**Annex 1 of resolution No. 333-2013 (COMIECO-LXVI)[[1]](#footnote-1)**

**CENTRAL AMERICA RTCA 11.03.59:11**

**TECHNICAL**

**REGULATION**

**PHARMACEUTICALS. DRUGS FOR HUMAN USE. HEALTH REGISTRATION REQUIREMENTS.**

CORRESPONDENCE: This regulation does not necessarily correspond with any other legislation or international regulations.

**ICS 11.120.01 RTCA 11.03.59:11**

Central American Technical Regulation, edited by:

* Ministry of Economy and Commerce Agency, MINECO (Guatemala)
* El Salvador Technical Regulation Agency, OSARTEC (El Salvador)
* Ministry of Trade and Industry, MIFIC (Nicaragua)
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* Ministry of Economy, Trade and Industry, MEIC (Costa Rica)

**REPORT**

The respective technical committees of technical regulations of the Central American countries, and their successors, are the agencies responsible for conducting the study or the adoption of technical regulations. They are formed by representatives from the academic, consumer, private enterprise and Government sectors.

This document was approved as Central American Technical Regulation, RTCA 03.11.59: 11 “Pharmaceuticals. Medicinal Products for Human Use. Requirements for Registration”, by the Subgroup on Medicines and Allied Products and the Subgroup on Standardisation Measures. The formalisation of this technical regulation required the ratification by the Council of Ministers for Economic Integration (COMIECO).

PARTICIPATING MEMBERS

**For Guatemala**

Ministry of Public Health and Social Welfare

**For El Salvador**

National Directorate of Medicinal Products

**For Honduras**

Ministry of Health

**For Costa Rica**

Ministry of Health

**For Nicaragua**

Ministry of Health

1. **OBJECTIVE**

Establish conditions and requirements under which the registration of medicaments for human use will be granted.

1. **SCOPE**

Applies to drugs for human use that are manufactured or imported by individuals or entities for marketing in the Central American Territory. Compounded preparations are excluded from this Regulation.

NOTES:

1. Biological and biotechnological drugs shall be registered in accordance with the national legislation of each State Party.
2. If a State party does not have a national law for the registration of biological and biotechnological medicinal products, these rules will be applied to those products.
3. In the case of nutritional or dietary supplements, as there are no regionally harmonised rules, the laws of each state party shall apply.
4. **DOCUMENTS TO BE CONSULTED**
   1. **RTCA 11.03.39:06 pharmaceuticals. Regulation of validation of analytical methods for the evaluation of the quality of medicinal products.**
   2. **RTCA 11.01.02:04 Pharmaceuticals. Labelling of Pharmaceuticals for Human Use.**
   3. **RTCA 11.01.04:10 Pharmaceuticals. Existing Stability Studies of Medicines for Human Use.**
   4. **RTCA 11.03.56:09 Pharmaceuticals. Medicinal Products for Human Use. Verification of Quality.**
   5. **RTCA Pharmaceuticals. Medicinal Products for Human Use. Good Manufacturing Practices for Pharmaceutical Industries.**
5. **DEFINITIONS**
   1. **Packaging:** All operations, including filling and labelling, are required to convert a bulk product into a finished product.
   2. **Regulatory authority:** authority responsible for the health regulations in each country or region.
   3. **Regulatory authority of regional reference:** it is the competent and effective national regulatory authority which performs the functions of health regulations recommended by PAHO/WHO, to ensure the quality, safety and efficacy of drugs and biological products.
   4. **Stringent regulatory authority:** those defined in the prequalification process of pharmaceutical products from WHO.
   5. **Good manufacturing practices:** a set of procedures and standards designed to ensure the uniform production of batches of pharmaceutical products that meet the quality standards.
   6. **Certificate of Free Sale:** document issued by the Regulatory Authority of the country or region of origin, or the source, which certifies that the drug is approved for sale in that country; in the case of production by third parties or affiliates and that the product is not commercially available in the country of origin, it may be issued by the regulatory authority of the country of the owner.
   7. **Certificate of Pharmaceutical Product (CPP or CoPP):** certification modelled by WHO and issued by the Regulatory Authority of the country or region of origin, or the source, as part of the system of quality certification of pharmaceutical products traded internationally, in the case of third party manufacturing or subsidiaries and that the product is not marketed in the country of origin, it may be issued by the Regulatory Authority of the country of the owner.
   8. **Certificate of Good Manufacturing Practices (GMP)**: document issued by the Regulatory Authority of the country in which the manufacturing laboratory is located, which certifies that the laboratory complies with Good Manufacturing Practices.
   9. **Co-packaging**: presentation of two or more previously registered products that are sold together for treating a specific disease.
   10. **Contract manufacturing**: legal document concluded between the owner of the drug and the manufacturer which establishes the conditions, commitments and other circumstances for the manufacture of one or more products.
   11. **International Non-proprietary name**: name recommended by WHO for the active ingredients of medicines.
   12. **Official document**: one issued by the Competent Authority of the State.
   13. **Labelling or tagging**: any recording or legend that identifies the product, which is printed, stuck or engraved on the primary container or packaging and/or the secondary container or packaging.
   14. **Primary container or primary packaging**: container into which the finished pharmaceutical form of the drug is directly placed.
   15. **Secondary container or secondary packaging**: container within which the primary packaging containing the drug in its finished pharmaceutical form for distribution and marketing is placed.
   16. **Chemical entity**: functional group of the active ingredient that is responsible for the physiological or pharmacological effect. It means a chemical entity that share those polymorphs, isomers and those derivatives attached to the chemical entity that constitute an ester, ether, salt, (including a salt with hydrogen bonds or coordinate), or other derivative such parts as non-covalent complex, among others.
   17. **Pharmaceutical equivalent**: medication that contains identical amounts of the same active ingredients of the product to which it is equivalent, the same salt or ester of the active ingredient in the same dosage forms, but that may or may not contain the same excipients. As a result, two pharmaceutical equivalents may show different bioavailabiities, magnitudes and temporal profiles of their pharmacological activities.
   18. **Manufacture or workmanship**: all operations involved in the purchase of materials and products, production, packaging, quality control, approval, storage, distribution of the finished product and related controls.
   19. **Manufacture by third parties**: national or foreign manufacture performed within the limits of a previous contract between the owner and manufacturer of the drug, the owner being responsible for the product.
   20. **Insert, leaflet or instructive**: scientific and technical information attached to the finished product, which must contain the information necessary for the safe and effective use of the medicinal product.
   21. **Manufacturer laboratory:** entity authorised with facilities designed to perform all operations involving the manufacture of pharmaceuticals.
   22. **Multisource drug**: product which is the pharmaceutical equivalent but which may or may not be therapeutic equivalent. Multisource drugs that are therapeutic equivalents are interchangeable.
   23. **Orphan drug**: one which is intended to treat a disease that is rare, severe, or results in disability, and whose commercial interest is unlikely, or without stimulus. It is intended for a small group of patients but responds to public health needs.
   24. **Post-registration changes**: changes to the health record of a pharmaceutical product subsequent to registration.
   25. **Product Monograph**: scientific description – technical safety profile and efficacy of a drug or pharmaceutical.
   26. **Country of origin**: the country where the product is manufactured. In cases where the method involves more than one manufacturer, the country is one in which the bulk of the manufacturing of the product is performed.
   27. **Country of departure**: the country in which the product is distributed, prepared, or exported. Provided that these involved are in the manufacturing process; at least until the primary packaging.
   28. **Country of owner**: country where the owner of the product is resident.
   29. **Compounds**: medicinal product prepared by the pharmacist in a pharmacy for a prescription or medical prescription for an individual patient.
   30. **Active ingredient**: substance with a specific pharmacological effect or that without activity, upon administration in the organism it acquires it undergoes changes in its chemical structure.
   31. **Pharmaceutical product or medicine**: simple or compound, natural, synthetic substance, or mixture of these, with defined dosage form, used to diagnose, treat, prevent disease or modify a physiological function of human beings.
   32. **Bulk product**: product that has gone through all stages of production except the primary packaging.
   33. **Finished product**: product which is in its final packaging, labelling, and ready to be distributed and marketed.
   34. **Responsible practitioner**: pharmacist or chemist responsible for the process of registration with the regulatory authority, authorised by the owner of the medicinal product or his legal representative through a power granted according to the law of each State party.
   35. **Registration**: approval by the regulatory authority of a country for the marketing of a drug, once it has passed the evaluation process relative to the quality, efficacy and safety.
   36. **Legal representative**: natural or legal person residing in the country which handles the registration, authorised by the owner of the drug, through a power awarded according to the laws of each State party, accountable to the Regulatory Authority.
   37. **Container closure system**: a set of packaging materials that contain and protect the dosage form, including both the primary packaging and secondary packaging, if the latter serves to provide additional product protection.
   38. **Product owner or registrant**: natural person or legal owner of the product.
6. **SYMBOLS AND ABBREVIATIONS**
   1. OMS: World Health Organisation
   2. FDA: United States Food and Drugs Administration
   3. ATC: Anatomical Therapeutic Chemical Classification System
   4. EMA: European Medicines Agency
   5. BPM: Good Manufacturing Practices
   6. DCI: International Non-proprietary Name
   7. USPDI: Drug Information for the Health Care Professionals
   8. AOAC: Association of Analytical Chemists
7. **GENERAL PROVISIONS**
   1. For import, distribution, marketing, promotion and prescription, any medicinal product requires prior registration with the regulatory authority.
   2. The registration of drugs will have a validity of five years, and the regulatory authority reserves the right to suspend or cancel the registration when there are health, scientific, technical or legal reasons that duly justify.
   3. Any certificate or official document required must be valid at the time of submission. Official documents shall be valid once granted by the Regulatory Authority of the country where it is issued. In cases where the duration is not specified, it will be 2 years for the purpose of registration, from the date of issue.
   4. Any official or legal document must be submitted in original or certified copy pursuant to the laws of each State party.

The document must be submitted in Spanish/Castilian or accompanied by its respective translation issued in accordance with the laws of each State party language.

* 1. No corrections to the certificates or official documents presented are permitted, unless they are supported by the same body that issued the original document.
  2. Any official or legal document issued abroad must be legalised in compliance with specific national regulations.
  3. In cases where it applies, and for purposes of registration of a specific drug, the applicant is allowed to refer to original documents stated in current files of the Regulatory Authority. In this case the applicant should refer to management in which the original document was delivered, presenting a photocopy of it.
  4. In the case of products to be registered which are not marketed in the country of origin or departure, the regulatory authority will evaluate the rationale provided.
  5. These correspond to the same record:
     1. Different commercial presentations of medicines with the same concentration and the same pharmaceutical form.
     2. Medications with the same quali-quantitative formula and different flavour and/or colour.
  6. **Official specifications**

For the purpose of this regulation the specifications that are recognised as official are:

* + 1. **For quality assurance:**

**For registration of medicines whose methods of analysis of the finished product are pharmacopoeial, they must be described in the version that includes latest specifications and tests to assess the quality of the drug for the specific dosage form. In cases where the latest version is not used, the applicant must justify this omission, stating which is pharmacopoeia and edition is used, provided it complies with the provisions of the Central American Technical Regulation of Verification of Quality and the list of official specifications. The Regulatory Authority will assess the justification provided. In cases where the medicines are described in more than a pharmacopoeia, the pharmacopoeia used should indicate the most current and complete specifications to verify product quality.**

**The official specifications are:**

1. German Pharmacopoeia
2. Argentina Pharmacopoeia
3. British Pharmacopoeia
4. United States Pharmacopeia (USP) and National Formulary of the US (USP / NF)
5. Spanish Pharmacopoeia
6. European Pharmacopoeia
7. French Pharmacopoeia
8. Swiss Pharmacopeia
9. International Pharmacopoeia
10. Japanese Pharmacopoeia
11. Mexican Pharmacopoeia
12. Chinese Pharmacopoeia
13. Food Chemical Codex (FCC)
14. AOAC
15. and others that, in consensus, countries agree to include.
    * 1. **For drug evaluation:**

**The following literature may be used for the evaluation of the monograph:**

1. Drug Information for the Health Care Professionals (USPDI)
2. Drug Information (AHFS).
3. Martindale. The Extra Pharmacopoeia.
4. Pharmacological regulations of Central America and the Dominican Republic.
5. Pharmacology books that are scientifically based.
6. Full articles from journals scientifically grounded.
   1. The name of the medication to be registered must not cause confusion with other medication already registered, either in its written or spoken form, hence the name of the medication to be registered must meet the following conditions:
      1. The registration of medicines with a same trademark name and different active principles is not allowed, nor is accepted the use of a brand name that has been used previously for products of different uses.
      2. Registration is only accepted the using the same brand name, in the case of declared over-the-counter medications that are used with similar therapeutic indications even though they contain different active principles (lines of treatment).
      3. The registration of poly-counter drugs used as part of a therapeutic action name is accepted.
      4. The use of the name of the owner or their initials accompanied by the International Non-proprietary name of the active principles accepted in the name of a drug.
      5. The medicine name, logos or other statements should not have therapeutic implications that could generate confusion in the instructions for use.
      6. The name of the medication to be registered must match all the documentation submitted, otherwise an explanatory note signed by the owner or legal representative duly authenticated if authorised must be submitted, which specifies that all documents correspond to the same medication.
      7. A drug can be designated with a brand name or a recommended international non-proprietary name. When a trademark is used, it should not be confused with a recommended international non-proprietary name, or it should not be misleading about the therapeutic properties or the nature of the drug.
   2. **Co-packaged medicines**
      1. In case of co-packaged medicines you must register each medicine separately and subsequently apply for a modification of the registry for the co-package.

If some of the products are not registered you must register and then request co-packaging. The expiry date issued will be the registered drug that expires first.

* + 1. If the marketing of several products for a specific treatment is sought in one package and products are not already registered, you must start the registration process, meeting the requirements of each product included in the package.
  1. The labelling of medicines to which this regulation refers shall be governed as indicated in the Central American Technical Regulation in force on Labelling of Pharmaceutical Products for human use.

All information on the label or printed on the packaging of the drug or insert, leaflet or instruction for professionals or patients, must adhere to approved information in the registry.

* 1. If the same product is manufactured in different branches or countries, you must deal with Sanitary Registration for each country or manufacturing laboratory.

NOTE: El Salvador does not apply this provision, since its registration procedure accounts for alternate manufacture.

* 1. To ensure the quality of medicines, regulatory authorities can verify compliance with good manufacturing practices by the means they deem necessary, including on-site inspection of laboratories established manufacturers inside and outside of the Central American countries, by applying the Central American Technical Regulations in force for Pharmaceutical Medicinal Products for Human Use; Good Manufacturing Practices for the Pharmaceutical Industry.

The Regulatory Authority may request regulatory authorities (as regional benchmark) and strict regulatory authorities accredited by WHO, for the verification of compliance with Good Manufacturing Practices of pharmaceutical laboratories that they have inspected

* 1. Regarding intellectual property, the current regulations of each country applies.
  2. Regarding studies of therapeutic equivalence the current regulations of each country applies.
  3. The administrative procedure for the application for registration, renewal and amendments will be made according to domestic legislation of each State party.
  4. Failure to comply with this regulation will lead to the implementation of sanctions in each State party.

1. **HEALTH REGISTRATION REQUIREMENTS**

The requirements for health registration are:

* 1. Request signed and stamped by the Professional Responsible containing the information detailed in Annex 2 of this Regulation.
  2. Powers evidencing legal and/or technical representation granted by the natural or legal owner(s), according to the laws of each country (original or certified copy of the document).
  3. WHO Certificate for Pharmaceutical Products, the original or certified photocopy of the legalised document must be submitted.

In the event that this type of certificate is not issued, the presentation of the following is supported:

* + 1. Certificate of Free Sale. If a certificate is presented attesting to two or more products (authenticated and /or certified photocopy of the legalised document), it will be accepted.
    2. Certificate of Good Manufacturing Practice for each of the establishments involved in the manufacture of the product, for the pharmaceutical form and specific type of product registration issued by the Regulatory Authority of the country or countries in which the manufacturing process is carried out, original legalised or certified copy thereof, indicating that it complies with good manufacturing practices.
  1. Contract manufacturing or otherwise extract of the parts of the contract manufacturing agreement, as applicable, in original or authenticated or certified photocopy of the legalised document, containing at least the following information:

1. Signed by the owner and the manufacturer jointly or separately.
2. Commitment to compliance with Good Manufacturing Practices.
3. Establish the conditions of production, analysis when applicable, or any other technical management related to these.
4. It should describe the handling of raw materials, packaging materials, bulk material and finished product and in the case that they are rejected.
5. Allow entry for the registrant to the premises of the contractor (hired) for audits.
6. Allow entry for the contractor (hired) to the registrant’s premises.
7. List each of the products or services of analysis of the contract.
   1. Complete quantitative and qualitative formula of the product per dose unit. The original, signed and stamped by the professional responsible for the laboratory, manufacturer or owner of the product must be submitted. In addition state the following:
      1. All ingredients must be described with their internationally accepted common or generic name and should not be presented with acronyms and abbreviations, units must be given according to the International System (SI). In case of active ingredients in the form of salts, esters or other, the equivalent amount of the molecule to the therapeutic dose to which it refers should be declared.
      2. Composition of the delivery system for modified release products.
      3. Qualitative composition of empty capsules.
      4. Qualitative composition of printing inks in capsules, tablets and coated tablets.
      5. Qualitative declaration of class 2 or 3 organic solvents used in the manufacturing process.

The registration of medicines which use organic solvents class 1 will not be allowed.

NOTE: The organic solvents mentioned in the previous paragraph are established in USP from edition 31.

* + 1. Excess active ingredients used in manufacturing.
    2. In the case of creams and ointments, the concentration must be expressed per gram, 100g or percentage. Lotions, eye drops, topical sessions and parenteral infusions should express their concentration per mL, 100 mL or percentage.

The complete formula may be provided in the Certificate of Free Sale or the WHO Certificate of Pharmaceutical Product, which will exempt one from presenting it individually.

* 1. Product Monograph.

The information contained in the monograph must be based on the official books. In case of conflict with such books or if the drug is not described in them, they must submit scientific information to back it up, which will be evaluated by the Regulatory Authority.

All monographs must correspond to the dosage form of the drug to be registered, however, it may include other presentations or concentrations provided that they are being registered. The following information must be contained:

1. Internationally accepted common or generic name and concentration of the drug.
2. Dosage form.
3. Structure, chemical name of the active ingredient or failing that attach the sheet to declare this information.
4. Clinical Pharmacology.
5. Instructions
6. Contraindications
7. Cautions and warnings.
8. Interactions.
9. Adverse effects.
10. Dosage and administration.
11. Recommendation in case of overdose according to the toxicological profile.
12. Abuse and addiction.
13. Date of revision of the monograph.
14. Complete list of references.
15. Therapeutic category according to Anatomical and Therapeutic Classification (ATC), in the pharmacological subgroup (updated version).
16. Form preparation

NOTE: When the requested information is not applicable to the characteristics of the product, it may be omitted in the monograph.

* 1. Methods validated according to the Central American Technical Regulations Validation of Analytical Methods for assessing the quality of existing drugs, attaching the report of the corresponding validation study analysis.
  2. Organoleptic, physical, chemical, biological and microbiological specifications of the finished product that comply with the provisions of the Central American Technical Regulation Quality Verification force. Medicines with concentrations higher than 30% of alcohol; as well as those who by their nature they are antiseptic, are exempt from filing microbiological specifications.
  3. Packaging labels/primary, secondary, and insert packaging in original or their drafts, according to the existing Central American Technical Regulation on Labelling of Pharmaceutical Products for Human Use.
  4. Stability Study Report under the existing Central American Technical Regulations Stability Studies of Drugs for Human Use.
  5. Safety and efficacy studies. All reports of clinical studies must have been made in a period not exceeding 10 years, or greater than this period with due justification. The reports should refer to the same medicine that is submitted for sanitary registration, in the following cases:
     1. For drugs whose safety and efficacy has not been documented in the official literature the following must be submitted:

1. Conclusive reports of results from preclinical studies.
2. Conclusive reports of results from clinical studies phases I, II and III.

NOTE: These studies will be accepted in electronic form, provided that the regulatory authority has free access to the information.

* + 1. In case of medications with previously recognised chemical entities whose active ingredient corresponds to new polymorphs, isomers, and those derivatives with parts attached to the chemical entity that constitute it as ester, ether, salt (including a salt with hydrogen bond or coordinated bonds), or another non-covalent derivative, such as complexes, among others, and are not described in the official literature reports conclusive reports of results from clinical studies phases I, II and III must be presented.
    2. For medicines that contain active principles previously registered but have one or more of the following features:

1. New fixed combinations of active ingredients.
2. New pharmaceutical form with an already registered route of administration.
3. New pharmaceutical form with a new route of administration.
4. New pharmaceutical form with a new form of release.
5. New powers or concentrations of active ingredients previously registered.
6. New powers or concentrations of active ingredients that are registered with the same route of administration, pharmaceutical form and dosage.
7. New release form with the same route of administration of a previously registered drug.
8. New routes of administration with an already registered dosage form.

Conclusive reports of clinical studies that verify the objective or objectives according to the variations above for the product in evaluation and to demonstrate to the authority its quality, safety and efficacy should be submitted.

* + 1. If in the evaluation of the documentation it is found that the information presented is not conclusive, the Regulatory Authority may request additional clinical studies. In the event that there is no scientifically appropriate presentation of any additional clinical study, the applicant should state the grounds for assessment by the Regulatory Authority.
    2. A request for which safety and efficacy information is not submitted should be considered by States as an application for the registration of a multisource pharmaceutical product. The regulatory authorities may grant the registration to a multisource pharmaceutical product that:

1. Be a pharmaceutical equivalent to a product having the following characteristics:

* That the regulatory authority has the data on safety and efficacy.
* It has been previously granted a health registration in the State party for registration and
* Which is not protected by patents or test data;

OR

1. Is a pharmaceutical product that meets the following conditions:

* An innovative product that has not been registered in the country and that the health authority considers an exception or in cases of medical needs.
* The applicant presents a document issued or published by a regulatory authority of any country, showing that there exists an innovative product that has been authorised for marketing in that country. This document must demonstrate a positive benefit risk ratio of the product to be registered. The regulatory authority of the State Party may require that the innovative product have a minimum marketing term that shows the risk-benefit ratio of the product to be registered. Specific national legislation established for these purposes will be applied in relation to the protection of test data.
* There are internationally recognised data (published in official books or by stringent regulatory authorities or guidelines), which guarantees the safety and efficacy of the pharmaceutical product to be registered.

1. Primary standards or standardised commodities.
2. Standards of related substances and/or degradation products, when the methodology requires it.

In both cases with their respective traceability by means of a photocopy of the certificate of analysis, except for official pharmacopoeia samples that do not have these certificates.

The Regulatory Authority assessed according to health risk, the requirement to present standards of related substances and/or degradation products.

* 1. Samples of the finished product, according to the harmonised quantity to perform the analyses, according to the existing Central American Technical Regulations of Verification of the Quality of Medicines.

When the official laboratory does not have the technology or the installed capacity for the analysis of certain medications, the regulatory authority will have the power to request external national or foreign laboratories which possess this technology, accredited by the competent entities, observing the number of samples that the laboratory has established. Shipping costs and samples will be paid by the manufacturer or importer, the result of the analysis will be recognised in the States party.

NOTE: In the case of Costa Rica requirements 7.12 and 7.13 are requested post-registration of the medication.

* 1. A copy of the finished product.

For those medicines internationally classified as radioactive or biological weapons the Regulatory Authority may exempt the presentation of this requirement. For medication requiring a cold chain, as well as cytotoxic and biological medication, containers without the product with the closure system with which they are being marketed will be accepted.

NOTE: In the case of Guatemala and El Salvador, the requirement is not requested because the test samples are used.

In the case of Costa Rica the requirement for the registration process is not requested.

* 1. Proof of payment

1. **REQUIREMENTS FOR CO-PACKAGED GOODS**
   1. Proof of payment
   2. Application signed and dated by the responsible professional, containing the information detailed in Annex 2 of this regulation.
   3. Draft co-packaging labels and insert, in accordance with the existing Central American Technical Regulation on Labelling of Pharmaceutical Products for Human use.
   4. Scientific information to support the treatment schedule. payment
2. **REQUIREMENTS FOR RENEWAL OF HEALTH REGISTRATION**

The renewal of the registration of a medication can be negotiated at least three months before maturity.

Once the health registration is past its expiration date, the renewal application will not be accepted and it shall be processed as a new entry.

* 1. When the drug maintains information and features that have been approved during the term of registration, to apply for renewal one must submit:
     1. Proof of payment.
     2. Application for renewal of the health registration signed and stamped by the Responsible Professional, containing the information detailed in Annex 2 of this regulation.
     3. Affidavit issued by the owner or his legal representative or by the professional responsible for the registration through power issued by the owner of the product, assuming that the information and product characteristics have not changed since the last request for amendment submitted to the Regulatory Authority.

If the affidavit is issued abroad it must be duly legalised.

* + 1. WHO Certificate for Pharmaceutical Products or alternatively Certificate of Free Sale and Certificate of Good Manufacturing Practices in accordance with the provisions in 7.3, valid at the time of submission.
    2. Product labelling as it is being marketed, in original according to the existing Central American Technical Regulation on Labelling of Pharmaceutical Products for Human use.

Note: If the product has not been placed on the market, the draft texts for printing of the primary and secondary and insert packaging in Spanish, accompanied by an affidavit of the owner of the product indicating that the product has not been marketed, will be accepted.

* + 1. Stability Study Report according to existing Central American Technical Regulations, signed by the technician responsible for the stability study so designated by the owner. This requirement applies only to products that have not yet submitted a long-term study on earlier sanitary registrations or renewals.
  1. In cases where the medication presents changes in the registration and the regulatory authority is unaware, the request for change must be made simultaneously with the renewal. In the same way, but the affidavit may be presented, in both cases the following requirements must be met:
     1. Proof of payment.
     2. Application for renewal of registration and non-submitted changes, signed and stamped by the responsible professional.
     3. WHO Certificate for Pharmaceutical Products or alternatively Certificate of Free Sale and Certificate of Good Manufacturing Practices in accordance with the provisions in 7.3, valid at the time of submission.
     4. Product labelling as it is being marketed, in original according to the existing Central American Technical Regulation on Labelling of Pharmaceutical Products for Human use.

Note: If the product has not been placed on the market, the draft prints of the primary and secondary and insert packaging in Spanish, accompanied by an affidavit of the owner of the product indicating that the product has not been marketed, will be accepted.

* + 1. Stability Study Report according to existing Central American Technical Regulations, signed by the technician responsible for the stability study so designated by the owner. This requirement applies only to products that have not yet submitted a long-term study on earlier sanitary registrations or renewals.
    2. Quantitative and qualitative formula shall be submitted in accordance to the requirements set out in paragraph 7.5.
    3. Organoleptic, physical, chemical, biological and microbiological specifications of the finished product comply with the provisions of the existing Central American Technical Regulation on Quality Verification. Medicines with concentrations higher than 30% of alcohol; as well as those which by their nature they are antiseptic, are exempt from filing microbiological specifications.
    4. Powers evidencing legal and/or technical representation granted by the owner natural or legal persons, according to the laws of each country; in case where there is no record or any changes in the designation.
    5. Contract manufacturing or otherwise extract concerning the parties to the contract manufacturing, where applicable, as set out in paragraph 7.4.
    6. According to the requested amendment the documents shall be submitted according to Annex 1.

1. **REGISTRATION HEALTH PERIOD**

The registration will have a term of 5 years from its provision, and may be renewed for similar periods. In cases of violations of rules and regulations or sanitary laws, the regulatory authority will proceed to the cancellation of the same.

1. **REASONS FOR NOT GRANTING HEALTH REGISTRATION**
   1. There is a discrepancy between the analytical results and the documentation submitted. This reason does not apply in the case of Costa Rica.
   2. There is a lack of therapeutic efficacy or safety according to the literature reference.
   3. The studies or research to be presented in support of the application are incomplete, or insufficient to demonstrate the quality, safety and efficacy of the product.
   4. The documentation submitted as required by regulations is incomplete, incorrect or not current.
2. **REASONS FOR CANCELLATION OF THE REGISTRATION**
   1. The product proves to be harmful or unsafe under normal conditions of use, following due process according to the laws of each country.
   2. It has been demonstrated that the product is not therapeutically effective.
   3. Where it is shown that that the product has no authorised qualitative or quantitative composition or when guarantees of quality and stability are breached, as declared in the file, following due process according to the laws of each country.
   4. It is shown that the data and information contained in the registration dossier are wrong or false.
   5. That on previous issuance of a warning, continue violating the existing Central American Technical Regulation on Labelling of medicines.
   6. That for any other reason constitutes a foreseeable risk to the health or safety of persons.
   7. When falsity is found in the affidavit filed for renewal of the registration.
   8. When the owner of the registration requests it.
3. **EXCEPTIONS TO THE REGISTRATION**

The regulatory authority may authorise the import and use of medicine without registration in the following cases:

* 1. Donations
  2. National emergencies and officially declared public necessities
  3. Orphan drugs for States Parties
  4. Medications used in clinical studies with approved protocols
  5. In cases of medical justification.
  6. Samples for registration procedures.
  7. Drugs purchased through the PAHO Revolving Fund.

1. **SUBSEQUENT AMENDMENTS TO THE REGISTRATION**

Any change in the information that is made after the health registration shall conform to the provisions of the Classification and Requirements (Annex 1).

1. **DEROGATION**

This Central American Technical Regulation repeals only provisions on the requirements for health registration, renewal and changes to medication for human use, of the internal regulations of each State party, with the exception of provisions on intellectual property and bioequivalence.

1. **MONITORING AND VERIFICATION**

The monitoring and verification of this Central American Technical Regulation corresponds to the Regulatory Authorities of States Parties in accordance with their law.

**ANNEX 1**

**(Regulations)**

**REQUIREMENTS FOR CLASSIFICATION AND MODIFICATIONS TO HEALTH REGISTRATION**

The responsible professional may apply for post-registration changes if the power granted by the owner of the product gives him that authority.

1. Changes requiring approval by the Regulatory Authority.

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| **TYPE OF CHANGE** | **REQUIREMENTS** |
| 1. Expansion in the commercial presentation   Variation in the amount of packaging units, weight or filling volume. | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. 4. Document issued by the owner or his Legal Representative stating the change. |
| 1. Changes or modifications to the product name | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Document issued by the owner or his Legal Representative stating the change. 4. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. |
| 1. Change of business name of manufacturer, packager or owner | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Legal document certifying that the change is duly authenticated. 4. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. |
| 1. Changes in the monograph and insert. | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Monograph and insert updated with the changes identified. 4. Document issued by the owner or his Legal Representative certifying the change. 5. List of bibliographic reference, otherwise, studies pursuant to the registration requirements that support the change. |
| 1. Change in the useful life period. | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Report of the updated Stability Study according to the existing RTCA. 4. Document issued by the owner or his Legal Representative certifying the change. |
| 1. Change in storage conditions. | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. New report of the Stability Study according to existing RTCA. 4. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. 5. Document issued by the owner or his Legal Representative certifying the change. |
| 1. Change of primary packager | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Current Good Manufacturing Practices certificate of the new packager. 4. Contract with the new packager, according to the provisions of paragraph 7.4, registration requirements. 5. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. 6. Document issued by the owner of the product or its Legal Representative indicating the provisions for change of primary packager in the existing RTCA Stability Studies of Medicines for human use. |
| 1. Change of secondary packager | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Contract with the new packager, according to the provisions of paragraph 7.4, registration requirements. 4. New original secondary container/packaging labels or their drafts, as applicable, according to existing RTCA Labelling of Pharmaceutical Products for human use. 5. Current Good Manufacturing Practices certificate of the new packager. 6. Document issued by the owner or his Legal Representative stating the change. |
| 1. Change in type of primary packaging material or container closure system. | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Stability Study Report according to existing RTCA Stability Studies of Drugs for Human Use. 4. New original primary container/packaging labels or their drafts, as applicable, according to existing RTCA Labelling of Pharmaceutical Products for human use. 5. Document issued by the owner or his Legal Representative stating the change. |
| 1. Addition of new primary packaging | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Stability Study Report according to existing RTCA Stability Studies of Drugs for Human Use. 4. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. 5. Document issued by the owner or his Legal Representative stating the change. |
| 1. Change of ownership | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. 4. Document issued by the owner or his Legal Representative stating the change. 5. Contract with the new owner, according to the provisions of paragraph 7.4, registration requirements. |
| 1. In the case of manufacturing for third parties: 2. Change of manufacturer. 3. Change of manufacturer and country of origin. | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. WHO Certificate for Pharmaceutical Products, in accordance with paragraphs 7.3, 7.3.1, 7.3.3, 7.3.4, when applicable. 4. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. 5. Certificate of Good Manufacturing Practices of the new manufacturer according to paragraph 7.3.2. 6. Stability Study Report according to existing RTCA Stability Studies of Drugs for Human Use. 7. A specimen of the finished product. 8. Finished product samples for analysis in accordance with the existing provisions of the RTCA Quality Verification (In the case of Costa Rica, this does not apply). 9. Analytical methodology validated according to paragraph 7.7. 10. Contract with new manufacturer, according to the provisions of paragraph 7.4, registration requirements. 11. Standards according to those detailed in paragraph 7.12. 12. Document issued by the owner or his Legal Representative stating the change. |
| 1. Change of sales modality | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Information justifying the change issued by the owner or his legal representative. 4. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. |
| 1. Change of excipients | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Quali-quantitative formula per unit of dose according to paragraph 7.5. 4. If the change is greater than 10% put into practice the existing RTCA Stability Studies of Drugs for Human Use. 5. Original samples of finished product with specifications according to the provisions of the existing RTCA Quality Verification. 6. Standard reference of the active ingredient with its respective certificate according to number. 7. Technical justification for the change.   Note: Item 4.1 and 4.2 of this section do not apply to Costa Rica.   1. Updated and validated analytical methodology, if applicable. 2. Finished product specifications updated, if applicable. 3. Document issued by the owner or his Legal Representative stating the change. |
| 1. Change of information on the primary and secondary labelling. | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. 4. Technical documentation supporting the change issued by the owner or his legal representative. |
| 1. Change in manufacturing site within the same country. | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Current certificate of Good Manufacturing Practices. 4. Affidavit of the owner or Legal Representative of the product to the effect that manufacturing conditions in which the stability study is presented are unchanged, or alternatively presentation of the stability study according to the existing RTCA Stability Studies of Medicines for Human Use. 5. Document issued by the owner or his Legal Representative stating the change. |
| 1. Change in the legal representative or responsible professional | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Power granted according to the laws of each State party attesting the change. |
| 1. Changes or updates to the specifications of the finished product | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. New specifications of the finished product that complies with the provisions of the existing RTCA on Quality Verification. 4. Document issued by the owner or his Legal Representative stating the change. |
| 1. Changes or updates to the analytical methodology | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Full description of the analytical methods (when it is not Pharmacopoeia) taking into account the provisions of the existing RTCA on Quality Verification. 4. Validation documentation as defined in the existing RTCA Validation of Analytical Methods for Evaluating the Quality of Medication. 5. Justification supporting the change. 6. Document issued by the owner or his Legal Representative stating the change. |
| 1. Expansion of Therapeutic Indications | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. Updated insert and therapeutic monograph. 4. Clinical studies to support the new indication. 5. Document issued by the owner or his Legal Representative stating the change. |
| 1. Change of origin | 1. Proof of payment. 2. Request signed and stamped by the responsible professional. 3. WHO Certificate for Pharmaceutical Products, in accordance with paragraphs 7.3, 7.3.1, 7.3.3, 7.3.4, when applicable. 4. New original primary, secondary container/packaging labels or their drafts according to existing RTCA Labelling of Pharmaceutical Products for human use. 5. New stability study according to the existing RTCA Stability Studies of Medicines for Human Use. 6. A specimen of the finished product. 7. Finished product samples for analysis in accordance with the existing provisions of the RTCA Quality Verification (In the case of Costa Rica, this does not apply). 8. Analytical methodology validated according to paragraph 7.7. 9. Standards according to those detailed in paragraph 7.12. 10. Document issued by the owner or his Legal Representative stating the change. |
| 1. Change of active principal ingredients and its salts, dosage form and strength of the product | A new registration is required. |

1. **Changes to be notified to the regulatory authority and do not require prior approval.**

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| **TYPE OF CHANGE** | **REQUIREMENTS** |
| 1. Change of the material or dimensions of the secondary packaging | 1. Notice signed and stamped by the responsible professional. 2. Document issued by the owner or his Legal Representative stating the change. 3. Packaging or drafts. |
| 1. Change in the labelling of the primary or secondary packaging design | 1. Notice signed and stamped by the responsible professional. 2. Document issued by the owner or his Legal Representative stating the change. 3. Packaging or drafts. |
| 1. Discontinuation of registered submissions | 1. Notice signed and stamped by the responsible professional. 2. Document issued by the owner or his Legal Representative stating the change. |
| 1. Change in product safety information. | 1. Notice signed and stamped by the responsible professional. 2. Document issued by the owner or his Legal Representative stating the change. 3. Monograph and insert with the change indicated. |
| 1. Change or extension of dealer | 1. Notice signed and stamped by the responsible professional. 2. Legal document certifying the change or extension issued by the owner or his legal representative. |

**ANNEX 2**

**(REGULATIONS)**

**INFORMATION TO INCLUDE IN THE APPLICATION FOR REGISTRATION.**

1. Product details
   1. Name of the product.
   2. Name of the active ingredients when it contains one or two active substances.
   3. Pharmaceutical form.
   4. Route of administration.
   5. Presentation of the product.
   6. Proposed shelf-life and storage conditions.
   7. Therapeutic group.
   8. Form of sale.
   9. Product Type (innovator, multisource etc.).
   10. Registration category (new, renewal).
   11. Analytical method (Pharmacopeial and non Pharmacopeial).
   12. Reference standard, if applicable.
2. Data of the manufacturer and packager:
   1. Name(s) of the laboratory (laboratories) involved in manufacturing.
   2. Address, telephone, fax and email.
   3. Manufacturing stage.
   4. Country of manufacturer's laboratory.
   5. Health Licence Number or Permit Health for Operation and expiration date (where national).
3. Details on the owner of the product:
   1. Name
   2. Address, telephone, fax and email.
   3. Country
4. Details on the distributors:
   1. Name of the distributor(s).
   2. Address, telephone, fax and email.
   3. Health Licence Number or Permit Health for Operation and expiration date (where national).

Note: For Honduras and El Salvador, these details are optional.

1. Details of the Legal Representative:
   1. Name.
   2. ID Card number.
   3. Address, telephone, fax and email.
2. Details of the responsible professional.
   1. Name.
   2. ID Card number
   3. Address, telephone, fax and email.
   4. Pharmaceutical chemical enrolment or registration number
3. Caption to give it status of affidavit at request.

**-— END OF THE TECHNICAL REGULATIONS--**

1. COMIECO – Consejo de Ministros de Economía de Centroamérica, or Council of Ministers of Trade of Central America [↑](#footnote-ref-1)