



# The Role of Regulatory Sciences from the Perspective of the Cuban Medicines Regulatory Agency: The Impact of COVID-19 in Promoting Innovation, Cooperation and Scientific Thinking

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## Abstract

The authors aim to familiarize the reader with the Center for the State Control of Medicines, Medical Equipment and Devices (CECMED) and the agency's perspective regarding the development and implementation of regulatory sciences as an interactive tool to promote cooperation and scientific thinking. The authors share their viewpoint on the preparedness of Latin American regulatory agencies by assessing innovation (i.e. novel biopharmaceuticals, vaccines, etc.), analyzing the challenges which are impacting healthcare and patients, and posing suggestions for a collaborative regional and international approach. To conclude, the authors' share recommendations for the implementation of regional initiatives aimed at supporting regulatory science, with the goal to promote the exchange of scientific cooperation as a vital element to maximize regulatory skills and competencies.

**Keywords** Regulatory science · National regulatory agency · Innovation · COVID-19 · Cooperation · Scientific thinking

## Background

In 1987, Uchiyama defined “regulatory sciences” as the process for assessing scientific optimization and technological developments through accurate prediction, evaluation, and decision-making process, based on scientific evidence with the aim to impact human health. [1] For the past thirty years, within the context of regulations, both for medicines and medical devices, the term regulatory sciences has been evolving proactively. Essentially, regulatory sciences have helped to optimize the analysis of regulations within the scientific regulatory landscape, adapting to and promoting innovation. Also, regulatory sciences as a component of scientific knowledge and thinking, it is a paramount tool,

harmonizing the dialogue between health agency regulators and key stakeholders, including the research industry, academia, manufacturers, distributors of medicines and medical devices. Regulatory science supports the accelerated development of products that can positively impact healthcare globally.

On one hand, we are clearly witnessing the emerging potential of innovative medicines, therapies and technologies to help advance population health and quality of life. These innovative products can provide effective treatment for a specific illness with significant improvement over existing treatments or providing a verifiable therapeutic option for diseases where there is no effective treatment or in a subgroup of patients with unmet medical needs [2].

In Cuba, the application of regulatory sciences to health regulations was implemented in 1989 with the inauguration of the Center for the State Control of Medicines, Medical Equipment and Devices (hereinafter, the CECMED), the Cuban regulatory authority, a branch of the Cuban Ministry of Public Health. The CECMED, was created to implement policies, procedures, and legislation to promote public health of the Cuban people by guaranteeing the quality, safety, and efficacy of health care products throughout the entire life cycle, that is, from clinical research and development to clinical use by the Cuban population [3]. In doing so,

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the CECMED has been playing a vital role in the national strategy supporting the creation of a research and development pipeline of novel quality product candidates developed by the Cuban biotechnology industry [4] CECMED's core areas within the context of regulatory sciences are focused on the diversification and integration of regulatory monitoring, risk–benefit evaluations, transparency of decision making, acceptability of adaptive clinical trial designs, new approaches to data collection in post-authorization stages, advancing patient-centered approaches and leveraging regulatory advice in response to novel scientific and technological challenges.

In September 2019, under Decree 10/2020 authorized by the Council of State of the Republic of Cuba [5] the CECMED officially established the prioritization of regulatory sciences and innovation as two emerging scientific disciplines in order to support the integration of scientific research throughout the entire regulatory framework process. The aforementioned decree plays a key role supporting the national strategy to strengthen Cuba's biopharmaceutical industries research and development.

CECMED's current concept of regulation has been directed towards the development and implementation of regulatory sciences, based on an interactive approach. The incorporating of regulatory sciences in a regulatory agency promotes new propositions, initiatives and strategies creating an interactive environment between drug sponsors and other stakeholders, fundamentally redefining the relationship between regulators and industry. This adaptive process was implemented at the CECMED for novel biopharmaceutical and technological advancements, creating an open, interactive collaboration for the assessment of the entire regulatory process.

This novel approach engages the regulatory reviewer from early project development stages, providing a number of benefits including a better understanding of the scope of the innovation, its scientific and technological benefits, it allows the exchange of ideas and an open dialogue among researchers and reviewers, promotes process efficiency, increased transparency thereby facilitating the benefit-risk-assessment and decision-making process.

## CECMED's Strategic Leadership

Emerging novel treatments and therapies offering hope for better patient outcomes, but present a real challenge for Latin American regulators, due to the lack of specific regulations presently in place. Without a doubt, this fact cannot be neglected, as clearly, the COVID-19 pandemic has challenged the life sciences research and development

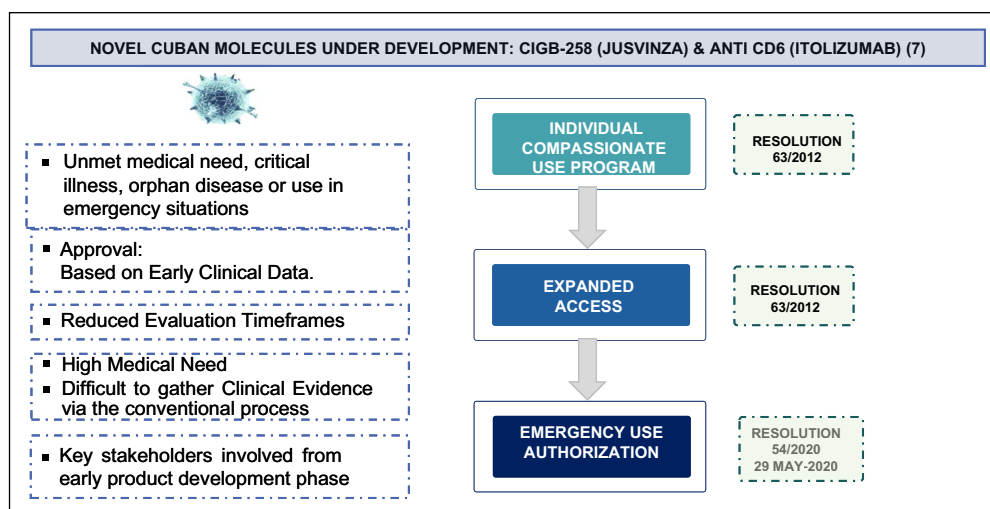
capabilities in every possible way, and most definitely, regional regulators cannot ignore this crucial reality. Furthermore, the COVID-19 pandemic has made evident the need for stronger collaborative regulatory efforts at the national, regional and global levels. From a regional regulatory perspective, countries like Brazil, Mexico and Argentina have established regulatory pathways such as adaptive clinical trial authorizations and emergency use authorizations for handling the increased number of drug candidates and vaccines for potential use against SARS-CoV2. The Pan American Health Organization (PAHO) has encouraged development plans for regulatory preparedness and response during pandemics and other health emergency situations, including ways to implement reliance mechanisms for emergency use of medicines and other health technologies [6].

CECMED's integration and its institutional alignment with the Cuban National Emergency Plan against COVID-19 has enabled the development of a coherent decision-making system with enough flexibility and adaptability to accelerate access to novel treatments for patients without compromising the safety, quality and efficacy of medicinal products and medical devices [7].

The rapid-regulatory response, as part of the national emergency program, created a broad framework to encompass the complexities of regulatory activities, with the necessary flexibility required to adapt to the continuous pandemic changes. Within this framework, the reconceptualization of regulatory strategies by the CECMED, based on real time evidence and knowledge and informed by the concepts of regulatory science, have helped to predict, explain and share the development of new data, encouraging a proactive and inherently collaborative regulatory culture. Consequently, the adaptability of known regulatory methodologies, the integration with national mechanisms and the priorities established by the CECMED, have facilitated the speed of development of novel therapies, treatments and products.

For innovative products in the context of the COVID-19 pandemic, a comprehensive regulatory framework was implemented by the CECMED addressing compassionate use and expanded access approvals, authorization for emergency use for existing products with possible effect on the treatment of seriously and critically ill COVID-19 patients on a case-by-case analysis based on rigorous real-time scientific assessments of product performance (Fig. 1). In summary, the CECMED's regulatory framework, has promoted timely integration with the overall national emergency health strategy, providing efficient management of approval timeframes for products and scientifically robust regulatory and public health decisions granting access to new therapeutic alternatives for the Cuban public healthcare system during the pandemic.

**Fig. 1** COVID-19 Patient Early Access Program implemented at CECMED



## The CECMED's Office of Innovation

At the forefront of regulatory sciences across the Latin American region, in October 2019, the CECMED implemented a pioneering initiative, the establishment of the Office of Innovation. First of its kind in Latin America, the CECMED's Office of Innovation has built a comprehensive regulatory framework geared at accelerating innovation and enabling the successful transition of novel products from research and development to clinical practice. This is a key step to enable patients' early access to innovative medicines. [2]

The leading role of the Office of Innovation of the CECMED is to serve as a driving force supporting biotechnology and pharmaceutical innovation in Cuba (prospectively, the Latin American region,) positively influencing and promoting regulatory support from early stages of research projects, defining specific needs and regulatory gaps, guiding and strengthening product development strategies. In today's rapidly evolving scientific environment, innovation based on scientific regulatory approaches is essential, as well as recognizing the importance of collaboration between regulators and key stakeholders during the design, the research and development stages of novel product candidates.

Both the FDA's Breakthrough Therapy Designation [8] and the European Medicine Agency (EMA) Prime scheme [9] share a common approach with the CECMED's Office of Innovation. Specifically, these pathways, reinforce regulatory and scientific support to foster accelerated drug development for patients' early access to medicines, addressing an unmet medical need. Also, ensuring that the scientific data generated by a drug sponsor fulfills the necessary standards required for a marketing authorization.

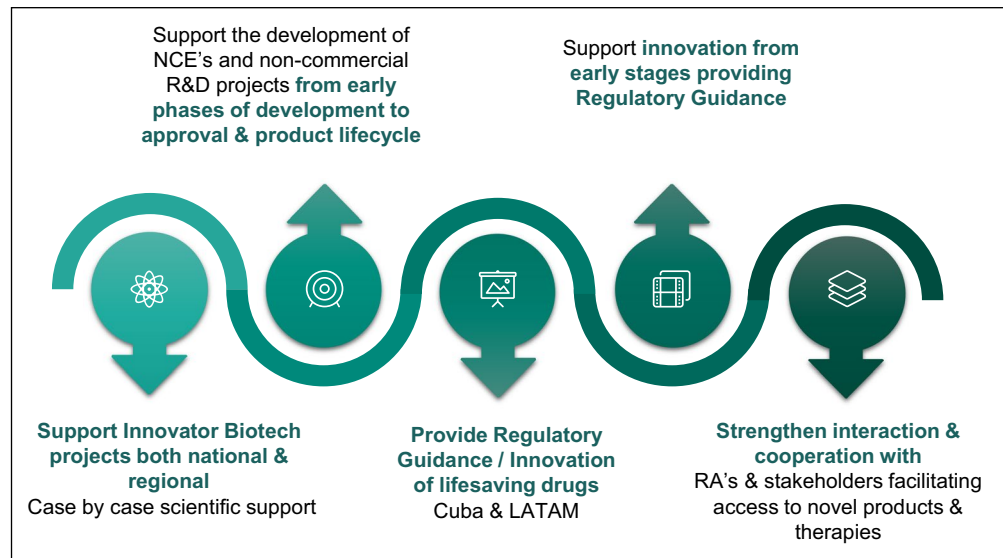
In the specific case of the CECMED, the Office of Innovation has implemented a two-fold approach. First, the Office of Innovation acts as a liaison to support Cuban industries' novel research and development priority projects and products, aimed at benefitting the Cuban public health system. Furthermore, promoting a collaborative approach and relationship with drug developers and researchers from the Cuban biotechnology and pharmaceutical industry. Referring to Fig. 2 for insights, key considerations and the process implemented by the CECMED's Office of Innovation shift from an adaptive capacity building scheme to an evolving scientific environment.

Second, the CECMED's Office of Innovation aims to be an active regional player interacting with other Latin American national regulatory authorities (NRAs) collaborating with assessments of novel drug product candidates to help strengthen regional/country specific public healthcare systems and patient early access.

In regards to the Latin American region (within the framework of a globalized world), we strongly believe that after the COVID-19 pandemic the development of a regulatory culture for medicines and health technologies based on risk analysis, scientific evidence and sufficient flexibility to interact and embrace technological advancements should become a top priority in every country's regulatory agenda.

Taking into consideration the existing regulatory collaboration initiatives across the Latin American region, such as the Pan American Network for Drug Regulatory Harmonization (PANDRH) and the Competent Authorities of Medicines in the Ibero-American Countries (EAMI Network), in order to support the development of a sustainable Latin American regional regulatory innovation ecosystem to strengthen existing country-specific regulatory frameworks, functions, and national and sub-regional health policies [10,

**Fig. 2** CECMED Office of Innovation: from adaptive capacities to an evolving scientific environment



11], we recommend the creation of a regional initiative, focused on the regulatory joint assessment of innovation for early patient access, the “Regional Innovation Task Force”.

This Regional Innovation Task Force could be organized as a pilot project within the framework of EAMI Network, without duplicating the PANDRH initiatives. The proposal is envisioned as a first step to create an innovation regulatory platform, where joint cooperation and reciprocity turn into vital elements for maximizing regulatory skills and competencies. The Innovation Task Force could help prioritize innovation and horizon-scanning of innovative products, finding practical and updated solutions to complex real-life healthcare threatening situations, such as therapeutic and diagnostic solutions for COVID-19 patient treatment. As such, as trust builds, the Innovation Task Force could provide a practical strategy (and prospectively, a common platform) to build adaptive capacities, having the ability to respond to the COVID-19 pandemic or other emerging public health emergencies. In the future, this Regional Innovation Task Force could become a platform through which collaborative or joint work sharing reviews of important innovative products may occur.

To conclude, to spearhead the pilot Regional Innovation Task Force initiative within the regional framework of the EAMI Network, the recommendation is to collaborate with the CECMED's Office of Innovation to extend existing regulatory sciences technical & scientific expertise with other NRAs based on the accomplishments of CECMED during the COVID-19 pandemic.

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