OVERVIEW OF THE REGISTRATION PROCESS OF GENERIC DRUGS IN BRAZIL
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**DEFINITION**

Generic Drug is a drug similar to a reference or innovative product, that contains the same active principle, in the same dose and pharmaceutical form, it is administered by the same route and with the same dosage and therapeutic indication of the reference drug, presenting efficacy and safety equivalent to the reference drug, and may be interchangeable with it.

The interchangeability, that is, the safe substitution of the reference drug by its generic, is ensured by therapeutic equivalence tests, which include *in vitro* comparison, through pharmaceutical equivalence studies and *in vivo*, with the bioequivalence studies presented to the National Health Surveillance Agency (ANVISA).

Designated by the Brazilian Common Denomination (DCB) or, in its absence, by the International Non-Proprietary Name (INN).
INSTITUTIONS INVOLVED IN THE REGISTRATION PROCESS

Ministry of Health

Brazilian Health Surveillance Agency (ANVISA)

General Management of Drugs and Biological Products (GGMED)

ANVISA:
Promotes the protection of the health of the population through the sanitary control of the production and consumption of products and services subject to sanitary surveillance, including the environments, processes, inputs and technologies related to them.

GGMED:
Coordinates, supervises, controls and evaluate the activities related to the registration and post-registration, inspection, norms and standards establishments, quality, safety and efficacy concerning the sanitary surveillance of active pharmaceutical inputs, drugs (including radiopharmaceuticals), biological products and clinical research in drugs involving humans.
1) Official documents in a foreign language used for registration purposes, dispatched by the health authorities, must be accompanied by translation sworn in the form of the law.

2) The applicant for registration should consult the list of reference drugs available at the Anvisa website, to check if there is a reference drug chosen in the concentration and pharmaceutical form for the drug to be registered. In the absence of elected reference drug, a request for election of reference drug must be filed with Anvisa.

3) The batch size to be considered for registration approval of generic drugs and similar should be based on the batch size used to prove pharmaceutical equivalence and bioequivalence.

4) It will not be admitted for registration as a generic drug or similar:

   I. biological products, immunotherapy, plasma derivatives and human blood
   II. herbal medicines
   III. specific drugs
   IV. dynamized drugs
   V. simplified notification drugs
   VI. antiseptics for hospital use
   VII. products with diagnostic purposes and radiological contrasts
   VIII. Radiopharmaceuticals
   IX. medicinal gases
   X. other classes of drugs that have specific legislation for your registration
In Brazil the registration dossier is structured in eCTD format and it has two main parts:

**Part 1 - Administrative Part:**
It corresponds to Module 1 and includes compilation of all administrative data and local information.

**Part 2 - Technical Part:**
It corresponds to Module 2, Module 3, Module 4 and Module 5 that include summaries of pre-clinical studies; CMC information; nonclinical data and reports; and clinical information and reports.

In case of Generic Drugs, there are only Module 1, Module 3, and Module 5 (BE studies).
**REGISTRATION PROCESS**

**Phase 2: Steps of Registration**

**APPLICANT ACTIVITY**
Applicant Company will file new drug submission with Brazilian Health Surveillance Agency - ANVISA

**GEPEC ACTIVITY**
Safety, efficacy and pharmacological evaluations conducted by Office of new drug research and clinical trials

**CMED ACTIVITY**
Chamber of Drug Market Regulation (CMED) discusses drug price with applicant

**ANVISA ACTIVITY**
ANVISA carry out facility inspections

**ANVISA ACTIVITY**
ANVISA approves drug and grant marketing authorization

**EXTERNAL CONSULTANT ACTIVITY**
Advice from external consultants used on ad hoc basis

**CATEME ACTIVITY**
Technical chamber of medicines provides expert advice
### ADMINISTRATIVE DOCUMENTS

**ITEM**

- Application forms FP1 and FP2 completed, stamped and signed
- Proof of payment of Anvisa fee from the Health Surveillance (TFVS)
- Status of the medicinal product: imported or locally manufactured
- Good Manufacturing Practice (GMP) certificate issued by ANVISA, or copy of the request for Anvisa GMP inspection
- Copy of GMP certificate in country of origin for imported products
- Proof of registration in the country of origin for imported drugs (CPP)

Declaration signed by the legal representative that the company will submit within 10 days after the submission of the registration the following additions:

- 10470 - Addition to the registration application with the Registration Documentation Information Form (FIDR), exclusively by electronic means
- 11212 - Addition of package leaflet, labelling and trade name, exclusively by electronic means
- 10415 - Addition of relative bioavailability study or Biowaivers
- 11314 - Addition of study for qualification of impurities and degradation products
## REGISTRATION PROCESS

### Documents Required

<table>
<thead>
<tr>
<th>TECHNICAL REPORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Documentation on the active pharmaceutical ingredient</td>
</tr>
<tr>
<td>IFA Quality Control by the Drug Manufacturer</td>
</tr>
<tr>
<td>Quality control of excipients by the Manufacturer of the finished product</td>
</tr>
<tr>
<td>Quality Control of Primary, Secondary, Packaging Material</td>
</tr>
<tr>
<td>Technical Report on the development of the formulation</td>
</tr>
<tr>
<td>Description of Manufacturing and Packaging process</td>
</tr>
<tr>
<td>Process Validation Report</td>
</tr>
<tr>
<td>Quality Control of the Finished Product performed by the Manufacturer</td>
</tr>
<tr>
<td>Product Quality Control performed by Importer</td>
</tr>
<tr>
<td>Stability studies of the finished product</td>
</tr>
<tr>
<td>Documentation and evidence regarding manufacturing site of the drug or active pharmaceutical ingredient (API), according to specific legislation in force for post-registration changes</td>
</tr>
<tr>
<td>Diluent/reconstituent solutions</td>
</tr>
<tr>
<td>Pharmaceutical Equivalence</td>
</tr>
<tr>
<td>Pre-bioequivalence dissolution profile</td>
</tr>
<tr>
<td>Biowaivers - pharmaceutical form</td>
</tr>
<tr>
<td>Biowaivers for other dosages</td>
</tr>
<tr>
<td>Final bioequivalence or biowaivers report based on the biopharmaceutical classification system</td>
</tr>
</tbody>
</table>
PACKAGING

<table>
<thead>
<tr>
<th>ITEM</th>
<th>Primary Package</th>
<th>Secondary Package</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>II.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>III.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>IV.</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>V.</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>VI.</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>VII.</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>VIII.</td>
<td>&quot;ADULT USE&quot;</td>
<td>✗</td>
</tr>
<tr>
<td></td>
<td>&quot;ADULT USE AND PEDIATRIC APPROPRIATE OF ____&quot;, indicating the minimum age, in months or years; or</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>&quot;ADULT AND PEDIATRIC USE &quot;, in the case of medication without age restriction</td>
<td>✓</td>
</tr>
<tr>
<td>IX.</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>ITEM</td>
<td>Primary Package</td>
<td>Secondary Package</td>
</tr>
<tr>
<td>------</td>
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</tr>
<tr>
<td>X. Conservation care, indicating the temperature range and storage conditions</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>XI. Name and address of the company holding the registration in Brazil</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>XII. Name and address of the manufacturing company, when it differs from the company holding the registration, preceded by the phrase &quot;Made by:&quot; and inserting the phrase &quot;Registered/Imported by:&quot; before the data of the company holding the registration</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>XIII. Name and address of the company responsible for the packaging of the drug, when it differs from the company holding the registration or manufacturer, preceded by the phrase &quot;Packed by:&quot; and inserting the phrase &quot;Registered/Imported by:&quot; before the data of the company holding the registration</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>XIV. Number of the National Register of Legal Entities (CNPJ) of the holder of the registration</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>XV. Expression &quot;Brazilian Industry&quot;, when applicable</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>XVI. Name of the technical manager, registration number and acronym of the Regional Pharmacy Council of the company holding the registration</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>XVII. Telephone number of the Customer Service (SAC) of the company holding the registration or its responsibility</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>XVIII. Acronym &quot;MS&quot; added to the Ministry of Health registration number as published in the Official Gazette (DOU)</td>
<td>✗</td>
<td>✓</td>
</tr>
</tbody>
</table>
LABELING

- The letters for the generic denomination of the active principles should be easy to read, in uppercase letters;
- The concentration must be arranged below the generic name of the active ingredients;
- Prints of the generic name of each active ingredient and its concentrations should be repeated on the labels of the primary destructible packaging, with more than one dose, allowing the identification of the drug throughout the treatment.

**Warning phrases:**

"ALL MEDICATION MUST BE KEPT OUT OF CHILDREN’S ACCOUNT", in uppercase letters;

"Information to the patient, indications, contraindications and precautions: see package insert"; or

"Information to the health professional, indications, contraindications and precautions: see package insert";

In case of contraindication, precaution or warning for the use of active ingredients, therapeutic class and excipients, the warning phrases foreseen in a specific rule must be included in bold.
It is **forbidden**:

1. Include images of people using the drug;

2. Include stamps, word marks, figurative or mixed of governmental institutions, philanthropic entities, foundations, associations and medical societies, non-governmental organizations, associations representing the interests of consumers or health professionals and quality certification stamps, except if required by specific standards;

3. Include images or figures that refer to the indication of the taste of the drug;

4. Use expressions or images that may suggest that a person's health may be affected by not using the drug; and,

5. Use labels with a layout similar to a drug with the same active ingredient, pharmaceutical form and concentration, previously registered by another company;

6. They may not appear on the labels of the drugs, names, symbols, figures, graphic representations or any indications that may make the information false and incorrect, which allow false interpretation, misunderstanding, error and confusion in relation to the true nature, composition, origin, quality, form of use, purpose and characteristics of the drug;
LABELING

- Yellow stripe (PANTONE 116C*) in which “Medicamento Genérico” is read. (highlighted in pink in the picture beside)

- Stripe with width equal to 1/5 of the largest total side, covering the main side and the sides of the package. (highlighted in pink in the picture beside)

- It is allowed to print legal texts on the sides, if necessary.

- The phrase “Medicamento Genérico Lei 9.787 de 1999” must appear on the packaging. (highlighted in blue in the picture beside)

- As generics have no brand, what you read on the packaging is the active ingredient of the drug. (highlighted in orange in the picture beside)

* The use of the color PANTONE 116C yellow is forbidden outside the yellow stripe and in packaging of drugs other than generics.
The drugs that can only be sold under medical prescription, the yellow stripe should be juxtaposed just **above** the red stripe (as shown in the picture 1 below).

The drugs based on narcotics and psychotropics, the yellow band should be juxtaposed just **below** the black stripe (as shown in the picture 2 below).
## TIMELINES

<table>
<thead>
<tr>
<th>Registration Validity</th>
<th>Registration Validity</th>
</tr>
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<tbody>
<tr>
<td>10 years (may be revalidated for equal and successive periods)</td>
<td>180 days before the validity date of the registration</td>
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</table>

### Registration Post-approval Changes

<table>
<thead>
<tr>
<th>Registration</th>
<th>Post-approval Changes</th>
<th>Registration</th>
<th>Post-approval Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>120 days</td>
<td>60 days</td>
<td>365 days</td>
<td>180 days</td>
</tr>
</tbody>
</table>

### PRIORITY REVIEW
- Registration: 120 days
- Post-approval Changes: 60 days

### STANDARD REVIEW
- Registration: 365 days
- Post-approval Changes: 180 days
REFERENCES

ANVISA Website. Resolution RDC 200/2017. Link:

ANVISA Website. Resolution RDC 47/2001. Link:
http://antigo.anvisa.gov.br/documents/10181/2718376/RDC_47_2001_COMP.pdf/60aca8aa-fa5e-4c8a-8f4b-e7fde7d717cf

ANVISA Website. Resolution RDC 71/2009. Link:
http://antigo.anvisa.gov.br/documents/10181/2718376/%282%29RDC_71_2009_COMP.pdf/3ff7e308-df4e-4a3c-bac3-b779d9d5c7f1

ANVISA Website. Resolution RDC 317/2019. Link:

Federal Government. Law No. 9.787, of February 10, 1999. Link:
http://www.planalto.gov.br/ccivil_03/leis/l9787.htm

ANVISA Website. Documentation for Generic Drug Registration. Link:
Thank You

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