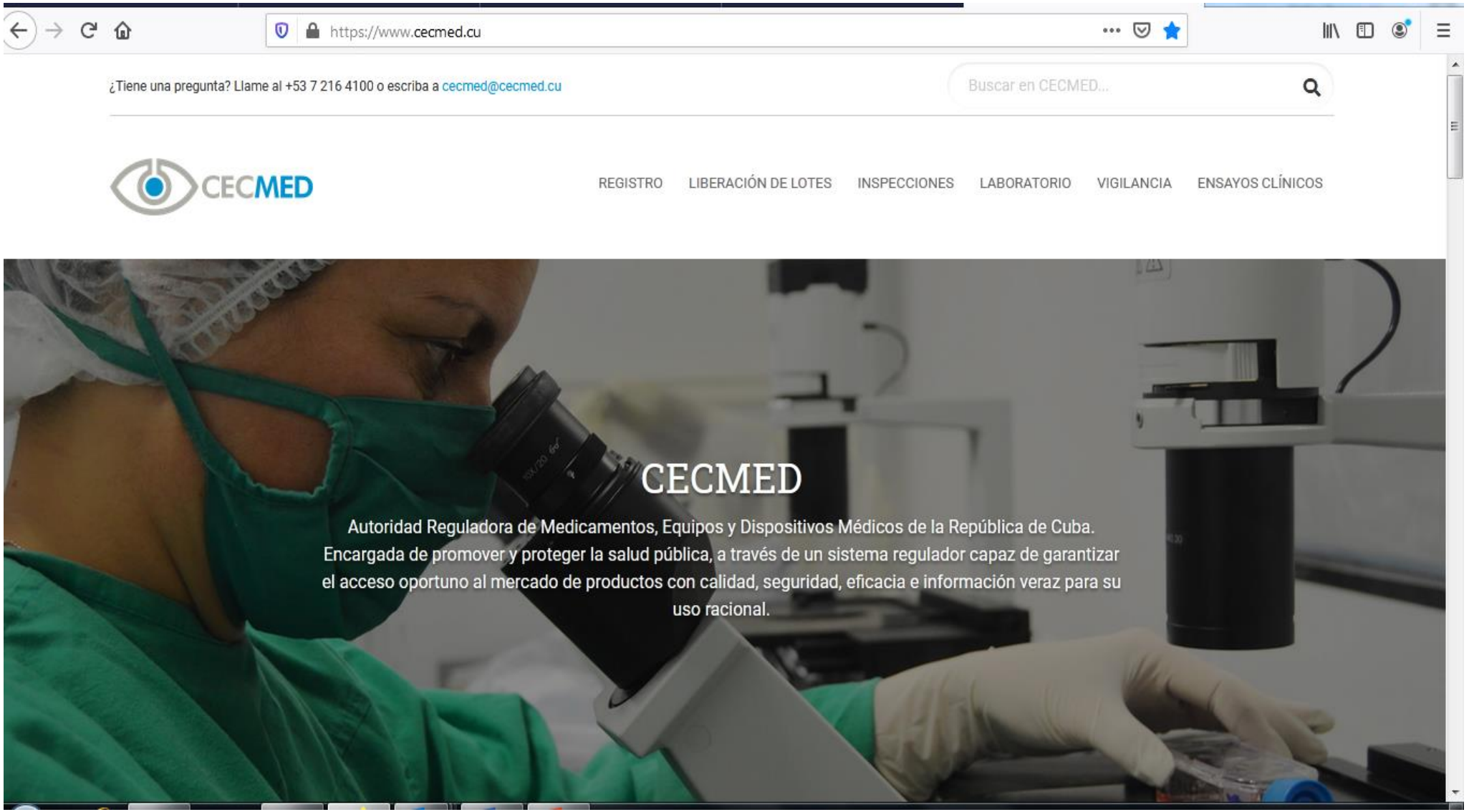
website: www.cecmed.cu



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THANK YOU