Regulatory Advances in Drug Regulation

Accelerated Pathways of Approval

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Director-President / Brazilian Health Regulatory Agency - ANVISA
Brazil at a glance

Population: 208,892,578
26 states and the Federal District - 5,570 municipalities
Life expectancy at birth: 75.99 (70.85 in MA to 79.37 in SC)
GDP total: US$ 1.9 tri (0.38 tri in SP to 1.9 bi in RR)
GDP per capita: US$ 9,290
Population on the poverty line: 25.4% (family income: US$ 5.5 per day)

SUS – National Public Health System:
“Health as a citizen’s right and the government’s responsibility”: free and universal access to health care.

Source: IBGE
Brazilian Drug Market

- **7º World Market**: 5th in 2020
- **US$ 18.7 bi**: Industrial pharmaceutical market in Brazil in 2016
- **4 bi**: Number of units of drugs sold (packaging) by the industry in 2016
Brazilian Drug Market

Variation between first quarter of 2016 and same period in 2015
Source: CNI, 2016
In order for these technologies to be used in SUS, in addition to being licensed by Anvisa, they must be evaluated and approved by CONITEC (National Committee for Technology Incorporation).

License – ANVISA

Evaluation of the quality, efficacy and safety of a medicine or health product aiming at marketing authorization

Incorporation – CONITEC

Analysis of the effectiveness of the technology, comparing it with the treatments already incorporated in SUS. If the new technology demonstrates superiority in relation to the technologies already offered in SUS, the magnitude of expected benefits and risks, the cost of its incorporation, and the budgetary and logistical impacts that it will bring to the system will also be evaluated.
Accelerated Pathways of Approval

RDC 204/2017 – Framework for prioritization of registration, variations and clinical trial authorization

Establishes the criteria for eligibility for the **Priority Pathway**:
The product must meet at least one of the eligibility criteria (e.g. Drug product for neglected disease; vaccine incorporated in the National Immunization Program)
- Drug product registration: 120 calendar days (cd);
- Variations/Post-approval changes: 60 cd;
- Clinical Trial Authorization: 45 cd for first evaluation

RDC 205/2017 – Establishes special procedure for clinical trials authorization, GMP (Good Manufacturing Practice) certification and Registration of new medicines for the treatment, diagnosis or prevention of rare diseases.

Defines the eligibility criteria for this special pathway and **special requirements** (ongoing stability studies; concluded fase II with ongoing fase III clinical trials)
- GMP Certification: 120 cd
- Clinical Trial authorization: 30 cd for first review cycle; 30 cd for companies to respond to questions; 30 cd for final decision.
- Drug product registration: 60 cd for first evaluation; 30 cd for companies to respond to questions; 45 cd for final decision.
- Must have pre submission meeting, CTD format
## Accelerated Pathways of Approval

<table>
<thead>
<tr>
<th>Previous rules (RDC 37/2014)</th>
<th>Current rules RDC 204/2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>75 days</strong> for authorization requests and <strong>90 days</strong> for post-authorization requests, to manifest for the first time</td>
<td><strong>120 days</strong> for authorization requests and <strong>60 days</strong> for post-authorization requests, to inform the final decision</td>
</tr>
</tbody>
</table>

**System of points, according to the criteria**

**Drug authorization prioritization:**
- Fractionable pharmaceutical forms;
- Rare, neglected diseases;
- Emerging or reemerging diseases;
- Basic, specialized, or strategic component for the Health Ministry;
- Vaccines within the National Immunization Program;
- First 3 generic drugs;
- First similar drug;
- API manufactured in the country;
- Risk of shortage in the National Public Health System.

**Prioritization to authorize drugs for:**
- Pediatric population;
- Neglected diseases; (rare diseases – RDC 205/17)
- Emerging or reemerging diseases;
- Public health emergencies;
- Serious debilitating conditions;
- Vaccines to be included in the National Immunization Program;
- First 3 unprecedented generic drugs;
- Risk of shortage in the market.
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<td><strong>Prioritization of drug post-authorization requests:</strong></td>
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</tr>
<tr>
<td>▪ Fractionable pharmaceutical forms;</td>
<td>▪ Rare diseases;</td>
</tr>
<tr>
<td>▪ Rare, neglected, emerging, or reemerging diseases;</td>
<td>▪ Pediatric population;</td>
</tr>
<tr>
<td>▪ Use extended to the pediatric population;</td>
<td>▪ Neglected diseases;</td>
</tr>
<tr>
<td>▪ Basic, specialized, or strategic component for the Health Ministry;</td>
<td>▪ Emerging or reemerging diseases;</td>
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<tr>
<td>▪ Vaccines within the National Immunization Program;</td>
<td>▪ Serious debilitating conditions;</td>
</tr>
<tr>
<td>▪ The only generic and similar drugs in the market;</td>
<td>▪ Public health emergencies;</td>
</tr>
<tr>
<td>▪ First similar drug;</td>
<td>▪ Vaccines to be included in the National Immunization Program;</td>
</tr>
<tr>
<td>▪ The only API manufacturer;</td>
<td>▪ The only generic drug;</td>
</tr>
<tr>
<td>▪ Risk of shortage in the Unified Health System.</td>
<td>▪ Reference drugs unavailable in the market;</td>
</tr>
<tr>
<td></td>
<td>▪ Risk of shortage in the market.</td>
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</table>
# Accelerated Pathways of Approval

## Previous rules (RDC 37/2014)

**Prioritization of drug clinical research authorization requests:**

- Rare, neglected, emerging, or reemerging diseases;
- For the pediatric or adolescent population;
- Basic, specialized, or strategic component for the Health Ministry;
- Vaccines within the National Immunization Program;
- Productive Development Partnerships;
- Phase I in the Brazilian territory;
- Radical or incremental innovation manufactured in the country.

## Current rules RDC 204/2017

**Prioritization of clinical research authorizations:**

- Neglected diseases;
- Emerging or reemerging diseases;
- Public health emergencies;
- Serious debilitating diseases;
- Pediatric population; and
- Vaccines within the National Immunization Program.
## Accelerated Pathways of Approval
### Rare Diseases – Market Authorization (RDC 205/2017)

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<th>Previous rules (RDC 37/2014)</th>
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<tr>
<td>Pre-submission meeting: there were no provisions</td>
<td>Pre-submission meeting: compulsory</td>
</tr>
<tr>
<td></td>
<td>For imported drugs: up to 60 days after the first authorization request to another authority</td>
</tr>
<tr>
<td>Period to submit the request (company): there were no provisions</td>
<td>Period to submit the request (company): 30 days after the pre-submission meeting</td>
</tr>
<tr>
<td>First manifestation (Anvisa): 75 days after analysis prioritization approval</td>
<td>First manifestation (Anvisa): up to 60 days after the authorization request was filed</td>
</tr>
<tr>
<td>Compliance with the requirements (company): up to 120 days</td>
<td>Compliance with the requirements (company): up to 30 days after receipt</td>
</tr>
<tr>
<td>Assessment of compliance (Anvisa): there were no provisions</td>
<td>Assessment of compliance (Anvisa): up to 45 days</td>
</tr>
<tr>
<td>Submission of price dossier (company): there were no provisions</td>
<td>Submission of price dossier (company): concomitant with the authorization request</td>
</tr>
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# Accelerated Pathways of Approval: Rare Diseases - Clinical Research (RDC 205/2017)

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<td>Pre-submission meeting: there were no provisions</td>
<td>Pre-submission meeting: compulsory</td>
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<td>First manifestation (Anvisa): 45 days after analysis prioritization approval (RDC 37/2014)</td>
<td>First manifestation (Anvisa): up to 30 days after the request was filed</td>
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<tr>
<td>Compliance with the requirements (company): up to 120 days</td>
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<td>Assessment of the compliance with the requirements (Anvisa): there were no provisions</td>
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Prioritization criteria

Clinical trials

- Rare, neglected, emerging or reemerging disease
- Exclusively with pediatric or adolescents
- Phase I in Brazil
- National Immunization Program
Prioritization criteria

**Registration**

- Rare, neglected, emerging or reemerging disease
- Productive development partnership
- First generic
- National Immunization Program
- Second generic
- Strategic for SUS
- Component of pharmaceutical assistance
- Third generic
- First similar
- Fractional presentation
- Innovation
Scenario without price cap regulation for an orphan drug

- In Brazil, SCMED/ANVISA established the ceiling price for medicines

US$ 176 million
Recent Regulatory Advances

Simplification of procedures

Resolution RDC nº 73/2016 (post-approval changes)
✓ Complexity-based analysis

Resolution RDC nº 107/2016 (simplified notification)
✓ 37 new molecular entities in the “low risk” category (a 50% increase in the list)

Evaluation of new registrations and post-approval changes of lesser complexity by new units (CRMEC and CPMEC)
OS Nº 45, February 2018 (Service Orientation)

- Establishes a Optimized Review Pathway for Biological Products (registration and variations/post approval changes)
- Reliance Pilot Project (one year)
- Eligibility criteria: Registered in the USFDA and EMA; same indications; dosage; adverse reactions; precautions.
- AR Approval Reports should be provided
- Submissions received: None
Backlog Reduction

➢ Law 13.411/2016 established new timeline targets and the General Office of Drugs implemented several strategies to reduce the backlog and increase efficiency;

➢ Grouping of the applications in the backlog into 4 groups according to submission date; pharmaceutical form; similarity of the manufacturing process; Active Pharmaceutical Ingredient; number of submission per company;

➢ Teleworking with an increase of 20% of the assessors individual productivity;

➢ Task force to increase the number of assessors evaluating drug applications.
Thank you!

contacts

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