DAJ-SM-446-2017

EXECUTIVE DECREE No. _____- S

The president of the Republic

AND THE MINISTER OF HEALTH

In use of the powers conferred by articles 11, 140 paragraphs 3), 8), 18) and 20), and 146 of the Political Constitution; 11, 25, 27 and 28 paragraph 2, subsection b) of Law No. 6227 of May 2, 1978, "General Law of Public Administration"; 1, 2, 4, 82, 112, 346, 355 and 366 of Law No. 5395 of October 30, 1973, "General Health Law"; Law No. 8279 of May 2, 2002, "National System for Quality"; Law No. 7475 of 20 December 1994, "Approval of the Final Act incorporating the Results of the the Uruguay Round of Multilateral Trade Negotiations "; Law No. 8220 of 4 March 2002, "Protection of the citizen from excess requirements and procedures administrative "; Executive Decree No. 38414 of February 28, 2014, "Public Resolution No. 333-2013 (COMIECO-LXVI) of 12/12/2013 and annexes: Reg. RTCA 11.03.59: 11 Pharmaceutical Products, Drugs for human use. Req. Reg. Sanitary Annex 1. Procedure for Mutual Recognition of Sanitary Regs medicines annex 2 ".

CONSIDERING:

1. That it is an essential function of the State to ensure the protection of the health of the population and contribute to improving the quality of pharmaceutical products that national and foreign laboratories manufacture and market in the country.

2. That the Public Administration has the responsibility to guarantee the welfare of citizens, without unnecessarily hindering the conditions of competitiveness for the development of the economic activity of the country.

3. That the Constitutional Chamber has established that the Ministry of Health has the duty to exercise effective control over the registration of medicines that will be destined the importation and internal consumption, for the treatment of illnesses and diseases. The above, in order to ensure that the drugs that are going to be marketed, comply with a registration procedure that allows establishing the quality of the product and all aspects related to the effect on the health of the people who consume them.

4. That Report 32 of the Expert Committee on Specifications for the Pharmaceutical Preparations of the World Health Organization, in point 3 and mainly, in Annex 2, establish the importance of plant inspections, in relation to Good Manufacturing Practices, noting that "the inspection and

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authorization of manufacturing facilities on the basis of compliance with the Good Manufacturing Practices constitute a vital element in the control of medicines."

5. That through Executive Decree No. 38414-COMEX-MEIC-S of 28 December February 2014, Resolution No. 333-2013 (COMIECO-LXVI) dated 12 December 2013 and its Annexes: "Central American Technical Regulation RTCA 11.03.59: 11 Pharmaceutical Products. Medicines for human use. Requirements sanitary registry ", which establishes in article 6.15 that to guarantee the quality of the medicines, the Regulatory Authorities may verify compliance with the Good Manufacturing Practices by the means they deem necessary, including the inspection at the facilities of the manufacturing laboratories established inside and outside of the Central American countries, applying Executive Decree No. 38732-S-COMEX-MEIC of July 2, 2014 that publishes Resolution No. 339-2014 (COMIECO-LXVII) of the 04/25/2014 and its Annexes: "Central American Technical Regulation RTCA 11.03.42: 07 Pharmaceutical products. Medicines For Human Use. Good practices Manufacturing for the Pharmaceutical Industry ". The Regulatory Authority may request Regulatory authorities of regional reference and strict regulatory authorities accredited by the WHO, the verification of compliance with Good Practices of Manufacture of Pharmaceutical Laboratories that they have inspected.

6. That Article 12.3 of the aforementioned Executive Decree establishes within the causes of cancellation of sanitary registration the breach of the guarantees of quality and stability stated in the file, and 12.6 also provides for any reason justified that it constitutes a foreseeable risk for the health or safety of people.

7. That all drug manufacturing laboratories, both national and international, foreigners must comply with the standards established in the current regulations of Good Manufacturing Practices, for the commercialization of said products in the National territory.

8. That there is a Convention for the Pharmaceutical Inspection and a Scheme for Cooperation for the Pharmaceutical Inspection (jointly called PIC / S for its acronyms in English) which constitute international instruments between countries and inspection authorities whose mission is to lead international development, the implementation and maintenance of harmonized BPM standards and systems of quality of inspection bodies in the field of medicines.

9. That to implement the aforementioned provision of Article 6.15 of the Regulations Central American Technician RTCA 11.03.59: 11 Pharmaceutical Products. Medicines for human use. Health registration requirements, it is necessary to develop a procedure that regulates the inspection of facilities in manufacturing laboratories.

10. That by virtue of the principles of economy, speed and efficiency, the Ministry of Health has determined that the inspection activities of Good Practices of Manufactured by both the strict regulatory authorities accredited by the WHO, as the authorities that are part of PIC / S, or those authorized third parties accredited before the Costa Rican Accreditation Entity or before another accrediting entity recognized by it, guarantee the application of a standard equal to or greater than that allowed by the Costa Rican institutional framework and regulations in this area and, in particular, the Good Manufacturing Practices in force.

11. That in accordance with the provisions of article 12 bis of the Decree Executive No. 37045 of February 22, 2012 and its amendment "Regulation to the Law of Protection of the Citizen of Excess of Requirements and Administrative Procedures ", this regulation complies with the principles of regulatory improvement, according to report No. DMR-DAR-INF-147-17 issued by the Department of Regulatory Analysis of the Regulatory Improvement Directorate of the Ministry of Economy, Industry and Commerce.

SO:

DECREE:

Article 1 - Approve the following Technical Procedure:

PROCEDURE FOR THE VERIFICATION OF THE COMPLIANCE OF THE GOOD MANUFACTURING PRACTICES OF MEDICATIONS FOR USE HUMAN.

1. OBJECTIVE

Establish the rules regarding the verification process of compliance with the Good Pharmaceutical Manufacturing Practices in order to guarantee the quality of the medicines, as one of the factors to reduce the risks associated with manufacturing.

2. SCOPE OF APPLICATION

Applies to manufacturing plants belonging to national or foreign laboratories who manufacture or market pharmaceutical products in the national territory, for effects of ensuring the quality of medicines.

3. REFERENCES

For the proper interpretation and application of this procedure you should consult the following documents:

3.1 Executive Decree N ° 38732-S-COMEX-MEIC of July 2, 2014, which publishes Resolution No. 339-2014 (COMIECO-LXVII) of April 25, 2014 and its Annexes: Central American Technical Regulation RTCA 11.03.42: 07 Pharmaceutical Products. Medicines For Human Use. Good Manufacturing Practices for the Industry Pharmaceutical

3.2 Executive Decree No. 38414-COMEX-MEIC-S of February 28, 2014, which publishes Resolution No. 333-2013 (COMIECO-LXVI) dated December 12, 2013. Central American Technical Regulation RTCA 11.03.59: 11 Pharmaceutical Products. Medicines for human use. Sanitary registration requirements.

4. DEFINITIONS

For the purposes of this procedure, the following definitions are established:

4.1 Regulatory authorities of regional reference: national regulatory authorities competent and efficient in the performance of health regulatory functions recommended by PAHO / WHO, to guarantee the quality, innocuousness and effectiveness of the medicines and biological products, described in Annex A.

4.2 Strict regulatory authorities: those defined in the prequalification process of pharmaceutical products from WHO, described in Annex B.

4.3 Regulatory authorities members of the PIC / S: those described in http://www.picscheme.org/members.php which have been accepted as part of the initiative, after successfully completing a competency assessment (Annex C).

4.4 Good Manufacturing Practices: set of procedures and standards intended for ensure the uniform production of batches of pharmaceutical products that comply with the Quality standards.

4.5 Inspection report: written document whose purpose is to describe information objective, in a clear and orderly manner, about the circumstances observed in the inspection to the drug manufacturing laboratory.

4.6 Inspection: field activity, whose objective is to verify that a laboratory

The manufacturer complies with all the elements of the Good Manufacturing Practices of the pharmaceutical industry, in force.

4.7 Inspectors: professionals with the technical knowledge and experience necessary to carry out the inspections of Good Manufacturing Practices in laboratories manufacturers, using the Verification Guides defined by the Ministry of Health.

4.8 Manufacturer laboratory: authorized entity with designed facilities, to perform all the operations that involve the manufacture of medicines.

4.9 Ministry: Ministry of Health of Costa Rica.

4.10 CIP / S: Informal cooperation agreement between Regulatory Authorities in the field of Good Manufacturing Practices for Medicinal Products for Human and Veterinary Use (BPM). It is open to any Authority that has a BPM inspection system comparable to the rest of the participating authorities.

4.11 Pharmaceutical product or medication: Simple or compound substance, natural, synthetic, or a mixture thereof, with a definite pharmaceutical form, used to diagnose, treat, prevent diseases or modify a physiological function of human beings.

4.12 Authorized Third Parties: Individuals and / or legal entities with technical competence for the health inspection, control and surveillance; who must be accredited as a unit of Inspection before the Costa Rican Accreditation Entity or other accrediting bodies previously recognized by the ECA through the recognition agreements multilateral.

5. SYMBOLS AND ABBREVIATIONS

5.1 BPM: Good Manufacturing Practices.

5.2 ECA: Costa Rican Accreditation Entity.

5.3 WHO: World Health Organization.

5.4 PAHO: Pan American Health Organization.

5.5 CIP / S: Convention for the pharmaceutical inspection and cooperation scheme for the pharmaceutical inspection (jointly named by its acronym in English).

6. PROVISIONS FOR INSPECTION.

To guarantee the quality of medicines, the Ministry of Health will be able to verify the compliance with Good Manufacturing Practices by the means that it considers necessary, including inspection at the facilities of the manufacturing laboratories established inside and outside the country by applying Executive Decree No. 38732-S-COMEX-MEIC of July 2, 2014 that publishes Resolution No. 339-2014 (COMIECO-LXVll) of 04/25/2014 and its Annexes: "Central American Technical Regulation RTCA 11 / .03.42: 07 Pharmaceutical Products. Medicines For Human Use. Good practices of Manufacture for the Pharmaceutical Industry ".

The Regulatory Authority may request the reference regulatory authorities regional and strict regulatory authorities, verification of compliance with Good Manufacturing practices of pharmaceutical laboratories that they have inspected, as support to consider the need to carry out the inspection.

6.1 Select the means to verify compliance with Good Practices of Manufacturing.

When the Ministry considers that, to guarantee the quality of medicines, it is

It is necessary to verify compliance with GMP through an inspection.

communicate to the owner of the products or to his legal representative and the manufacturing laboratory indicating the purpose, scope and methodology of the inspection, and that they must choose any of the following options:

to. Inspection by the Ministry of Health: Receive the inspection carried out by the sanitary authorities of the Ministry of Health of Costa Rica assuming the costs of the same as indicated in Annex D, in which case the Ministry must indicate the proposed period for the inspection, submitting the inspection and scope plan, the constitution of the team of inspectors and the costs and payment conditions associated with said inspection.

b. Inspection by other authorities: Submit within a period of no more than three months a certified copy of the GMP compliance inspection reports issued by the Strict Regulatory Authorities or the regulatory authorities members of the PIC / S, including the aspects indicated in the objective and scope of the Inspection notified. The inspection reports issued by these Authorities they must be the most recent available for the manufacturing laboratory. In case of have been issued outside the national territory, they must be legalized or apostilled in the country of the manufacturing site, in the country of the owner of the product or in

the country or countries of the authorities that carried out the inspection. The reports will be Accepted in Spanish or English.

In the event that the report contains information of a confidential nature that does not be known to the owner, the Ministry of Health may accept that the report

be sent directly by the manufacturing laboratory.

c. Inspection by authorized third parties: Submit within a period not exceeding three months a certified copy of the inspection report of Good Practices of Manufacture issued by an authorized third party that includes the aspects indicated in the purpose and scope of the inspection notified. Inspection reports issued by the authorized third party must not be more than one year old. issued and if they have been signed outside the national territory, they must be legalized or apostilled. The authorized third party must not have conflicts of interest with the laboratory inspected. The costs and fees for the inspection will be agreed between the authorized third party and the owner of the product or laboratory to inspect.

6.2 Communicate to the Ministry the selected alternative:

The owner of the product or his legal representative will communicate within a period no longer than 20 days the selected alternative, presenting, according to the alternative, the following Requirements:

to. Inspection by the Ministry of Health: Document signed by the representative the holder of the product, in which the commitment to cover is expressed, in a

no longer than three months after the approval according to point 6.3, the costs indicated by the Ministry for the purpose of the verification inspection of the GMP.

b. Inspection by other authorities: Document indicating the commitment of present the certified copy of the inspection report made by any of the Strict Regulatory Authorities or regulatory authorities that are members of the

PIC / S, indicating the name of the evaluating authority, the inspection period and that the result is satisfactory for the purpose and scope of the inspection notified by the Ministry according to point 6.1.

c. Inspection by authorized third parties: Document indicating the commitment of present the certified copy of the inspection report made by any of the authorized third parties, indicating the name of the authorized third party, the period of inspection and that the result is satisfactory for the purpose and scope of the inspection notified by the Ministry according to point 6.1. You must also submit a statement sworn where the authorized third party indicates the non existence of conflicts of interest with the laboratory inspected, according to Annex E.

6.3 Approval of the alternative:

The Ministry evaluates the proposed alternative and, within a period of 10 business days, will notify the administered the acceptance or not of it.

In case the Ministry rejects the alternative, it must accompany the notification with a reasoned justification, indicating the alternative (s) that proceed. In such case the managed shall have the right to appeal such a resolution in accordance with the General Law of Public administration.

6.4 Execution of the approved alternative:

To verify compliance with the BPM, the approved alternative will be applied as follows:

to. Inspection by the Ministry of Health: The inspection must be carried out according to what is established in the inspection plan and the term indicated by the Ministry and following the GMP verification guide established in the "Regulation Central American Technician RTCA 11 / .03.42: 07 Pharmaceutical Products.

Medicines For Human Use. Good Manufacturing Practices for the Industry Pharmaceutical ", and the procedure MS.NI.FIMPR.02.02.25 Good Inspection Manufacturing practices to drug manufacturing laboratories.

b. Inspection by other authorities: The inspection must be in accordance with the objective and the scope of the inspection requested by the Ministry of Health and the report of the must clearly demonstrate compliance with the Good Practices of Manufacturing of said authority.

c. Inspection by authorized third parties: The inspection must be in accordance with the objective and the scope of the inspection requested by the Ministry of Health and the report of the must clearly demonstrate compliance with the Good Practices of Manufacturing according to the BPM verification guide established in the "Regulation Central American Technician RTCA 11 / .03.42: 07 Pharmaceutical Products. Medicines For Human Use. Good Manufacturing Practices for the Industry Pharmaceutical. "

6.5 Approval of inspection reports.

Upon completion of the inspection or review of the documentation provided, the Ministry has a term of 20 business days to issue the corresponding resolution.

6.6. Verification of remedial plans.

After the issuance of the resolution, in case the Ministry requests the presentation of a remedial plan to correct the non-conformities found, the owner of the product or your legal representative will have fifteen working days for the presentation of said plan, the which will be revised to be approved or rejected by the Ministry in the fifteen days skilled after its reception. If necessary, the Ministry may perform a new verification to verify compliance with the commitments established in the approved remedial plan, applying what is established in this

Regulation.

7. APPLICATION OF SANITARY MEASURES.

7.1 In case of failure to comply with the approval criteria established in the regulations current and in case such breach involves any critical criteria, the Ministry may suspend the sanitary registration of the products manufactured in said plant of the laboratory manufacturer, under the scope of the inspection carried out until it demonstrates that has corrected the nonconformities found in the inspection.

7.2 In case of persisting the breach of quality guarantees as indicated in the previous point, generating a foreseeable risk for the health or safety of persons, the Ministry will proceed to cancel the medical records of the medicines manufactured in said plant.

7.3 In the event that for reasons attributable to the manufacturer, the Ministry can not carry out the inspection or receipt of satisfactory reports and when doubt persists on the guarantees of quality or a foreseeable risk to the health or safety of people, we will proceed

suspend the sanitary registries of the medicines elaborated by said plant of the laboratory until the situation is corrected.

ANNEX A
(Informative)

PAHO Level IV Authorities

1. ANMAT: National Administration of Drugs, Food and Technology Medical (Argentina)
2. ANVISA: National Health Surveillance Agency (Brazil)
3. COFEPRIS: Federal Commission for Protection against Health Risks (Mexico)
4. INVIMA: National Institute for Drug and Food Surveillance (Colombia)
5. ISP: Institute of Public Health (Chile)

6. CEMCED: Center for State Control of Drugs, Equipment and Devices

Doctors (Cuba)

Note: This list may vary depending on the updates made by PAHO.

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ANNEX B
(Informative)

Strict regulatory authorities.

1. EMA. European Medicines Agency

2. FDA. Food and Drug Administration of the United States of America

3. Ministry of Health, Labor and Welfare of Japan

4. Swissmedic: Swiss Agency for Therapeutic Products.

5. Health Canada.

6. TGA: Therapeutic Products Administration of Australia.

7. IMCA: Icelandic Agency for the Control of Medicines.

8. Norwegian Agency of Medicines.

9. Health Office / Department of Medicines of Liechtenstein

Note: This list may vary according to the updates made by WHO.

Annex C.

(Informative)

Regulatory authorities members of the PIC / S.

1. ANMAT: National Institute of Medicines of Argentina. National Institute of Medications (INAME).
2. TGA: Australian Therapeutic Goods Administration. Department of Health Office of Manufacturing Quality
3. AGES: Austrian Medicines and Medical Devices Agency. Österreichische Agentur für Gesundheit und Ernährungs-sicherheit.
4. AFMPS: Belgian Federal Agency for Medicines and Health Products. Agence Fédérale des Médicaments et des Produits de Santé. Federal Agentschap voor Geneesmiddelen in Gezondheidsproducten (FAGG).

5. Health Canada: Canadian Health Products and Food Branch Inspectorate (HPFBI).

6. TFDA: Taiwan Food and Drug Administration. Department of Health

7. HALMED: Agency for Medicinal Products and Medical Devices of Croatia. Agencija za lijekove i medicinske proizvode.

8. CyPHS: Cypriot Pharmaceutical Services. Ministry of Health.

9. SÚKL: Czech State Institute for Drug Control. Státní Ústav pro Kontrolu Léčiv.

10. ISCVBM: Czech Institute for State Control of Veterinary Biologicals and Medicines

11. DHMA: Danish Health and Medicines Authority.

12. SAM: Estonian State Agency of Medicines.

13. FIMEA: Finnish Medicines Agency. Finland

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14. ASNM: French National Agency for Medicines and Health Products Safety. Agence Nationale de sécurité du medicament et des produits de santé (ANSM)

15. ANSES: French Agency for Food, Environmental & Occupational Health Safety. Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail

16. BMG: German Federal Ministry of Health. Bundesministerium für Gesundheit (BMG)

17. ZLG: Central Authority of the Laender for Health Protection regarding Medicinal Products and Medical Devices. Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten, comprising:

Baden-Württemberg, Bayern,

Berlin, Brandenburg, Bremen, Hamburg, Hessen,

Mecklenburg-Vorpommern, Niedersachsen,

Nordrhein-Westfalen, Rheinland-Pfalz, Saarland,

Sachsen, Sachsen-Anhalt, Schleswig-Holstein, Thüringen

18. EOF: Greek National Organization for Medicines. Εθνικός Οργανισμός Φαρμάκων (EOF)
19. PPBHK: Pharmacy and Poisons Board of Hong Kong.
20. NIPN: Hungarian National Institute of Pharmacy and Nutrition.
21. IMA: Icelandic Medicines Agency.
22. NADFC: Indonesian National Agency for Drug and Food Control. Badan Pengawas Obat dan Makanan Republik Indonesia.
23. HPRA: Health Products Regulatory Authority. Ireland

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24. ISCP: Israeli Institute for Standardization and Control of Pharmaceuticals.
25. AIFA: Italian Medicines Agency, Italian Agenzia del Farmaco.
26. MHLW: Japanese Ministry of Health, Labor and Welfare.
27. PMDA: Japanese Pharmaceuticals and Medical Devices Agency.
28. MFDS: Korea Republic of Ministry of Food and Drug Safety.
29. ZVA: State Agency of Medicines of the Republic of Latvia.
30. AG: Liechtenstein's Office of Healthcare. Amt für Gesundheit.
31. SMCA: Lithuanian State Medicines Control Agency.
32. NPCB: Malaysian National Pharmaceutical Control Bureau (NPCB)
33. MAM: Maltese Medicines Authority.
34. IGZ: Dutch Health Care Inspectorate. Inspectie voor de Gezondheidszorg (IGZ)
35. Medsafe: New Zealand's Medicines and Medical Devices Safety Authority.
36. NOMA: Norwegian Medicines Agency.
37. MPI: Polish Main Pharmaceutical Inspectorate.
38. INFARMED IP: Portuguese National Authority of Medicines and Health Products,

IP

39. National Autoridade do Medicamento e Produtos de Saúde IP.

40. NAMMD: Romanian National Agency for Medicines and Medical Devices.

41. HAS: Singapore's Health Sciences Authority.

42. SIDC: Slovak State Institute for Drug Control.

43. JAZMP: Slovenian Agency for Medicinal Products and Medical Devices. Javna agencija Republike Slovenije za zdravila in medicinske pripomočke.

44. MCC: South African Medicines Control Council.

45. AEMPS: Spanish Agency for Medicines and Health Products (AEMPS)

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46. MPA: Swedish Medical Products Agency.

47. Swissmedic: Swiss Agency for Therapeutic Products.

48. SAUMP: Ukrainian State Administration on Medicinal Products.

49. MHRA: Medicines and Healthcare products Regulatory Agency.

50. US FDA: US Food and Drug Administration.

Annex D.

(Normative)

Conditions for conducting GMP inspections by the Ministry of Health of Costa Rica

The manufacturing laboratories inspected by the Ministry will cover the costs corresponding to carry out the inspections. Such amounts will be governed by Law regulator of travel expenses and transportation expenses for all State officials, Law No. 3462 of November 26, 1964, and the Regulations of the Travel and Transportation Expenses for current public officials issued by the General Comptroller of the Republic and must be deposited in the account in dollars or colones of Trust 872-3, MINISTRY OF HEALTH, CTAMS-BNCR, within a no longer than 1 month for laboratories located in the country and no longer than 3 months for foreign laboratories, from the notification of the resolution of the beginning of the inspection process.

The bank accounts of the Ministry of Health Trust - CTAMS - Banco Nacional de Costa Rica, in which must be deposited for inspections of laboratories located in national territory or foreigners, as the case may be, are the following:

1. Account in colones 000-213715-6 Trust 872-BNCR-Ministry of Health.

2. Account in US dollars 000-617477-5 Trust 872-BNCR-

Ministry of Health.

If the manufacturing laboratory plant is located outside the country, air tickets they must be provided by the latter after approval of the itinerary by the Ministry.

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The laboratory must have a translator who facilitates the inspection when the language in the country where the laboratory is located, it is different from Spanish. You must also submit all its operating procedures, manufacturing guidelines, analytical techniques and any another technical document that is required within the scope of the inspection, in language Spanish or English.

2. 3

Annex E.

(Normative)

Format of the Affidavit of Non-Conflict of Interest

AFFIDAVIT OF NON-CONFLICT OF INTEREST

I _____ with identification number

_____, as an INSPECTOR ACCREDITED AS A UNIT OF

INSPECTION BEFORE THE COSTARRICIAN ENTITY OF ACCREDITATION (ECA) OR

BEFORE ANOTHER ACCREDITING ENTITY RECOGNIZED PREVIOUSLY BY THE

ECA THROUGH MULTILATERAL RECOGNITION AGREEMENTS, FOR

PERFORM INSPECTIONS TO VERIFY THE COMPLIANCE OF THE

GOOD MANUFACTURING PRACTICES FOR MEDICINES established in

the current regulations in Costa Rica, I declare that during the time that I am

developing the functions that correspond to me:

• I declare that I do not have any real, potential or potential conflict of interest situation

evident, including any financial or other interest or other relationship, with the

establishment to be inspected called _____.

• I agree to inform the Ministry of any change in the circumstances

previous

I hereby accept and agree to the conditions and provisions contained in

this document, knowing the legal responsibilities that may be incurred by

its non-compliance

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PLACE AND DATE:

NAME AND SIGNATURE:

Article 2 - Governing from six months after its publication.

Given in the Presidency of the Republic. San José, on the thirteenth day of the month of November two thousand seventeen.

LUIS GUILLERMO SOLÍS RIVERA

DRA. KAREN MAYORGA QUIRÓS
MINISTER OF HEALTH