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Defective medicines are among us! Analysis of combating defects in drug packaging in terms of the Sanitary Administrative and Consumer Law

Medicamentos com defeitos estão entre nós! Uma análise do combate aos defeitos em embalagens de medicamentos à luz do Direito Administrativo Sanitário e do Consumidor

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ABSTRACT

Introduction: Providing quality, safe, and effective medicine is the purpose of the production and supply chain; however, errors happen. This work addresses action against defects observed in medicines' primary and secondary packaging from the perspective of health and consumer administrative legislation and their practical consequences in the consumer relationship. **Objective:** To demonstrate the contribution of health and consumer administrative legislation, with emphasis on Good Manufacturing Practices (GMP) for medicines and the Consumer Protection Code, ensuring adequate and safe information to patients and how suppliers and consumers can influence the control of defects and safe administration of medicines, before, during, and after sale. **Method:** Adoption of descriptive and explanatory research, a documental nature bibliographical using checklist for direct observation register, about a qualitative and quantitative approach. **Results:** It was identified that current resolution about GMP applied at medicines have 34 control mechanisms that contribute to avoiding defects in packaging operations, an advance for patient safety. In addition, in all legislative frameworks analyzed, there was a protection of consumerist principles of transparency in information, objective good faith and security. However, there were gaps in the use and knowledge of information and safety devices in packaging materials. Highlighting the practice of changing medications without regulatory provisions as a problem for communicating product defects to the manufacturer and increasing health risk. **Conclusions:** Despite legislative evolution to combat defects, consumers and pharmacies need more knowledge, awareness, and adequate use of complaint channels. The return/exchange of medicines is a potential sanitary risk that needs to be confronted and perhaps better regulated.

KEYWORDS: Defects; Medicine Packaging; Drug Consumption; Good Manufacturing Practices for Medicines; Consumer Protection Code

RESUMO

Introdução: Disponibilizar medicamento com qualidade, seguro e eficaz é a finalidade da cadeia de produção e suprimento, entretanto, erros ocorrem. O trabalho aborda o combate a defeitos em embalagens primárias e secundárias de medicamentos, sob o prisma da legislação administrativa sanitária e consumerista e seus desdobramentos práticos na relação de consumo. **Objetivo:** Demonstrar contribuição da legislação administrativa sanitária e consumerista, com destaque às Boas Práticas de Fabricação (BPF) de medicamentos e ao Código de Defesa do Consumidor, na garantia da informação adequada e segurança do paciente e como fornecedores e consumidores influenciam no controle de defeitos e segurança de uso do medicamento, antes, durante e após a venda. **Método:** Adoção de pesquisas descritivo e explicativa, de natureza documental, bibliográfica, com auxílio de lista de verificação para registro de observação direta,

sob uma abordagem qualitativa e quantitativa. **Resultados:** A resolução vigente que dispõe sobre as BPF de medicamentos possui 34 mecanismos de controle que contribuem para evitar defeitos em operações de embalagem, uma evolução para a segurança do paciente. Em todo o arcabouço legislativo analisado, percebeu-se a tutela dos princípios consumeristas da transparência na informação, boa-fé objetiva e segurança. Por outro lado, lacunas no uso e no conhecimento dos dispositivos informativos e de segurança dos materiais de embalagem foram identificadas. Destacou-se que a prática de troca de medicamentos, sem previsão normativa, prejudica a comunicação do defeito ao fabricante e aumenta o risco sanitário. **Conclusões:** Apesar da evolução legislativa no combate aos defeitos, consumidores e profissionais de dispensação carecem de mais conhecimento, conscientização e utilização dos canais adequados de reclamação. A troca de medicamentos é um potencial risco sanitário que necessidade ser enfrentado e talvez, mais bem regulamentado.

PALAVRAS-CHAVE: Defeitos; Embalagem de Medicamentos; Consumo de Medicamentos; Boas Práticas de Fabricação de Medicamentos; Código de Defesa do Consumidor

INTRODUCTION

The drug packaging process, with its diversified operations and high flow of materials and sometimes people, is always a critical point in the pharmaceutical industry, capable of affecting the quality of the finished product. In this sense, there is great concern about possible operational failures that could lead to an increase in the number of defects due to deficiencies in the packaging processes[1].

This study assumes the term defect[2,3] as one that affects the quality of the product in a generic way, encompassing the terms non-conformity[4] and quality defect[2,3], all of which are common in the literature on the subject.

The presence of defective items is a reality associated with production processes in general, and it's no different for medicine packaging operations. For example, the following can be listed[5,6,7,8]: mix-ups of packaging materials, leaks, caps that are too tight, empty or incomplete bottles or tubes, absence of labels, absence of accessories such as measuring cups, syringes, and others, empty or missing tablets, broken tablets, damaged tablets, absence of coding, absence of package leaflets, incomplete or empty packaging, packaging with broken tamper-evident seals.

In view of this, there is a need to control the generation of defective items as much as possible, in the light of regulatory requirements, with the support of improvement tools and the use of sensors.

However, despite all the effort expended in the manufacturing environment, it is not uncommon for medicines to be recalled due to faulty coding, missing units, and mixed packaging materials[9].

To illustrate the importance of the subject, mention should be made of the World Health Organization (WHO) program entitled "Global Patient Safety Challenge on Medication Safety"[10], which reports that costs related to medication administration errors represent 42 billion dollars (around R$ 136 billion) a year and that both health professionals and patients can make mistakes that result in serious harm, such as prescribing, dispensing, preparing, administering, or consuming the wrong medication or inappropriately, which can result in physical disability and even death.

In line with this program, presented at the WHO's Third Global Patient Safety Challenge, the Brazilian National Health Surveillance Agency (Anvisa) recently published Resolution of the Collegiate Board (RDC) No. 768, of December 12, 2022[11], which establishes rules for the labeling of medicines. By the way, the regulatory agency's comment[12] when the new rule was being prepared is interesting:

> The proposals are in line with the WHO's Third Global Patient Safety Challenge, which aims to reduce serious and preventable harm related to medicines by 50%. They are also in line with the guidelines of the National Patient Safety Program (PNSP) in Brazil, established by Ministry of Health Ordinance No. 529 of April 1, 2013.

It is therefore of the utmost importance to understand that the absence of a package leaflet in a cartridge can deprive the consumer of the possibility of administering the medicine correctly; the absence of tablets in a closed blister can influence the patient's treatment; defects in the sealing of primary packaging can degrade the medicine; mixtures of packaging materials can induce the administration of the wrong medicine.

Fortunately, protective measures are advancing to mitigate the defects and consequences of medicines. As presented in this paper, administrative health and consumer standards are increasingly working to protect patient health. There are measures, for example, to improve the availability of information: the use of the Tall Man Lettering (TML) technique - which uses capital letters to help differentiate the names of similar medicines - and the implementation of digital package leaflets.

In terms of patient safety, the harmonization of Good Manufacturing Practices (GMP) for medicines, in line with the best international guidelines, is a good example of regulatory progress. In the same vein, there is a structured system to protect consumers when defects reach them, such as recalls, complaints, and notification of technical complaints.

The packaging line: people, products, and processes

The act of packaging takes place on what are known as packaging lines, which vary greatly in configuration according to what is required. According to RDC No. 658 of March 30, 2022[4], packaging is all the operations, including filling and labeling, that a bulk product must go through to become a finished product. In summary, it can be said that the typical packaging line needs: materials, i.e. product and packaging material within specifications; utilities, such as electricity, compressed air, among others, according to usage standards; and also people[13]. The same authors[13] indicate that the objective of any medicine packaging line can be briefly described as filling, closing, identifying, and protecting the product safely to guarantee the predetermined specification at an adequate cost. In this sense, it is clear that an operation with the least amount of loss possible should always be one of the objectives to be pursued.

Therefore, the introduction of control measures in the standards certainly contributes to controlling and combating defects, given the range of possibilities for defects in the product at the production stage.

Defects in medicine packaging in the light of administrative health and consumer law

The Constitution of the Federative Republic of Brazil (CRFB)[14] lists the Right to Health and Consumer Protection as Fundamental Rights, in Arts. 6 and 5, XXXII, respectively, as they have been recognized by the legislator as essential to the human person and to life in society. Along these lines, José Afonso da Silva[15] provides a good overview of the concept: "[...] as those rights pertaining to legal situations without which the human person cannot be realized, cannot live and, sometimes, cannot even survive".

Regarding health, Article 200, I of our Charter[14] states that it is the responsibility of the Unified Health System (SUS), in addition to other duties, under the terms of the law: "I - To control and inspect procedures, products, and substances of interest to health and to participate in the production of medicines, equipment, immunobiologicals, blood products, and other inputs".

This understanding and importance of the production and public access to medicines as an integral part of the Health System was corroborated by the National Medicines Policy, approved by Ordinance No. 3,916, of October 30, 1998,[16] of the Ministry of Health. In item 3.7, it includes Good Manufacturing Practices for Medicines (GMP) as a systematic way of guaranteeing the quality, safety, and efficacy of medicines, with the avoidance of mixtures of packaging materials, the certainty of the contents inside, and the correct identifications included in the packaging being the main concerns of this standard.

It should be noted that updates and revisions are routinely carried out in an attempt to adapt the normative needs to new concepts and technological and social developments. It is therefore interesting to understand how references in Brazilian Administrative Health Law, from Law No. 6,360 of September 23, 1976[17], considered by Geyer[18] to be a landmark in Brazilian administrative health legislation, to the current RDC No. 658/2022[4], have dealt with GMP requirements over time.

Although GMP is widespread worldwide, the search for regulatory convergence and the sharing and adoption of best preventive practices is a real challenge[19,20]. In this sense, several countries, including Brazil, are currently adopting globally recognized principles and requirements in their internal standards, in line with the guidelines of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) and the Pharmaceutical Inspection Co-operation Scheme (PIC/S)[21,22] .

In general terms, the ICH has as its central mission the promotion of public health through the harmonization of technical regulations, ultimately seeking to reduce industrial and governmental costs related to health and research and development, as well as meeting the public expectation of minimizing the delay in making safe and effective products available to the patient[23]. The main activities of the PIC/S are: international harmonization, through the establishment of reference guides in the area of GMP, and making inspection systems around the world equivalent[22].

The fact is that RDC No. 658/2022[4] has content that complies with the PE 009 family guide from PIC/S[24], especially in the operational text, which includes packaging operations, the required procedures and controls, and the mechanism for complaining about defective items.

The production cycle, acquisition, and consumption of medicines follow the rules of Administrative Health Law, as we have seen up to this point. However, medicine is a consumer good, a product, acquired and used by an individual or legal entity, a consumer, and produced and marketed by another individual or legal entity, the supplier, who is held responsible for defects in their products or services[25]. This sets up a consumer relationship, according to articles 2 and 3 of Law No. 8.078, of September 11, 1990[26] - known as the Consumer Protection Code (CDC) - and therefore all the activities involved in the product to be marketed to the final recipient are also covered by Consumer Law.

The CDC[26] is based on the 1988 Federal Constitution[14], which provides for the protection of the consumer, the vulnerable party in a consumer relationship. Although it is a rule of general application, it is certainly applicable to users of medicines purchased in commercial establishments, since this is characterized as a consumer relationship. In this sense, all the guiding principles of this branch of law, as well as the other consumer rules, including those relating to defects, are perfectly applicable to medicines.

Mass production and consumption leave the consumer at a disadvantage, since the supplier holds the technical knowledge in

their own hands. There is an absolute lack of consumer control over the products and services that are placed on the market, in other words, the consumer is vulnerable, and it is on this vulnerability that consumer law is based[2,27].

A good reflection on the above, which demonstrates the power of technical knowledge and information on the part of those who supply and vulnerability on the part of those who consume, was brought up by Leroyd[28]:

> People who prescribe or are prescribed a drug have little chance of detecting whether or not it is defective. People who take a medicine trust the doctor who prescribed it and the pharmacist who dispensed it. The doctor and pharmacist, in turn, place their trust in the manufacturer, who plays a key role in ensuring that the medicine is fit for purpose and safe to use.

Thus, both the administrative health regulations, which are said to be specific, and the CDC[26], which is said to be general, are moving towards a common goal: consumer protection for the safe use of medicines.

It should be noted that the notion of safety has a certain relativity, as there is no totally safe product or service. The rules of common experience show that consumer goods always have a residue of insecurity[27]. In this sense, it is intrinsic to a mass process, such as the production of medicines, that units with some degree of defect will be produced. This probability increases the more participatory human action is.

Defects can be classified into three types: design defects, production defects, and marketing or information defects. In the first, the defect is embedded in the very conception of the product; in the second, it stems from a failure at a certain stage of the production process and can be caused by machine or human error; in the last, it stems from insufficient or inadequate information on the use of a product[29].

In turn, the predominant understanding in legal circles is that the CDC[26] is a principiological norm, i.e. based on principles (ethical and moral values) and the force they have in the legal system[27].

Therefore, since the medicine is the product of a consumer relationship, it is subject to certain principles governing the contract between supplier and consumer, such as the well-established principles of objective good faith, transparency in information and safety to the health and life of the consumer, all of which are set out in the CDC[26]. Chart 1 summarizes the basic consumer principles.

Therefore, the CDC creates duties for suppliers, such as providing sufficient and adequate information, under penalty of liability for its insufficiency. This is why certain medicines must indicate on the packaging or package leaflet all the side effects they may cause[27].

Similarly, from the point of view of the direct impact of the principles of information and safety on the object under study,

Chart 1. Basic principles of consumer law.

	**Principle of objective good faith:** this is understood as behavior that is objectively appropriate to the standards of ethics, loyalty, honesty and collaboration required in consumer relations[27].
	**Principle of transparency in information:** this means clear and correct information about the product being sold and the protection of transparency and trust is an offshoot of the impact of objective good faith in consumer relations[3].
	**Principle of safety:** found in article 12, paragraph 1, of the Consumer Defense Code[26] and directly related to the existence of product defects and liability for improper consumption.

Source: Adapted by the authors from images on the websites direitodetodos.com.br; tjdft.jus.br and farmacêuticas.com.br.

there is: the manufacturer's duty to guarantee legible information both on printed packaging materials (under a formal final artwork approval) and on online coded data, such as: manufacturing and expiry dates, batch number, and any warnings allowed by specific regulations[11]; the manufacturer's duty not to make medicines available on the market that are vulnerable to consumer safety and health, hence the need for warnings and seals against packaging breaches[11]; the manufacturer's duty to supply medicines within the given specifications, ensuring that they have the quantity and quality determined by the pre-established standards[4], the duty to ensure that medicines under special control are not returned to the supplier due to consumer withdrawal[30] and others.

Even so, it is a fact that there have been lawsuits over defects arising from the packaging of medicines, as in a specific case in which the plaintiff purchased a medicine without its contents, claiming the return of the amount paid, in double, as well as compensation for moral damages[31].

In turn, the preventive function plays a fundamental role in the constant fight against defective items that are made available. To this end, there are two important instruments considered to be suppliers' duties: the product recall policy, with legal provision in article 10 of the CDC[26], governed by Ordinance No. 618, of July 1st, 2019[32], of the Ministry of Justice and Public Security and the Consumer Service, currently regulated by Decree No. 11.034, of April 5, 2022[33].

Another, and no less important, public instrument developed by Anvisa is the notification which, for the purposes of this work, consists of the act of communicating the occurrence of technical complaints about medicines, through the system called Notivisa.

Technical complaints are understood to be alterations to products or company irregularities, such as the following non-exhaustive list: unregistered products, counterfeit medicines, alterations to the consistency of the product, peeling off the label, presence of a foreign body, defect in the cap, incorrect labeling (e.g. absence of batch number, expiry date), instructions for use, and unsuitable packaging[34,35].

Thus, there are many instruments for constantly combating the defects that are the subject of this study. It's just a question of whether all of them are being used in society.

Therefore, the objectives of this work are to demonstrate the contribution of administrative health and consumer legislation, with emphasis on GMP for medicines and the CDC, in guaranteeing adequate information and patient safety and how suppliers and consumers influence the control of defects and safety in the use of medicines, before, during, and after sale.

METHOD

The methodology proposed to achieve the objectives is qualitative and quantitative in approach. In terms of objectives, it is descriptive and explanatory. In terms of procedure, it is documental, bibliographical, and uses a checklist to collect data through direct observation. Below are descriptions of the methodologies used to achieve the objectives described.

To demonstrate the contribution of administrative health and consumer legislation, we searched for laws, resolutions and other relevant rules on the Anvisa[36] and Ministry of Health[37] websites.

To define the GMP regulatory frameworks, the current RDC No. 658/2022[4] was used as a reference and, for comparison purposes, other standards were considered that had content with the requirements to produce medicines.

In RDC No. 658/2022[4], we looked for articles that dealt with issues related to work, namely: mechanisms for investigating product defects and process failures; requirements for packaging operations and the necessary records; mechanisms for investigating consumer complaints.

For other regulations directly related to packaging operations, information, and safety mechanisms introduced into packaging materials during production operations were sought. The search for laws, resolutions, and other relevant regulations took place in June 2023, covering the period from January 1, 2013, to June 2, 2023, in the database of the Health Legislation System - SLEGIS[37], using the keywords: "packaging", "drug packaging" and "good manufacturing practices" and the origin "Anvisa" and "MS". The search for Anvisa normative acts[36] was carried out in June 2023 and covered the period from January 1, 1998, to June 2, 2023, using the macro-themes: "cross-cutting themes" and "medicines". On the website of the Chamber of Deputies of Brazil[38], the search was carried out in June 2023, covering the period from January 1, 1998, to June 2, 2023, under the filters: federal legislation, ordinary laws, no express repeal, and using the keywords: "medicines", "packaging of medicines", "consumption of medicines", "consumer right to medicines".

In order to demonstrate how suppliers and consumers influence the control of defects and safety of use of the drug, before, during, and after sale, the technique of passive observation of the phenomena was adopted, in which the investigator, inserted in commercial sales establishments in the state of Rio de Janeiro, made his own records based on a checklist, for two years, intermittently, between May 2021 and May 2023.

The proposed non-participatory observation technique makes use of the senses to grasp certain aspects of reality. It consists of seeing, hearing, and examining the facts, the phenomena that are to be investigated[39]. Also according to the pair of authors[39]:

> It is also known as passive observation. The researcher is not part of the group being observed but remains on the outside. They witness the event, but don't take part in it, they don't get involved in the situation, they play the role of spectator. The procedure is systematic. This type of observation is used in research that requires a more detailed and precise description of phenomena or in hypothesis testing. In this data collection technique, it is assumed that the researcher knows exactly what information is relevant to achieving the proposed objectives. In this sense, before carrying out systematic observation, it is necessary to draw up a plan for its execution.

The data collected was related to the defects which are the subject of this study, how the consumers complain about them, and how they are handled by suppliers. This evaluation used a qualitative approach, with critical analysis of thematic content.

It should be noted that, when conducting the non-participatory observation technique, there was no interference by the author in the phenomena observed, and the confidentiality of the sources observed was maintained.

RESULTS AND DISCUSSION

The first result to be presented and discussed is the historical-comparative study of regulatory frameworks, from Decree No. 20.397 of January 14, 1946[40], to the current RDC No. 658/2022[4], looking at the articles that encompass GMP in packaging operations. To this end, Chart 2 summarizes the control mechanisms to avoid defects, adopted as comparison parameters, considering the text of RDC No. 658/2022[4].

The result of this analysis is shown in Figure 1 and indicates that the 34 requirements in Chart 2 were gradually introduced at increasingly detailed levels, which demonstrates the concern for clarity of information and the search for operational standardization.

A literal interpretation of the rule was adopted and, in this sense, those that proved to be incomplete or imprecise, based on the text described in RDC No. 658/2022[4], were classified as "partially present".

Chart 2. Articles analyzed from RDC 658/2022 packaging operations.

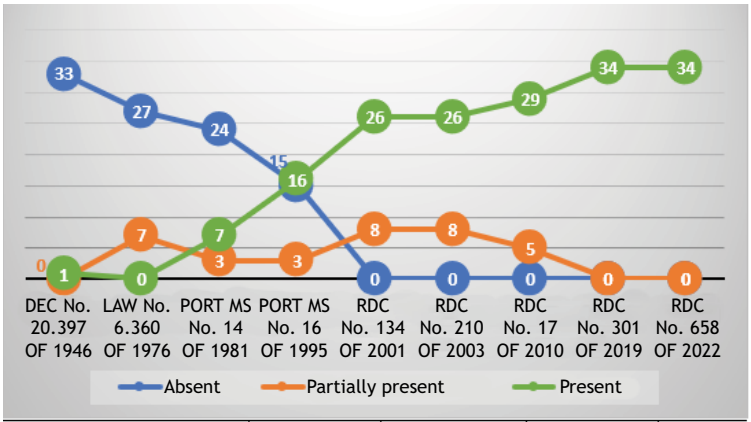
No.	Defects to avoid	Requirement in RDC 658/2022	Reference article	Control mechanism to prevent defects
1	Defective mixtures and products	An appropriate level of root cause analysis is applied during the investigation of deviations, suspected product defects and other process problems	8, XIV	Failure investigation and risk analysis
2	Mixtures	Depending on the level of risk, it may be necessary to dedicate facilities and equipment to packaging operations in order to control the risk posed by some medicines	71A, para. 3	Risk analysis
3	Mixtures	Drug packaging facilities must be specifically designed and built so that mix-ups are avoided	82	Segregated lines
4	Defective products	Production areas must be well lit, particularly where in-line visual checks are carried out	83	Adequate ambient lighting
5	Mixtures	Specific instructions and full identification of the item to be processed (product name, including batch number of bulk and finished product)	136	Personalized documentation
6	Mixtures	Complete list of all necessary packaging materials	136	List of components
7	Defective mixtures and products	Examples (models) or reproductions of printed packaging materials with indications of where to insert the batch number and expiration date	136	Coding instruction
8	Mixtures	Station and equipment checklist for line cleaning	136	Line cleaning routine
9	Defective mixtures and products	Checklist of area points and equipment for line clearance	136	Line release routing
10	Defective products	In-process control test script with instructions for sampling and acceptance limits	136	In-process control test script
11	Mixtures	Batch packaging record for each batch or part of a batch processed	138	Activity records
12	Mixtures	Record of batch identification, date and times of packaging operations	139	Activity records
13	Defective mixtures and products	Identification of the employees who carried out each significant step in the process and, if appropriate, who verified these operations	139	Identification of the executor of the critical activity
14	Defective products	Records of line tests and compliance with pre-established parameters	139	Test records
15	Mixtures	Records of equipment and lines used	139	Equipment records
16	Defective mixtures and products	Where possible, samples of printed packaging materials used, including examples of batch coding, expiry date and any additional overprinting	139	Attachment of samples of coded packaging materials
17	Defective products	Notes on any problems or unusual events, including details, with signed authorization for any deviation from the packing instructions	139	Records of deviations and unusual events
18	Mixtures	Reconciliation of printed packaging materials, which can be dispensed with if automation is in place	139	Reconciliation of materials
19	Mixtures	Reconciliation of the bulk product used, which can be dispensed with if automation is implemented	139	Bulk product reconciliation
20	Mixtures	Batch yield	139	Batch yield
21	Mixtures	Different products should not be packaged in close proximity, unless there is physical segregation	205, pu	Segregated lines
22	Mixtures	The name and batch number of the product being handled must be displayed at each station or packaging line	207	Lines identified
23	Mixtures	All products and packaging materials to be used must be checked on delivery to the packaging department	208	Checking packaging materials
24	Defective mixtures and products	Line clearance, including line cleaning, must be carried out according to an appropriate checklist	206	Line cleaning
25	Defective products	Visual verification of coding (batch, manufacture and expiry date) and the need for more regular intervals for manual operation of this activity	211	Visual process control for coding
26	Mixtures	Special care should be taken when using die-cut labels and when printing outside the production line	212	Care when handling single labels
27	Defective mixtures and products	Challenges in electronic devices (sensors)	213	Sensor challenges

Continue

Continuation

28	Defective products	Printed or embossed information on packaging materials must be distinctive and resistant to fading or erasure	214	Information printed on packaging materials
29	Defective products	*Online* control of the product during packaging, to view at least: the appearance of the packaging, whether it is complete, coding, whether products and materials are correct and line monitor challenges	215	*Online* control during packaging
30	Mixtures	Samples taken from the packaging line cannot be returned	216	Care of samples taken offline
31	Mixtures	Products that have been involved in an unusual event can only be reintroduced into the process after special inspection, investigation and approval by authorized personnel	217	Investigation of products with unusual events
32	Mixtures	Any significant discrepancy between reconciliation of bulk product and material to be printed (where applicable) and batch yield should be investigated	218	Investigation of faults detected in reconciliation
33	Mixtures	Any unused coded packaging materials must be destroyed	219	Disposal of printed and unused packaging materials
34	Defective mixtures and products	Written complaint investigation procedure and action plan	326 e 327, 331	Investigation of defects due to complaints

Source: Prepared by the authors, 2023.



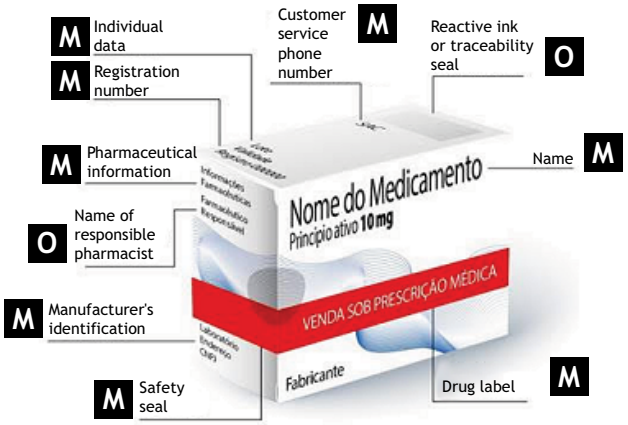
Regulatory framework	Missing requirements	Requirements Partially present	Present requirements	Total
DEC No. 20.397 OF 1946	33	0	1	34
LAW No. 6.360 OF 1976	27	7	0	34
PORT MS No. 14 OF 1981	24	3	7	34
PORT MS No. 16 OF 1995	15	3	16	34
RDC No. 134 OF 2001	0	8	26	34
RDC No. 210 OF 2003	0	8	26	34
RDC No. 17 OF 2010	0	5	29	34
RDC No. 301 OF 2019	0	0	34	34
RDC No. 658 OF 2022	0	0	34	34

Source: Prepared by the authors, 2023.
Dec: Decree; PORT MS: Ministry of Health Ordinance; RDC: Collegiate Board Resolution.

Figure 1. Temporal analysis of the introduction of packaging requirements in administrative health regulations based on RDC No. 658/2022.

RDC No. 134, of July 13, 2001[41], should be highlighted, which presented 26 requirements that were present and eight that were partially present, giving a total of 34 requirements and demonstrating that, from that moment on, the absence of requirements was definitively overcome.

When analyzing the differences between the two latest versions of GMP (RDC No. 301, of August 21, 2018[42], and RDC No. 658/2022[4]) and those immediately preceding them (RDC No. 17, of April 16, 2010[43], RDC No. 210, of August 4, 2003[44], and RDC No. 134/2001[41]), the following can be seen:



Source: Image taken from Sincofarma SP.

Figure 2. Example of mandatory (M) and optional (O) devices and information on secondary packaging.

1. The inclusion of Risk Management, requirements 1 and 2 of Chart 2;

2. The explicit inclusion of the checklist requirement for online tests, present in requirements 8 and 9 combined with 24 of Chart 2;

3. The inclusion of automation as an ally in the control of faults and defects and productivity, present in requirements 18, 19, and 29 of Chart 2.

Such inclusions represent a strong gain in line defect control.

To analyze other normative acts, we searched for a list of norms introduced, in force and during the period described in the method. A total of 37 regulations were collected and analyzed, with the following distribution in terms of the main consumer right protected: safety (21), information (12), safety and information (4), which indicates the constant attempts to protect patients' health with measures that ensure the effective use of the medication, whether through GMP rules, traceability or pharmacovigilance. There is also a clear concern to guarantee clear and transparent information for the public, using packaging materials for this purpose.

In this regard, RDC 768/22[11] contains several articles on the inclusion of mandatory and optional information on primary and secondary packaging materials. Articles 3, 4, 5, 7 and 18, among others, clearly highlight the principle of transparency in information. Figure 2 illustrates some of this mandatory (M) and optional (O) information.

Thus, the analysis of the legislation studied shows an evolution in the quantity and quality of discussions and the drafting of rules so that medicines are packaged and made available safely and with a wide range of information for the consumer patient.

In order to understand whether at the end of the chain, at the last barrier between supplier and patient, there is a relationship between these and the mitigation or not of visible defects in medicines, passive observation of the phenomena was carried out, in different environments and at different times, over an alternating period of two years with the support of the following checklist:

1. Is important information on packaging materials often shared and understood by consumers?

2. Is it usual to exchange medicines, even if they are not defective?

3. Have any defects been observed in the conduct of the supplier and/or consumer that are detrimental to the safety of the medicine?

4. Does the consumer demonstrate awareness and use of the Customer Service contact details on the packaging?

5. Does the consumer demonstrate knowledge and use of Anvisa's technical complaint channel?

From the observations made, from a technical point of view, seeking to remove the subjective nature, it can be concluded that, at all times during the study, there was no general or widespread habit of consulting the information present on the packaging materials, either when reading the package leaflet or when understanding the range of devices present on the secondary packaging, signaling a lack of knowledge or interest in the importance of a seal, the watermark, the meaning of the different labels, and other information.

Regarding the exchange of defective medicines, this calls for a more in-depth debate. From what we have seen, drugstores' policy of exchanging medicines seems to be a widespread practice, respecting the established deadline. This fact, by the way, has already been the subject of a note from Anvisa[45] and needs to take into account health and legal aspects.

Concerning the exchange of defective medicines, we would like to highlight a few passages from this note[45] that are fully in line with the CDC[26] :

> The Consumer Protection Code (CDC), which establishes consumer protection rules, described in Law 8.078/90, states in its article 18 that "suppliers of durable or non-durable consumer products are jointly and severally liable for defects in quality or quantity that make them unfit or unsuitable for the consumption for which they are intended or diminish their value, as well as for those arising from the disparity with the indications on the container, packaging, labeling, or advertising message, respecting the variations arising from their nature, and the consumer may demand the replacement of the defective parts". This determination assures the consumer that in the case of dispensed medicines in which the patient subsequently finds a deviation in quality, the pharmaceutical establishment must accept the return and give the customer the right to choose between: replacing the medicine (with another) of the same kind in perfect conditions of use; immediately refunding the amount paid or making a proportional reduction in the price at the time of purchase. Some quality deviations observed in medicines are changes in appearance, color, smell, taste, number of tablets in the package, volume or presence of foreign body, or shelf life of the product.

Thus, there is no discussion about exchanging the defective medicine for another or for its value, rendering it unusable. Such conduct has legal backing in the CDC and has been observed in the course of this work.

On the other hand, the problem occurs when there are no defects in the medicine and the consumer wants to exchange it, either because of interrupted treatment, leftover units, or a wrong purchase. In this case, two situations must be analyzed: for medicines under control (Ordinance No. 344 of May 12, 1998[30], or antimicrobials[46]) and other medicines, whether they are sold on prescription or over the counter.

In the first case, regulations prevent the exchange and no non-compliance with these regulations was observed on the occasions under analysis. In line with this, the Anvisa note[45] contains the following comments:

> For controlled medicines, according to two health regulations: article 44 of Ordinance SVS/MS 344/98 and article 90 of Ordinance SVS/MS 6/99 state that, in these cases, the consumer must refer the controlled medicine to the Health Surveillance Office in their region.
>
> Ordinance SVS/MS 344/98
>
> Art. 44. When, for whatever reason, the administration of medicines based on substances included in the lists in this Technical Regulation and its updates is interrupted, the local health authority must advise the patient or their guardian on the destination of the remaining medicine.
>
> Ordinance SVS/MS 06/99
>
> Art. 90. When, for whatever reason, the administration of medicines based on substances included in the lists of Ordinance SVS/MS 344/98 and its updates is interrupted, the prescriber and/or the local health authority must recommend that the patient or their guardian deliver these medicines to the competent Health Surveillance body. The health authority will issue a document confirming receipt and will then decide on the appropriate destination (destruction or donation).
>
> Similarly, antibiotics entering and leaving pharmacies and drugstores also need to be recorded in the SNGPC, and RDC 20/2011 provides for the possibility of return only in cases of quality deviations:
>
> Art. 20. Individuals may not return industrialized or manipulated antimicrobial drugs to drugstores and pharmacies.
>
> Paragraph 1. This article does not apply to returns due to deviations in quality or quantity that make them unfit or unsuitable for consumption, or due to disparities with the indications on the container, packaging, labeling or advertising message, which must be assessed and documented by the pharmacist.
>
> Paragraph 2. If the return is found to be appropriate, the pharmacist may not reintegrate the medicine into the marketable stock under any circumstances, and must immediately notify the competent health authority, informing them of the product's identification data, so as to enable the relevant health actions to be taken.

For other medicines, the situation is different, since there is no legal impediment to exchange medicines, and it is therefore up to the supplier to do so. The observation made in this study showed that it is common to exchange medicines that are not under special control when the consumer finds themselves in a situation where they have made the wrong purchase or in the case of leftovers. This practice, however, increases the health risk, in other words, it affects the patient's own health safety. Once again, Anvisa's note[45] contributes to understanding:

> The main reason why medicines cannot be exchanged so easily, like cell phones and other products, is that there is a so-called health risk, which is concerned with the safety of the consumer's own health.
>
> This situation becomes effective, for example, when the consumer of the medicine, after purchasing the product and leaving the pharmacy or drugstore, takes responsibility for that item away from the pharmacist, who is supposed to ensure that the medicine is properly packaged. In this way, since this professional has no way of validating the quality of the product, this exchange is not possible, as there is no guarantee that the consumer has observed the storage precautions for its preservation and, therefore, that any new patient who takes that medicine will have their health preserved.

Therefore, in the practice observed, whether for marketing or cultural reasons, the health risk of inadequate storage of the

item to be returned to the shelf occurs in medicines without special control, representing most presentations and sales.

Another behavioral vice that can have consequences for consumer safety is the practice of sealing secondary packaging that, for reasons of transport and storage or even due to a deficiency in the manufacturing process, reaches the final point of consumption with a broken seal or failed glue. Exposing this material to be sealed and replaced at the point of sale is putting something other than the condition in which it was produced out to the public.

In terms of consumer law, it can be concluded that such practices violate two of the basic principles: objective good faith and security.

In order to combat such conduct, it is also suggested that the behavioral issue be explored in greater depth, followed by a massive campaign showing the importance of the original seal and the risks of mixtures that can occur with the advent of reprehensible conduct. In this regard, the recent RDC No. 768/2022[11] reads as follows:

> Art. 84. Secondary packaging must contain a closing mechanism, which cannot be recovered after it has been broken, to detect any attempt to open the packaging, in order to guarantee its inviolability. (emphasis added)
>
> Paragraph 1. When the medicine is made available exclusively in primary packaging, the opening or violation of which is not easily discernible, it must contain a closing mechanism, in accordance with the characteristics set out in the *caput* of this article.

This practice has been observed on numerous occasions, which suggests a behavior driven by the "just stick it" culture, ignorance of the consequences and pressure to avoid the momentary loss or late replacement of the medicine. The images in Figure 3 show how this common problem appears at the end of the supply chain.

Directing the analysis towards the SAC tool, there is a notable normative appreciation, reflected both in the recent RDC No. 768/2022[11] and in the general precepts of the CDC. In this regard, the excerpts below from the administrative rule[11] stand out, including an article dedicated to information for the visually impaired:

> Art. 5. The following information is mandatory on one of the other sides of the secondary packaging label (back, sides, bottom, or top):
>
> [...]
>
> VI - the telephone number, or pictogram representing it, of the Customer Service Center (SAC) defined by the company holding the registration or notification; (emphasis added)
>
> Art. 85. The labels on the secondary packaging of medicines that are dispensed to the user must contain a Braille system that complies with the guidelines of the Brazilian Braille Commission (CBB):
>
> [...]
>
> Paragraph 3. The concentration, pharmaceutical form, SAC and other information required for secondary packaging labels may be printed on the packaging using the Braille system.
>
> Art. 86. In the event of a limitation in the printing field of all the information required in art. 85 of this Resolution, a technical justification must be presented (emphasis added)
>
> Paragraph 2. The concentration and the SAC may be made available by means of a QR Code that is directed to the companies' institutional portal, allowing for specific service for the target public, focusing on the information approved in the register, as provided for in article 8, item IX of this Resolution (emphasis added).

Despite this, in practice, the term SAC - and technical complaint - seems far removed from everyday life. No mentions or explanatory interventions were observed in the environments analyzed. This may be due to lack of knowledge, the degree of importance attached by the parties to the relationship or even the immediate satisfaction of exchanging the damaged item, which, to a certain extent, "takes away the interest"

Source: Prepared by the authors, 2023.

Figure 3: Broken seal or failed glue on secondary packaging.

of complaining, after all the problem has been "solved". This point requires further reflection, says articles 18 and 19 of the CDC respectively[26]:

> Art. 18. Suppliers of durable or non-durable consumer products are jointly and severally liable for defects in quality or quantity that make them unfit or unsuitable for consumption or diminish their value, as well as for those arising from disparity with the indications on the container, packaging, labeling or advertising message, respecting the variations arising from their nature, and the consumer may demand the replacement of the defective parts.
>
> Art. 19. Suppliers are jointly and severally liable for defects in the quantity of the product whenever, respecting the variations arising from its nature, its net content is less than the indications on the container, packaging, labeling or advertising message.

According to the law, in the event of defects in the medicines claimed at the point of sale, these suppliers are also responsible for delivering the medicine that is suitable for use. In this sense[3]: "It should not be forgotten, moreover, that in the case of product defects, there is solidarity between all those involved in the supply, such as the manufacturer, the producer and the trader."

Thus, when a drug is returned at the point of sale, on the one hand there is a direct benefit for the most vulnerable party in the relationship (the patient), both because of the speed with which it can be replaced and because of the convenience, but on the other hand there is a loss in communicating this failure to the manufacturing company and to the regulatory body, thus preventing these actors from becoming aware of what has happened and from promoting both continuous improvement and the demand for corrective action.

In this sense, it can be said that the CDC[26], in the application of articles 18 and 19, allows speedy access to a right to have the correct medicine in conditions of use quickly in the hands of the patient, but at the same time does not encourage, even indirectly, the use of important channels such as SAC and the notification of technical complaints. In order to work on this topic in future research, it is suggested that we reflect on the standardization of social awareness notices on the importance and use of complaint channels in search of a cycle of continuous improvement capable of increasingly combating the defects that are unfortunately made available to the population.

CONCLUSIONS

The acquisition of a quality, safe, and effective medicine is the raison d'être of an entire production and supply chain, however, possible operational failures can occur and generate an increase in the number of defects, with varying degrees of harm to the consumer, which are made available to the market year after year.

This work aimed to understand the mechanisms for combating a class of defects: those that are visible to the consumer's eye and come from faults in various packaging material devices.

To this end, an analysis was made not only of the rules of Administrative Health Law, both from the Ministry of Health and Anvisa, but also of ordinary federal laws, such as the CDC and other related laws.

A second aspect considered was the analysis carried out at the point of supply to the public, in the pre-sale, sale, and post-sale of medicines, seeking to understand the application of Consumer Law combined with Administrative Health Law and how the two branches are used by the players in the consumer relationship, both the supplier and the patient.

Of the two aspects analyzed, the latter proved to be vulnerable, and there is room for reflection and improvement on the standardization and return/exchange policy for medicines, a lot of work on the knowledge, and awareness of the consuming public and dispensing professionals regarding the practices adopted when they come across defects, and there is also a great need to publicize and value the complaint channels, especially SAC and notification of technical complaints.

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Authors' Contribution

Figueredo A, Macedo EV, Costa JCS - Conception, planning (study design), acquisition, analysis, data interpretation, and writing of the paper. All the authors approved the final version of the paper.

Conflict of Interest

The authors inform that there is no potential conflict of interest with peers and institutions, political or financial, in this study.