Review of requirements for drug registration according to RTCA 11.03.59.18

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Abstract
Medications are substances or products to diagnose, cure, mitigate, treat, or prevent diseases. For its marketing and distribution in a country, a marketing authorization is required to ensure compliance with territorial legislation. In the case of Central American nations, there is Central American Technical Regulation (RTCA, for its Spanish acronym) 11.03.59.18. Therefore, the objective was to identify compliance with the requirements established in such guidelines by Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama. To this end, an exhaustive review of the document was made.

Then, a list of the main obligations for the registration and renewal procedures of medicines for human use that apply to the States Parties to the General Treaty of Central American Economic Integration was established. Next, other specific provisions indicated by the legislation and regulatory authorities of the states mentioned above were investigated. This search was complemented by communication with regulatory affairs officers in each nation. After their review, it was shown that, despite the countries' compliance with the aspects established in the RTCA, it is usual to find some differences in the processing linked to each territory's legislation, adding complementary elements that must be incorporated. Thus, its comparison and delimitation are a basis for analyzing which aspects could be subject to harmonization and convergence by Central Americanregulatory authorities.

Keywords: regulatory affairs, medicines, marketing authorization, Central American Technical Regulation, harmonization.

Introduction

The medications, according to the U.S. Food and Drug Administration (FDA), are substances or products used to diagnose, cure, mitigate, treat or prevent diseases. they may affect the body structure or some function (United States Food and Drug Administration, 2017). Within the Costa Rican legal framework, there are other definitions. Based on what the N° 5395 General Law establishes it is defined as 'any substance or natural product, synthetic or semi-synthetic and any mixture of such substances or products used for the diagnosis, prevention, treatment and relief of pathologies or abnormal physical states, or its symptoms and for the people's organic function reestablishment or modification' (Asamblea Legislativa de Costa Rica, 2022). Marketing authorization that guarantees compliance with what is established in its legislation is required

to be commercialized and distributed to different countries. It corresponds to a process in which the presented information is assessed and validated, ensuring its quality, safety, and efficacy. The procedure is performed by the National Regulatory Agencies (NRA) to grant wholesale distribution authorization and purchase within the territory (Red Panamericana de Armonización de la Reglamentación Farmacéutica, 2013).

The regulatory affairs departments of pharmaceutical industries are responsible for collecting and submitting the documentation required by regulatory authorities to obtain authorizations. Thus, ensuring that safe and efficacy products are available to the population (Narang et al, 2021).

Central American Technical Regulation (RTCA) 11.03.59.18, aims to establish conditions and requirements to grant marketing authorization for medicines intended for human use. This applies to those who manufacture or import, either natural or legal persons for its commercialization in Central America. Within its scope of application, magistral, biological and biotechnological preparations are not included if there is registry legislation (Council of Ministers Central American Economic Integration, 2021).

In addition, it is important to keep authorizations in force through renewals, according to the guidelines of each territory. This ensures that the information and the validity of the market authorization are updated. (Presidencia de la República y Ministerio de Salud, 2022).

The medications are health affair products, because their composition, usage, and function may affect people's health. For this reason, they are strictly regulated (Narang et al, 2021). Despite the harmonization implemented in Central America through the RTCA for member states, each country still has its own regulations. This results in the requirements varying depending on the country.

Hence, the objective of this research is to identify the compliance with requirements established in the RTCA 11.03.59.18 by Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama, to provide information about these procedures from the regulated parties or marketing authorization holders' perspective.

Materials and methods

An exhaustive revision for the RTCA 11.03.59.18 was carried out (Council of Ministers Central American Economic Integration, 2021), which is the current version, coming into force on January 3rd, 2022. The revision set the basis to establish a preliminary list of the main obligations for registration and renewal processes for human use medication that applies for The State Parties to the General Treaty of Central American Economic Integration. Afterwards, the differences in matters of specific provisions implemented by each legislation were determined. Subsequently, to verify the similarity degree's provisions required by the State Parties about this document, different dispositions given by the legislation and regulatory authorities from Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama were found. The revised documents are listed in Figure 1. This research was complemented by the communication with the regulatory affairs officers in each nation.

Figure 1. Legislation, guidelines and complementary material reviewed for the examination in registration, renewal, and post- marketing authorization changes in human use medications

Country	Legislation, guideline, or complementary material issued by the regulatory authority
Costa Rica	Medicines' first batch marketing processes guidance (Unidad de Normalización y Control, 2019)
El Salvador	Decree 34: Foreign Market Authorization Special Guidelines (Ministerio de Salud, 2013)
Guatemala	Government Agreement N° 712-99: Medicines and Byproducts Health Control Guidelines (Presidente de la República, 1999) Technical Norm 36-2010: Pharmaceutical Products and Byproducts Market Surveillance (Departamento de Regulación y Control de Productos Farmacéuticos, 2010) Pharmaceutical Reference Standard Health Registration Renewal Request (F-AS-f-05, version 14-2021) (Unidad de Autorizaciones Sanitarias, 2021a) Pharmaceutical Products' Registration Renewal Request (F-AS-f-09, versión 18-2021) (Unidad de Autorizaciones Sanitarias, 2021b) Pharmaceutical Reference Standard Market Authorization Request (F-AS-f-04, versión 21-2022) (Unidad de Autorizaciones Sanitarias, 2022)
Panama	Law 1 from January 10th, 2001: About Medications and Other Human Health Products (Asamblea Legislativa, 2001) Executive Decree Nº 95 (Ministerio de Salud, 2019).

Results

Central American Technical Regulation 11.03.59.18 (RTCA by its acronym in Spanish) compliance with the established requirements by Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama.

The following figures are based on the RTCA requirements to determine the compliance that the corresponding States Parties maintain. Also, with the help of the information provided by the Regulatory affairs officers from the concerning States, those requirements with additional provisions were complemented based on the health authorities and its legislation. Figures 2, 3 and 4 contain the information. The footnote's objective at the end of each figure is to provide a useful tool for those who are in charge of chemical synthesis substances marketing authorization in Central America.

Figure 2. Comparison of the requirements compliance for the co-packaged medications registration in the Central American countries

Requirement	Costa Rica	El Salvador	Guatemala	Honduras	Nicaragua	Panama
Signed and stamped request by the regulatory affairs officer	Yes	Yes [1]	Yes	Yes	Yes	Yes
Co-packaging and draft labels insert	Yes	Yes	Yes	Yes	Yes	Yes
Scientific information supporting the treatment scheme	Yes	Yes	Yes	Yes	Yes	Yes
Receipt slip	Yes	Yes	Yes	Yes	Yes	Yes
Additional requirements according to the regulatory authority						
Document issued by the holder or the legal representative who declares the change	N/A	N/A	Yes[2]	Yes	N/A	N/A

[1]It includes the attorney in fact signature of the importing country.
[2]This requirement is included and the procedure is carried out as a post-registration change that requires previous approval by the
National Regulatory Agencies (NRA).

Figure 3. Comparison of the requirements compliance for medications registration or new registrations in the Central American countries

Requirement	Costa Rica	El Salvador	Guatemala	Honduras	Nicaragua	Panama
Signed and stamped request by the regulatory affairs officer	Yes	Yes[1]	Yes	Yes	Yes	Yes
Powers of attorney granted by the holder that ascertain legal or technical representation to the natural or legal persons according to the regulatory legislation of the country[2]	Yes	Yes	Yes	Yes	Yes	Yes
Certificate of a pharmaceutical product or World Health Organization (WHO)-CPP model , original or authenticated copy [3]	Yes	Yes	Yes[4]	Yes	Yes	Yes
Certificate of Free Sale or CLV (by its acronym Certificat de Libre Vente, in French) (submitted when the CPP is not issued)[5]	Yes	Yes	Yes[6]	Yes	Yes	Yes
Certificate of Good Manufacturing Practices or GMP (in case the CPP is not issued), issued by the regulatory authority of the country or countries where the manufacturing is carried out. [7, 8]	Yes	Yes	Yes [4]	Yes	Yes	Yes
Manufacturing contract or extract related to the manufacturing contract[9]	Yes	Yes	Yes	Yes	Yes	Yes
Complete qualitati-ve-quantitative formula per unit of dose [10]	Yes	Yes[11]	Yes	Yes	Yes	Yes
Product's monographs, substantiated on official literature [12]	Yes	Yes	Yes	Yes	Yes	Yes[13]
Analysis methods in accordance with the current RTCA (Council of Ministers Central American Economic Integration, 2008a)	Yes[14]	Yes[14]	Yes	Yes[14]	Yes[14]	Yes

Organoleptic, physical, biological and microbiological finished product specifications, in accordance with the current RTCA (Council of Ministers Central American Economic Integration, 2008a)	Yes	Yes	Yes[15]	Yes	Yes	Yes
Primary, secondary and insert packaging labels, either the original or draft labels, in accordance with the current RTCA (Council of Ministers Central American Economic Integration, 2014)	Yes	Yes	Yes	Yes	Yes	Yes
Stability study report in accordance with the current RTCA (Council of Ministers Central American Economic Integration, 2011)	Yes	Yes	Yes	Yes	Yes	Yes[16]
Safety and efficacy studies, as per sections from 7.11.1 to 7.11.5 of RTCA	Yes	Yes	Yes	Yes	Yes	Yes
Finished product samples (according to harmonized amount) to carry out the analysis in accordance with the current RTCA (Council of Ministers Central American Economic Integration, 2008a)[17]	Yes	Yes	Yes	Yes	Yes	Yes
Analytical standards: a) Primary or standardized raw materials b) Related substances and/or degradation products (the authority evaluates their need according to health risk)[18]	Yes	Yes[19]	Yes[20]	Yes[21]	Yes	Yes
Receipt slip	Yes	Yes	Yes	Yes	Yes	Yes
Finished product sample	N/A	N/A	N/A	N/A	Yes[22]	Yes

[1] It includes the regulatory affairs officer's signature from the importing country.
[2] Original or authenticated copy.
[3] In Costa Rica, El Salvador, Guatemala and Honduras it is also accepted when it has been issued by a reference regulatory authority even when it is not the country of origin, or title holder in cases of first-time registration whose safety and efficacy have not been documented in official literature yet.
[4] Must be only the original document.
[5] An authenticated or certified copy of the legalized document is accepted in case the CLV authorizes two products or more
[6] Only allowed if a country of origin is not part of the WHO Quality Certification System for Pharmaceutical Products thus does not issue CPP.
[7] Must be an original legal document or authenticated copy.
[8] Presented if the CPP does not contain information related to the GMP, in the case it is not a WHO format CPP or when there are establishments which are involved in the manufacturing that are not from the country where the CPP is issued.
[9] To present original or authenticated copy with the information from section 7.4 from the RTCA when applicable.
[10] Original signed and stamped by the manufacturing laboratory regulatory affairs officer or product's holder (sections 7.5.1 to 7.5.7 of the RTCA). It is not submitted if it is complete in the CPP or CLV.
[11] It is included, despite being complete in the CPP or CLV.
[12] It must correspond to the pharmaceutical form of the medication to be registered and may include other presentations or concentrations.
For products registered with a strict regulatory authority listed by the WHO, the holder can use published monographs from this authority (Section 7.6 of the RTCA)
[13] It requires to include warnings regarding published excipients issued by the current European Medicines Agency (EMA) guidelines. It also requests to include active ingredient safety notes issued by the Ministry of Health (when applicable).
[14] It is necessary to present a disclaimer when a RTCA established trial is not performed.
[15] Signed and stamped by the regulatory affairs officer.
[16] Only the climate zone IV b applies for long-term studies in controlled conditions.
[17] Requested post-registration certificates, except for Guatemala and Panama, where they are requested at the beginning of the process, before its approval.
[18] Presented with their respective analysis, excluding official pharmacopeia samples, and are requested after the marketing authorization certificate has been obtained.
[19] Each raw material must be labeled with: name, manufacturing laboratory, batch, manufacturing date, expiration date, purity and storage recommendations. The data and the analysis certificate must match.
[20] Requested at the beginning of the process.
[21] Requested at any moment during the registry lifespan, according to the quality control analysis submission by the laboratory in charge.
[22] An approval must be requested when packaging colors do not match with records'. Also, the specimen expiration date must be greaterthan a year regarding the presented date.

In terms of artwork presentations, there are significant variations according to each country.

For Nicaragua draft label and a copy of any finished product presentation must be facilitated, for Costa Rica and Honduras only drafts are provided, and concerning El Salvador, the alveolar distribution of blisters packs must be attached. In addition, in Panama both drafts and originals are provided, thus complying with the copy of the finished product, and in Guatemala the revision date and the version must be stated on the insert along with the drafts.

Figure 4. Market authorization renewals in Central American countries requirement compliance comparison

Requirement	Costa Rica	El Salvador	Guatemala	Honduras	Nicaragua	Panama
Market authorization renewal request signed and stamped by the title holder or legal representative.	Yes	Yes[1]	Yes	Yes	Yes	Yes
Affidavit issued by the title holder, legal representative or registry officer regulatory affairs officer stating that the product's information or characteristics have not been modified since the previous modification request [2]	Yes	Yes[3]	Yes	Yes	Yes	Yes
CPP as the WHO model, original or authenticated copy[4]	Yes	Yes	Yes[5]	Yes	Yes	Yes
CLV (presented when CPP is not issued) [6]	Yes	Yes	Yes[7]	Yes	Yes	Yes
GMP certificate (presented when CPP is not issued) issued by the country's regulatory authority or countries where manufacturing is carried out. [8]	Yes[9,10]	Yes[9,11]	Yes[9,10]	Yes[9,10]	Yes[9,10]	Yes[9,11]
Original product labeling (primary, secondary and insert) as it is marketed, according to current RTCA (Council of Ministers Central American Economic Integration, 2014)[12]	Yes	Yes	Yes	Yes	Yes	Yes
Current stability study report for product renewals that have not previously presented a long term study according to the current RTCA (Council of Ministers Central American Economic Integration, 2011)	Yes[13]	Yes	Yes	Yes	Yes	Yes[13]
Receipt slip	Yes	Yes	Yes	Yes	Yes	Yes

Renewals with modification requirements	It includes the above requirements, with the exception of the affidavit of no changes					
Qualitative and quantitative composition by unit dosage form[14]	Yes	Yes[15,16]	Yes	No	Yes	Yes[17]
Organoleptic, physical, biological and microbiological finished product specifications, according to current RTCA (Council of Ministers Central American Economic Integration, 2008a)	Yes	Yes[17]	Yes[18]	No	Yes	Yes[17]
Powers that ascertain legal and/or technical representation by the title holder to the natural or legal persons according to their country's legislation[19]	Yes[15]	Yes	Yes[20]	Yes[15]	Yes	Yes[15]
Contract Manufacturing Agreement or extract related to the contract manufacturing agreement[21]	Yes	Yes	Yes	No	Yes	Yes

[1] It includes the regulatory affairs officer's signature from the importing country.
[2] Must be legalized if it is issued abroad.
[3] It may also be signed as well by the regulatory affairs officer from the importing country.
[4] In Costa Rica, El Salvador, Guatemala and Honduras it is also accepted when it has been issued by a strict regulatory authority even when it is not the country of origin, or title holder in cases of first-time registration whose safety and efficacy have not been documented in official literature yet.
[5] Must be only original documents.
[6] An authenticated or certified copy of the legalized document is accepted in case the CLV authorizes two products or more
[7] Only allowed if a country of origin is not part of the WHO Quality Certification System for Pharmaceutical Products thus does not issue CPP.
[8] Must be original legal document or authenticated copy.
[9] Presented if the CPP does not contain information related to the GMP or in case the CPP is not in WHO format.
[10] Presented where the manufacturing stakeholders are not from the country that issued the CPP.
[11] Presented if the CPP is not issued or if it does not count with the GMP compliance form from the manufacturing stakeholders.
[12] Labels in Spanish are accepted stating that the product has not been marketed through an affidavit issued by the regulatory affairs officer.
[13] A disclaimer must be issued stating the studies are found in their records.
[14] Original document signed and stamped by manufacturer's officer or title holder (section 7.5.1 a 7.5.7 from RTCA). Not presented if it is completed within CPP or CLV
[15] Presented within renovation with or without changes.
[16] Included even though it is stated within CPP or CLV.
[17] Applies according to the requested post-marketing changes.
[18] Signed and stamped by the regulatory affairs officer.
[19] When there is a designation change or when it is not in the records (original document or authenticated copy)
[20] Also presented if no changes have been made to the product in the last five years.
[21] Present original document or authenticated copy with information from RTCA section 7.4 when applicable.

Concerning the labeling, Costa Rica requires the finished product pictures submission as is in the market. In case it is not being marketed yet, the drafts are issued next to a packaging's non-commercialization declaration when applicable. On the other hand, in El Salvador it is necessary a non-commercialization statement which must contain an estimated date to begin this activity (if applicable). In Nicaragua, an affidavit is necessary only when the medication has never been marketed. Otherwise, it is necessary to present a physical sample of any size. Additionally, for Guatemala, Honduras and Panama the drafts must be sent. In Guatemala the revision date and its version number must be stated in the insert.

Discussion

Co-packaged medication registry As shown in Figure 2, all the requirements for the co-packaged medications are met. It applies to those that possess two or more previously authorized formulations and are combined to be sold and used in a specific medical disorder (Council of Ministers Central American Economic Integration, 2021). These presentations are useful to make the adherence to a treatment easier (Adkins, 2019).

The procedure requests must be signed by the regulatory affairs officer and the attorney in fact only in El Salvador whilst the RTCA requires only the regulatory affairs officer's signature. In addition, Guatemala states the registry must include a statement by the title holder specifying a change is being requested.The differences can be attributed to a legal disposition or complementary local regulation by the country (Figure 1) and it is applied by the NRA. Hence, additional information is needed to comply with the requirement. This situation also occurs in the following procedures:

Registry of medications

The compliance with the requirements by the regulatory entities from the concerning territories is evident in figure 3. Regarding some divergences, the RTCA allows to present a CLV when a CPP is not issued, although in Guatemala and Panama this presentation has its conditions, as detailed in the figure's footnotes. The CPP is intended to confirm the marketing authorization status and compliance with GMP principles or equivalent standards, supporting the regulatory processes in importing countries (Human Medicines Division, 2023).

The CPP promotes the convergence and simplification of practices to enhance the pharmaceutical market globalization, the regulatory environment and the lifespan management of the product (Rodier et al, 2021).

On the other hand, The CLV is a document which certifies that it is freely commercialized in the exporting country. Consequently, it is registered there (Ministerio de Salud, 2023). Its counterparts do approve a CLV in the presented documentation, which may mean the requirement is interpreted differently by the Member States. The WHO recommendations address its use when the exporting nation is not subscribed to the certification scheme of the organization; hence, the CPP is not issued (Red Panamericana de Armonización de la Reglamentación Farmacéutica, 2013).

Regarding the monographs to present, they contain information about the quality of a medication, including identity, purity and performance; also, the trials to validate a medication and that its components are in accordance with the necessary criteria (United States Pharmacopeia, 2023). Panama asks to attach the information to the safety notes of the main ingredients issued by the Health Ministry.

This is vital, because during the products' lifespan constant monitoring is carried out during the pharmacovigilance, regardless whether they count on a marketing authorization or not. This is a public health activity whose objective is to identify, quantify, assess, and seek the associated risks to its use (Presidencia de la República & Ministerio de Salud, 2015).

The main objective is to identify the adverse reactions other than the previously described and to generate the causal hypothesis between a substance administration and the occurrence of an undesirable effect. It also determines the relationship among these reactions and the conditions, the medication circumstances or pathologies in the human being (Ramírez Bianchini et al, 2016). An established system is crucial to effective regulatory structures, as it guarantees effective monitoring of the safety and effectiveness of
health products, as well as the favorable benefit/risk profile of each one (Stegmann et al, 2022).

The pharmacovigilance regulatory function involves the reporting of suspected medication adverse reactions. This information is under periodic review by the entity with the objective of identifying safety issues derived from its usage. Other activities are related to the post-marketing studies, constituted by clinical or epidemiological studies under regular usage conditions (Presidency of the Republic & Ministry of Health, 2015).

Another aspect is the analytical methodology, which establishes different methods, including the active ingredient quantification (Sánchez-Hoyos et al, 2016) and the determination of formulation impurities (Quiñones-García et al, 2015). The tests suggested by the current RTCA must be complied with, according to the specifications of each, following the official pharmacopeias or the manufacturer or the holder statements in the marketing authorization (Council of Ministers Central American Economic Integration, 2008a). Thus, if a required test is not carried out, a letter must be attached to justify why it is not included. It applies for Costa Rica, El Salvador, Honduras and Nicaragua.

The labeling of pharmaceutical products corresponds to a tag, punching, or other descriptive or graphic material that is written, oilboarded, embossed, relief printed, or printed on the medication, its container or its package which purpose is to inform people
(Herrera Víquez et al, 2020). The revision for the current RTCA is vital (Council of Ministers Central American Economic Integration, 2014) for all countries that present label drafts and, concerning El Salvador, the alveolar distribution in the primary packaging as a blister must be identified. At the same time, Guatemala requires that the insert contains its version number and revision date.

Regarding its stability, the studies contribute to determine its shelf life, evaluating packaging and sealing elements covering as well the physical, chemical, microbiological, therapeutic, and toxicological specifications (Peeraer, 2023). Consequently, it is vital to ensure the product or main ingredient keep their properties within the quality standards and it also allows data acquisition about its storage (Council of Ministers Central American Economic Integration, 2011).

To determine physical, chemical, biological and microbiological properties during the expiration period the studies must be performed in controlled storage environments. This implies the compliance with the guidelines depending on the climate zone where the manufacturer is located and where the medication is distributed (Council of Ministers Central American Economic Integration, 2011).

The RTCA state parties correspond to the climate zone IV - warm/humid. This is divided in (Council of Ministers Central American Economic Integration, 2011):

▶ IV a: warm/humid with a 30 ± 2° C y 65 ± 5 % relative temperature and humidity storage conditions, respectively.
▶ IV b: warm/humid with a 30 ± 2,1º C y 75 ± 5 % relative temperature and humidity storage conditions, respectively.

Panama has a very humid tropical climate and adopts the climate zone IV b according to its legislation, it possesses more critical humidity and temperature aspects to evaluate stability (Ministerio de Salud, 2009). This information was added because Panama was not previously a member of the States party to the RTCA.

Regarding the finished product samples, these are required for quality control analysis and to verify that the medication complies with the submitted information. However, each has their own procedure and stakeholders. Sanitary registration renewals Based on obtained information, a division on renewals with and without variations was carried out.

Renewals without variations

The nations which comply with the requirements raised by the RTCA can be observed on figure 4. Among the found differences is the responsible for signing the renewal application documents and the statement of affidavit which indicates the formulation has not varied since the last authorized modification. In El Salvador, any application for each of those procedures (including registration and post marketing authorization variations) must be signed for the regulation affairs officer and the attorney in fact. The RTCA states the statement of affidavit is issued by the holder, the legal representative or the regulation affairs officer. Hence, it can be signed by the importing country's power of attorney.

On the other hand, the original CPP must be presented in Guatemala, while in the other members an original or copy is allowed, according to the RTCA. The CLV, as well as for new registration procedures, if the country can issue the CPP is not allowed for Guatemala and Panama.

In relation to GMP requirements, they do not differ among territories and comply with what the RTCA establishes. However, it is important to note that if a CPP does not include GMP information, the certificates of the laboratories involved in its manufacturing must be presented. This scenario may occur when the CPP does not follow the WHO model or when laboratories outside the country of origin, where the CPP is issued, are involved in the manufacturing process.

Conversely, the labeling has a partial compliance, since the RTCA requires original labeling and this only occurs in Nicaragua where a sample of any presentation is required. In the rest of the countries, drafts or pictures of their current commercialization are submitted. If it is not being marketed, an affidavit stating it is submitted and only drafts are submitted.

Its revision is imperative since all the submitted information must be verified to ensure its compliance in labeling guidelines, that they are according to the last approved drafts and they are being adequately marketed.
The stability study is complied with in all countries as a complement, but in Costa Rica and Panama a disclaimer is issued to state that (in controlled conditions) it is already on file. If the long term stability study has not been presented, it must be done at that time. Finally, in Honduras the file as a whole is required. Moreover, a disclaimer can be sent that the qualitative-quantitative formula, analysis methods and analytical validation (evaluations to verify an analytical test system is adequate for its purposes and is capable of providing beneficial and legitimate data) (Rao, 2018), the monograph and specifications (define limits to establish whether the trials are acceptable) (Oosterhuis, 2017) are already on file.

Variations

In Renewals due to Variations the same documentation is submitted, except the affidavit that has not undergone any changes. Moreover, it is imperative to provide when applicable the qualitative-quantitative formula (list of ingredients with their respective quantities or concentrations) (Arias, 1999), the finished product specifications, the powers of attorney, and the manufacturing contract. This is true in all cases except Honduras where a renewal and the changes must be submitted as different procedures making the latter to be presented if it is necessary according to the changes.

Finally, it is necessary to evaluate the local norms' existence. For example, in Guatemala and Panama the waste management plan is required. This includes medication that has been expired, unused, spilled, recalled, damaged, contaminated or any other reason (Mohammed, 2021). Guatemala requires as a complement the same requirements as in new registries: safety information, the last safety and efficacy analysis if they have not been documented. The main difference is that at any given time the analytical standards could be required for their analysis. However, not all renewed products are subjected to analysis. On the other hand, within the renewals with variations the analytical methodology, its validation and monograph are required.

Conclusions

After the requirements review with the different member states regulatory affairs officers it is demonstrated that, despite the country's compliance concerning the established aspects in the RTCA, it is common to identify divergences in the procedures related to the legislation of each one, including complementary requirements, as it was demonstrated in this research results. Due to this, its comparison and delimitation are the basis to analyze the aspects that may be subject to harmonization or convergence by the Central American regulatory authorities.

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