Medicinal product regulation and product liability in Brazil: overview

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Country Q&A | Law stated as at 01-Jun-2017 | Brazil

A Q&A guide to medicinal product regulation and product liability law in Brazil.

The Q&A gives a high level overview of key issues including pricing and state funding, manufacturing, marketing, clinical trials, advertising, labelling, and product recall and liability.

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, visit *Pharmaceutical IP and Competition Law in Brazil: overview*.

To compare answers across multiple jurisdictions, visit the Medicinal product regulation and product liability *Country Q&A tool*.

The Q&A is part of the global guide to life sciences law. For a full list of jurisdictional Q&As visit *www.practicallaw.com/lifesciences-guide*.

Regulatory overview

1. What are the main legislation and regulatory authorities for pharmaceuticals in your jurisdiction?

Legislation

The Brazilian regulatory framework regarding pharmaceuticals is evolving steadily to become more transparent, efficient and convergent with international standards. The current framework is extensive and complex compared to 18 years ago, when the Federal Government created the regulatory agency ANVISA.

Two constitutional clauses establish the foundation for the framework:

- **Article 196, Federal Constitution 1988 (FC 1988).** This underpins citizens' constitutional right and the government's duty to implement health policies aimed at reducing the risk of illness and other hazards for the whole population, as well as to provide equal and universal access to programmes and services to promote, protect and recover health.

- **Article 197, FC 1988.** This enshrines the government's duty to regulate the provision of health services and products, whether directly or through third parties, and provides for the Brazilian regulatory framework for medical devices, pharmaceutical products and pharmaceutical active ingredients.

The key legislation is:

- **Federal Law No. 6,360 of 23 September 1976, with relevant amendments through its 40-year existence.** This is the main statute related to pharmaceutical products in Brazil. It provides for, among other things, the production, commercialisation, advertising, labelling, inspection, quality control, penalties, importation and marketing approvals of medicines, drugs, pharmaceutical active ingredients, medical devices, cosmetics, household products and other products. This law is regulated by Decree No. 8,077 of 2013.
- **Law No. 5,991 of 17 December 1973, amended by Law No. 13,097 of 19 January 2015.** This establishes sanitary control related to the trade of drugs, medicines, pharmaceutical active ingredients and medical devices.
- **Law No. 6,437 of 20 August 1977.** Sets out the penalties for infringing sanitary federal statutes and corresponding regulations, including criminal sanctions.
- **Law No. 9,294 of 1996.** Imposes restrictions on the use of, and advertising for, smoking products, alcoholic beverages, medicine, therapies and agricultural pesticides. This law is regulated by Decree No. 2,018 of 1996.

Regulatory authorities

Law No. 9,782 of 26 January 1999 (Law No. 9,782/99) established the National Sanitary Surveillance Agency (ANVISA) (*www.anvisa.gov.br*). It is linked to the Ministry of Health, despite operating as a financially autonomous regulatory agency.

ANVISA's statutory role is to protect and promote public health by regulating the production and marketing authorisation of pharmaceuticals, food, household products, cosmetics, medical devices, smoking products and new technologies that impact on its mandate.

ANVISA's main responsibilities are defined in Law No. 9,782/99, recently amended by Law No. 13,411/16, which set out provisions enforcing transparency and performance standards with minimum criteria to measure compliance with those standards and the consequences for not complying with them.

In general, a marketing authorisation from ANVISA is required to produce and commercialise pharmaceutical products in Brazil, or import pharmaceutical products into Brazil. Every company seeking a pharmaceutical marketing authorisation must comply with good manufacturing practices (GMP) and other GxP standards set out in ANVISA's guidelines.

Among other activities, ANVISA is responsible for the sanitary control of the production and marketing of products and services subject to sanitary surveillance, including related premises, processes, pharmaceutical active ingredients and technologies, as well as:

- Controlling ports, airports and borders and co-ordinating the National System of Sanitary Surveillance.
- Establishing rules, proposing, monitoring and executing policies and activities concerning health surveillance.
- Authorising the operations of companies manufacturing, distributing and importing medicines.
- Approving the import and export of medicines, granting marketing approval for medicines and granting and cancelling GxP certificates.

- Closing down, as a sanitary surveillance measure, manufacturing plants and any premises involved in the management, importation, storage, distribution and sale of health-related products and services, if the relevant legislation is violated, or if they constitute a likely health risk.
- Analysing patent applications related to pharmaceutical products and processes, jointly with INPI (Brazilian Patent and Trademark Office, BPTO) (prior consent analysis).

2. Briefly outline how biologicals and combination products are regulated in your jurisdiction.

In 2010, ANVISA updated the regulations for biological products, and different regulatory pathways for new biological products and their similar products were established (*Resolution No. 55 of 16 December 2010*). For new biological products, the usual pathway, based on a full dossier submitted by the applicant, is required. For similar biological products, the following two regulatory pathways were introduced:

- **Individual development pathway.** A reduced dossier can be submitted. The applicant must submit full data regarding quality issues but this does not have to be comparative. The number of non-clinical and clinical studies submitted can be reduced, depending on how much data is available on the pharmacological properties, safety and efficacy of the originator product. At least one comparative Phase III study (equivalence, superiority or non-inferiority) with the originator biological product is mandatory (except for hemoderivatives, vaccines and biological products for oncological use). When available, the results of phase IV studies should be submitted.
- **Comparative pathway.** A comparator product must be elected. The applicant must use comparability in terms of quality, safety and efficacy between the comparator biological product and the biological product.

Two other recent pieces of legislation are also relevant:

- Resolution No. 49 of 20 September 2011, as amended by Resolution No. 24 of 14 May 2013. This provides for post-registration changes and inclusions, suspensions and reactivations of manufacture and cancellation of registration of biological products.
- Resolution No. 50 of 20 September 2011, as amended by Resolution No. 25 of 14 May 2013. This provides for procedures and conditions for conducting stability studies for registration or post-registration changes of biological products.

Combinations products are not subject to a specific regulation. However, to establish the pathway, a relevant aspect to be considered is whether the device would be commercialised within the drug packaging or independently. In the latter, the device would have to be in accordance with Resolution No. 185 of 22 October 2001 that establishes general conditions for approval, marketing and review of medical devices.

3. Briefly outline how medical devices and diagnostics are regulated in your jurisdiction. Is there any specific regulation of health IT issues and mobile medical applications?

Medical devices and diagnostics, except diagnostic reactants for in vitro use, are regulated by Resolution No. 185 of 22 October 2001, as amended by Resolutions No. 207 of 17 November 2006 and No. 40 of 26 August 2015.

Each medical/diagnostic device is assigned to one of four regulatory classes (Class I, II, III or IV) based on increasing scale of risk the device poses to the patient and/or user. Class I includes devices with the lowest risk and Class IV includes those with the greatest risk.

Class I and II devices are not subject to registration, but as provided by ANVISA Resolution No. 40 of 26 August 2015 and Normative Instruction No. 2 of 31 May 2011, a cadastro (simplified route) must be submitted.

In addition, all medical devices, regardless of the class must comply with principles of safety and effectiveness, as provided by Resolution No. 56 of 6 April 2001.

Certain devices, particularly electro-medical ones, require certification following INMETRO (National Institute of Metrology, Quality and Technology)'s and ABNT (Brazilian Association of Norms Techniques)’s standards.

Mobile medical applications created to generate diagnostics are considered by ANVISA as medical devices and must comply with the regulations, seeking approval. Conversely, ANVISA has issued a brief statement that mobile applications with leisure and sporting purposes are not subject to regulation.

Pricing, state funding and reimbursement

4. What is the structure of the national healthcare system, and how is it funded?

Although the Constitution establishes that health is everyone's right, the Brazilian public healthcare system is mostly used by citizens who cannot afford private healthcare. Historically, an average of 55% of healthcare expenditure incurred by Brazilians refers to private medical insurance (Law No. 9,656 of 3 June 1998 establishes the rules for private insurances and healthcare plans), which is often subsidised by employers (including all branches of government) and expenditure funded directly by the end user of a product or service.

The national healthcare network is commonly referred as SUS, a Unified Healthcare System, organised according to the following principles (*Article 198 FC 1988, Law No. 8,080 19 September 1990* and *Law No. 8,142 of 28 December 1990*):

- Decentralisation, with a single management in each sphere of government.

- Full service, with priority given to preventive activities.
- Participation of the community.

Care provided under SUS splits between public and private sectors. Its statutory definition comprises "health activities and services, provided by public and federal entities and institutions, both by states and counties, of the direct and indirect administration of the foundations maintained by the government". In this sense, when the public structure is insufficient, the private sector may act as a supplementary resort.

Federal, State and County executive governments maintains SUS through a variety of taxes and contributions. Funds are transferred from the National Health Insurance Found to the other regional governments.

SUS relies on publicly owned facilities, such as hospitals, hiring private contractors for specific needs.

The health activities and services provided by SUS are organised regionally and hierarchically with a unified management structure, exercised by each government sphere of the following institutions:

- In relation to the Federal Union, by the Ministry of Health.
- In relation to the states, Federal District and municipalities, by the respective health offices.

5. How are the prices of medicinal products regulated?

The prices of new medicinal products and new presentations of medicines are strictly regulated in Brazil. Prices are set by the Pharmaceutical Market Regulation Council (CMED), after the marketing authorisation is issued by ANVISA.

CMED was created by Law No. 10,742 of 6 October 2003, and is composed of members of the Ministries of Health, Justice and Finance and the Chief of Staff to the President. CMED is responsible for monitoring and regulating the pharmaceutical market and establishing parameters and criteria for setting and adjusting the prices of medicines in Brazil, to stimulate competition in the market. Prices are reviewed annually in March and this review considers diverse factors, such as level of inflation, productivity and sector competition.

In 2016, for the first time the price readjustment index was above inflation, reaching a maximum of 12.5% for some products.

In 2017, although the official index awaits publication, the market expects a maximum adjustment of 4.7%.

To commercialise a medicine, after the publication of the marketing authorisation by ANVISA, a company must file the following economic data (*Article 16, VII, Law No. 6,360/76, as amended by Law No. 10,742/03*), which must be taken into consideration by CMED when setting or adjusting prices:

- The price charged by the company in foreign countries.

- The cost of the active ingredients.
- The cost per patient of the treatment with the product.
- The potential number of patients to be treated with the product.
- The price that the company intends to charge in the market, including tax.
- The commercialisation plan, including advertising and sales costs.
- The list of all the competitor products with their respective prices.
- Information on intellectual property, especially patents covering the product.

However, some products are not subject to the analysis of CMED, such as herbal, homeopathic, and medicines subject to simplified notification at ANVISA.

Depending on the product, CMED Resolution 04/2006 imposes a flat and compulsory discount to be applied to all sales to government entities in all federative levels.

6. When is the cost of a medicinal product funded by the state or reimbursed? How is the pharmacist compensated for his dispensing services?

There is no direct or indirect reimbursement to end users or pharmacists in Brazil. Medicines in Brazil, in general, are subject to the same tax burden as other non-essential goods, such as alcoholic beverages or clothes.

Conversely, Article 6, clause D of Law No. 8,080 of 19 September 1990 establishes that SUS has an obligation to provide integral therapeutic assistance, which in combination with Article 196, Federal Constitution that mandates universal access to healthcare services and measures, includes access to pharmaceuticals. The Brazilian population therefore has the right to receive free medicines.

Brazil adopted a National List of Essential Medicines in 1964, called Rename since 1975. The National Medicines Policy of the Ministry of Health, established by Ordinance No. 3,916 of 1998 has the adoption and constant review of Rename as a priority to guide access within SUS.

Throughout the years, several programmes for patients with chronic diseases (for example, diabetes, asthma, epilepsy and Alzheimer's disease) were created, including an HIV/AIDS programme, responsible for the free distribution of antiretroviral medicines, which is recognised as the leading programme worldwide.

The federal government buys nearly 40% of the medicines in Brazil. The distribution is made by the federal, state and county public hospitals.

The purchase of medicines by the Ministry of Health and public health institutions is carried out through competitive bidding in a procurement process under the FC 1988 (Federal Law No. 8,666/93, as amended). The supplier with the lowest price, who proves that the medicine meets the legal and technical requirements of the procurement, wins the

bid. Federal Law No. 9,787/99 states that a public bid for the purchase of medicines must include the international non-proprietary name (INN).

A system called low-cost pharmacy was also introduced under Decree No. 5,090/04. It is currently regulated by Ordinance No. 971/12, as amended by Ordinance No. 1,146/12. Under this system, the federal government buys medicines from the industry and distributes or sells them to patients at a lower cost, through a network of pharmacies.

However, integral and universal access to therapeutic assistance does not mean access to all kinds of treatments. There are several medicines and treatments that SUS does not provide.

Law No. 12,401 of 28 April 2011, which reviewed Law No. 8,080 of 19 September 1990, updated the legal landscape and rationale to incorporate other lists involving specialised and strategic treatments within SUS's lists of mandatorily available treatments.

Law No. 12,401/2011 also created CONITEC (National Committee for Technologies Incorporation) to perform HTA (Health Technology Appraisal) in Brazil. Since then, CONITEC is responsible for advising the Ministry of Health in the incorporation or disinvestment of health technologies into the SUS and development of clinical guidelines. The Committee receives studies submitted by applicants and, after analysing HTA aspects, takes a position on inclusion or exclusion of health technologies.

HTA is a continuous process of analysing and summarising the potential health benefits and the economic and social consequences inherent in employing certain technologies, while considering the following aspects: safety, accuracy, efficacy, effectiveness, costs, cost-effectiveness, aspects of equity, and the ethical and cultural and environmental impacts involved in their use.

However, the existing HTA route has some idiosyncrasies and is often a barrier to citizens' access to healthcare. HTA inadequacies have been considered a key factor in causing citizens/patients to seek court orders against the government to provide them with treatments not listed in SUS.

This trend, the *Judicialização da Saúde*, is widely discussed in Brazil, as it often opposes the individual constitutional right to healthcare against public expenditure and sanitary concerns.

The Supreme Federal Court (STF) is currently assessing two appeals, recognised as matters of general application, focusing on the economic burden of such treatments and whether the government could be ordered to provided medicines not approved by ANVISA.

Clinical trials

7. Outline the regulation of clinical trials.

The interest in clinical trials has increased sharply in Brazil in the last couple of years, due to ANVISA's new regulation and CONEP's initiatives to streamline the ethical approval.

Legislation and regulatory authorities

Clinical trials are regulated by the National Health Council, linked to the Ministry of Health, through Resolution No. 466/2012, which sets out the main guidelines for clinical research, particularly concerning the ethical aspects of research involving humans.

Through Resolution No. 9 of 20 February 2015, ANVISA ruled on the technical requirements for clinical trials with medicines. Through this resolution Brazilian standards are brought up to meet those established by international guidelines and aimed to encourage the development of clinical trials in Brazil, besides promoting Brazilian participation in clinical trials carried out simultaneously in different countries.

Authorisations

Every clinical trial to be performed with medicinal and health products in Brazil, regardless of its subject (whether new medicines or new or therapeutic indications, for example), must be submitted to ANVISA's prior evaluation by means of a clinical development dossier. ANVISA's Co-ordination of Research and Clinical Trials (COPEC) analyses all the required documentation, as well as the sanitary risks involved, before granting the approval.

Among other issues of relevance, Resolution No. 9/2015 defines a deadline by which ANVISA must conclude the analysis of the submitted dossiers regarding the projects on clinical trials to be conducted in Brazil. According to the resolution, Phase III studies involving synthetic drugs conducted in other countries which are part of the submitted dossiers, should have their reviews concluded by ANVISA at the most in 90 days.

As to Phase I and Phase II studies with biologicals, or those performed only in Brazil, ANVISA must conclude their evaluation in no more than 180 days. Studies however cannot be initiated before complete evaluation from ANVISA.

In addition, as a condition of obtaining ANVISA's approval, the company must file a detailed protocol before the Ethics Committee (CEP) of the institution in which the clinical trial will be performed, to have all ethical aspects of the trial analysed. Every CEP must be registered at the National Ethics Commission (CONEP), linked to the Ministry of Health and the Health National Council. This protocol must contain the freely given and informed consent of the trial subjects (or their legal representatives) on every detail of the clinical trial, such as objectives, procedures to be adopted, alternative methods to be eventually adopted, risks, assistance offered to the subject, freedom to withdraw from the trial, and so on (*see below, Consent*).

Consent

The consent set out in Resolution No. 466/2012 covers international documents such as the Universal Declaration on the Human Genome, the International Declaration on Human Genetic Data and the Universal Declaration on Bioethics and Human Rights. However, it no longer refers to the Declaration of Helsinki in its latest version of 2008, referring only to versions up to the year 2000. It must contain the following information:

- Rationale aims and methods to be used in the research.
- Any foreseeable risks or discomfort to the subject, as well as benefits that might reasonably be expected, associated with participation in the research.
- Existing alternative methods.

- Medical follow-up and care to be provided to the subjects of research, as well as the identity of those responsible for these actions.
- Assurance of information concerning the methodology, before and during the research, including the possibility of inclusion in a control or placebo group.
- Freedom of the individual to refuse participation or withdraw his consent, at any time during the research, without any penalty or loss of benefits to which he would otherwise be entitled.
- Extent to which confidentiality of records will be maintained, to safeguard the privacy of the research subjects.
- Forms of reimbursement of current expenditure resulting from participation in the research.
- Types of indemnity to cover possible injury resulting from the research.

Trial pre-conditions
Insurance coverage is not required, but the sponsor must declare himself responsible for assistance in the case of complications or damage caused during the trial, including adverse reactions.

Procedural requirements
The sponsor must file annual reports about the trial, as well as a final report with the conclusion of the trial, along with a special report concerning adverse reactions. Senate Bill (PLS 200/2015) aims to streamline trial approval and add legal certainty to this topic. Despite being under discussion, the Bill is a key driver towards more efficiency and dialogue to enhance the system.

Manufacturing

8. What is the authorisation process for manufacturing medicinal products?

Application
The company must obtain an operating authorisation from the Ministry of Health. Once this authorisation is granted, the company must obtain a licence from the local sanitary surveillance body (state, county or municipalities), which ultimately allows the company to start its manufacturing activities. State and country rules must also be observed. Further, the company must obtain a GMP (Good Manufacture Practices) certificate from ANVISA, after ANVISA inspects the manufacturer's plant.

Conditions
To obtain an operating authorisation and licence, the company must (*Articles 2, 50, 51 and 52, Law No. 6,360/76, as amended by Law 13.097/15*):

- Specify its industrial activities and the kind of products it wishes to manufacture.
- Prove its technical, scientific and operational capability.

- Satisfy other requirements set out in ANVISA's internal rules.

The company must also obtain approval from the state sanitary surveillance body for the building's projects and plants. County rules must also be observed.

Restrictions on foreign applicants
Foreign manufacturers can market medicinal products in Brazil as imported goods, through local subsidiaries or local commercial representatives. To do so, they must obtain a GMP certificate from ANVISA. ANVISA may use the inspection report of some regulatory authorities as a base document for analysis and granting of the GMP certificate. The local subsidiaries or local commercial representatives must obtain an operating authorisation and licence, as well as marketing authorisation for each imported product. The specific regulation on imported products is ANVISA's Resolution No. 81 of 5 November 2008, as amended by Resolution No. 28, of 28 June 2011.

Key stages and timing
It takes roughly between six months to one year to:

- File the operating authorisation request at the Ministry of Health (ANVISA).
- Obtain Ministry of Health approval.
- File the operating licence at the local sanitary surveillance body.
- Obtain the licence.
- Publish it in the *Official Gazette*.

Fee
ANVISA charges fees for granting the operating authorisation, for each type of activity performed by the company. These fees are established in ANVISA's new Ordinance No. 45/2017.

Period of authorisation and renewals
The operating authorisation (AFE) is valid indefinitely for local manufacturers. However, for some others activities, AFE must be renewed annually.

Monitoring compliance and imposing penalties
ANVISA, as well as state and municipal entities, are responsible for inspecting and enforcing compliance with food and drug laws.

ANVISA, as well as state and municipal entities, can impose administrative penalties (such as fines) for a statutory sanitary infringement, after due administrative prosecution. Civil and criminal penalties can also be imposed, but only after civil or criminal court proceedings (not directly by ANVISA).

Marketing

Authorisation and abridged procedure

9. What is the authorisation process for marketing medicinal products?

Application
The application (on forms PF1 and PF2) for each category of medicine is available at ANVISA's website.

Authorisation conditions
For a medicine to be registered, it must be proven, by means of scientific and analytical evidence, to be safe and effective for its intended use, and have sufficiently high quality, activity and purity for human use (*Article 16, Law No. 6,360/76*).

ANVISA's resolutions set out the specific and technical requirements for obtaining marketing approvals for:

- New medicines (*Resolution No. 60 of 10 October 2014*).
- Generic medicines (*Resolution No. 60 of 10 October 2014*).
- Branded drugs (so-called similar medicines) (*Resolution No. 60 of 10 October 2014*).
- Biological products (*Resolutions No. 55 of 16 December 2010 and No. 49 of 20 September 2011, amended by Resolution No. 24 of 14 May 2013*).

In the Official Gazette of 13 October 2014, ANVISA published Resolution No. 60/2014, an update of the technical requirements for marketing authorisation of new medicines, generic medicines and branded drugs (similar medicines). The resolution replaces Resolution No. 136 of 29 May 2003, Resolution No. 16 of 2 March 2007 and Resolution No. 17 of 2 March 2007 on the matter.

Key stages and timing
The key steps in the procedure for obtaining marketing approval are:

- Filing the application and additional documentation.
- Analysis by ANVISA.
- Publishing the approval in the *Official Gazette*.

The whole process generally takes from one to two years, depending on the category of the medicine and on possible office actions that may be issued during ANVISA's analysis.

However, Law No. 13.411/2016, which recently amended Laws No. 6.360/76 and 9,782/99, creates categories and imposes specific deadlines to be followed by ANVISA while assessing marketing approval/post approval requests: ordinary (365/180 days) and priority (120/60 days). A specific provision allows for the postponement of those deadlines once, for one third of the statutory limit, under strict conditions. ANVISA has not yet established the provisions to set criteria to classify products within the above categories to implement Law No. 13,411/2016.

The registration term for all other products regulated by Law No. 6,360/76 continues to be 90 days.

Fee
ANVISA charges fees for issuing and revalidating marketing approvals. The fees vary depending on the type of product, according to ANVISA's new Ordinance No. 45/2017.

Period of authorisation and renewals
By means of Law 13,097/15, ANVISA will define the deadline for marketing authorisation renewals, not exceeding ten years, depending on the nature of the product and the health risk involved in its use.

For medicines, the marketing authorisation is valid for a five-year term (*Law 6,360/76*).

Monitoring compliance and imposing penalties
ANVISA, as well as the state and municipal bodies, are responsible for inspecting and enforcing compliance with food and drug laws. This includes monitoring the existence or lack of the necessary marketing authorisation.

ANVISA, as well as the state and municipal bodies, are also responsible for imposing administrative penalties for any statutory sanitary infringement, after due administrative prosecution.

10. What commitments and pharmacovigilance obligations apply after a company has obtained marketing authorisation? Are there further conditions concerning how the drug is distributed and accessible to patients?

ANVISA can undertake a control analysis of commercialised batches in official laboratories, to monitor the quality and compliance of the medicine with the medicine registration. When necessary, ANVISA can require companies to train ANVISA technicians, to enable them to undertake this monitoring.

Pharmaceutical industries also have a stake in the pharmacovigilance system, informing ANVISA of any problems with medicines. Law No. 6,360/76 establishes that these companies must notify the sanitary authorities of any adverse reactions caused by medicines. The rules governing pharmacovigilance on medicinal products for human use are set out in Resolution No. 4 of 10 February 2009, for which guidelines are established in Normative Instruction No. 14 of 27 October 2009.

Any post approval changes involving alterations, inclusions or cancellations must follow the procedures specified in Resolution No. 73/2016, amended by Resolutions No. 121/2016 and No. 100/2016.

If medicines are not marketed within a certain period, marketing approval may not be renewed. Under Law 13,411/2016 regime, a renewal of a marketing approval will only be possible if there is evidence the medicine was commercialised for the last two thirds of the marketing approval validity. In other words, the registration holder will have to provide evidence its drug has been commercialised for the last 40 months before the marketing approval expiration. There is no guideline on how such provision will be implemented yet.

11. Which medicinal products can benefit from the abridged procedure for marketing authorisation and what conditions and procedure apply? What information can the applicant rely on?

Scope of abridged procedure
Medical products seeking marketing approval as generics or similar medicines (*Resolution No. 60 of 10 October 2014*) can benefit from an abbreviated marketing approval procedure.

Conditions and procedure
Similar medicines. These must contain the same following characteristics as the reference medicine registered with ANVISA:

- Active ingredients.
- Concentration, dosage form, route of administration, strength and therapeutic, preventive or diagnostic indication.

A similar medicine can only differ in characteristics related to size and form of the product, expiry date, packaging, labelling, excipients and vehicles, and must always be identified by its trade mark.

As per Resolution No. 58 of 10 October 2014, ANVISA determined the possibility of interchangeability of similar medicines with reference drugs, which means that similar drugs can have the same status as generics, once they have been shown to be therapeutically equivalent to the reference products, having the same efficacy and safety.

This change in policy reflects a 2003 decision by ANVISA setting the end of 2014 as a deadline for similar medicines to submit bioequivalence tests for agency approval, which has always been required for generics.

Generic medicines. These are products similar to a reference/innovative product, which must be interchangeable with the reference/innovator product. Generics are usually produced after the expiration or waiver of patent protection or other exclusive rights, since their effectiveness, safety and quality are proven. They can be designated by either:

- DCB, that is, the Brazilian Common Denomination of the drug substance or the pharmaceutically active ingredient approved by ANVISA.
- In the absence of a DCB, the International Non-proprietary Name (INN) of the drug substance, or the pharmaceutically active ingredient recommended by the WHO.

To prove interchangeability for generic medicines, ANVISA requires the submission of bioavailability and bioequivalence assays:

- **Bioavailability.** This indicates the rate and extension of absorption of an active ingredient in dosage form, based on its concentration/time curve in the systemic circulation, or its excretion in urine.

- **Bioequivalence.** This demonstrates the pharmaceutical equivalence of products presented in the same pharmaceutical form, showing:
  - the same qualitative and quantitative composition of active ingredient(s); and
  - comparable bioavailability when studied under the same experimental design.

Further details on the specific procedure to be followed are in ANVISA Resolution No. 60/2014.

12. Are foreign marketing authorisations recognised in your jurisdiction?

A Brazilian marketing approval must still be obtained from ANVISA for a medicine with a foreign marketing approval. In the case of imported medicines and active pharmaceutical ingredients, in addition to the usual registration requirements, the company must also prove that the product is already registered in the country of origin (*Article 18, Law No. 6,360/76*) and complies with the GMP standards in that country.

Parallel imports

13. Are parallel imports of medicinal products into your jurisdiction allowed?

IP laws prohibit parallel imports into Brazil. Trade mark and patent rights can be used to oppose parallel imports. An importer can have the IP law enforced against it.

ANVISA is responsible for the pharmacovigilance of imported pharmaceutical products in Brazil, including airports and ports (*Law No. 9,782/99*). ANVISA has been enforcing a very stringent rule which requires the importer of medicines to provide detailed information on, among other things, the source of the drug and the owner of the marketing authorisation (*Resolution No. 81 of 5 November 2008, amended by Resolution No. 28 of 28 June 2011*). If the importer satisfies the requirements of Resolution No. 81, ANVISA will issue an import licence and release the pharmaceutical products.

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, see *Pharmaceutical IP and Competition Law in Brazil: overview*.

Restrictions on dealings with healthcare professionals

14. What are the restrictions on marketing practices such as gifts, sponsoring, consultancy agreements or incentive schemes for healthcare establishments or individual medical practitioners?

Advertisements, visits by representatives, distribution of free drug samples or other gifts and sponsoring of meetings and seminars are all permitted, provided that this interaction does not influence a medical practitioners' prescription decisions inappropriately.

However, the advertisement and indirect sale or the granting, offer, promise or distribution of promotional gifts, benefits and advantages to professionals are prohibited (*Resolution No. 96/2008, as amended by Resolution No. 23/2009*).

The distribution of institutional gifts, that is, gifts that do not advertise medicine, and of scientific papers, magazines or publications and technical books used for professional updates, are allowed (*Normative Instruction No. 5 of 20 May 2009*).

Free samples, distributed exclusively to prescribing practitioners, must contain at least 50% of the original packaging content, except for antibiotics (enough for complete treatment is mandatory) and contraceptives (full contents of the original package are mandatory). The packaging of these samples must contain the non-removable expression "free sample". Resolution No. 60 of 26 November 2009 prohibits the distribution of free samples of:

- Non-prescription products.
- Biological products that require special care for maintenance and transport.
- Medicine prepared by compounding pharmacies.

Further, it is not possible to distribute free samples of unregistered medicines at ANVISA, as well as non-commercialised presentations of them.

The distribution of medicine subject to special control is subject to more strict rules (*Ordinances No. 344 of 12 May 1998, as amended by Resolution No. 147 of 20 March 2017*). Compliance with such rules does not exempt companies from full compliance with other determinations of Resolution 60/2009.

There are several laws, rules and regulations that address prohibitions or restrictions in providing items of value to public officials at the different branch and federative levels. This situation is considered in many cases a conflict of interest and may be relevant, as many healthcare professionals simultaneously hold positions in public service and work in private practice.

Sales and marketing

15. What are the restrictions on selling medicinal products? Are there specific regulations for the sale of medicinal products on the internet, by e-mail and by mail order?

According to ANVISA's Resolution No. 44 of 17 August 2009, pharmacist technicians can perform activities that are not exclusive to pharmacists, including dispensing/selling prescription medicines. However, the pharmacist technicians must be under direct supervision of the registered pharmacist technically responsible or a substitute (also a pharmacist), whose presence is required during opening hours of the commercial establishment. The sale of prescription medicines can only be made on presentation of a prescription.

The sale of medicine over the internet can only be undertaken by websites from pharmacies and drugstores with fixed commercial establishments, which are open to the public.

In addition, the company providing the service must provide a direct and immediate method of communication between the patient and a pharmacist. Drugs subject to special control (*Ordinance No. 344 of 12 May 1998, as amended by Resolution No. 147 of 20 March 2017*) cannot be sold on the internet.

The site should use only the electronic domain *com.br*, and must show on the main page, among other things, the following data and information:

- Name and registration number in the Pharmaceutical Council of the pharmacist in attendance.
- Alert messages and health recommendations from ANVISA.
- That prescription medicines will only be released on presentation of a receipt, and the means by which it can be presented to the establishment (fax, e-mail or otherwise).

Advertising prescription medicine over the internet is prohibited, unless the advertisement is only accessible by professionals who are able to prescribe or to dispense medicine (*see Question 16, Internet advertising*).

Resolution No. 96/2008 does not expressly mention e-mail messages, but it can be inferred that the term internet in this resolution includes e-mail messages (*see above, Internet*).

There are no particular rules referring to marketing medicinal products by mail order.

Advertising

16. What are the restrictions on advertising medicinal products?

Legislation and regulatory authority

Law No. 9,294 of 1996 and Decree No. 2,018 of 1996 impose restrictions on the use and advertising of smoking products, alcoholic beverages, drugs, therapies and agricultural pesticides, under section 4 of Article 220 of the FC 1988.

The rules relating to the advertising of medicinal products are contained in Resolution No. 96/2008 enforced by ANVISA. Medicines cannot be advertised unless they have a marketing authorisation from ANVISA.

ANVISA often sets fines for industries perceived as marketing ethical medicines to the general public, even where these involve disguised, non-direct advertising. A common practice used to avoid the advertising rules is to partner with medical societies to campaign for awareness and prevention of diseases, without specifically mentioning products. The National Council for Advertising Self-Regulation (CONAR), founded in 1980, has the authority to enforce the Brazilian Code of Advertising Self-Regulation, adopted in 1978. CONAR's objective is to eliminate the placing of advertisements and campaigns with misleading, offensive and abusive content, or that could, among other things, distort competition.

Restrictions

According to Law No. 9,294/1996, only OTCs can be advertised to the lay public. Accordingly, Resolution No. 96/2008 establishes, among others, several proscribed conducts related to OTC advertising, as follows:

- Stimulate and/or induce the indiscriminate use of medicines.
- Suggest or encourage diagnosis by the general public.
- Include images of people using the medicine.
- Employ words that encourage consumption of the medicine, for example, "have", "take", "use ", "try", and so on.
- Advertise a drug as being new, if it has been on the market for more than two years (except for new therapeutic indications).
- Suggest that the patient's health could be endangered if he does not take the advertised medicine.

Prescription drugs can only be advertised to professionals who are able to prescribe or dispense medicines. Advertisement requirements in this case are similar to those imposed on OTC drugs. Among other things, it is required to state the:

- Active principle name according to DCB or DCI.
- Indications and contra-indications of the product.
- Posology.

Further, under Precedent No. 2 of 15 August 1988 and the Code of Advertising Self-Regulation, advertising prescription-only pharmaceuticals to the lay public can be immediately withdrawn by CONAR.

Internet advertising
Advertising prescription medicine over the internet is prohibited, unless the advertisement is only accessible by professionals who are able to prescribe or to dispense medicine (*Resolution No. 96 of 17 December 2008*). Pharmaceutical industries commonly operate restricted-access websites. Advertisements for non-prescription medicine on the internet must contain a warning concerning the active ingredient of the product.

Data protection

17. Do data protection laws impact on pharmaceutical regulation in your jurisdiction?

Brazilian statutory legislation provide for the protection of undisclosed test data that needs to be submitted to the Brazilian regulatory authorities to obtain official approval for the marketing of pharmaceutical products, patented or not. In fact, ANVISA is under an obligation to keep this sort of information secret. Conversely, data package exclusivity for pharmaceutical products for human use is rather controversial.

It is important to highlight that the Civil Code (*section 21*) and the Federal Constitution (*Article 5, item X*) grant rights to privacy, according to which everyone has the right to keep secret certain information concerning their personal lives, which can certainly include aspects of their own health. The Good Clinical Practice of the Document of the Americas and Resolution No. 422/2012 of the National Health Council also grant confidentiality for the information of volunteers for clinical trials.

Packaging and labelling

18. Outline the regulation of the packaging and labelling of medicinal products.

Legislation and regulatory authority
Packaging and labelling requirements are set out in ANVISA's Resolution No. 71 of 22 December 2009, which is currently under review. Enforcement can be made by ANVISA and the other sanitary authorities across states and counties.

Information requirements
Packaging must contain certain minimum information, including:

- The medicine's brand name (except for generics).
- The name of the active ingredient.
- The name and address of the owner of the marketing approval.
- The name of the manufacturer and place where the medicine is manufactured (country, state and city, in the case of imported products).
- The name and registration number of the pharmacist responsible for the medicine.
- The batch number.
- Manufacturing and validity dates.
- Marketing approval number.
- Information regarding the medicine's formula and composition, including weight and volume.
- Security stamp.
- The storage conditions, indicating the temperature range and storage conditions indicated by the medicine's stability study.
- The telephone number of the customer service of the marketing approval holder.

Other conditions
There are also specific requirements for prescription medicines, and specific warnings regarding children, free samples and routes of administration. All the information that does not fit in the external packaging must be contained in the insert packaging. As well as Portuguese, the packaging must contain information in Braille (*Article 24, Resolution No. 71/09*).

Product liability

19. Outline the key regulators and their powers in relation to medicinal product liability.

ANVISA is the main regulator and can, among other things:

- Order a recall.
- Impose penalties for non-compliance, in accordance with Law No. 6,437/1977.
- Seize medicinal products.
- Suspend their distribution, commercialisation, and use.

20. Are there any mandatory requirements relating to medicinal product safety?

Several rules and regulations oblige companies to comply with principles of safety and effectiveness (Law No. 6,360/1976; ANVISA's Resolutions No. 17/2010, and 56/2001, among others).

When there is sufficient evidence or confirmation of non-compliance posing a health risk, and if marketing authorisation has been cancelled due to safety and efficacy issues, Resolution No. 55 of 17 May 2005 applies, which governs drug recall.

In that sense, notification of non-compliance/cancellation of marketing authorisation, including the reasons for non-compliance and classification of the health risk, must be submitted by holders to both ANVISA and the local sanitary authority:

- By e-mail, immediately after acknowledgement of the sufficient evidence/confirmation of non-compliance, or publication of marketing approval cancellation due to lack of safety and efficacy. The following must be included:
    - product name, registration number, presentation, batch number, manufacturing date, expiry date and manufactured or imported amount; and
    - a description of the non-compliance;

- By a specific form submitted to a particular ANVISA office, within 48 hours of the acknowledgement of the sufficient evidence/confirmation of non-compliance, or publication of marketing approval cancellation due to lack of safety and efficacy.

The publication of recall warnings by the marketing authorisation holder requires prior approval from ANVISA. The warning must be submitted to ANVISA for its approval within 72 hours of the acknowledgment of significant evidence/confirmation of non-compliance, or publication of marketing authorisation cancellation due to absence of safety and efficacy.

The entire recall procedure must be closely monitored by the marketing authorisation holder, by means of periodic reports and a final report to ANVISA after the procedure ends.

Non-compliance with sanitary rules incurs penalties, under Law No. 6,437/1977.

21. Outline the key areas of law applicable to medicinal product liability, including key legislation and recent case law.

Legal provisions
Liability for defective medicinal products can arise under:

- The Civil Code (*Law No. 10.406 of 10 January 2002*).
- The Consumer Protection Statute (*Law No. 8,078 of 11 September 1990*).
- The Criminal Code (*Decree-Law No. 2,848/1940*, as amended by several subsequent laws, particularly *Law No. 8,072/1990* and *No. 9,677/98*, which classify crimes against public health as serious crimes).
- Law No. 8,137 of 27 December 1990, which defines crimes against consumer relations.
- Law No. 6,437 of 20 August 1977, which provides sanitary offences and its respective penalties.

Recent case law
In Brazil, case law is not binding. However, recent court decisions covering medicine product liability include:

- Superior Court of Justice (STJ), Internal Appeal on Appeal No. 126815, 2013: defect in a contraceptive product, liability and compensation against the laboratory.
- São Paulo State Court of Appeals (TJSP) Appeal No. 70048214464, 2013: defect in a contraceptive product, liability and compensation against the laboratory.
- Superior Court of Justice (STJ) Appeal No. 1302596, 2015: Class Action VIOXX, medicine with a defect.

Substantive test
A pharmaceutical product is considered to be defective when it is unfit or inadequate for consumption, or when there are contradictions between the product and its packaging information. It can also be considered counterfeit when it has been deliberately and fraudulently mislabelled with respect to identity and/or source, including drugs:

- With correct ingredients but fake packaging.
- With the wrong ingredients.
- Without active ingredients or with insufficient active ingredients.

22. Who is potentially liable for defective medicinal products?

According to the Civil Code, whoever violates a right or causes damage to another, voluntarily or by omission, negligence, recklessness or malpractice, must make reparations for the damage.

Under the Criminal Code, the following are potentially liable for defective pharmaceutical products (*Article 273, Criminal Code*):

- Anyone who falsifies, corrupts, adulterates or alters a product intended for therapeutic or medicinal uses.
- Anyone who imports, sells, displays for sale, stores for sale or, in any way, distributes or delivers for consumption a falsified, corrupted, adulterated or altered product.
- Anyone who commits these actions with products which:
- do not have registration from ANVISA;
- do not comply with the registered formulae;
- do not have the necessary identity and quality required for their commercialisation;
- have reduced therapeutic value or activity; or
- are products of unknown origin, or are acquired from an establishment that does not have the necessary operating authorisation.

The Brazilian or foreign manufacturer, producer, importer and seller of the defective pharmaceutical products are jointly liable (*Consumer Protection Statute*).

23. What defences are available to product liability claims?

There is no liability if any of the following is proven (*Article 12, Consumer Code*):

- The product has not been placed on the market.
- The product has no defect.
- The defect or damage arises exclusively from the consumer's fault.

24. How can a product liability claim be brought?

Limitation periods

There is a five-year limitation period for consumers bringing claims for damages caused by defective products. For criminal complaints, the limitation period can rise up to 20 years, depending on the maximum penalty applied to the crime (*Article 109, Criminal Code*).

Class actions

Class actions are allowed, and are quite common, for groups of consumers claiming damages (civil liability) for defective products.

25. What remedies are available to the claimant? Are punitive damages allowed for product liability claims?

The claimant can file a civil lawsuit claiming damages (civil liability). The Public Prosecutor's Office is responsible for bringing criminal lawsuits.

Although it is possible to find some decisions applying punitive damages, this is a controversial issue in Brazil.

Reform

26. Are there proposals for reform and when are they likely to come into force?

Currently, there are several bills related to IP, food and drug matters being considered by Congress. The most important ones are the following:

- Bill No. 4,961/2005, which aims to amend the IP Law, so that substances or materials isolated from nature which meet the patentability requirements and are not mere discoveries are patentable. This Bill is currently awaiting the opinion of the Chamber of Deputies' Committee on Economic Development, Industry and Trade. It is doubtful whether it will be adopted into law.
- Bill No. 139/1999, which proposes amendments to Law No 9,279/1996.
- Bill No. 3,995/2008, attached to Bill 139/1999, which proposes the exclusion from patentability of new therapeutic uses of known compounds and novel polymorphic forms. It is doubtful whether it will be adopted into law.
- Bill No. 3,943/2012, attached to Bill 139/1999, which aims to amend Article 229-C of the IP Law, to specify that the prior consent analysis carried out by ANVISA in pharmaceutical patent applications includes examination of patentability requirements.
- Bill No. 5,402/2013, attached to Bill 139/1999, which proposes substantial amendments to the IP Law, including:
    - limitation of the patent term at 20 years maximum;

- non-patentability of new property or use of a known substance, or simple use of a known process, except if it does not result in a new product; and
- harmonisation, by ANVISA/BPTO Joint Ordinance, of ANVISA's prior consent mechanism for pharmaceutical patents (Article 229-C) with ANVISA's Resolution No. 45/2008 as amended by Resolution No. 21/2013.

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, visit *Pharmaceutical IP and Competition Law in Brazil: overview*

**The authors would like to extend special thanks to Lucas Calabria and Lívia Figueiredo, for their assistance in writing this chapter.*

Online resources

Brazilian Presidency's website
W *www4.planalto.gov.br/legislacao*

Description. This is the Brazilian Presidency's website. All federal laws and presidential decrees currently in force are available at this address. The legislation is constantly updated, but it is provided in Portuguese only.

ANVISA
W *www.anvisa.gov.br*

Description. All resolutions enacted by ANVISA are made available at its official website. However, the material is provided only in Portuguese. Its contents are regularly updated.

INPI
W *www.inpi.gov.br*

Description. INPI makes available all its resolutions, including its guidelines for examination, at its official website. The address is updated frequently, but most material is only available in Portuguese. Versions of the Brazilian Patent and Trademark Act in English, French and Spanish are available. Those versions are only for information purposes and do not have any binding effect.

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Professional qualifications. Brazilian Bar Association, 2005.

Areas of practice. Transactional, regulatory and IP matters affecting the life sciences industries, dealing with clinical trials, compliance, pharmacovigilance, economic regulation, technology transfer (notably related to the local industrial policy, called PDP) and government procurements.

Non-professional qualifications. Graduated in Law (JD) at the State University of Rio de Janeiro (UERJ, 2005); Master of Laws (LL.M.) in Competition Law and Regulation, University of Lisbon (2012); Master of Laws (LL.M.) in Intellectual Property, University of London, Queen Mary (2013).

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Recent transactions

- Succeeded in two lawsuits representing a major Brazilian jeweller unduly accused of copyright infringement.
- Negotiated an agreement for the construction of a new shipyard in Brazil.
- Negotiated an agreement for the setting-up of a new technological company in the oil and gas industry.

Languages. Portuguese, English, German

Professional associations/memberships. Honorary President of the Brazilian-German Chamber of Commerce in Rio de Janeiro; President of the Ethics Committee of ASIPI; Vice-President of the Brazilian Association of Industrial Property Agents; FICPI; Member of the Council and Chairman of the Industrial Property and Piracy Committee of the Rio de Janeiro State Bar.

Publications. *Direito Tributário Internacional e a Tributação da Transferência de Tecnologia (International Tax Law and the Taxation of Technology Transfer), 1996.*

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