

OVERVIEW OF THE BRAZILIAN HEALTH REGULATORY AGENCY ON SANITARY SURVEILLANCE (ANVISA) ON GOVERNANCE AND CAPACITY BUILDING FUNDAMENTAL RIGHTS: LEGAL POLICY AND INTERNATIONAL HARMONIZATION SYSTEMS

PANORAMA DO PROCESSO LEGISLATIVO SOBRE GOVERNANÇA E CAPACITAÇÃO EM DIREITOS FUNDAMENTAIS DA AGÊNCIA NACIONAL DE VIGILÂNCIA SANITÁRIA (ANVISA): POLÍTICAS PÚBLICAS E SISTEMAS DE HARMONIZAÇÃO INTERNACIONAL

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ABSTRACT: The research examines the relevant elements inspiring the Brazilian health legislation and exposes the principles and goals of public policies from the analysis of competencies, structure and regulatory roles assigned to ANVISA, the Brazilian Health Regulatory Agency, a public regulatory and executive body in charge of regulation, placing on the market authorization and monitoring of health products, pesticides, biocides, medicines and cosmetics, among others. In a strongly globalized market, the main mission of the Agency is to ensure the quality, efficacy and safety of health products & services marketed in the country. The research also explores the alignment of ANVISA with the principles of good practices, its role in formulating internal policies and the global trends of this market, with particular attention to the coordinating role of international organizations for harmonization and standardization.

KEYWORDS: Governance; Legal and Public Policy; International Harmonization Systems.

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RESUMO: A pesquisa analisa brevemente os principais elementos da legislação brasileira em saúde e está dentro das prioridades da política de saúde, com base no estudo das competências, estrutura e função reguladora atribuída à ANVISA, Agência Nacional de Vigilância Sanitária, órgão público com funções executivas encarregadas da autorização de colocação no mercado, monitoramento e controle de dispositivos médicos, pesticidas, biocidas, medicamentos e cosméticos, entre outros. Num mercado fortemente globalizado, a principal missão da Agência é garantir a qualidade, a eficácia e a segurança dos produtos e serviços de saúde. Para tanto, a pesquisa explora os princípios das boas práticas aplicadas na ANVISA, seu papel na formulação de políticas internas e as características globais do mercado de medicamentos, produtos de saúde ou cosméticos, em estreita coordenação com as organizações internacionais de harmonização, dentro das funções que foi confiado.

PALAVRAS-CHAVE: Governança; Políticas públicas; Harmonização Regulatória Internacional.

Introduction

One of the Brazilian Health Regulatory Agency on Sanitary Surveillance (ANVISA) functions is the possibility of constant interaction with society, in terms of health promotion to ensure the fundamental citizenship rights. On this way, ANVISA understands regulatory convergence process as the international technical alignment movement that takes into account best practices, principles and internationally recognized standards with the legislative harmonization. It is very importante because ANVISA exercises control of ports, airports and borders and interlocution with the Ministry of Foreign Affairs and foreign institutions to deal with international matters in the area of health surveillance.

If technically justified, in regulatory harmonization and convergence process enable the application or adaptation of local regulatory requirements to improve the special functions of regulatory system are:

- Regulatory and inspection action on services provided, products and therapeutic inputs of health interest;
- Permanent assessment of the need for risk prevention; and
- Possibility of constant interaction with society, in terms of health promotion, ethics and citizenship rights.

On the international field, the regulatory harmonization - which provides that exactly the same technical requirements are adopted, with the use of identical language by countries and without flexibility for adjustments based on national specificities - regulatory convergence predicts that different measures can be adopted to achieve the same goal, without the loss of regulatory power or national sovereignty. This research address investigation how is function and which is the connections of ANVISA harmonization and regulatory convergence processes.

2. Brazilian Health Regulatory Agency on Sanitary Surveillance - ANVISA

In Brazil, health is a social fundamental right, inscribed in the Federal Constitution of 1988, which also instituted the Brazilian National Health System (SUS) as a means of realizing this right². Health becomes the right of everyone and the duty of the State and must be supervised, regulated and controlled in accordance the Brazilian Constitution on articles 196 to 200.

In order to regulate the structure and functioning of the SUS, the Organic Law of Health - Law No. 8,080, of September 19, 1990 - which provides for the conditions for the promotion, protection and recovery of health, and the organization and operation of health correspondents. In the art. 6, which are included in the field of performance of SUS, epidemiological surveillance, sanitary surveillance, the health of the worker and comprehensive therapeutic care, including pharmaceutical. The Law defines the role and scope of health surveillance:

Art. 6º. Health Surveillance is understood as a set of actions capable of eliminating, reducing or preventing health risks and of intervening in health problems caused by the environment, production and circulation of goods and the provision of services of health interest, covering:

- I- the control of consumer goods that, directly or indirectly, relate to health, comprising all steps and processes from production to consumption; and
- II- the consumption of the provision of services that are directly or indirectly with health³.

ANVISA's role it to promote the protection of the population's health by execu-

²RAMALHO, Pedro Ivo Sebba (Org.) Regulação e agências reguladoras: governança e análise de impacto regulatório. São Paulo: RT, 2009, p. 45.

³Aviabile on: <http://www.planalto.gov.br/ccivil_03/constituicao/constituicao.htm>. Accessed on August, 23rd, 2017.

ting sanitary control of the production, marketing and use of products and services subject to health regulation, including related environments, processes, ingredients and technologies, as well as the control in ports, airports and borders. The scope of ANVISA actions are:

- Pre-market authorization for products prior to its manufacturing, market exposure or delivery to consumers
- Inspections to ensure manufacturing quality; products' post-market and post-use activities (monitoring, oversight, complaints' receipt, etc.)
- Oversight to enforce compliance with sanitary regulations
- Control of the import, export and circulation of ingredients and goods subject to health regulation
- Health regulation actions in services for outpatient care (routine or emergency) and hospitalization; diagnostic support and therapeutic services that entail the incorporation of new technologies
- Coordination of special programmes to monitor the quality of regulated products and services
- Control actions in ports, airports and borders, to ensure the sanitary control of facilities, services and means of transportation, products' import and the protection of travelers' health
- Adoption of preemptive and control measures for outbreaks, epidemics and public health emergencies⁴.

In addition, the Agency exercises control of ports, airports and borders and the dialogue with the Ministry of Foreign Affairs and foreign institutions to deal with international affairs in the area of sanitary surveillance present throughout the national territory.

The Brazilian Health Regulatory Agency on Sanitary Surveillance - ANVISA - is an autarchy linked to the Ministry of Health, being that this relationship is regulated by Management Agreement. The Agency's institutional purpose is to promote health protection of the population through the sanitary control of production and commercialization of products and services subject to sanitary conditions, including

⁴List of scope of ANVISA actions are available on: <
<http://portal.anvisa.gov.br/institucional>>. Accessed on August, 29th, 2017.

environments, processes, inputs and technologies. Due this, the Brazilian Health Regulatory Agency on Sanitary Surveillance has these challenges:

- Simplification of critical working processes;
- Reduction of waiting times for granting market authorizations, performing inspections and issuing import licenses;
- Moving forward in promoting international regulatory convergence, consolidating advancements achieved, alignment to best practices, and joining harmonization initiatives;
- Reaching a workforce size compatible to the extent of the regulatory activity;
- Strengthening post-market and post-use vigilance models; and
- Consolidating a service policy in accordance with good governance, access to information, transparency and communication values⁵.

Following a worldwide trend, ANVISA pursues strategies to modernize the processes of issuing market authorization to regulated products, maintaining their quality, safety and efficacy.

In this process, it is worth highlighting the following stakeholders: the regulated sector, in charge of delivering safe products and services; the National Congress, legislative body that should act based on qualified technical information; and the society, which must be increasingly aware of health risks and must be able to evaluate the products and services consumed⁶.

3. The international policy making system: Harmonization and Convergence in Brazilian Health Regulatory Agency on Sanitary Surveillance - ANVISA

3.1 Overview of ANVISA International History on XXI Century

ANVISA aims at reaching the highest standards for sanitary regulation, in line with the best scientific evidence available to date. The results achieved in the last years show an advance in the international leading role of the Agency: ANVISA INTERNATIONAL ACTIVITIES ON XXI CENTURY⁷.

⁵List of ANVISA challenges available on: <<http://portal.anvisa.gov.br/institucional>>. Accessed on September, 25th, 2017.

⁶COSTA, E. A., *Vigilância Sanitária: temas para debate* [online]. Salvador: EDUFBA, 2009. 237 p. ISBN 978-85-232-0652-9. Available from SciELO Books: <<https://static.scielo.org/scielobooks/6bmrk/pdf/costa-9788523208813.pdf>>. Accessed on August, 15th, 2017.

⁷Information available on: <<http://portal.anvisa.gov.br/institucional>>. Accessed on August, 29th, 2017.

According to the information provides by the Agency itself, the main milestones in its regulatory competences are:

2010: Recognized as Regulatory Authority of Regional Reference (NRArr) by the Pan American Health Organization (PAHO)

2012: Founder member of the International Medical Device Regulators Forum (IMDRF)

2015: Regulatory and monitoring tasks assigned to Anvisa for mutual recognition and equivalence monitoring for pharmaceutical ingredients marketed to/from the UE. Becomes also member of International Cooperation on Cosmetics Regulation (ICCR)

2016: Becomes a member of International Council for Harmonization (ICH)

3.2 Important aspects of harmonization and regulatory convergence processes worldwide

The sector of medicines & health products is a highly delocalised sector under harmonized international standards⁸. The differences in authorization requirements between different States pose a great obstacle for patent and licensed holders for the global marketing of those products. Different specifications for the same product between the EU, Japan, USA (FDA) or Brazil, for example, are in fact an barrier to trade, since different specifications operates depending on the place of final marketing. Hence the need for private companies to control that a certain pharmaceutical product is marketed exactly to the market for which it has been designed and tested⁹.

Some medications may be approved for certain indications in a given country but for others in another. The product needs to be pre-designed before its manufacture and placing on the market. Certain drugs (especially orphan drugs) have serious problems of availability in certain markets because the pharmaceutical company finds extremely costly to meet the specific demand requirements, which are in turn economically unviable¹⁰. The labeling also differs. So, for the pharma companys, it

⁸Cockburn, I; Henderson, R, Publicly Funded Science and the Productivity of the Pharmaceutical Industry. In: Innovation Policy and the Economy, Jaffe, Lerner and Stern (Coord), Cambridge (MA): MIT Press, 2001, p. 34-35.

⁹For example, the administration of epoetin-alpha resulted in cases of severe anemia in patients who injected the drug under the skin, rather than intravenous. Regulators in Australia and Europe banned the subcutaneous use of the anti-anemia principle, epoetin alfa (Eprex). In January 2003, Health Canada issued a warning against intravenous use in patients with chronic renal failure (CRF), recommending a risk-benefit assessment prior to subcutaneous administration.

¹⁰Cockburn, I. et all. Pharmaceuticals and Biotechnology. In: US Industry in 2000 - Board on Science, Technology and Economic Policy, Washington (DC): National Research Council, 1999, p. 148.

is of paramount importance to adopt and implement common international standards, a role that has been assumed by international harmonizing organizations and especially by the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), whose standards promote the equal access to the markets with have equivalent specifications. However, the application of other ancillary requirements poses also an additional obstacle.

A) International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)

ICH has a special status in International Law, resulting from the obligations assumed by the States that join the organization, which in any event is considered as a private organization. The adopted standards are usually of common application by the EU, Japan and USA, and other 10 additional countries (Australia, India, Korea, Mexico, Russia or China are part of ICH). It is a special case of international obligation.

In practice implies that all the main world producers have adopted common requirements for approval and marketing. Those rules have the consideration of binding soft law in the domestic pharmaceutical law since a legislative act refers to them directly, including the content and structure of Common Technical Document (CTD) that many regulatory agencies (including ANVISA) has been adopted. For the time being, more than 60 Guidelines has been published, classified in the 4 technical sections¹¹: Quality - 23 Guidelines; Safety - 14 Guidelines; Efficacy - 20 Guidelines; Multidisciplinary - 5 Guidelines Brazil, however, has not adhered to more of these standards.

Other applicable standards are: Electronic Standards for the Transfer of Regulatory Information (ESTRI, E2B), and MedDRA (Standardized Medical Terminology)

A) Common Technical Document (CTD)

The Common Technical Document (CTD) describes the documentation, organised by modules and sections that an applicant must fulfil for the marketing authorization of a medicine for human use in each of the states that have adhered to ICH.

¹¹The Guidelines are accesible at <http://www.ich.org/products/guidelines.html>. For example, the Standard Q10 Pharmaceutical Quality System, has been adopted only by (information available on line): EC, Europe - Adopted by CHMP, July 2008, issued as CHMP/ICH/214732/04 / MHLW/PMDA, Japan - Adopted 19 February 2010, PFSB/ ELD Notification No. 0219-1 & PFSB/ NCD Notification No. 0219-1 / FDA, US - Published in the Federal Register, 8 April 2009, Vol. 74, No. 66, p. 15990-1 / Health Canada, Canada - Implemented 15 February 2016 File #: 16-101419-273 / Swissmedic, Switzerland - Refer to the press release on Swissmedic, Switzerland's website. Accessed on July, 29th, 2017.

The eCTD is defined as an interface for the transfer of regulatory information from the industry to the regulatory agencies and, at the same time, facilitates the creation, revision, life cycle management and electronic filing file. This application starts in June 2003; applicants have the option to submit an eCTD in parallel with the presentation document (CTD)

B) Other Standards / ISO - International Organization for Standardization

The IDMP standards of ISO are a set of common and global standards for data transmission and common terminologies to identify and exchange exclusive information on medicinal products. The five ISO IDMP standards should improve the connectivity between systems at the European Union level and define common elements for the unique identification and exchange of regulated information. Those standards are: Information on regulated pharmaceutical products (ISO 11616); Information on regulated medicines (ISO 11615); Hazardous substances (ISO 11238); Pharmaceutical dosage forms, presentation units, routes of administration and packaging (ISO 11239); Units of measure (ISO 11240)

C) The position with respect to European Union Law in relation to the competencies of ANVISA in the global market¹²

The Directive on counterfeit medicinal products (2011/62), amending Directive 2001/83 / EC, provides in Article 111b for the inclusion of “equivalent” third countries. From 2 July 2013, third countries may only export API to the EU taking into account: (a) the country’s rules for good manufacturing practice; (b) the regularity of inspections to verify compliance with good manufacturing practice; (c) the effectiveness of enforcement of good manufacturing practice; (d) the regularity and rapidity of information provided by the third country relating to non-compliant producers of active substances.

D) Role of pharmacopoeias

The European Pharmacopoeia provides a legal and scientific reference for the quality of medicinal products. The Pharmacopoeia is legally binding in 37 Member

¹²Directive 2001/83 and Regulation 726/2004 (medicinal products for human use) Directive 2001/82/CE and R. 726/2004 (Veterinary use products) (The Directive 90/385/CEE Active Implantable Medical Devices (AIMDD) Directive 93/42/CEE Medical Devices (MDD) and Directive 98/79/CE In Vitro Diagnostic Medical Devices (IVDMD), will be replaced after a 3 or 5 transitional period by Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, and Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices)

States that have signed, within the Council of Europe, the Convention on the elaboration of a European Pharmacopoeia (Convention no. 50, CoE)¹³ and its additional Protocol (Protocol of the Convention for the preparation of the European Pharmacopoeia - no 134 CoE)¹⁴. The European Directorate for Quality of Medicines and Healthcare (EDQM) was created by the European Convention of the Pharmacopoeia. Those standards are recognized as scientific reference worldwide. The European Union (EU) recognizes the binding nature of the Monographs adopted by the European Pharmacopoeia as prior requirement to request authorization for placing in the market of a new medicinal product.

E) Other relevant harmonization systems: chemical products - classification and labelling (GHS)

The Globally Harmonized System of Classification and Labeling of Chemicals (GHS) was adopted in December 2002 by a UN Committee of Experts and formally approved by the UN ECOSOC2 in July 2003. The World Summit on Sustainable Development held in Johannesburg in 2002 urged countries to implement the new EMS as soon as possible with a view to making the system fully operational in 2008¹⁵.

The Strategic Approach to International Chemicals Management (SAICM) was adopted by an international conference held in Dubai in 2006, which has among its objectives “to promote the application of the common definitions and criteria contained in the GHS”. is hosted by the United Nations Environment Programme. All chemical substances must be identified with a CAS code, a unique numerical identification for chemical compounds, preparations and alloys. (in English CAS-Chemical Abstracts Service). In addition, other classifications are: substances of great concern (SVHC) which is a chemical (or part of a group of chemicals) for which it has been proposed that use within the European Union shall be subject to authorization under the REACH Regulation. Classified a substance as SVHC by the European Chemicals Agency (ECHA) is the first step in the procedure to restrict the use of this chemical.

¹³The Council of Europe is an international organization established in 1949, which today has 47 member states. Its main objective is to create a common democratic and legal space throughout the European continent, guaranteeing respect for its fundamental values of human rights, democracy and the rule of law. The Convention is accessible at:<http://ec.europa.eu/world/agreements/prepareCreateTreatiesWorkspace/treatiesGeneralData.do?step=0&redirect=true&treatyid=480>

¹⁴Accessible at: <http://ec.europa.eu/world/agreements/prepareCreateTreatiesWorkspace/treatiesGeneralData.do?step=0&redirect=true&treatyid=8022> >. Accessed on August, 9th, 2017.

¹⁵See UNECE: https://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html >. Accessed on August, 20th, 2017.

3.3 ANVISA harmonization and regulatory competencies: application, function and connections

ANVISA's international activities include active participation in bilateral, regional and multilateral forums in which harmonization and regulatory convergence processes occur, which establish the technical and scientific references for the regulation of the Agency¹⁶. This action is coordinated with competent institutions of the Federal Government and includes the preparation of subsidies and the preparation of proposals for international instruments to be negotiated, the defense of Brazilian health interests in commercial forums and the systematic monitoring of compliance with related commitments to the activities pertinent to the field of sanitary regulation agreed by the Brazilian Government

ANVISA understands harmonization and regulatory convergence as the international technical alignment movement that takes into account best practices, principles and internationally recognized standards in the regulatory process. In addition to international alignment, regulatory convergence enables the application or adaptation of local regulatory requirements¹⁷.

Unlike the process of regulatory harmonization - which provides that exactly the same technical requirements are adopted, with the use of identical language by countries and without flexibility for adjustments based on national specificities - regulatory convergence predicts that different measures can be adopted to achieve the same goal, without the loss of regulatory power or national sovereignty. International reference building forums work to bring together knowledge, data and experts from different countries in order to build international technical and scientific references that can be used by regulators for their decision-making. Below are the main international forums for regulatory harmonization and convergence that have regular participation by ANVISA.

The list of the regulatory harmonization and convergence¹⁸ that have regular participation by ANVISA is:

A) International Coordination of Medicines Regulatory Authorities - ICMRA

The International Coalition of Drug Regulatory Authorities is an informal policy

¹⁶BRANDÃO, Dagoberto de Castro. Dificuldades, progressos e desafios da Agência Nacional de Vigilância Sanitária (ANVISA). Monografia (Especialização em Direito Público) - Pontifícia Universidade Católica de Minas Gerais (PUC-MG), 2013, p. 60.

¹⁷Op. cit. Brandão, 2013, p. 66.

¹⁸List of ANVISA connections with International or Foreign Organisms available on: <<http://portal.anvisa.gov.br/relacoes-internacionais/convergencia-regulatoria>>. Accessed on August, 9th, 2017.

mechanism for discussing strategic issues for health authorities. It is a high level of participation and representation in the field of drug regulation with the objective of strengthening a network of contacts of drug regulatory agencies, managing the challenges and future trends in drug regulation in search of shared solutions.

It is a privileged forum for brainstorming among key leaders in regulatory agencies. The Steering Committee is composed of the following countries: Australia, Brazil, Canada, China, European Union, European Commission, Ireland, Italy, Japan, Netherlands, Singapore, South Africa, United Kingdom, United States. Membership of ICMRA is voluntary and its face-to-face meetings occur twice a year¹⁹.

B) International Coalition for Research in Regulatory Science - GCRSR

The GCRSR is an international forum of regulatory authorities in the USA, Japan, Brazil, the European Union, Australia, New Zealand, Canada, Argentina and Singapore. This coalition includes the theme “research in regulatory science” that currently occupies important space on the international agenda of the countries.

These countries understand regulatory science as the science of developing new tools, standards, and approaches to assessing product safety, effectiveness, quality, and performance. It is applied to make regulatory decisions by agencies and agencies, and can extend to many fields where scientific data are used to develop policies and standards to protect the population. In the field of pharmaceutical regulation, it can be defined by the need for scientific data that can be used by a regulatory agency to develop regulations on the safety of a medical product or food. In-person meetings take place once a year²⁰.

C) CODEX ALIMENTARIUS

Joint FAO/WHO body created with two objectives: to promote consumer health and ensure fair trade practices. To achieve these objectives, Codex develops references to requirements, parameters and practices that simultaneously reduce the risk of food consumed and do not pose barriers to international food trade. In addition to being an international food reference for its 188 members, Codex is the reference recognized in the theme by the WTO. In view of the structure for discussion of Codex in Brazil, Anvisa’s participation takes place in specific groups, coordinated by the Brazilian Codex Alimentarius Committee (CCAB).

¹⁹Aviabile on: <<http://www.icmra.info/drupal/>>. Accessed on August, 19th, 2017.

²⁰Aviabile on: <<https://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeofScientificandMedicalPrograms/NCTR/WhatWeDo/ucm289679.htm>>. Accessed on August, 10th, 2017.

The Codex Committees of which Anvisa participates are: Codex Alimentarius Commission; Codex Committee on General Principles; Committee on Inspection for Import and Export of Food and Certification Systems; Committee for Latin America and the Caribbean; Committee on Pesticide Residues; Committee on Food Labeling; Committee on Nutrition and Special Diets; Committee on Food Hygiene; Committee on Additives; Committee on Pollutants; Committee on Methods of Analysis and Sampling; Committee on Residues of Veterinary Drugs in Food²¹.

D) United Nations Commission on Narcotic Drugs - CND

The Commission on Narcotic Drugs (CND) is a subsidiary body of the United Nations Economic and Social Council and meets annually at its Vienna headquarters to address issues relating to the control of the lawful and illicit aspects of the production, distribution and consumption of controlled substances, psychotropic substances, narcotics and precursors²².

E) Technical Barriers to Trade Committees - TBT - and Sanitary and Phytosanitary Measures - SPS - of the World Trade Organization - WTO

The purpose of the TBT and SPS Agreements can be broadly described as ensuring that technical regulations, standards and conformity assessment procedures do not create unnecessary obstacles to international trade, while providing Members with appropriate regulatory discretion to protect life and human, animal and plant health, national security, the environment, consumers, and other interests of public policy.

The participation of Anvisa seeks to ensure that Brazilian positions reflect health interests and do not take into account purely commercial aspects. It is important to advocate internationally for the regulation of the Agency so that it is understood as a legitimate measure to protect the health of the population and prevent it from being considered as an unjustified barrier to international trade. In addition, Anvisa has the possibility to discuss possible concerns regarding the regulations of other countries that may entail obligations for the Agency or impediments to international trade in health. The meetings of each Committee occur three times a year.²³

²¹Available on: <<http://www.fao.org/fao-who-codexalimentarius/en/>>. Accessed on August, 15th, 2017.

²²Available on: <<http://www.unodc.org/unodc/en/commissions/CND/>>. Accessed on August, 18th, 2017.

Both are available on: <https://www.wto.org/english/tratop_e/tbt_e/tbt_e.htm> and <https://www.wto.org/english/tratop_e/sps_e/sps_e.htm>. Accessed on August, 20th to 25th, 2017.

F) *International Conference of Drug Regulatory Authorities - ICDRA*

The ICDRA aims to promote annual meetings of WHO Member State Drug Regulatory Authorities to discuss and discuss ways to strengthen their collaboration, guiding the work of WHO regulatory authorities, and other stakeholders in determining priorities for action in regulation national and international level of medicines, vaccines, biotechnology and phytotherapeutic medicines²⁴.

G) *Framework Convention on Tobacco Control - FCTC*

In order to regularly review the implementation of the Framework Convention on Tobacco Control, the Conference of the Parties, a body composed of all Parties to the Convention, is hereby established which makes the necessary decisions to promote its implementation, and may adopt protocols and annexes and carry out amendments to the text of the Convention.

Their regular sessions are held at two-year intervals. Regular meetings of tobacco control laboratories (TobLabNet) and national tobacco regulations (TobReg) are also held periodically in the implementation of Convention mechanisms²⁵.

H) *International Cooperation on Cosmetic Regulation - ICCR*

International regulatory forum of Canada, the European Union, Japan, the United States and Brazil (full member since 2015) working together to promote regulatory convergence in the area of cosmetics in order to maximize consumer protection while minimizing barriers to trade. The technical discussions take place in specific ad hoc groups, which present their conclusions at the annual meetings²⁶.

I) *International Cooperation of Phytotherapeutic Regulators - IRCH*

IRCH is a voluntary technical group that organizes itself as a network with the objective of protecting and promoting the public health and safety of herbal medicines, looking for instruments to improve its regulation. Created in 2006 and organized by WHO, the IRCH meets annually to identify, discuss and prioritize topics associated with the quality, safety and efficacy of herbal medicines; exploring common solutions and strategies for the regulation of these products²⁷.

²⁴Available on: <http://www.who.int/medicines/areas/quality_safety/regulation_legislation/icdra/en/>. Accessed on August, 13th, 2017.

²⁵Available on: <<http://www.who.int/fctc/en/>>. Accessed on August, 16th, 2017.

²⁶Available on: <<http://www.iccrnet.org/>>. Accessed on August, 22nd, 2017.

²⁷Available on: <<http://www.who.int/medicines/areas/traditional/irch/en/>>. Accessed on August, 27th, 2017.

J) *International Forum of Health Product Regulators - IMDRF*

Regulators participation forum from several countries to discuss and implement regulatory convergence actions in the area of medical devices, in operation since 2012, replacing the Global Harmonization Taskforce (GHTF). Today, it has as members: Brazil, Australia, Canada, China, Singapore, United States, Japan, Russia and European Union. The official observers at the forum are WHO, APEC, and there are also affiliated organizations, PAHO and AHWP.

It currently has seven active working groups: Software as Product for Health; NCAR System Review; Electronic Submission of Registration (RPS); Patient Records; Development of common codes for adverse health product events; Good Regulatory Practice of Registry Analysis - Competence and training requirements for pre-market registry analysts and product specialists; Improvement of the quality of international standards for medical devices for regulatory use. Its management structure is composed by: Management Committee, Presidency and Secretariat. The face-to-face meetings of the Steering Committee occur once every six months²⁸.

L) *International Forum of Drug Regulators - IPRF*

Its purpose is to create an environment for the exchange of information among members, promoting regulatory cooperation. It is characterized as a forum to seek greater effectiveness in the implementation of internationally agreed regulatory technical guidelines (ICH and other initiatives), thus contributing to greater coordination among the various global efforts in the area of medicines.

It assists in the identification of topics where regulatory convergence and international cooperation are desirable, through discussions in specific working groups on the following topics: biosimilars, cell therapies, gene therapies, nano drugs. They are members of Australia, Brazil, Canada, Singapore, Korea, the United States, Japan, Mexico, Russia, Switzerland and the European Union, as well as a regional and WHO harmonization initiatives²⁹.

M) *Group of Experts on Pharmaceutical Products and Chemical Substances of CICAD*

The Inter-American Drug Abuse Control Commission (CICAD) of the Organization of American States (OAS) has a Group of Experts on Pharmaceutical Products and Chemical Substances dedicated to addressing and solving specific problems or iden-

²⁸Available on: < <http://www.imdrf.org/>>. Accessed on August, 17th, 2017.

²⁹Available on: < <https://www.i-p-r-f.org/en/> >. Accessed on August, 20th, 2017.

tifying and responding to new trends, threats or regional problems in this matter. To this end, experts meet annually, discuss and develop resources, tools, guides and other materials that, once approved by the CICAD Commission, are made available for use by Member States as reference materials or best practices³⁰.

N) Agrochemicals Program of the Organization for Economic Co-operation and Development (OECD) - Working Group on Agrochemicals

Under the Agrochemicals Program of the Organization for Economic Co-operation and Development (OECD), a Working Group was established which meets annually to supervise practices in this area.

The group is composed of government representatives from OECD member countries, the European Commission and other international organizations, industry observers, interested publics and organized civil society. Its discussions include the evaluation of chemicals, information on risk reduction activities, development of registration requirements and other common guidelines³¹.

O) International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use - ICH

Its mission is to develop recommendations aimed at achieving greater convergence in the understanding and application of technical drug requirements, ensuring that safe, effective and high-quality products are developed and recorded with resource efficiency.

Its guidelines are the result of technical consensus among the experts who participate in more than 20 active working groups, and the guides are subsequently implemented by the governments of its members.

Created in 1990 by the regulatory authorities and industry associations in Europe, Japan and the US, in October 2015 the ICH announced substantial organizational changes, which enabled Anvisa to apply for membership, and was accepted in November 2016. Currently, ICH members are: Europe, Japan, the United States, Canada, Switzerland, Brazil, Korea and China, as well as industry members and observers³².

³⁰Available on: < http://www.cicad.oas.org/Main/Template.asp?File=/reduccion_oferta/grupoexpertos/ge_quimicos-farmacos_spa.asp >. Accessed on August, 21st, 2017.

³¹Aviable on: < <http://www.oecd.org/env/ehs/pesticides-biocides/agriculturalpesticidesprogramme.htm> >. Accessed on August, 23rd, 2017.

³²Available on: < <http://www.ich.org/home.html> >. Accessed on August, 25th, 2017.

Formal substance group on substandard/spurious/falsely-labeled/falsified/counterfeit (SSFFC) which discusses good practice issues to combat drug counterfeiting and protection of public health interests. It includes technical groups that are dedicated to the discussion of topics and development of reference documents in several aspects related to the problematic of the SSFFC, especially of virtual form. Meetings of the Mechanism are annual, but there may be occasional meetings of its technical groups³³.

Q) MERCOSUR³⁴

Anvisa participates especially in the Working Subgroups - SGT No. 3 “Technical Regulations and Conformity Assessment” and No. 11 “Health”, linked to the Common Market Group (GMC).

SGT no. 3 has the task of harmonizing Technical Regulations and Conformity Assessment Procedures and coordinating actions related to the industrial and agricultural sectors, and Anvisa’s issues are dealt with in the Food Commission and in Temporary Working Groups with specific mandates. The face-to-face meetings take place twice a semester.

SGT no. 11 has as its general task to harmonize laws and guidelines, promote technical cooperation and coordinate actions related to health care, goods, services, raw materials and products for health, professional practice, epidemiological surveillance and sanitary control.

The themes of Anvisa are treated by the Commission on Health Surveillance and its Subcommittee on Sanitary Control of PAF; in the Commission of Health Care Services and its Subcommittee on Evaluation and Use of Technologies in Health Services; in the Health Products Commission - its Ad Hoc Groups (Psychotropic and Narcotic, Pharmacopoeia, Medical, Cosmetic and Sanitary Products) and Temporary Working Groups (BP Distribution and Fractionation of IFAs and BPF Pharmaceutical Area). The face-to-face meetings are held once per semester.

There is also the participation of ANVISA in the scope of the Commissions of the Meeting of Ministers of Health dealing with the International Sanitary Regulation, Donations and Transplants, Blood and Hemoderivatives, Tobacco Products³⁵.

³³Available on: < <http://apps.who.int/gb/SF/> >. Accessed on August, 22nd, 2017.

³⁴In Mercosur, “health products” are all those products regulated by Anvisa, except for food. What Anvisa calls “products for health” is referred to in Mercosur as “medical products”.

³⁵Available on: < <http://www.mercosur.int/innovaportal/v/6432/11/innova.front/cooperacion-en-el-mercotur> >. Accessed on August, 27th, 2017.

R) *Pharmaceutical Inspection Cooperation Scheme - PIC/S*

It is a forum that seeks the harmonization of pharmaceutical inspection procedures through training and training opportunities to promote the development of common standards in the area of Good Manufacturing Practices. This process also facilitates the construction of a network of work and of mutual trust among the inspectors; the exchange of information and experience in GMP; and a role in improving quality systems for regulatory authorities responsible for GMP inspection through the training of their inspectors.

ANVISA is in the process of joining the PIC/S - the evaluation questionnaire for the national inspection system has already been finalized. After recognition of the equivalence of the Brazilian control to the European standard applied in the IFAs area, the Agency should receive the audit of the PIC/S inspectors team to validate the inspection procedures and documentation, as reported in the adherence questionnaire³⁶.

S) *International Program of Generic Drug Regulators - IGDRP*

International Forum of Drug Regulatory Authorities of South Africa, Australia, Brazil, Canada, China, Singapore, Colombia, Korea, United States, Japan, Mexico, Russia, Switzerland, Taiwan and New Zealand, as well as WHO as an observer, was created to promote regulatory cooperation and convergence, exploring opportunities for better regulation and compatibility of requirements for registration of generic drugs.

The entity has operated as a pilot between the years 2011 and 2014, and today is consolidated, with concrete expectations that the activities developed lead to the convergence of requirements and approaches on the theme, more efficient use of resources, reduction of duplication of efforts and of the time of analysis of generic drug registration processes, and greater access to these drugs by the population³⁷.

T) *Single Health Products Audit Program - MDSAP*

Cooperation program between Brazil, the United States, Australia, Canada and Japan to enable a single auditing of health products by a third-party Audit Body recognized by these countries to meet all the regulatory requirements of participating countries and this result can be used for the regulatory demands of these

³⁶Available on: < <https://picscheme.org/> >. Accessed on August, 27th, 2017.

³⁷Available on: < <http://www.igdrp.com/> >. Accessed on August, 27th, 2017.

countries. The pilot of the program ended in December 2016. ANVISA has issued regulations to allow the use of the results of the program in the processes of Certification of Good Practices in the Manufacture of Health Products.

In 2014, RDC Anvisa nº 15 was published. allows the Agency to use valid audit reports issued by third parties to grant Certificates of Good Manufacturing Practices for Health Products, provided that they are issued by organizations recognized by Anvisa. This resolution was complemented by Resolution RE No. 2,347 / 2015, which recognizes the MDSAP for the purpose of complying with DRC No. 15 above.

As a practical result, manufacturers who are interested in joining the products in the Brazilian market, when requesting the Certification of Good Manufacturing Practices have the possibility of contacting an auditing body recognized by Anvisa to perform an audit in their establishment, and the result of this audit will subsidize the analysis of the concession of the Certificate. In these cases, since the report is valid, the company does not have to wait for the inspection carried out by Anvisa to receive the Certification. ANVISA has published the recognition of the Audit Bodies evaluated and approved by the participating countries³⁸.

U) Pan American Regulatory Agency - PARF

The PARF Network was established in 1999 to support regulatory convergence and cooperation processes in the Americas region. The Regulatory Authorities of the countries of the Americas and the different drug interest groups (including the pharmaceutical industry, patient and professional associations, and the academic community) are participating in the initiative.

The Pan American Conference is the ultimate forum for exchange of experiences and discussion, preparation of guides and joint adoption of strategies to strengthen the regulatory capacities of countries. It takes place every two years and its mission is to promote debate on issues of pharmaceutical regulation, covering aspects of quality, safety and efficacy of pharmaceuticals.

The Network's main decision-making body is the Steering Committee, which meets annually and has representatives from each subregion of the Americas³⁹.

³⁸http://www.who.int/immunization_standards/vaccine_regulation/dcvrn/en/. Accessed on August, 25th, 2017.

³⁹Available on: < http://www.paho.org/hq/index.php?option=com_content&view=article&id=11818&Itemid=41774&lang=es >. Accessed on August, 30th, 2017.

Final considerations

About the institucional relationship, ANVISA, in order to carry out its institutional mission, acts in alignment with various governmental agencies. Among them are the Ministry of Health, the Ministry of Planning, Development and Management, the Ministry of Agriculture, Livestock and Supply, and control bodies such as the Federal Audit Office.

ANVISA follows the international rules and international reference building forums work to bring together knowledge, data and experts from different countries in order to build international technical and scientific references that can be used by regulators for their decision-making. International negotiations are to use existing international tools to assist the Agency to develop its final role in regulating, monitoring and supervising products subject to health surveillance, avoid duplication of efforts and make better use of available resources, with a focus on to reconcile protection and health promotion with national economic development.

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REFERENCES

ANVISA. *Agência Nacional de Vigilância Sanitária*. Available on: <<http://portal.anvisa.gov.br/institucional>>. Accessed on August, 25th, 2017.

_____. *Processo de Convergência Regulatória*. Available on: <<http://portal.anvisa.gov.br/relacoes-internacionais/convergencia-regulatoria>>. Accessed on August, 9th, 2017.

BRANDÃO, Dagoberto de Castro. *Dificuldades, progressos e desafios da Agência Nacional de Vigilância Sanitária (ANVISA)*. Monografia (Especialização em Direito Público) - Pontifícia Universidade Católica de Minas Gerais (PUC-MG), 2013.

BRASIL. *Segurança sanitária: desafios em um mundo sem fronteira - cooperação entre as agências reguladoras de medicamentos*. Brasília: Agência Nacional de Vigilância Sanitária. 2012.

____. *Constituição da República Federativa do Brasil de 1988*. Available on: <http://www.planalto.gov.br/ccivil_03/constituicao/constituicao.htm>. Accessed on August, 23rd, 2017.

CND - *United Nations Commission on Narcotic Drugs*. Available on: <<http://www.unodc.org/unodc/en/commissions/CND/>>. Accessed on August, 18th, 2017.

COCKBURN, I. et al. *Pharmaceuticals and Biotechnology*. In: US Industry in 2000 - Board on Science, Technology and Economic Policy, Washington (DC): *National Research Council*, 1999.

____; Henderson, R, *Publicly Funded Science and the Productivity of the Pharmaceutical Industry*. In: Jaffe, Lerner and Stern (Coord), *Innovation Policy and the Economy*, Cambridge (MA): MIT Press, 2001.

CODEX ALIMENTARIUS. Available on: <<http://www.fao.org/fao-who-codexalimentarius/en/>>. Accessed on May, 15th, 2017.

COSTA, E. A. *Vigilância Sanitária: temas para debate* [online]. Salvador: EDUFBA, 2009. 237 p. ISBN 978-85-232-0652-9. Available from SciELO Books: <<https://static.scielo.org/scielobooks/6bmrk/pdf/costa-9788523208813.pdf>>. Accessed on May, 15th, 2017.

GCRSR - *International Coalition for Research in Regulatory Science*. Available on: <<https://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeofScientificandMedicalPrograms/NCTR/WhatWeDo/ucm289679.htm>>. Accessed on August, 10th, 2017.

GROUP OF EXPERTS ON PHARMACEUTICAL PRODUCTS AND CHEMICAL SUBSTANCES OF CICAD. Available on: < http://www.cicad.oas.org/Main/Template.asp?File=/reduccion_oferta/grupoexpertos/ge_quimicosfarmacos_spa.asp >. Accessed on August, 21st, 2017.

ICCR - *International Cooperation on Cosmetic Regulation*. Available on: < <http://www.iccrnet.org/> >. Accessed on August, 22nd, 2017.

ICDRA - *International Conference of Drug Regulatory Authorities*. Available on: <http://www.who.int/medicines/areas/quality_safety/regulation_legislation/icdra/en/>. Accessed on August, 13th, 2017.

ICH - *International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use*. Available on: < <http://www.ich.org/home.html> >. Accessed on August, 25th, 2017.

ICMRA - *International Coordination of Medicines Regulatory Authorities*. Available on: <<http://www.icmra.info/drupal/> >. Accessed on August, 19th, 2017.

IGDRP - *International Program of Generic Drug Regulators*. Available on: < <http://www.igdrp.com/> >. Accessed on August, 27th, 2017.

IMDRF - *International Forum of Health Product Regulators*. Available on: < <http://www.imdrf.org/>>. Accessed on August, 17th, 2017.

IPRF - *International Forum of Drug Regulators*. Available on: < <https://www.i-p-r-f.org/en/> >. Accessed on August, 20th, 2017.

MERCOSUL - *Mercado Común del Sur*. Available on: < <http://www.mercosur.int/innovaportal/v/6432/11/innova.front/cooperacion-en-el-mercosur> >. Accessed on August, 27th, 2017.

OCDE - *Organisation for Economic Co-operation and Development*. Available on: < <http://www.oecd.org/env/ehs/pesticides-biocides/agriculturalpesticidesprogramme.htm> >. Accessed on October, 23rd, 2017.

PARF - *Pan American Regulatory Agency*. Available on: < http://www.paho.org/hq/index.php?option=com_content&view=article&id=11818&Itemid=41774&lang=es >. Accessed on August, 30th, 2017.

PIC/S - *Pharmaceutical Inspection Cooperation Scheme*. Available on: < <https://picscheme.org/> >. Accessed on August, 27th, 2017.

RAMALHO, Pedro Ivo Sebba (Org.) *Regulação e agências reguladoras: governança e análise de impacto regulatório*. São Paulo: RT, 2009.

WHO - *World Health Organization*. Available on: < <http://www.who.int/medicines/areas/traditional/irch/en/> >. Accessed on August, 27th, 2017.

_____. Available on: < <http://apps.who.int/gb/SF/> >. Accessed on August, 22nd, 2017.

_____. Available on: < http://www.who.int/immunization_standards/vaccine_regulation/dcvrn/en/ >. Accessed on August, 25th, 2017.

WTO - *World Trade Organization*. Available on: < https://www.wto.org/english/tratop_e/tbt_e/tbt_e.htm > and < https://www.wto.org/english/tratop_e/sps_e/sps_e.htm >. Accessed on August, 20th to 25th, 2017.

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