

ANVISA





Regulatory Reliance

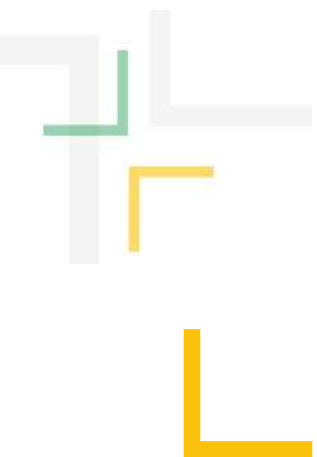
New regulation in Brazil.

- 20/09/2023
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Regulatory Convergence

- Regulatory Convergence is a major value of Anvisa
- WHO – World Health Organization
- ICMRA - International Coalition of Medicines Regulatory Authorities
- ICH - International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
- PIC/S - Pharmaceutical Inspection Co-operation Scheme
- IPRP - International Pharmaceutical Regulators Program



Reliance – goals:

The propose is to fully assess studies, data and documents prepared to meet specific conditions for products to be commercialized in Brazil and benefit from equivalent assessments already carried out by trusted regulators.

GOALS:

- To strengthen regulatory capacities
 - To make better use of limited resources
 - To avoid duplication of efforts
 - To promote expedite access to medicines
 - To increase convergence practices among regulators
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- By expediting assessment of products having reliance as a tool, it is expected to dedicate enough human resources to also expedite the assessment of products that are developed aiming to be approved first in Brazil.



Previous initiatives:

Several dissociated initiatives with limited outcomes:

- Medicines,
- Medical Devices
- Food
- Pharmacopeia ...

For Medicines: Service Order #45/2018

- Establishes optimized procedure for authorizations and post approvals changes for products approved by FDA **and** EMA
- Necessity of the detailed reports
- Differences between the approvals must be justified and the proposal approved by Anvisa



Previous initiatives:

Problems identified during the beginig of the initiative:

- Low adherence in the first year
- Lack of information - documentation issued by the reference authorities do not identify the approved change
- Confused documentation in the submission
- Absence of one of the agencies approval
- Difficult for the companies to provide the reference agencies reports

Conclusion: The process needed to be improved to get better results



Previous initiatives:



Following years:



After some open meetings with companies' associations – Increase in the numbers (more than 600 until 2023), but still a small portion considering the potential



Use of the process in specific initiatives



Acquired Experience – Used in the consolidation for the definitive initiatives



Recent Initiatives for medicines:

Regulation	Status
RDC n° 741: General criteria for the admissibility of an analysis carried out by an Equivalent Foreign Regulatory Authority, through a reliance assessment pathway.	In force since August 10, 2022
RDC n° 750: temporary optimized reliance assessment pathway for applications of marketing authorization (registration) and post-approval changes of API, Medicines and Biological Products	In force since September 19, 2022.
Normative Instruction: Establishes the criteria applied for the reliance assessment pathway for registration and post-approval changes application of API, Medicines and Biological Products	Final document will be approved soon by Anvisa's Board of Directors



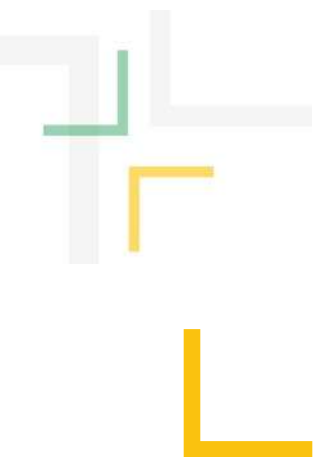
RDC 750 In force since September 19, 2022.

Temporary

To address the pandemic impact/Pilot for the Normative Instruction

Not Applied to:

- vaccines
- medicines and biological products without complete clinical data (Without phase III or ongoing studies)
- ATMP



RDC 750 – Results

- 190 submissions
- 9 for new molecules
 - 1 not accepted (report not submitted)
 - 2 accepted and submissions were approved
 - Others accepted and under review
- 181 for post Approval Changes
 - 36 accepted and 32 submissions were approved and 4 under review
 - 3 were quit by the companies and 9 finished without assessment (submissions already under review)
 - 11 not accepted – absence of the assessment report, reports from agencies not considered equivalent and lack of data to guarantee the sameness



Public Consultation n° 1.108

Verification: confirmation of the applicability of the assessment outcomes of another authority for regulatory decision making in the national context;

Abridged assessment: assessment of data on quality, safety and efficacy or performance, considering information in the assessment reports of the reference regulatory authority.

Note: the final decision will be taken by Anvisa independently of the Reference Regulatory Authority conclusions.

***The procedure will not be applied for ATMP**



Equivalent Foreign Regulatory Authority (AREE)

- AREE: foreign regulatory authority or international entity that has regulatory practices aligned with those of Anvisa.



To be considered Equivalent to Anvisa (AREE), a Regulatory Authority must:



I - carry out pre- and post-market regulatory activities, in a manner consistent with those adopted by Anvisa;

II - have a transparent regulatory system, guided by good regulatory practices, with measures that prevent conflicts of interest;

III - adopt international standards and norms equivalent to those currently adopted by Anvisa applicable to API, medicines and biological products and their active substances, those established by the International Council for Harmonization of Technical Requirements for Medicines for Human Use (ICH) and the Organization World Health Organization (WHO);

IV - has established a formal and practical structure of technical cooperation with Anvisa, supported by a Memorandum of Understanding, or equivalent document, that allows the exchange of confidential information;

V – can interact in English, Spanish or Portuguese; and

VI - is not prevented from submitting, or allowing them to be submitted, the necessary documents and reports required by this resolution



Equivalent Foreign Regulatory Authority (AREE)

New AREE can be included in the guideline



The decision to include or not a new AREE is from Anvisa's Board of Directors that will consider the reports from the offices responsible to assess the submission and the Anvisa International Affairs Office.



AREE that are considered to be equivalent (RDC 750 and Public Consultation)*

- I - European Medicines Agency EMA (centralized analysis processes), applicable to medicines and biological products;
- II - Health Canada, applicable to medicines and biological products;
- III - World Health Organization - WHO, applicable to API and medicines;
- IV - European Directorate for the Quality of Medicines & HealthCare - EDQM, applicable for API;
- V - Swiss Agency for Therapeutic Products - Swissmedic, applicable to medicines and Biologicals;
- VI - Medicines and Healthcare products Regulatory Agency – MHRA, United Kingdom: applicable to medicines and biological products;
- VII - US Food and Drug Administration - FDA: applicable to medicines and biological products.

* Others may be included after the Public Consultation if established criteria are fulfilled.



AREE Documentation:

- “Sameness”: product must have essential characteristics identical to those evaluated by the reference regulatory authority;
 - The applicant must confirm that the product is the same or sufficiently similar.
 - Same qualitative and quantitative composition, same strength, same pharmaceutical form, same intended use, same manufacturing process, same suppliers of active pharmaceutical ingredients, same quality of all excipients.
 - Additionally, the results of supporting studies of safety, efficacy and quality, indications and conditions of use should be the same.
 - The impact of potential differences should be assessed and justified by the applicant.



AREE Documentation:

If the medicine is approved in more than one AREE:

- The applicant can choose the AREE to be used as reference for the optimized assessment procedure.

- The documentation must be complete – essential conditions

- If part of the documentation is redacted, the applicant may use other AREE documents to fulfill the requirements

- If there is difference between the approval of two or more AREE, the applicant must technically discuss the differences and justify the AREE selection



Submission:



Complete submission: all documentation provided for ordinary pathways must be submitted and in addition the assessment reports from AREE.



Despite Anvisa's participation in important initiatives, such as the Orbis Project, the current regulation does not address collaborative assessment or work-sharing yet.



Assessment Procedures – Reliance:



The complete analysis using the reliance procedure is applied when the regulatory documentation submitted is enough to assess all the requirements – Quality, Safety, Efficacy



The partial assess can be used when the submitted documentation is enough for one or more sections of the application but not sufficient for all the essential aspects.



If it's not possible to guarantee the sameness of the product, then Anvisa will review the submission using the regular procedures.



SOVEREIGNTY

- Decisions on regularization requests submitted under the optimized analysis procedure is the exclusive responsibility of Anvisa and is not necessarily linked to the decisions and conditions approved by the AREE.



Challenges:

Regional requirements, which inhibit wider adoption of reliance;

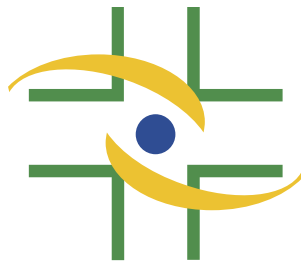
Control of the lifecycle;

Possible lack of adherence of companies to the pathway; and

Reports of the Reference Regulatory Authority redacted or incomplete.



Thank You!



ANVISA

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