COLLEGIATE BOARD RESOLUTION – RDC No. 135 OF 29 MAY 2003

Approves the Technical Regulation for Generic Medicinal Products.

The Collegiate Board of Directors of the Brazilian Health Regulatory Agency, in the use of the attributions vested in it under Article 11, item IV of Anvisa Regulation approved by Decree No. 3,029 of 16 April 1999, and Article 111, item I, letter "b", Paragraph 1 of the Internal Regulation approved by Presidential Decree no. 593 of 25 August 2000, republished on 22 December 2000, as decided upon in a meeting held on 6 March 2003,

Whereas Law no. 6,360 of 23 September 1976 and its Regulation approved by Decree no. 79,094 of 5 January 1977, which establishes the legal basis for granting marketing authorization for medicinal products;

Whereas Law no. 9,787 of 10 February 1999, which establishes the legal basis for instituting generic medicinal products in Brazil;

Whereas the same Law in its Article 2, which determines its regulation by the federal organization responsible for health surveillance;

Whereas generic medicinal products are a priority of the Brazilian Ministry of Health's policy on medicinal products;

Whereas the need to ensure the quality, safety, and efficacy of generic medicinal products as well as to ensure their interchangeability with their respective reference products;

Adopts the following resolution and I, Director-President, determine its publication:

Article 1. The attached Technical Regulation for Generic Medicinal Products is hereby approved.

Article 2. This Resolution determines that the companies interested in the marketing authorization for Generic Medicinal Products must fully comply with the provisions of this Regulation.

Sole Paragraph. For the purposes of the provisions in this Regulation, the companies must be based on the technical procedures described in specific guides approved by the Collegiate Board and published in the Federal Official Gazette.

Article 3. This Resolution determines that only those centers authorized by ANVISA may undertake pharmaceutical equivalence and relative bioavailability/ bioequivalence trials.

Sole Paragraph. The companies interested in undertaking trials must petition for their accreditation at ANVISA and comply with the legal requirements pertinent to their activity.

Article 4. Resolution RDC no. 84 of 19 March 2002 is hereby revoked.

Article 5. This Resolution enters into force on the date of its publication.

CLAUDIO MAIEROVITCH PESSANHA HENRIQUES

ANNEX

TECHNICAL REGULATION FOR GENERIC DRUGS

Scope

This regulation has the purpose to establish the technical precepts and procedures for the marketing authorization for Generic Medicinal Products in Brazil, as follows:

I. Definitions used in the marketing authorization for Generic Medicinal Products.

II. Pre-marketing authorization measures.

III. Documentation for marketing authorization.

IV. Medicinal products that will not be accepted as Generic.

V. Post-marketing authorization measures.

VI. Criteria for the prescription and dispensation of Generic Medicinal Products.

This Regulation encloses Annex I, entitled "Title page of the marketing authorization and post-marketing authorization of Generic Medicinal Products".

The definition of the technical procedures for compliance with the technical requirements related to marketing authorization and post-marketing authorization are available in specific guides published in the Federal Official Gazette.

I – Definitions used in the marketing authorization for Generic Medicinal Products

1. Bioavailability: "it indicates the rate and the extension of absorption of an active ingredient in a dosage form, based upon its concentration/ time curve in the systemic circulation or its excretion in urine ". (Law no. 9,787 of 10 February 1999)

2. Common Brazilian Denomination (DCB): "name of the pharmaceutical substance or active pharmaceutical ingredient approved by the federal agency in charge of health surveillance." (Law no. 9,787 of 10 February 1999)

3. International Nonproprietary Name (INN): "name of the pharmaceutical substance or active pharmaceutical ingredient recommended by the World Health Organization." (Law no. 9,787 of 10 February 1999)

4. Therapeutic equivalence: two medicinal products are considered therapeutically equivalent if they are pharmaceutically equivalent and, after administration of the same molar dose, their effects concerning efficacy and safety are essentially the same. This is assessed through appropriate bioequivalence studies, pharmacodynamic trials, clinical trials, or *in vitro* studies.

5. Pharmaceutical equivalents: medicinal products containing the same active ingredient, that is, the same salt or ester of the same therapeutically active molecule, in the same amount and pharmaceutical form, and they may or may not contain identical excipients. They must comply

with the same updated specifications of the Brazilian Pharmacopoeia or, in the absence of these, with those of other codes authorized by the legislation in force, or with other applicable quality standards related to identity, dosage, purity, potency, uniformity of content, disintegration time, and dissolution rate, when applicable.

6. Medicinal product: "pharmaceutical product technically obtained or elaborated for the purposes of diagnosis, cure, treatment, or prevention of disease". (Law no. 5,991 of 17 December 1973). It is a finished pharmaceutical form that contains an active ingredient, generally in association with pharmacotechnical adjuvants.

7. Bioequivalent medicinal products: pharmaceutical equivalents that, when administrated in the same molar dose, in the same experimental conditions, do not present significant statistical differences concerning bioavailability.

8. Reference Drug: "innovating product granted marketing authorization by the federal agency in charge of health surveillance and commercialized in Brazil, the effectiveness, safety, and quality of which have been scientifically confirmed to the competent federal agency, at the moment of marketing authorization". (Law no. 9,787 of 10 February 1999)

9. Generic Medicinal Product: "medicinal product similar to a reference or innovating product, expected to be interchangeable with the latter, usually produced after the expiration or waiver of patent protection or of other exclusiveness rights, the effectiveness, safety, and quality of which having been confirmed, and designated by DCB or, in its absence, by the INN". (Law no. 9,787 of 10 February 1999)

10. Innovating Medicinal Product: medicinal product commercialized in the Brazilian market, composed of at least one active pharmaceutical ingredient that has been the object of a patent (even if no longer valid) on behalf of the company responsible for its development and introduction in the market of the country of origin. An innovating medicinal product is generally considered a reference medicinal product. However, in its absence, ANVISA shall indicate the reference medicinal product.

11. Similar Medicinal Product: "that which contains the same active ingredient(s), presents the same concentration, dosage form, administration route, posology, and therapeutic indication as, and is equivalent to the medicinal product granted marketing authorization by the federal agency in charge of health surveillance, and it may differ only in characteristics related to size and form of the product, shelf life, packaging, labeling, excipients, and vehicles, and it must always be identified by fantasy name or trade mark". (Wording given by Provisional Measure no. 2,190-34 of 23 August 2001)" (Law no. 9,787 of 10 February 1999)

II – Pre-marketing authorization measures

Before applying for the marketing authorization for a generic medicinal product, the company must:

1. Consult the list of reference medicinal products available at the Anvisa website to check if there is this indication in the concentration and pharmaceutical form for the product it intends to be granted marketing authorization as generic. In its absence, submit a petition for the indication of a reference medicinal product at Anvisa, presenting the following data both for the test medicinal product and for the supposed reference medicinal product: company, product,

active ingredient, pharmaceutical form, concentration, and proof of commercialization/ distribution in Brazil of the medicinal product indicated as reference.

2. Request a medicinal product import license (IL) to Anvisa for the conduction of *in vitro* and *in vivo* studies.

3. Present the Notification of Production of Pilot Batches in compliance with the GUIDE FOR THE NOTIFICATION OF PILOT BATCHES OF MEDICINAL PRODUCTS, when applicable.

The company will have the choice of submitting the bioequivalence study protocol.

III – Marketing authorization

a) The process to request the marketing authorization for national and imported generic medicinal products shall consist of the documentation described below. Applications with incomplete documentation shall not be analyzed.

b) A maximum of three manufacturers shall be accepted for the presentation of active ingredient manufacturers.

1. Proof of payment of the Health Surveillance Inspection Fee (original) or proof of exemption, when applicable;

2. Copy of the company's up-to-date Operation License (Health Permit);

3. Copy of the company's Functioning Permit or of the Special Functioning Permit, when applicable, published in the Federal Official Gazette.

4. Copy of the Good Manufacturing and Control Practices (GMCP) certificate issued by Anvisa for the production line in which the medicinal product intended for marketing authorization will be manufactured.

5. For imported medicinal products:

5.1. Submit the Medicinal Product Marketing Authorization Certificate including the manufacturing site, which must be the same manufacturing site of the medicinal product intended for marketing authorization in Brazil.

5.2. Specify the stage of the medicinal product to be imported as finished product, product in bulk, or in primary package;

5.3. Copy of the Good Manufacturing and Control Practices (GMCP) certificate issued by ANVISA for the production line in which the medicinal product intended for marketing authorization will be manufactured.

5.4. Copy of the Good Manufacturing Certificate issued by ANVISA for the packaging line facilities of the company requesting marketing authorization, in case of bulk product or in primary package;

5.5. Copy of the Good Manufacturing and Control Practices (GMCP) certificate issued by ANVISA of at least one production line, for the facilities of the company requesting marketing

authorization, in case of imports of bulk product or product in primary package, in which the marketing authorization petitioner has a permit to manufacture medicinal products or needs to subcontract its distribution, storage, and/ or packaging.

5.6. Present the quality control specifications and methodology used by the importer. These must be the same ones submitted for the approval of marketing authorization.

6. Copy of the Notification of Production of Pilot Batches with the ANVISA protocol number, if existent.

7. Copy of the up-to-date Technical Responsibility Certificate issued by the Regional Pharmacy Council of the federated unit where the pharmacist acts professionally.

8. Compliance with the conditions established in the legislation in force on the control of Transmissible Spongiform Encephalopathy (TSE).

9. FP1 and FP2 petition forms.

10. Model of the package insert, label, and cartridge. The information in the package insert of the generic medicinal product can be no less than that contained in the package insert of the reference medicinal product. Anvisa has the right to request complementary data whenever there are technical recommendations to do so. A copy of the reference medicinal product's package insert must be included in the documentation.

11. Production report

11.1. Standard formula; production process; equipment used in the medicinal product's manufacture with details of the maximum individual capacity; and definition of the size of the industrial batch;

11.2. Complete description of the master formula with designation of components, respecting the denominations in the DCB, INN, or the name listed in the Chemical Abstract Substance (CAS), in this order of priority;

11.3. Description of the amount of each substance expressed in the metric system or standard unit, with indication of its function in the formula and the respective quality specification reference described in the Brazilian Pharmacopoeia or, in its absence, in another official code authorized by the legislation in force;

11.4. Copy of the complete production and quality control reports, including the order of production, detailed production process, and in-process controls referring to the three pilot batches manufactured or to three industrial batches produced in the last three years. In case of medicinal products with three or more different concentrations and proportional formulas, submit the reports of the lowest and the highest concentration.

11.5. Additional documentation whenever there is more than one manufacturer of the active ingredient:

a) This documentation refers to the medicinal product batches that were not submitted to pharmaceutical equivalence and bioequivalence studies, in case of more than one manufacturer of the active ingredient(s).

b) This documentation does not include the three batches whose production and quality control reports were used in the pharmaceutical equivalence, bioequivalence, and stability studies.

11.5.1. Production and quality control report of a batch of the medicinal product manufactured with the active ingredient that corresponds to each manufacturer presented;

11.5.2. Results and assessment of the accelerated stability study of a batch of the medicinal product manufactured with the active ingredient that corresponds to each manufacturer presented, in compliance with the criteria established in the GUIDE FOR THE CONDUCTION OF STABILITY STUDIES;

11.5.3. Comparative dissolution profile with the medicinal product submitted to bioequivalence and pharmaceutical equivalence studies for solid pharmaceutical forms;

11.5.4. In case of suspension, test results verifying the size of the particles between one batch of the medicinal product submitted to bioequivalence and pharmaceutical equivalence studies, and one batch of the medicinal product manufactured with the active ingredient that corresponds to each manufacturer presented, for the lowest and the highest concentration of the product, when applicable.

12. Quality control report of the raw materials

12.1. Excipients

12.1.1. List the bibliographic reference (official compendium) of all excipients used in the formula of the medicinal product. In case of excipient not described in official compendia, submit the specifications and the analysis methods used.

12.2. Active Ingredient(s)

a) The company requesting marketing authorization must submit copies of the original documents listed below of the manufacturing company or companies of the active ingredient(s). The indication of a maximum of three manufacturing companies shall be accepted.

b) The documentation of the active ingredient must be submitted on the manufacturing company's letterhead paper.

12.2.1. General data of the manufacturing company including complete address of the manufacturing site of the active ingredient;

12.2.2. Synthesis route including description of the intermediary molecules and their chemical names;

12.2.3. Description of the specifications of the manufacturer;

12.2.4. Identification and the analytic methods used by the manufacturer;

12.2.5. Quantification and limits of the main contaminants according to the synthesis route of the active ingredient;

12.2.6. List of the solvents used in the process according to the synthesis route of the active ingredient;

12.2.7. Data on the stereoisomer content, in case of active ingredients that present chirality, whose proportion of stereoisomers may compromise the efficacy and safety of the medicinal product;

12.2.8. Information and determination of the probable polymorphs and the analytical methodology for active ingredients that present polymorphism;

12.2.9. Validation of the analytical method in case of active ingredients not described in official compendia.

12.2.10. Specify the manufacturer(s) of the active ingredient(s) used in the production of the medicinal product submitted to the pharmaceutical equivalence and bioequivalence studies, when applicable;

12.2.11. The manufacturer(s) of the active ingredient(s) has (have) the option of sending directly to Anvisa the documentation specified in this item, duly identified with the number of the process to which it is related.

13. Quality control report of the medicinal product

13.1. Specifications and analytical methods;

13.2. Present validation of the analytical methods used, in compliance with the GUIDE FOR THE VALIDATION OF ANALYTICAL AND BIOANALYTICAL METHODS;

13.3. Submit media with the specifications and analytical methods in MS-Word format. The media must be labeled with the following data: name of the company, name of the medicinal product; concentration(s); pharmaceutical form; type of method used to analyze content and dissolution; type of standard and indication of the methodology used (pharmacopoeia or company's internal method).

14. Stability studies

a) Medicinal products containing three or more different concentrations and proportional formulae may present only the results and assessment of the stability study of the lowest and the highest concentrations.

14.1. Present the results and assessment of the accelerated stability study of the three pilot batches and timeframe of the long duration stability studies, including expected shelf life, in compliance with the criteria established in the GUIDE FOR THE CONDUCTION OF STABILITY STUDIES;

14.2. In case of generic medicinal products imported in bulk, present the results and assessment of the accelerated stability study in its final commercialization packaging, in compliance with the provisions in the GUIDE FOR THE CONDUCTION OF STABILITY STUDIES;

14.3. Submit the results and assessment of the long duration stability study, including the shelf life established for the national medicinal products already granted marketing authorization in Brazil, as well as the imported ones;

14.4. In case of medicinal products the shelf life of which exceeds 24 months, present the completed long duration stability study. In case of stability studies conducted in a manner that does not comply with the conditions established in the GUIDE FOR THE CONDUCTION OF STABILITY STUDIES, through justification, the maximum shelf life granted shall be of 24 months;

14.5. In case of medicinal products with three or more different concentrations and proportional formulae, present the results and assessment of the stability study of the lowest and the highest concentration.

15. Data concerning the primary packaging

15.1. Describe the specifications and analytical methods used in the quality control of the primary packaging.

16. Pharmaceutical equivalence report

a) Any medicinal product that comes in the form of a coated tablet whose reference medicinal product is a simple tablet or vice versa may be granted marketing authorization as a generic medicinal product, provided that the coating does not present a gastro-protective function.

16.1. Present a technical report containing the results and assessment of the pharmaceutical equivalence study conducted with the reference medicinal product commercialized in Brazil, in compliance with the provisions in the GUIDE FOR THE CONDUCTION OF THE STUDY AND ELABORATION OF THE PHARMACEUTICAL EQUIVALENCE REPORT;

17. Report of biological, pharmacological, and technical tests

a) The types of medicinal products exempt from bioequivalence study and those cases in which this study may be substituted by a pharmaceutical equivalence test are defined in the GUIDE FOR THE EXEMPTION AND SUBSTITUTION OF BIOEQUIVALENCE STUDIES.

b) In cases where the exemption is based on the comparison of the dissolution profiles, this must be conducted in laboratories duly authorized by Anvisa using the same analytical methodology used in the pharmaceutical equivalence. In case of non-pharmacopoeial method, the comparative dissolution profile must be established by using the test and the reference medicinal products under various conditions. These must include at least three different dissolution media, in compliance with the GUIDE FOR DISSOLUTION TRIALS FOR IMMEDIATE RELEASE SOLID ORAL PHARMACEUTICAL FORMS.

c) Immediate release oral formulations with active ingredient(s) of high solubility, high intestinal permeability, and broad therapeutic window shall be exempt from bioequivalence studies, provided they have already been exempted from the relative bioavailability test by the regulatory organizations of the United States (FDA) and Europe (EMEA), and present documentation to confirm such exemption.

d) The bioequivalence study must be conducted on the same batch used in the pharmaceutical equivalence study.

e) Bioequivalence studies that fail to use an adequate design for statistical treatment shall not be accepted, even if the acceptance criteria are in accordance with those established.

17.1. Present a technical report with the results and assessment of the report of the bioequivalence study, conducted with the reference medicinal product commercialized in Brazil, in compliance with the provisions in the GUIDE FOR RELATIVE BIOAVAILABILITY/ BIOEQUIVALENCE TESTS OF MEDICINAL PRODUCTS. Anvisa may require complementary studies, if deemed necessary.

17.1.1. The company must attach the following to the report:

17.1.1.1. copy of FP1 and FP2 forms;

17.1.1.2. copy of the title page (model in Annex I of this Regulation);

17.1.1.3. pharmaceutical equivalence report of the products used in the bioequivalence study;

17.1.1.4. report of the comparative study of the dissolution profiles, between dosages, accompanied by table containing the individual values of all determinations, for the cases of petitions for bioequivalence exemption;

17.1.1.5. copy of the Good Medicinal Products Bioavailability and Bioequivalence Practices Certificate, or publication in the Federal Official Gazette or, in its absence, copy of the certification petition protocol.

IV – Medicinal products that shall not be accepted as generic

The following products shall not be admitted for marketing authorization as generic medicinal product:

1. medicinal products exempt from marketing authorization, in compliance with Article 23 of Law 6,360 of 23 September 1975;

2. small volume parenteral solutions and unitary large volume parenteral solutions, free from active ingredients, such as water for injection, glucose solutions, sodium chloride, other electrolytic compounds, or sugars;

3. biological products, immunotherapeutic medicinal products, plasma derivates, and human blood;

4. products obtained through biotechnology, except antibiotics, fungicides, and others determined by Anvisa;

5. herbal medicinal products;

6. medicinal products containing vitamins and/ or mineral salts;

7. antiseptics for hospital use;

8. oral contraceptives and endogenous hormones of oral use;

9. products for diagnostic purposes and radiological contrasts;

10. over-the-counter medicinal products, except:

10.1. simple antacids, antacids with antiflatulence preparations or carminatives, simple antiflatulence preparations and carminatives;

10.2. non-narcotic analgesics;

10.3. topical use non-steroidal anti-inflammatory medicinal products;

10.4. expectorants, cough sedatives;

10.5. topical antifungal medicinal products;

10.6. muscle relaxants;

10.7. oral and topical anti-parasitic medicinal products;

10.8. anti-histamines;

10.9. anti-spasmodic medicinal products.

V – Post-marketing authorization measures

1. After the publication of the marketing authorization, the manufacturing company of the generic medicinal product must submit the following to Anvisa:

1.1. proof of distribution of the first three batches manufactured so that Anvisa can collect samples for control analysis, at its discretion;

1.2. results and final assessment of the long duration stability study of the first three batches produced, in accordance with the timeframe approved by Anvisa. In case of medicinal products already granted marketing authorization, whose stability studies do not meet the provisions in the GUIDE FOR THE CONDUCTION OF STABILITY STUDIES, a new study must be submitted;

1.3. report on the occurrence of adverse reactions and therapeutic inefficacy.

1.4. the company shall have a period of 180 days, counting from the date the generic medicinal product's marketing authorization was published in the Federal Official Gazette, to prove the beginning of the medicinal product's commercialization by presenting three invoices to Anvisa. This period may be extended only once, at Anvisa's discretion, through express justification by the company, for no longer than the initial 180 days. Non-compliance shall result in cancellation of the marketing authorization.

1.4.1. official laboratories are exempt from presenting invoices, but must prove the production and distribution of the medicinal products.

2. Post-marketing authorization alterations, inclusions, notifications, and cancellations

a) The complete documentation referring to the description of the alterations, inclusions, notifications, and cancellations that the medicinal product has undergone, after having been granted marketing authorization, must be submitted to Anvisa, in compliance with the GUIDE FOR POST-MARKETING AUTHORIZATION ALTERATIONS, INCLUSIONS, NOTIFICATIONS, AND CANCELLATIONS OF MEDICINAL PRODUCTS.

b) The company may only commercialize the product with the proposed alteration and/ or inclusion after the publication of the petition approval in the Federal Official Gazette.

c) Various alterations and/ or inclusions of a same medicinal product may be requested, provided that the documentation pertinent to each one is presented.

d) If an alteration and/ or inclusion are found in the medicinal product that has not been previously communicated to Anvisa and approved by it, the company shall be penalized with the cancellation of the marketing authorization for the medicinal product.

3. The following alterations, inclusions, notifications, and cancellations require previous approval for their implementation by the manufacturer:

3.1. alteration in labeling;

3.2. alteration in shelf life;

3.3. alteration in conservation care;

3.4. alteration in the synthesis route of the active ingredient;

3.5. alteration in the manufacturer of the active ingredient;

3.6. alteration in the manufacturing site;

3.7. alteration by modification in the excipient;

3.8. alteration in the manufacturing process of the medicinal product;

3.9. alteration in the size of the batch;

3.10. alteration in the equipment used;

3.11. inclusion of a new commercial presentation;

3.12. inclusion of new packaging;

3.13. inclusion of new concentration already approved in Brazil;

3.14. inclusion of manufacturer of the active ingredient;

3.15. inclusion of batch size;

3.16. temporary suspension of manufacturing;

3.17. reactivation of the manufacturing of the medicinal product;

3.18. cancellation of the marketing authorization of the presentation of the medicinal product on request;

3.19. cancellation of the marketing authorization of the medicinal product on request.

4. Criteria and conditions for marketing authorization renewal

To renew the marketing authorization of a generic medicinal product, the company must present the following documentation:

4.1. Petition form duly completed;

4.2. Proof of payment of the Health Surveillance Inspection Fee or proof of exemption, when applicable;

4.3. Copy of the up-to-date Certificate of Technical Responsibility issued by the Regional Pharmacy Council;

4.4. Copy of the invoices proving the commercialization of the medicinal product. Submit a declaration concerning commercial presentations that were not commercialized, but the company is interested in keeping their marketing authorizations;

4.5 Whenever a medicinal product is not manufactured in the said period, Official Laboratories must present a justification for the fact that it was not commercialized;

4.6. Copy of the final version of the package insert that accompany the product in its commercial packaging;

4.7. A list of all the post-marketing authorization alterations and/ or inclusions that took place during the product's last valid period of marketing authorization, accompanied by a copy of the publication on the Federal Official Gazette or, in its absence, a copy of the protocol of the corresponding petition(s);

4.8. for imported medicinal products:

a) Copy of the Good Manufacturing Practices (GMP) certificate for the packaging line, issued by Anvisa for the facilities of the company requesting marketing authorization, in case of product in bulk or in its primary packaging;

b) Copy of the Good Manufacturing and Control Practices certificate of at least one production line, issued by Anvisa for the facilities of the company requesting marketing authorization, in case of products imported in bulk or in their primary packaging, in which the petitioner has an authorization to manufacture medicinal products or need to subcontract distribution, storage, and/ or packaging;

c) For imported medicinal products, present copies of physicochemical, chemical, microbiological, and biological quality control reports elaborated by the importer in Brazil;

4.9. results and assessment of the long duration stability study;

4.10. bioequivalence study conducted with the reference medicinal product commercialized in Brazil, in case the marketing authorization was granted based on bioequivalence study conducted with an international reference medicinal product.

5. Situations in which a new study may be required to confirm bioequivalence

a) Anvisa may require a new study to confirm bioequivalence of a generic medicinal product in the following situations:

5.1. whenever there is clinical evidence that the generic medicinal product does not present therapeutical equivalence in relation to the reference medicinal product;

5.2. whenever there is documented evidence that the generic medicinal product is not bioequivalent to the reference medicinal product;

5.3. whenever there is risk of harm to health;

5.4. whenever there are alterations and inclusions in the medicinal product that justify a new interchangeability proof.

VI – Criteria for the prescription and dispensation of generic medicinal products

1. Prescription

1.1. Within the Unified Health System (SUS), prescriptions must adopt the Brazilian Common Denomination (DCB) or, in its absence, the International Nonproprietary Name (INN).

1.2. In private health services, the professional in charge will determine whether to prescribe using the generic name or the brand name of the medicinal product;

1.3. If the professional prescribing the medicinal product decides for the non-interchangeability of his or her prescription, this must be specified for each item prescribed in a clear, readable, and unequivocal manner in his or her own handwriting, other forms of printing being forbidden.

2. Dispensation

2.1. The pharmaceutical professional shall be allowed to substitute the medicinal product prescribed with the corresponding generic medicinal product, except if there are restrictions expressed by the prescriber.

2.2. In these cases, the pharmaceutical professional must indicate the substitution made on the prescription, add his or her seal, name, and Regional Pharmacy Council inscription number, date, and sign the prescription.

2.3. In cases of prescription with the generic name, the dispensation of the corresponding reference or generic medicinal product shall be permitted.

2.4. It is the duty of the pharmaceutical professional to explain the dispensation in detail to the patient or user, as well as to provide all guidance necessary for the rational consumption of the generic medicinal product.

2.5. The substitution of the generic medicinal product must be based on the list of generic medicinal products granted marketing authorization by Anvisa.

2.6. The list of generic medicinal products must be made public by Anvisa in the media.

ANNEX I

COVER SHEET OF MARKETING AUTHORIZATION AND POST-MARKETING AUTHORIZATION PROCESSES OF GENERIC MEDICINAL PRODUCTS

Submission		Post-Marketing Authorization (indicate petition)	
Compliance with Requirement		Addendum	

Data on the petitioning company	
Petitioner	
Telephone	
Fax	
E-mail	
Technically Responsible Officer	
Date of publication of the GMCP certificate on the Federal Official Gazette	
Does the company have an outsourcing contract approved by Anvisa?	

Data on the process	
Generic medicinal product	
Country of origin of the medicinal product	
Pharmaceutical form	
Concentration	
Therapeutic class	
Name of the laboratory that conducted the bioequivalence study	
Country where the bioequivalence study was conducted	
Full name and address of the manufacturer of the active ingredient used in the medicinal product, with which the pharmaceutical equivalence and bioequivalence/ relative bioavailability study was conducted	
Batch number and manufacturing date of the medicinal product with which the pharmaceutical equivalence study was conducted	
Batch number and manufacturing date of the medicinal product with which the bioequivalence/ relative bioavailability study was conducted	

Data on the reference medicinal product company	
Reference medicinal product	
Manufacturing laboratory of the reference medicinal product	

Rectification:

Published on the Federal Official Gazette; Executive Power.

Republished on the Federal Official Gazette of 12 August 2003.