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Traceability in the Pharmaceutical Industry: Application to Radiopharmaceutical Production

Camila Zanette[1], Laura T. U. H. Melero[1], Elaine B. de Araújo[1], Jair Mengatti[1] and Kátia S. de S. Silva[1]

[1] Instituto de Pesquisas Energéticas e Nucleares (IPEN / CNEN - SP)
Av. Professor Lineu Prestes 2242
05508-000 São Paulo, SP
czanette@usp.br

ABSTRACT

The development of tools to promote the traceability of the drugs in the pharmaceutical industry during all the production chain is a necessary requisite. The traceability system is applied to enable the identification of the origin, destination and exact location of the drug. Traceability optimizes the process chain, reduces errors, is a requirement for quality process, promotes safety for the user and assists in pharmacovigilance. The health regulatory agency in Brazil (ANVISA) will implement a tracking system for medicaments with RDC nº 59 of 2009, to control distribution since the producer until the patients in order to prevent the traffic and adulteration of drugs. Thus, this study discusses the importance and impact of the new traceability system proposed by ANVISA in the production and distribution of radiopharmaceuticals from the Nuclear and Energy Research Institute (IPEN-CNEN). The radiopharmaceuticals have a difference track when compared with another drug classes. In this context, this RDC would increase the price of the medicines by up to 10%, since it provides deployment of a single stamp supplied by the Mint. Considering that radiopharmaceuticals are not sold to the final consumer (patients), but only for accredited medical clinics and nuclear medicine physicians, and the transport of radiopharmaceuticals is performed by specialized companies licensed by CNEN (National Nuclear Energy Commission), the use of the stamp to ensure authenticity and prevent falsification should not be appropriated and represents and additional cost for the radiopharmaceuticals.

1. INTRODUCTION

Product Traceability, or more commonly Track and Trace, is the ability to know the exactly localization of the product in the industry, in this case, the pharmaceutical industry, at any time (Track), furthermore, to know where the item has been (Trace) in the past (Figure 1). In other words, the traceability system is applied to enable the identification of the origin, destination and exact location of the medicament [1].

The development of tools to promote the traceability of the drugs in the pharmaceutical industry during all the production chain is a necessary requisite. In addition, in simpler situations, such as the need for recall of the entire lot of one medicament, a tracking system is very useful [2].

Traceability optimizes the process chain, reduces errors, is a requirement for quality process, promotes safety for the user and assists in pharmacovigilance [1, 2, 3].

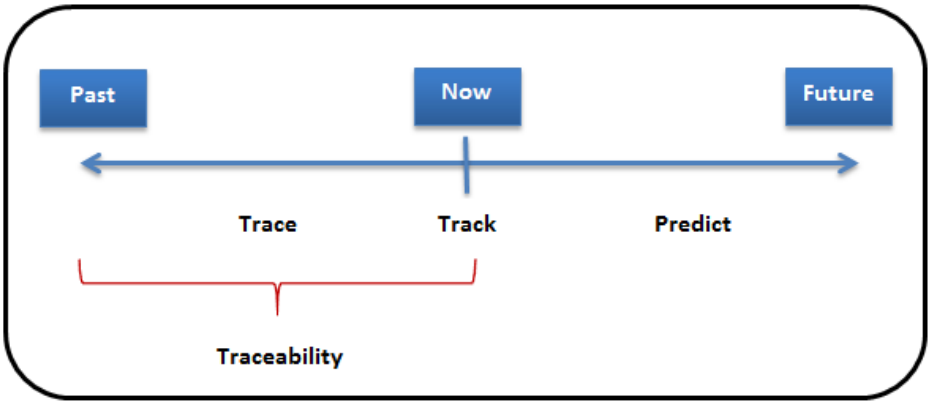

Figure 1. Track and Trace time dimension [2].

1.1. History

The traceability drugs is very important for ensure its quality to the patients. Thus, for the safety of the Public Health, laws about traceability had to be developed. Brazilian authorities and companies have to been long seeking for mechanisms to restrain illegality [4].

Initially, the Secretary of Sanitary Surveillance of the Ministry of Health published the Administrative Rule n^{o} 802/1998, which instituted the Control and Inspection System for the whole chain of pharmaceutical products. The only mention of traceability in this norm was the correct localization for the effective procedure interdict, collection or returns the drugs [5].

On November 22nd, 2002, the Resolution RDC n^{o} 320 established that the wholesalers of pharmaceutical products had to execute the commercial transaction and circulation operations with sale bills that presented the product's batch numbers [6].

Public Consult n^{o} 8 was published by Brazilian National Agency of Sanitary Surveillance (ANVISA) on the 4th of March, 2008, in order to get reviews and suggestion related to the minimum requirements to establish of mechanisms to track the pharmaceutical products chain and to ensure their authenticity [7].

The law n^{o} 11.903 from 2009 created the National System of the Medicament Control involves the production control, commercialization, dispensation and the prescription of the drugs. This law established that control would be realized through the exclusive identification system of the products, service providers and users with the utilization of the electronic capture, storage and transmission of data [8]. Therefore, the law establishes the tracking of all kinds of drugs existing in the Brazil, from the manufacture until the sale to the final consumer.

Currently, ANVISA published the Resolution RDC n^{o} 59 of 2009. This RDC provides the mechanism that enables the localization, identification and evidence about the product origin in anywhere of the pharmaceutical chain, in order to facilitate any gathering. This RDC proposes facilitate the product recalls, allow the drug tracking in whole pharmaceutical chain and contribute to reduce the fraud [9].

On January 13rd, 2010, the Normative Instruction (NI) nº 01/2010 published the deadline to install the System of Medicine Traceability [10]. Normative Instruction nº 08/2010 repealed only paragraphs about the deadline proposed in the previous NI [11]. In the same year, the Normative Instruction nº 11, October 29th, 2010, repealed the two previous statutes [12]. According to this Normative, the mint is the body delegated by ANVISA to be responsible for developing the technology, to produce, to deliver and to monitor the distribution of self-adhesive labels for security. The deadlines are that from January 15th 2012, all units of drugs in circulation in the country would have to rely on this safety label on its packaging.

ANVISA repealed the NI nº 11/2010 with Normative Rule nº 1/2011, thus the registering with the Brazilian mint is no longer necessary. In addition, obligation of the seal must also be suspended [13].

In this context, the Administrative Act has a reduced the economic impact of the identification, localization and removal of the products efficiently and effectively. The consumer security impact is increased; this way could save lives and preserved the consumer confidence. Likewise, the legal impact is increased since it provides compliance and regulatory requirements [2, 3].

1.2. Radiopharmaceuticals

The radiopharmaceuticals could be defined as a substratum that contains a radioactive atom in their structure and could be considered a vector that presents specificity by any organ or a physiologic function [14, 15].

As radiopharmaceuticals are prepared from radioactive elements that have a specific physic half-life time, the stability of the preparations varies from a few minutes until some days. Thus, these products have a short expiration time [14].

Considering its particular structure, these drugs should have a specific transport, because they need a radioactive monitoring to avoid accidents or inconvenient exposure due to the radioactivity nature of the product.

The radiopharmaceuticals have some particularities in their track. These specific drugs are not sold to the final consumer (patients), differentially of other medicament. The transport of radiopharmaceuticals is restricted to transport companies, previously authorized by the National Commission of Nuclear Energy (CNEN) for the transport of radioactive materials. The radiopharmaceuticals can only be distributed to nuclear medicine centers and clinics that have a nuclear medicine physician also previously authorized by CNEN to manipulate and prescribes radiopharmaceuticals. Because of special characteristics and restrict control in the commercialization and distribution of radiopharmaceuticals, they should be viewed with some particularity.

2. OBJETIVES

This work intends to discuss the importance and impact of the new traceability system proposed by ANVISA in the production and distribution of radiopharmaceuticals by Nuclear and Energy Research Institute (IPEN-CNEN).

3. DISCUSSION

After the protests of pharmaceutical companies in Brazil, ANVISA suspended temporarily the implementation of the security seals, as proposed in RDC nº 59 for the new traceability system with the publication of the Normative Instruction nº 1/2011 [13].

The labels defined in the RDC nº 59 will be relevant to the Medicines Unique Identifier (MUI), printed in legible numeric characters and two-dimensional code [9].

3.1. Two-dimensional Code

The two-dimensional code is a symbolic representation of any digital information in the form two-dimensional with high information capacity. The code can be read by optical equipment [16]. An example of two-dimensional code is Data Matrix, which is approached in RDC nº 59. A Data Matrix code is a two-dimensional matrix bar-code consisting of black and white modules arranged in either a square or rectangular pattern (Figure 2).

Figure 1. Example of the Data Matrix code [17].

Data matrix code requires less space on the packaging, has high storage capacity, auto correction, multidirectional reading and allows direct marking of components (without labels) [16, 17].

The RDC nº 59 of 2009 provides this deployment through a single stamp supplied by the Mint, would increase the price of the medicaments by up to 10% [3, 18].

3.2. Radiopharmaceuticals Traceability

The new traceability process are being evaluated. More efficient and effective alternative technologies are being considered for the screening of medicaments, that has to start in 2012, as determined by the resolution, but it repealed for the Normative Instruction n^{o} 1/2011.

In normal process, the track of the drugs begin in industry, pass to warehouse, go to wholesalers delivering the retail pharmacy until it reach the consumers, as illustrated in figure 3 [4].

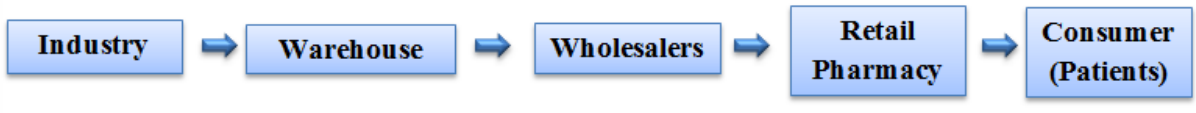

Figure 3. Normal track of the drugs [4].

On the other hand, the radiopharmaceuticals have a different logistic, these drugs are not commercialized directly to the patients. These products are marketed to the medical clinics and their use is restricted to that medical environment because they are radioactive drugs.

Because they have a short half-life time, many of them are not stored, except the lyophilized drugs. The freeze-dried substances are labeled with a radioactive atom and therefore are considered radiopharmaceuticals. This process is done in the clinic.

Thus, with these particularities, the radiopharmaceuticals have a different track and it is shown in figure 4.

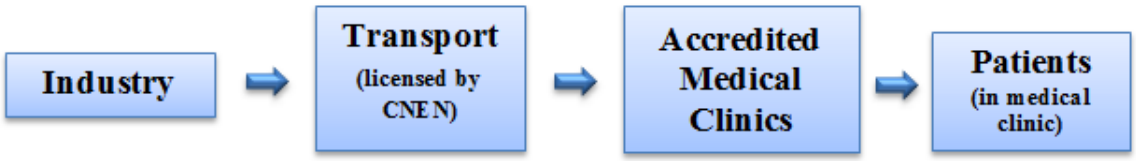

Figure 4. Radiopharmaceutical track scheme.

The use of the stamp to ensure authenticity and prevent falsification should not be necessary and represents an additional cost to the radiopharmaceuticals. Since radiopharmaceuticals are not sold to the final consumer (patients), but only for accredited medical clinics and nuclear medicine physicians, and also the transport of radiopharmaceuticals is performed by specialized companies licensed by CNEN (National Nuclear Energy Commission).

4. CONCLUSIONS

The radiopharmaceuticals are produced and distributed by authorized radioactive installations, with restriction and control transport and distribution, especially when compared with non-radioactive drugs. Thus, the use of the two-dimensional code, as determined in the RDC 59, should not be necessary to ensure authenticity and prevent falsification of the final product and will represent an additional cost to the radiopharmaceuticals.

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