Establishes the possibility and criteria for priority examination of petitions related to marketing authorization, post-authorization and prior consent of clinical studies of small molecule drugs and biologic products.

Current as of June 18, 2014
TABLE OF CONTENTS

ANVISA’s Board of Directors Rule #37 of 2014
Establishes the priority technical analysis for authorization, post-authorization and prior consent of clinical studies by ANVISA of small molecules drugs and biological products..............................................................5

Normative Instruction 03/2014
Provides the scoring criteria for prioritization of the technical analysis of the application for registration, post-registration and prior consent on clinical research for drugs and biological medicinal products..............13
Published on the Brazilian Federal Register of June 16th, 2014

Establishes the priority technical analysis for authorization, post-authorization and prior consent of clinical studies by ANVISA of small molecules drugs and biological products.

ANVISA’s Board of Directors Rule #37 of 2014
Article 1st - This rule approves criteria and procedures for priority technical analysis of applications for authorization of drugs and biological products, as the public relevance of the request, to ensure or increase access to pharmaceutical assistance pursuant to this Resolution.

Chapter I - Initial provisions

Section I - Purpose

Article 2nd - The purpose of this Regulation is to establish criteria and procedures and the score for applications of authorization, post-authorization and prior consent of clinical studies by ANVISA to small molecule drugs and biological products capable of having a prioritized analysis, according to public relevance.

Section II - Scope

Article 3rd - This Regulation applies to applications for authorization, post-authorization and prior consent of clinical studies by ANVISA of small molecule drugs and biological products.

Section III - Definitions

Article 4th - For the purposes of this rule, the following definitions are adopted:

I - Basic component of pharmaceutical assistance: the component is financing part of the National Policy for the Pharmaceutical Assistance of Brazilian Unified Health System (SUS), which sets the set of drugs of the National Reference, medicines composed of the National List of Essential Medicines, designed to meet the priority health problems prevalent and Primary Care;

II - Specialized component of pharmaceutical assistance: range of cares defined in Clinical Protocols and Therapeutic Guidelines, published by the Ministry of Health (MoH);

III - Strategic component of pharmaceutical assistance: includes drugs used for treatment of endemic diseases, which may have socioeconomical impact and possess control and treatment through the protocol and standards established by the MoH;

IV - Emerging or reemerging disease: term for new conditions of health status, usually of infectious origin, or condition already known to acquire or reacquire epidemiological significance in public health;

V - Neglected disease: term used to describe diseases that do not present economical attractiveness for the development of drugs or for achieving predominantly the population of developing countries;

VI - Orphan disease: term used to describe diseases of low prevalence in the population as parameter set by the Ministry of Health, which are usually chronic, progressive, degenerative and even crippling;

VII - Radical innovation: innovation resulting in a new molecule not registered in the country;

VIII - Incremental innovation: innovation that results in a new dosage form, new strength, new route of administration or new indication for a molecular entity ever recorded in the country;

IX - Unheard generic drug: corresponds to the first generic to be registered in the country for a determined active substance or combination, strength or dosage form;

X - Unheard drug branded copy similar: is similar to the first drug to be registered in the country for a determined API or combination, strength or dosage form;

XI - Technological core: steps to complete clinical development and manufacture of a determined product to the packaging step;

XII - Productive Partnerships for Development: those made between public and other institutions of same or even private companies and public institutions in order to allow access to priority technologies and reducing the vulnerability of the Unified Health System (SUS), by involvement of internalization of production or the development of new strategic technologies;

XIII - Basic Productive Process (PPB): minimum set of operations, the manufacturing facility, which characterizes the effective industrialization of a product; and

XIV - Strategic Products for the Brazilian Health System: those listed in the specific rule Ministry of Health, with the aim of supporting the development of the Industrial Complex Health.

CHAPTER II - GENERAL PROVISIONS

Article 5th - The prioritization of technical analysis to applications applies to small molecule drugs and biological products classified in one or more of the following criteria and that meet the minimum score of 10 points:

I - Application for marketing authorization:

a) Fractionated presentations;

b) First protocol of generic sold under medical prescription for determined Active Pharmaceutical Ingredient (API);

c) Second and third protocols of generic with the objective of increasing competition in the market for determined API;

d) First protocol of branded copy similar sold under medical prescription for determined API;

e) Inherent part of API of the Basic, Strategic or Specialized Components of the Pharmaceutical Assistance, published by the Ministry of Health, and when proven the risk of shortage of SUS;

f) API of the National Immunization Program, established and published by the Ministry of Health, and when proven the risk of shortage of SUS;

g) Used for orphan disease and neglected disease, emerging or re-emerging, and when proven the risk of shortage of SUS;

h) API integral part of the Basic, Strategic or Specialized Components of the Pharmaceutical Assistance, published by the Ministry of Health, and when proven the risk of shortage of SUS;

i) Necessary to avoid shortages in the domestic market of medicinal regarded as the single active ingredient or combination, concentration and dosage form; and

j) For the subject change of manufacturing site of active pharmaceutical ingredient (IFA) due to supply interruption, proven by the manufacturer IFA initiative, and when this is the only manufacturer registered for a particular drug;

k) For the subject use expansion for the pediatric population;

l) With radical innovation or manufactured in the country that meet your rule of origin or Basic Productive Process, since the core technology of the product is also manufactured in the country; and

m) When there is a proven risk of shortages of SUS;

n) Using only active pharmaceutical ingredient (s) produced by national manufacturers (s).

II - Application for post-marketing authorization:

a) Concerning the inclusion of new subject divisible presentation;

b) Single generic registered and sold under medical prescription for a particular asset or association, pharmaceutical ingredient, dosage form and concentration, whose priority analysis is essential to prevent market shortages;

c) Only similar registered and sold under medical prescription for a particular asset or association active pharmaceutical ingredient, dosage form and strength, whose priority analysis is essential to prevent market shortages;

III - Application for post-marketing authorization:

a) Concerning the inclusion of new subject divisible presentation;

b) Single generic registered and sold under medical prescription for a particular asset or association, pharmaceutical ingredient, dosage form and concentration, whose priority analysis is essential to prevent market shortages;

c) Only similar registered and sold under medical prescription for a particular asset or association active pharmaceutical ingredient, dosage form and strength, whose priority analysis is essential to prevent market shortages.
m) with incremental innovation or manufactured in the
country that meet your rule of origin or Basic Productive
Process, since the core technology of the product is also
manufactured in the country; and
n) is proved the risk of shortage of SUS;
a) to change the place of manufacture of active pharma-
ceutical ingredient (API) to replace the foreign manufac-
turer by domestic manufacturer, independent of supply
disruption by the original manufacturer.

III - Application of prior consent of clinical studies:

a) inherent part of the Basic, Strategic or Specialized
Components of the Pharmaceutical Assistance, pub-
lished by the Ministry of Health, and when proven the risk
of shortage of SUS;
b) inherent part of the National Immunization Program,
established and published by the Ministry of Health, and
when proven the risk of shortage of SUS;
c) used for rare and neglected, emerging or re-emerging
disease, and when proven the risk of shortage of SUS;
d) inherent part of the Productive Development Part-
nerships;
e) inherent part of the Strategic Goods List, under of the
SUS, and when proven the risk of shortage of SUS;
f) conducted exclusively in pediatric or adolescent pop-
ulation;
g) in Phase I development, conducted exclusively in Bra-
zilian territory;
h) with radical innovation or manufactured in the coun-
try that meet your rule of origin or Basic Productive Pro-
cess, since the core technology of the product is also
manufactured in the country;
i) with incremental innovation produced in the country
or who fulfill their rule of origin or Basic Productive Pro-
cess, but only if the technological core of the product is
also manufactured in the country;
j) with incremental innovation, in terms of letter "k", item i,
the letter "m" in item ii and the letter "l", item iii, relevance
will be evaluated as clinical and therapeutic advantage of
this innovation for the drug or biological product.

§ 4 The market shortages, discussed in items "b" and "c"
of item II of this article, will be configured when there is
a maximum of two (2) registered medicines or biologi-
cal products marketed in the country for a particular as-
set or association of active pharmaceutical ingredients
and dosage forms and these depend on the analysis of
post-registration application for the continuation of their
marketing.

§ 5 The analysis of post-petition record drug or biological
product may be prioritized, even when there is no proven
shortages as predicted in § 4, when this proven shortage
answers for at least 80% (eighty percent) of market sales
in the past two years on active pharmaceutical ingre-
dient or combination, concentration and dosage form
specified.

§ 6 When there are one or more registered and market-
ed generic drugs with the same active pharmaceutical
ingredient or association, in order to fit a new concen-
tration or new dosage form, as an unprecedented gener-
dic drug, the relevance for the expansion of the targeted
population will be evaluated.

§ 7 Pursuant to subsection "c" of item I, when there is
a single generic drug registered and marketed with the
same active substance or combination, concentration
and dosage form, priority review will be granted for the
second and third protocols registered to extend compe-
tition in the market, provided that the request for regis-
tration comes from a company of different economical
group from the one of the record.

§ 8 When there are similar drugs registered and traded
with the same active ingredient or association, to frame
a new concentration or new dosage form as a drug un-
heard of similar relevance for expanding the target popu-
lation will be evaluated.

§ 9 The analysis for registration or post-registration of a
generic drug may be prioritized, even if not classified as
unprecedented, since it’s proven that previously regis-
tered medications for certain active pharmaceutical in-
gredient or combination, concentration and dosage form
are not being marketed.

§ 10. To prove the point to which ‘j’ of section II refers, the
company that holds the registry of the medicinal prod-
uct concerned shall provide documentation of the active
pharmaceutical ingredient manufacturer justifying the
request for prioritization analysis.

Article 6th - The exceptional situations not provided for
in this Rule and of public importance may be prioritized
after evaluated by ANVISA.

Article 7th - The applications will be prioritized accord-
ing to ANVISA for the purpose of auditing analysis and
post-authorization of drugs or biological products.

Article 8th - For the applications for authorization and
post-authorization of drugs and biological products al-
ready prioritized, which have been filed, the applicant
may request the prioritization of the reopening of the
status of the application.

Article 9th - The requirements for prioritization of exam-
ination shall be made solely by electronic application at
ANVISA’s website.

§ 1 The requirements referred to in this article can only be
made by companies duly recognized by ANVISA as re-
ponsible for their petitions for which it intends to apply
the provisions of this Resolution.

§ 2 The companies concerned shall complete the elec-
tronic application at ANVISA’s website through login and
password that are already registered in the security sys-
tem for electronic application.

§ 3 The electronic application will be made by complet-
ing the required data in electronic form and attach PDF
files, as appropriate.

§ 4 Manual petitioning upon proof of inability to access
the electronic application on the ANVISA website will be
accepted.

Article 10 - Upon the petitioning company must indicate
the technical criteria set out in art. 5 ° who moved the
request prioritization.

Sole paragraph - Petitions requesting prioritization anal-
ysis shall be evaluated on the classification criteria set
out in Article 5 of this Resolution.

Article 11 - Results of the analysis and motivation re-
garding the request for prioritization will be released
monthly at ANVISA’s website, in particular link.

Sole paragraph - Any prioritization petition under this
resolution has impact on all subsequent acts related to
the prioritized application, such as compliance with of-
ce actions, administrative appeals and other petitions
related, except the petition to reopen the status of the
application.

Article 12 - The deadline for expressions of competent
organizational units regarding the analysis of petitions
that have the priority will be granted to:

I - 75 (seventy five) calendar days for applications for reg-
istration of drug or biological product;
II - 90 (ninety) calendar days calendar for applications
post-authorization; and
III - 45 (forty-five) calendar days for the previous consent
of clinical studies.

Sole paragraph - The term shall begin on the first work-
ing day after the publication of granting the application
prioritization.

Article 13 - Applications fitting the criteria set out in this
Resolution shall be examined by the relevant technical
areas according to the sum of the scores achieved by the validated criteria and publication date of the granting of the application prioritization.

**Article 14** - Applications that do not fit the criteria set out in this Resolution or cannot attain the established minimum score will be considered by the relevant technical areas, according to the chronological order of entry in ANVISA.

**Article 15** - Implementation of this Rule for prioritization, the application for grant of authorization, post-authorization and consent in clinical study of drug or biological product to be prioritized should be accompanied by all documents required by prevailing legislation, subject to rejection in case of non-compliance.

**CHAPTER III - FINAL AND TRANSITORY PROVISIONS**

**Article 16** - Resolution - RDC No. 57 of December 20, 2013, is revoked.

**Article 17** - This Rule comes into force on the day of its publication.

Dirceu Brás Aparecido Barbano
Chief Director
Establishes the scoring criteria for the priority technical analysis for authorization, post-authorization and prior consent of clinical studies by ANVISA of small molecules drugs and biological products.
The Board of the National Sanitary Surveillance, in the exercise of the powers conferred upon it by items III and IV, art. 15, in accordance with Law 9782 of January 26, 1999, and taking into consideration the provisions of Art. 5th, item IV, § 1 and § 3 of the Internal Regulations approved pursuant to Annex I to ANVISA’s Order 650 of May 29, 2014, published in the D.O.U. of June 2, 2014, and its updates; Art. 2nd, item III; Art. 7th, items III and IV of Law 9782, of January 26, 1999, and the ANVISA Better Process Regulation Agenda, according to the Order 422 of April 16, 2008, in meeting held on July 16, 2014, resolves:

Art. 1st It is established the scoring criteria for prioritization of the technical analysis of the application for registration, post-registration and prior consent on clinical research for drugs and biological medicinal products as referred to in Art. 5th of Directors Collegiate Resolution (RDC) RDC 37, of June 16, 2014.

I – Scoring criteria for registration of drugs and biological medicinal products application:

<table>
<thead>
<tr>
<th>Point</th>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td>Used for rare disease, excluded disease, emerging disease, re-emerging disease.</td>
<td>10,0</td>
</tr>
<tr>
<td>b)</td>
<td>Components of the Productive Development Partnerships.</td>
<td>10,0</td>
</tr>
<tr>
<td>c)</td>
<td>Employing exclusively pharmaceutical (s) active ingredient (s) produced by national manufacturer (s).</td>
<td>10,0</td>
</tr>
<tr>
<td>d)</td>
<td>With radical innovation, manufactured in the country or that serves a rule of origin or basic productive process, on the condition that the technological center of the product is also manufactured in the country.</td>
<td>10,0</td>
</tr>
<tr>
<td>e)</td>
<td>First Protocol of Generic, inedited sale, sale under medical prescription to a certain pharmaceutical active ingredient.</td>
<td>10,0</td>
</tr>
<tr>
<td>f)</td>
<td>With incremental innovation manufactured in the country or that serves the rule of origin or basic productive process, on the condition that the technological center of the product is also manufactured in the country.</td>
<td>8,0</td>
</tr>
<tr>
<td>g)</td>
<td>Second Protocol of Generic, inedited sale, sale under medical prescription to a certain pharmaceutical active ingredient.</td>
<td>8,0</td>
</tr>
<tr>
<td>h)</td>
<td>Components of the Strategic Products List, in the scope of the Public Health System (SUS).</td>
<td>6,0</td>
</tr>
<tr>
<td>i)</td>
<td>Components of the Basic, Specialized or Strategic Constituents of Pharmaceutical Assistance, published by Ministry of Health.</td>
<td>6,0</td>
</tr>
<tr>
<td>j)</td>
<td>Components of the Immunization National Program, settled by Ministry of Health.</td>
<td>6,0</td>
</tr>
<tr>
<td>k)</td>
<td>Third Protocol of Generic, inedited sale, sale under medical prescription to a certain pharmaceutical active ingredient.</td>
<td>6,0</td>
</tr>
<tr>
<td>l)</td>
<td>First Protocol of Similar, inedited sale, sale under medical prescription.</td>
<td>5,0</td>
</tr>
<tr>
<td>m)</td>
<td>With shattered presentations.</td>
<td>1,0</td>
</tr>
</tbody>
</table>

II – Scoring criteria for post-registration application of drugs and biological medicinal products:

<table>
<thead>
<tr>
<th>Point</th>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td>Indispensable to avoid a national market destocking of a drug or biological medicinal product considered special as for the active principle or as for the pharmaceutical association, concentration and form.</td>
<td>10,0</td>
</tr>
<tr>
<td>b)</td>
<td>Used for rare disease, excluded disease, emerging disease, re-emerging disease.</td>
<td>10,0</td>
</tr>
<tr>
<td>c)</td>
<td>Relative to the process of domestic drugs production of the Productive Development Partnerships.</td>
<td>10,0</td>
</tr>
<tr>
<td>d)</td>
<td>Single Generic registered, to be sold under medical prescription to a certain pharmaceutical active ingredient or to a pharmaceutical association; form and concentration necessary to avoid the market destocking.</td>
<td>10,0</td>
</tr>
<tr>
<td>e)</td>
<td>Relative to the increase of the use for the pediatric and/or adolescent population.</td>
<td>10,0</td>
</tr>
<tr>
<td>f)</td>
<td>With radical innovation, manufactured in the country or that serves a rule of origin or basic productive process, on the condition that the technological center of the product is also manufactured in the country.</td>
<td>10,0</td>
</tr>
<tr>
<td>g)</td>
<td>Change of place of pharmaceutical active ingredient (IFA) manufacturing because of the supplying interruption, by a confirmed initiative of IFA’s manufacturer and when this is the only manufacturer registered.</td>
<td>10,0</td>
</tr>
<tr>
<td>h)</td>
<td>Change of place of pharmaceutical active ingredient (IFA) manufacturing because of the substitution of a foreign manufacturer by a national manufacturer, even if there is a supplying interruption by the original manufacturer.</td>
<td>8,0</td>
</tr>
<tr>
<td>i)</td>
<td>With incremental innovation manufactured in the country or that serves the rule of origin or basic productive process, on the condition that the technological center of the product is also manufactured in the country.</td>
<td>8,0</td>
</tr>
<tr>
<td>j)</td>
<td>Component of the Strategic Products List, in the scope of the Public Health System (SUS).</td>
<td>6,0</td>
</tr>
<tr>
<td>k)</td>
<td>Component of the Basic, Specialized or Strategic Constituents of Pharmaceutical Assistance, published by Ministry of Health.</td>
<td>6,0</td>
</tr>
<tr>
<td>l)</td>
<td>Component of the National Immunization Program, settled by Ministry of Health.</td>
<td>6,0</td>
</tr>
<tr>
<td>m)</td>
<td>Single registered similar, to be sold under medical prescription to a certain pharmaceutical active ingredient or to a pharmaceutical association, pharmaceutical form and concentration, necessary to avoid the market destocking.</td>
<td>5,0</td>
</tr>
<tr>
<td>n)</td>
<td>For the inclusion of a shattered presentation.</td>
<td>1,0</td>
</tr>
</tbody>
</table>
III - Scoring criteria for prior consent on drugs clinical research:

<table>
<thead>
<tr>
<th>Point</th>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td>Used for rare disease, excluded disease, emerging disease, re-emerging disease.</td>
<td>10,0</td>
</tr>
<tr>
<td>b)</td>
<td>Components of the Productive Development Partnerships.</td>
<td>10,0</td>
</tr>
<tr>
<td>c)</td>
<td>Led exclusively into pediatric and adolescent population.</td>
<td>10,0</td>
</tr>
<tr>
<td>d)</td>
<td>When in Phase I, must be led exclusively in national land.</td>
<td>10,0</td>
</tr>
<tr>
<td>e)</td>
<td>With radical innovation, manufactured in the country or that serves a rule of origin or basic productive process, on the condition that the technological center of the product is also manufactured in the country.</td>
<td>10,0</td>
</tr>
<tr>
<td>f)</td>
<td>With incremental innovation manufactured in the country or that serves the rule of origin or basic productive process, on the condition that the technological center of the product is also manufactured in the country.</td>
<td>8,0</td>
</tr>
<tr>
<td>g)</td>
<td>Component of the Strategic Products List, in the scope of the Public Health System (SUS).</td>
<td>6,0</td>
</tr>
<tr>
<td>h)</td>
<td>Component of the Basic, Specialized or Strategic Constituents of Pharmaceutical Assistance, published by Ministry of Health.</td>
<td>6,0</td>
</tr>
<tr>
<td>i)</td>
<td>Component of the National Immunization Program settled and published by the Ministry of Health.</td>
<td>6,0</td>
</tr>
</tbody>
</table>

§ 1 Under point “1”, item I and point “n”, item II of Directors’ Collegiate Resolution (RDC) 37, of June 26, 2014, and considering the public interest, the applications for registration, post-registration for drugs or biological medicinal products with a proved risk of SUS destocking shall have a prior analysis and the scoring is not relevant.

§ 2 The result of the prioritization request is the total score of the prioritization criteria that are validated by a technical area.

§ 3 When the validation is according to the criteria described in point “c”, item I, is prohibited the inclusion or the change of a foreign manufacturer of pharmaceutical active ingredient (IFA), for 5 (five) years, except in case of SUS destocking or IFA supply interruption.

Art. 2nd This Normative Instruction takes effect on the date of its publication.

Dirceu Brás Aparecido Barbano
Chief Director