The medicine package leaflet and the regulation of its configurations in terms of form and content in Brazil[1]

A bula de medicamentos e a regulação de suas configurações em termos de forma e conteúdo no Brasil

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Abstract

The medicine package leaflet (MPL) is a technical – scientific document regulated by the government, directed at health professionals and patients in order to inform and instruct its users about the use of a medicine. Considering the importance and complexity of the MPL technical - scientific information for its users, there have been changes in the regulation of MPL´s content and representative elements. It is questionable, however, which representation the MPL technical – scientific information assumed for users' comprehension. In order to identify and analyze the various configurations the MPL has undergone over time due to the influence of regulatory frameworks, we looked at the representations the MPL technical – scientific information has taken to become adaptable to users' comprehension. A qualitative study was conducted, focused on surveying, identifying, organizing and reading the legal instruments that constitute the MPL national regulatory framework, observing changes in the regulation over time. The results show that its regulation has a legal history, which has been developing for seven decades, along with the establishment of institutions in health and health surveillance by the government. It is also observed that, in spite of MPL's regulatory process development occurring over long periods of time, since the foundation of the National Agency for Sanitary Surveillance (1999) and its public inquiries, this process started to be renewed and improved with a little more frequency. Thus, in the last ten years, MPL regulation has become more specific, regarding form and content.

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Keywords: Brazil; Medication Instructions; Legislative Information; Qualitative Method; Regulatory Process.

Resumo

A bula é um documento técnico – científico, direcionado a profissionais da saúde e pacientes, que acompanha o medicamento para informar sua composição, características e uso. Considerando a importância e complexidade dessas informações técnico-científicas, houve transformações na regulação de seu conteúdo e de seus elementos representativos. Questiona-se, contudo, quais as representações que a informação técnico-científica assumiu em relação à compreensão de seus usuários. Com o objetivo de conhecer e analisar as diversas configurações contemporâneas que a bula de medicamento tem sofrido sob influência dos marcos regulatórios ao longo do tempo, evidenciaram-se as representações que a informação técnico-científica da bula de medicamento vêm assumindo para compreensão de seus usuários. Para tanto, realizou-se este estudo qualitativo centrado em levantamento, identificação, sistematização e análise comparativa dos instrumentos jurídicos que compõem o marco regulatório nacional dessas bulas. Os resultados demonstram que sua regulação possui um arcabouço legal histórico, que vem se desenvolvendo há sete décadas, juntamente com a criação de órgãos de fiscalização em saúde e em vigilância sanitária. É possível notar que o desenvolvimento do processo regulatório das bulas de medicamento, apesar de ocorrer entre longos espaços de tempo, a partir da criação da Agência Nacional de Vigilância Sanitária (1999) e das consultas públicas, começou a ser realizado com um pouco mais de frequência. Assim, nos últimos dez anos, a regulação da bula de medicamento passou a ser mais específica, principalmente quanto aos aspectos de forma e conteúdo.

Palavras-chave: Brasil; Bula de medicamentos; Informação legislativa; Metodologia qualitativa; Processo regulatório.

Introduction

Nowadays, medicine can be characterized as a hybrid artefact, at the same time a public good, a consumer good and a scientific tool of treatment. As a public and consumer good, this artefact attracts the attention of public health policy administrators, of technical-scientific organizations, non-governmental organizations and national and international bodies which regulate biomedical products (Carpenter, 2010; Hawthorne, 2005). Public Health administrators and researchers and civil society organizations, concerned with the increasing and harmful effects of medicines on citizens' health, are paying more attention to the choices made by the pharmaceutical industry in terms of the drugs' form (tablet, capsule, lotion, cream, etc.) and excipients that may affect both the effectiveness and safety of a new substance launched on the market (Bates et al., 2001; Friedhoff, 2009; Wolfe et al., 2005). This convergence of what some see as humanitarian (Gunn and Masellis, 2008; Petersen and Lupton, 1996) and others as economic (Paolucci, 2010) interests triggered various campaigns on the international scene, of which two deserve a mention here: (1) formulation of the principle of pharmaceutical care (Hepler and Strand, 1990; WHO, 1993) – in which the pharmacist takes on a more active role in promoting health through direct interaction with the patient in order to solve or prevent problems related to the prescribed drug – and (2) improvements to the regulatory process concerning the medicine package leaflet (Hawthorne, 2005; Friedhoff, 2009; Carpenter, 2010) – in which this leaflet, indispensable when taking the drug, provides information, ordered according to specific norms, on chemical composition, precautions, warnings, cautions, ways to administer it and prepare it before ingestion.

On the other hand, despite industrialized medicines occupying a central place in the longevity and quality of life of the population (Weatherall, 1990), inappropriate or excessive use has resulted in adverse reactions which contribute to increased morbidity and mortality rates (WHO, 1969; Davies, 1999; Johnson and Bootman, 1997). These adverse reactions, caused by excessive consumption of medicines, is a national public health problem and, even when medicines are safely and correctly prescribed, correct use can depend on reading and understanding the medicine package leaflet.

The contents of the medicine package leaflet, in Brazil, is based on information from records of medicine approvals, previously submitted to the National Health Surveillance Agency, responsible for regulating, analyzing and approving them. The information from the records are technical-scientific, deriving from the results obtained in developing the medicine through clinical trials. This characterizes the medicine package leaflet as a document describing the medicine, as well as a product of Science and Technology (S&T) and the result of Research and Development (R&D). Even if the reader is informed, the leaflet is essential in accessing information about the medicine. Moreover, it is also an institutionalized document, as, according to Caldeira et al. (2008), over a period of seven decades its content has been regulated by norms established by government bodies and it is the result of various campaigns/activities by different agents/actors forming part of the chain of the production of the medicine. On the other hand, considering the nature and complexity of technical-scientific information, reading and understanding the medicine package leaflet may not be an easy task for certain users, especially for the layperson, which describes the majority of patients with regards technical-scientific content.

Caldeira et al. (2008) conducted research into the historical evolution of the legal regulation of the medicine package leaflet in Brazil, seeking to observe the influence of scientific development, globalization of information and different health care policies through a retrospective review of Brazilian health legislation, comparing the obligatory items, structure and content required by the norms to be included in the medicine package leaflet. Six norms were identified, published between 1946 and 2003, which established items to be included in medicine labels and leaflets. Based on this, an analysis of the obligatory items, required by health care institutes and regulatory bodies was conducted. The authors

stated that, due to intrinsic relationship between the record and the leaflet, the standardization of both was altered at practically the same time. As the requirements to guarantee effectiveness, safety and quality of medicines increased, the number of obligatory items in the leaflet also increased in order to better describe and define them, such as the creation of new information items (Caldeira et al., 2008).

In Brazil, the Law guarantees health care system users the right to information. However, guaranteeing "access" and "the right" to information is not limited to ensuring its material availability, but rather ensuring it being understood by the reader. A basic condition for this is that the information be configured in such a form that its users can understand and remember it when necessary. In the case of medicine package leaflets, the main users are patients, usually laypeople as far as technical-scientific content goes, as was remarked above. Thus, in order for the information on the leaflet to be accessible, it needs to be appropriate to the informational needs and degree of instruction of the various users. As there are regulations applying to the medicine package leaflet, which the pharmaceutical industry must adhere to, it is appropriate to question what configurations the technical-scientific information in the medicine package leaflet has taken on due to regulation and which are aimed at making it appropriate to today's reality.

Faced with this problem, given that regulation of the content and of the elements which the medicine package leaflet must include have evolved and changed, the aim of this art6icle id to discover and analyze the diverse contemporary configurations which the medicine package leaflet has had under the influence of regulation from the first published norm up to the current one, from the last decade.

The article is divided into two large sections. In section "Analysis of medicine package leaflet regulations", the methodology and results are shown. The results of the description and analysis are divided into two periods: "2.2 Description of regulations published between 1946 and 1997" and "2.3 Description of regulations published in the last ten years". A discussion is developed in item "3. Discussion", concerning the main results of the analysis of regulation. In the final section, "4. Final considerations", a synthesis of the analyses and a comparison between the regulatory processes in the periods (1946 to 1997 and in the last ten years) are used to present improvements detected in the process of constructing regulations, concerning the configurations which the technical-scientific information in the medicine package leaflet has taken on over time in order to acquire the realities of lay users, the patients.

Analysis of regulation of the medicine package leaflet

With the aim of discovering the various contemporary configurations which the medicine package leaflet has taken on under the influence of regulation, a qualitative study was conducted using secondary source documental analysis. The legal instruments which regulate the medicine package leaflet were found on the internet, on the page of the Diário Oficial da União (Official Federal Gazette) (http://portal.in.gov.br/) site, in the portal of information which is of public interest and on that which monitors public administration, JusBrasil (http://www.jusbrasil.com.br/diarios). Documents published between 1946 (year of publication in the Diário Oficial da União of the first regulation of medicine package leaflet) and 2009 (current legislation), were analyzed, giving a total of 9 legislative tools which represent the development of the regulatory process for the medicine package leaflet in Brazil. A retrospective reading of each legal instrument was performed and comparative analysis conducted. The data were organized into a chart, classified by "Year", "Type of legal instrument", "Regulatory body" and "Description" (Chart 1).

Results

Chart 1 shows, in chronological order, the nine legal instruments which make up the legal framework of the medicine package leaflet.

Chart 1 - Legal instruments concerning the medicine package leaflet published in the Diário Oficial da União

Year	Type of legal instrument	Regulatory body	Description
1946	Decree n. 20,391, 14 January 1946. Diário Oficial da União 1946; 19 Jan.	Ministry of Health - MH	Regulation of the Pharmaceutical Industry in Brazil approved by decree.
1959	Ordinance n. 49, 10 August 1959. Diário Oficial da União 1959; 17 Aug.	National Medicine and Pharmacy Surveillance Service - SNFMF	Regulates the presentation and examination of labels and leaflets for prescription and over the counter medicines, dietary, cosmetic and hygiene products and toiletries.
1984	Ordinance n. 65, 28 December 1984. Diário Oficial da União, Brasília, 31 Dec.1984. section 1. p. 19931.	National Department of Health Surveillance - SNVS	Set a standardized medicine package leaflet layout to be used by all medicines registered in Brazil.
1997	Ordinance n.110, 10 March 1997. Diário Oficial da União 1997; 8 Mar.	Department of Health Surveillance - SVS	Set a standardized medicine package leaflet text, the items of which to be rigorously adhered to, with regards order and content.
2001	Public consultation n. 95, 19 November 2001. Diário Oficial da União, Brasília, DF, 21 Nov. 2001.	ANVISA — National Health Surveillance Agency *	Public consultation held for criticisms and suggestions to be presented to the public so that the texts of medicine package leaflet for medicines available in the market could be re-evaluated considering the heterogeneity of information available to consumers and health care professionals
2002	Public consultation n.2, 18 January 2002. Diário Oficial da União, 9 Jan. 2002.		
2003	Board Resolution (RDC), n. 140, 29 May 2003. Diário Oficial da União 2003; 24 Sept.	ANVISA	Set a standardized medicine package leaflet text with regards to form and content and published a list of standardized medicines for the leaflet text.
2009	Public Consultation n.1, 23 January 2009. Diário Oficial da União 2009; 26 Jan.	ANVISA	Public consultation held for criticisms and suggestions to be presented regarding the proposed Resolution to approve rules for drawing up, publishing, updating and standardizing medicine package leaflets for patients and health care professionals.
2009	Board Resolution (RDC), n. 47, 8 September 2009. Diário Oficial da União DOU. No 172, 9-9-2009, section 1, p. 31.	ANVISA	Established rules for drawing up, publishing, updating, standardizing and making available medicine package leaflets for patients and health care professionals.

Source: Brazil, 1946, 1959, 1984, 1997, 2001, 2002, 2003, 2009b; ANVISA, 2010.

Description of regulations published between 1946 and 1997

According to Chart 1, from a chronological perspective, it can be seen that the process of regulating the medicine package leaflet in Brazil began in **1946**, when the Ministry of Health (MH) issued decree n. 20,397 establishing regulation of the Pharmaceutical Industry. In this decree, Brazil began to regulate information to create the medicine package leaflet, this information was approached as separate items, depending on the type of laboratory and/or pharmaceutical product: "industrial pharmaceutical laboratories"; "biological product laboratories"; "functioning of the laboratories"; "pharmaceutical chemical products"; "officinal products" ; "fraud, alteration, seizures, analyzes and expertise" and; "general provisions". As for the content of the medicine package leaflets, according to the above mentioned decree they may "only refer to the action of the com-

ponents, with the therapeutic indications strictly limited to the terms of the license". The labels of pharmaceutical preparations "obliged" to contain "the denomination by which they are characterized, formula, method of use, place manufactured, name of the responsible technician, number and date of the license and the statement 'prescription only' when required by the SNFM".

In **1959**, the National Medicine and Pharmacy Surveillance Service (SNFMF) issued Ordinance n. 49, regulating the presentation and examination of labels and medicine package leaflets for prescription and over the counter medicines, dietary, cosmetic and hygiene products and toiletries. This ordinance complements Decree n. 20,391/46, with regards to the models of labels and leaflets for pharmaceutical or similar products, which should contain the same wording (content) and satisfy the requirements presented above in the Decree. Ordinance n. 49 added that "it is optional to dispense with medicine package leaflets provided the labels or packages themselves contain all of the information required by the regulation in force, and appropriate disclosure is made at the time the models of the labels and cartons are approved".

Twenty-three years after Ordinance n. 49 was issued, in **1984**, the National Department of Health Surveillance (SNVS), an MH body, became responsible for regulating concerning information to be included in the medicine package leaflet. In this year, for the first time in Brazil, Ordinance n. 65 established a layout for leaflets for medicines which had been approved by the SNVS (Ordinance n. 65). This layout, structured in four parts, contained: (I) Identification of the Medicine; (II) Information for the Patient; (III) Technical Information; (IV) Legal Information. It is worth noting that this general structure has been in use since them. The payout is presented in detail, according to Ordinance n.65, in Chart 2, as follows;

In **1997**, the Department of Health Surveillance (SVS) re-issued the norm for the new Ordinance, number 110, keeping the same structure and the original content, but modifying the order of some items in the Technical Information section. It also added to and altered the wording in some requirements related to the information for the patient section. Two of these alterations are worth noting: to be obligatory and uniform, written in easily understood language for the general consumer; to insert some warnings in the technical information and information for the patients in upper case (Brasil, 1997).

It was noted that, in the first four publications (from 1946 to 1997), before ANVISA was created, these publications developed by the MH, the National Medicine and Pharmacy Surveillance Service – SNFMF, and by the National Department of Health Surveillance – SNVS, the legislation of the content of the medicine package leaflet was generalized, with no distinction between types of medicine or users. This generalization mainly occurred in the two first MH publications (Decree n. 20,397, 1946) and by the SNFMF (Ordinance n. 49, 1959), which only regulated the presentation and the label and leaflets of various different types of products, such as leaflets for prescription and over the counter medication, diet, cosmetic and hygiene products and toiletries.

Description of regulation published in the last ten years

Considering the chronological order of systemizing the legal instruments shown in Chart 1, the following items describe the regulatory process which has occurred in the last ten years. This process, which began in 2001, with a Public Consultation, is coordinated by ANVISA, and marks a change in the form of regulation practiced up to that time.

Public consultations and the Board Resolution - RDC n.140, ANVISA

In their official website, ANVISA explain that, before issuing a new norm, resolution or regulation, a public consultation is conducted to learn their opinions on the issue, and so that the citizen is familiar with the topics which are debated in the agency and can express their opinion using the website. A virtual discussion forum is created for each topic, which is open to everyone. When the period of the consultation is over, all contributions are analyzed.

As can be seen in Chart 1, in the first two years of the 21st century, ANVISA conducted two public consultations, in 2001 and 2002, respectively, to collect criticisms and suggestions on the proposal in force at that time (Ordinance n. 110/97). The aim

Chart 2 - Layout for medicine package leaflets, published in Ordinance n. 65 in 1984

Headings	Subheadings
[I] Identification of Product	Name of product
	Generic name (BCD for active substances)
	Pharmaceutical forms and presentation
	CHILDREN'S USE or ADULTS USE (prominent)
	Full composition
[II] Information for the Patient (obligatory and uniform for each active ingredient, written in easy to understand language for the general consumer).	Storage guidance before and after opening and/or preparation.
	Expiry date and validity after opening and/or preparation. Warning of the dangers of taking out of date medicine.
	Expected action of the medication: time until effects felt, etc..
	Inform you doctor of pregnancy while following this treatment or after (set time limit if necessary)
	Precautions while taking the medication
	What to do if you interrupt the treatment
	Inform your doctor if you notice any of the following symptoms (most important, in order of frequency or severity if necessary).
	" ALL DRUGS SHOULD BE KEPT OUT OF REACH OF CHILDREN " – prominent and also appears on the label
	Effects if taken with other substances (alcohol, food etc.)
	List contra-indications and precautions if necessary.
	General warning on the risks of self-medicating: "DO NOT TAKE ANY MEDICINE WITHOUT YOUR DOCTOR'S KNOWLEDGE. THIS MAY BE HARMFUL TO YOUR HEALTH".
[III] Technical Information (partly uniform for the active ingredient and partly following industry criteria according to DIMED instructions, written in technical terminology)	Indications - based on pharmacological actions and not diagnoses or symptoms (diagnosis may be used depending on DIMED agreement).
	Contraindications based clinical entities for which the drug cannot be used
	Precautions: age, pregnancy, breastfeeding, associated pathologies, abrupt interruption possibility of dependence.
	Drug Interactions citing substances or groups of substances and not specialties.
	Adverse Reactions: cite all substantiated adverse reactions in order of severity (if possible include incidence); always use technical language, replace the phrase "does not produce adverse reactions" with "intensity and frequency of adverse reactions as yet unknown"; quote the most common situations in the PATIENT INFORMATION.
	Dosage: dose and duration of treatment, methods of and other instructions for administration; if applicable, detail dosage for specific diseases and special situations (kidney or liver failure, etc.). Always in technical language.
	What to do in case of overdose and, if necessary, serious adverse reactions – general and specific guidance.
[IV] Legal Information	DIMED record number
	Name of company
	Address of company
	CGC Number
	Other statutory wording

Source: Brazil, 1984.

was to re-evaluate the texts of the leaflets for non-prescription medicines, due to the heterogeneity of information available to the consumer (the patient) and health care professionals (Ordinance n. 110/97, p. 34). It was only in 2003 that ANVISA drew up and issued a new resolution (Resolution RDC n. 140) broader and more specific in terms of content in relation to the four legal instruments published between 1946 and 1997, describing how the information in each section of the structure should be organized. For the first time, with the introduction of this resolution, norms, laws and principles established by the Health Law were cited, regarding the health care users' right to information and others from the Code of Consumer Protection, regarding the right to clear and sufficient information on different products and services, specifying quantity, characteristics, composition, quality and price, as well as risks they posed; it also included those of the World Health Organization - WHO regarding the importance of access to impartial, quality information to guide self-care and self-medication.

It was also noted that, for the first time in the Brazilian regulatory process, four types of content were specified in the medicine package leaflet, as a health legal document: one for the health care professional (containing technical-scientific information and guidance on medications and their rational use, available to health care professionals); another for the patient (containing technical-scientific information and guidance on medications, available to users in appropriate language, which is to say, easy to understand); a third was for the electronic database (containing the digital version of the text in the medicine package leaflet and other information concerning health education) and a fourth for the compendium of medicine package leaflets (published annually and edited by ANVISA, a set of leaflets from commercialized medicines, with the contents of both the leaflets for the patient and the leaflet for the health care professional).

Chart 3, below, shows, in sequence, the structure of the contents of medicine package leaflets according to the norms established by ANVISA in the penultimate resolution, published in 2003 (Resolution RDC Nº 140, 2003):

In Chart 3, we can see that the content of the structural text of the medicine package leaflet continues to be similar to the first layout, published in 1984 (see Chart 2), Ordinance n. 65, divided into four main items: 1. Identification of Product; 2. Information for the Patient; 3. Technical Information for health care professionals and 4. Legal information. In the "Information for Patients" item, it is suggested that the information be organized in a question and answer form. With regards to the form of the leaflets' content, the only recommendation was that the typeface be 1.5 millimeters, minimum.

ANVISA's 1st public consultation and Board Resolution – RDC 47/09

In January 2009, ANVISA conducted a new public consultation (Public consultation n. 1, 2009) presenting criticisms and suggestions regarding a new proposal for the Resolution concerning medicine package leaflets, which was published in September of the same year, RDC 47/09. Soon after issuing this new Regulation (RDC n. 47, 2009b), ANVISA made the report of the public consultation, (ANVISA, 2010), available on its official website (www.anvisa.gov.br). Among the data found and presented in the report, it was observed that, of the topics mentioned by the public regarding the proposal of the Resolution (a total of 46 key topics and 531 related proposals), the most frequently commented on was the "Form and Content" of the leaflet, with 130 proposals and, in second place, the Wording, with 56. This consultation, then, contributed to more attention being paid to the "graphic presentation of information in the leaflet" aspect by the body responsible for current regulation. It stands out that the results of the Consultation and ANVISA's decision (to give more relevance to the graphic presentation) show the importance of the graphic presentation of the information for medicine users.

The introduction to RDC 47/09 presents the same rules, laws and principles as the RDC 140/03 concerning rights and access to information, but it refers to three documents: the 1988 Constitution of the Federal Republic of Brazil as regards the right to health care; the text of the National Medicines Policy, on established directives, priorities and responsibilities, seeking to guarantee the safety and quality of medicines used in the country, en-

Chart 3 - Structure of the text of the medicine package leaflet, according to the norms of Resolution RDC N° 140, 2003

Headings	Subheadings
[I] Identification of Product	Commercial or brand name of the medicine.
	Pharmaceutical forms, method of administration, presentations commercialized Insert the phrase "For Children's or Adults' use", prominent.
	Composition
[II] Information for the Patient	Action of the drug
	Indications of the drug
	Risks of the drug
	Method of use
	Adverse reactions
	What to do in case of an overdose
	Instructions for storage and use
[III] Technical Information for Health Care Professionals	Pharmacological characteristics
	Efficacy Results
	Indications
	Contraindications
	Method of use and storing after opening
	Dosage
	Warnings
	Use in the elderly, children and other risk groups
	Drug interactions
	Adverse reactions to medications
	Overdose
	Storage
[IV] Legal Information	ANVISA/MH record number
	Responsible pharmacist and registration number in the Regional Unit of the Federal Council of Pharmacy.
	Full name and address of the manufacturer and the registrant.
	National Register of Legal Entities, CNPJ.
	Customer care telephone number
	Include the following wording where necessary: "Use restricted to hospitals"; "Prescription only"; "Dispensed only with prescription" (for official laboratories) and "Not for commercial use".

Source: Brasil, 2003.

couraging rational use and the population's access to those considered essential and, finally, the Standard Rules on the Equalization of opportunities for person with disabilities document, adapted for the General Meeting of the United Nations (UN, 1995).

With regards content, an alteration was made to the "Information for the Patient" item, which is obligatory in the pre-structured layout and made up of nine questions and answers (Chart 4). The requirement that the "Information for the Patient" section be structured as questions and answers in Resolution n. 140 (2003) precursor of the current Resolution n. 47, 2009b), was presented as an optional proposal for medicine manufacturers. Chart 4 shows the required content and structure in the RDC 47/09, as follows:

As for the format, the RDC 47/09 determined that the content of medicine package leaflets should: 1) use (a) Times New Roman font in the body of the text, with a minimum size of 10, not condensed

Chart 4 - Structure of the text of the medicine package leaflet, according to the norms of ANVISA Resolution RDC Nº 47

Headings	Subheadings
[I] Identification of Product	Commercial or brand name of the medicine.
	Generic name of the active substance(s), using the Brazilian Common Denomination.
	For herbal medicines, inform plant species and plant part used.
	For herbal medicines, registered based on traditional use, insert the phrases: "herbal medicines recorded based on traditional use." (in bold) "Prolonged use is not recommended while large scale clinical studies on safety have not been carried out."
	For streamlined drugs, include the following phrase, depending on the class of drug, in bold: Homeopathic Remedy "and" Anthroposophic Medicines "or" Antihomotoxic medicine
	Presentation
	Pharmaceutical form
	Concentration per unit or pharmaceutical units, as appropriate.
	Total weight, liquid volume or pharmaceutical units.
	Total number of dosing accessories included, as appropriate.
	Cite method of administration, using upper case and bold.
	Include the following in upper case and bold: "FOR ADULT USE ABOVE AGE...", indicating the minimum age, in months or years, for which the medicine was approved and registered to be used.
	Composition
	Active substance
	Excipients
	Pharmaceutical form whose physical state is liquid, in droplets, inform the equivalence of drops per milliliter (drops / mL) and a drop weight (mg / mL).
	For herbal medicines, inform the drug composition, indicating the actual weight ratio or volume of plant material used, the equivalent markers and description of the derivative.
	For streamlined medications, inform the qualitative and quantitative composition in active ingredients, according to the official nomenclature for the qualitative and inert ingredients. Mention power / scale for active ingredients. Mention below of the alcohol composition of the final product, for liquid formulations.
[II] Information for the Patient	1. What is this medicine used for?
	2. How does it work?
	3. When should this medicine NOT be used?
	4. Before taking the medicine
	5. Where, how and for how long can I store this medicine?
	6. How to take the medicine
	7. What if I forget to take it?
	8. What side effects may be caused by this medicine?
	9. What should I do if I take more than the recommended dose of this medicine?

(continues)

Chart 4 - Structure of the text of the medicine package leaflet, according to the norms of ANVISA Resolution RDC Nº 47 (continued)

Headings	Subheadings
[III] Technical information	1. Indications
	2. Efficacy results
	3. Pharmacological characteristics
	4. Contraindications
	5. Warnings and precautions
	6. Drug interactions
	7. Storing the medicine
	8. Dose and method of use
	9. Adverse reactions
	10. Overdose
[IV] Legal Information	Report the initials "MS" plus the number of the Ministry of Health record as published in Diário Oficial da União (D.O.U.), using the first 9 (nine) digits.
	Name, registration number and initials of the Regional Board of Pharmacy technician in charge of undertaking the record.
	Corporate name and address of the company holding the record in Brazil.
	CNPJ of the registrant
	For products manufactured and/or packaged by different companies, inform the company name manufacturer and place of manufacture of the product, citing the city and state, preceded, as appropriate, by: "Created by:" and "Packed by:"
	Customer care telephone number
	Include the following wording where necessary: "Use restricted to hospitals"; "Prescription only"; "Dispensed only with prescription" (for official laboratories).
	Include the phrases on sales restrictions, use and dispensation provided for in specific norms for controlled items.
	Include, except in texts leaflet to be submitted electronically to ANVISA, one of the following phrases, as appropriate, in bold: "This leaflet was approved by ANVISA on (day / month / year)" (stating the date of publication); "This leaflet was updated as Bula Standard approved by ANVISA on (day / month / year)."

Source: Brasil, 2009b.

and not expanded; (b) text with a minimum 10% spacing between the letters, (c) text spacing with an least 12 points between lines, (d) columns at least 8 millimeters wide; 2) text left aligned, hyphenated or otherwise; 3) using upper case and bold to highlight the questions and the items in the leaflet; 4) contain underlined or italic text only for scientific names; 5) be printed in black on white paper thick enough that the print on the reverse side does not show, if the leaflet covers more than one side; 6) when printing the leaflets in special format, with a larger font, Verdana should be used, with a minimum size of 24, with no columns in the text; 7) when printing Braille formats of the text, the arrangement of the dots and the spacing between the Braille cells should follow the directives of the Brazilian Braille Commission (CBB) and the Brazilian Accessibility Standards, issued by the Brazilian Association of Technical Norms (ABNT). The unprecedented nature of having norms for presenting the content of the medicine package leaflet in Braille for visually impaired users should be pointed out.

Discussion

In this section we present a discussion on the legal instruments issued by Brazilian health care and health surveillance supervisory bodies to regulate medicine package leaflet over the 63-year-period. We also highlight the regulatory process guided by public consultation, which informed the presentation of the technical-scientific information which forms the content, aiming to make it understandable to users/patients.

Throughout the regulatory process, which occurred relatively recently in the history of public health in Brazil, it was observed that the first four legal instruments concerning the contents of the medicine package leaflet, published between 1946 and 1997 by the MH, SNFMF, the SNVS and the SVS, treated the material in a generalized way, making no distinction between types of medicine or types of user. This generalist concept is more noticeable in the first two instruments, Decree n. 20,397/46 and in Ordinance n. 49/59. These norms, each in their own era, dealt not only with medicine package leaflets, but also with other types of pharmaceutical products, such as over the counter medicine, diet, cosmetic and hygiene products and toiletries.

The legal instruments published between 1984 and 1997 showed the structure of the content which should appear in the medicine package leaflet. It was only between the years of 2003 and 2009 that a national regulatory agency began to give instructions on how the technical-scientific information should be presented in terms of form and content. This change is of great importance, as Brazil is a continent-sized country, with serious public health, education and income distribution problems, which means the population has different and, very often, deficient perspectives of understanding and assimilating information.

Between 2001 and 2009, three public consultation were conducted. Two aiming to re-evaluate the text of non-prescription medicine package leaflets available commercially, due to the heterogeneity of the information available to consumers (patients) and health care professionals (Public consultation n.95, 19 November 2001; Public consultation n.2, 18 January 2002) and another aimed at approving the rules for drawing up, publishing, updating and standardizing medicine package leaflets for patients and health care professionals (Public consultation n.1, 23 January 2009a). Regarding the first two, ANVISA prepared and published a new resolution one year later, in 2003 (Resolution n. 140). It was both broader and more specific than any of the previous norms in terms of content (explaining how each item should be worded). Although Resolution n. 140, in 2003, already indicated the need to word information differently for different types of user ("Information for the Patient" and "Technical Information"), this only became obligatory with Resolution n.47, in 2009.

The requirement for the "Information for the Patient" content to be structured as question and answer stands out. According to ANVISA, this is the most simplified presentation for content aimed at patients. However, it is deemed necessary to analyze whether the content of the nine questions is sufficient to cover all the patients' information needs and, also, whether the form and the wording used by the manufacturer in the answers are appropriate to the information needs of the patients/users.

Based on comparative analysis, it was observed that the tables of rules for each of the legal instruments from 1946 onwards, that it was only 57 years later that graphic presentation was deemed relevant to the definition of form and content in medicine package leaflets. Chart 5 shows a synthesis of how this process occurred:

We associated this greater specificity in the RDC, passed in 2009, with the fact that aspects of "Form and content" were the most strongly criticized according to the report of Public consultation n. 1 (Brasil, 2009a). The actions of the pharmaceutical industry to bring medicine package leaflets in line with the new norms meant restructuring the standard pattern of leaflets then in force, based on legislation which had never used public consultation as part of the regulatory process.

Chart 5 - Synthesis of the regulatory process for the rules for presenting information in medicine package leaflets

Legal instrument	Year	Rules for presenting form and content
Decree n. 20.391	1946	Does not include rules on the presentation of the content
Ordinance n. 49	1959	
Ordinance n. 65	1984	
Ordinance n. 110	1997	
RDC n. 140	2003	Font size must be at least 1.5 millimeters
RDC n. 47	2009	Use Times New Roman font in the body of the text, minimum size of 10 points, not condensed and not expanded; Minimum spacing between letters of 10%; Minimum 12 point spacing between lines; Text columns of at least 80 millimeters width; Left aligned text, hyphenated or otherwise; Underlined and italic text only for scientific names; medicine package leaflet text should be printed in black on white paper, thick enough that text on the reverse is not visible, if the leaflet covers more than one side; When printing the leaflets in special format, with a larger font, Verdana should be used, with a minimum size of 24, with no columns in the text; When printing Braille formats of the text, the arrangement of the dots and the spacing between the Braille cells should follow the directives of the Brazilian Braille Commission (CBB) and the Brazilian Accessibility Standards, issued by the Brazilian Association of Technical Norms (ABNT).

Source: Brasil, 1946, 1959, 1984, 1997, 2003, 2009b.

Final considerations

This article is a continuity of the analysis begun by Caldeira et al. (2008), on health legislation in Brazil between 1946 and 2003, comparing content of medicine package leaflets required by legal standards.

In short, it could be said that the regulation of medicine package leaflets fulfills an historical legal framework which has been evolving over seven decades, together with the creation of health care and health surveillance supervisory bodies (SNFMF, SNVS, SVS and ANVISA), since the first publication in 1946. It can be noted that the development of the regulatory process regarding medicine package leaflets, although slow and with long periods elapsing between changes, takes place after the appearance of ANVISA, in 1999. The moment at which public consultations of the process began to be conducted a little more frequently. From then on, the "medicine package leaflet" as a document began to be treated with more specificity, both with regards to content and to format (related to aspects of graphic presentation), as the topic "form and content" of the leaflet received greater attention both in the published norms of the regulation in force and from users.

The legal instruments published between 1984 and 1997 show the structure of the content which should appear in the medicine package leaflet, but it was only between 2003 and 2009 that the national regulatory agency began to give instructions as to how the technical-scientific information should be presented, with regard to both form and content. This change is of great importance, as Brazil is a continent-sized country, with serious public health, education and income distribution problems, which means the population has different and, very often, deficient perspectives of understanding and assimilating information.

We judged that the inclusion of Public Consultations in ANVISA's methodology of developing regulation (RDC 140/03; RDC 47/09), was a positive step in the process of constructing a medicine package leaflet with the quality of information necessary for all users. User participation in this process can be a variable, not just a collaborator, but also facilitating making the information in the medicine package le-

aflets more appropriate to their understanding. On the other hand, it is necessary to evaluate whether medicine package leaflets currently being produced meet the configuration required by RDC 47/09, especially concerning the content of the "Information for the Patient" item (structured as question and answer), in other words, are they appropriate to the users/patients.

ANVISA's adopting this social control mechanism in providing public services is in line with the idea of the State and Society working together as partners, aiming to involve them in the process of constructing norms for medicine package leaflets with the goal of improving the process of drawing up, standardizing and updating them for the users. In listening to and considering public opinion as an aid to developing norms and making decisions choices on the part of the State and its public institutions, the chances of them being effective and better adapted to the diversity of Brazilian culture are higher. In the case of regulation concerning medicine package leaflets, according to Caldeira et al. (2008), it can and should be used as an instrument for the citizen, as it empowers the individuals to inform themselves on the use of the medicine, a hybrid technical-scientific artefact, linked to longevity and quality of life, indispensable to the progress of public health in modern society.

Compared with previous norms and to the respective institutions which issued them, it was observed that in the last ten years the current regulatory agency has paid more attention to them, and has updated them more frequently, especially aspects of wording, form and contents, considering the opinions of users using Public Consultation aimed at all Brazilian citizens. This fact signals a closer relationship between the State and Society in Brazil in the 21st century. Since then, ANVISA has taken on the idea which has guided relationships and inter-relationships between the State and society in Western societies for the last thirty years, expressed by words such as "participation", "empowerment", "participative budgeting", "human rights", "accountability", "social control" etc. (Machado, 2012). But, at the same time, it is important to consider to what extent more information on medicines are available to users through medicine package leaflet, and, over time, the greater is the need to alter and update the technical-scientific content, as new scientific knowledge is produced and revised by the pharmaceutical industry.

"Access to public information is increasingly recognized as a right in various parts of the world" (Brasil, 2011, p. 8). This us because a well-informed citizen certainly has better conditions for knowing about and accessing other basic rights, such as health care, education and a healthy environment. It is appropriate, then, to highlight the presentation of the principles regarding the right to and access to information in the two Resolutions developed by ANVISA, it is a milestone in the national regulatory process for medicine package leaflets, as it places Brazil in line with the international scene in terms of the legal evolution of this material.

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