NORMATIVE INSTRUCTION – IN NO. 292 OF 2 MAY 2024

Provides for the specific criteria and procedures to define the Equivalent Foreign Regulatory Authorities for the process of health inspection of manufacturers of active pharmaceutical ingredients, Cannabis products for medicinal purposes, medicinal products, and biological products, as well as the optimized analysis procedure for the purposes of Good Manufacturing Practices Certification.

The Collegiate Board of Directors of the Brazilian Health Regulatory Agency, in the use of the attributions vested in it under Article 7, item III, and Article 15, items III and IV, of Law no. 9,782 of 26 January 1999, and considering the provisions of Article 187, item VII, and Paragraph 1 of the Internal Regulation approved by Collegiate Board Resolution – RDC no. 585 of 10 December 2021, adopts the following Normative Instruction, as decided upon in a meeting held on 30 April 2024, and I, the acting Director-President, determine its publication.

CHAPTER I

INITIAL PROVISIONS

Section I

Objective and Scope

Article 1. This Normative Instruction establishes, in accordance with Collegiate Board Resolution – RDC no. 741 of 10 August 2022:

I – the specific criteria and procedures to define the Equivalent Foreign Regulatory Authorities (EFRA) for the purposes of health inspection and Good Manufacturing Practices Certification (GMPC) of active pharmaceutical ingredients (APIs), Cannabis products for medicinal purposes, medicinal products, and biological products; and

II – the levels of regulatory reliance and criteria to apply the optimized analysis procedure for applications for API GMPC, Cannabis products for medicinal purposes, medicinal products, and biological products.

Section II

Definitions

Article 2. For the purposes of this Normative Instruction, the following definitions are adopted:

I – Health inspection: set of technical and administrative procedures that aim at the protection of individual and collective health, through *in loco* (or, in specific cases, remote) verification of compliance with health legal and regulatory benchmarks relating to the activities developed and the health conditions of facilities, processes, and products. Inspection allows the adoption of guidance measures and correction of situations that may cause damages to the population's health; and

II – Regulatory Reliance Building Program: set of stages aiming at strengthening regulatory reliance with the view to assess the regulatory equivalence between Anvisa and another EFRA, with the purpose of moving towards a Mutual Recognition Agreement – MRA.

CHAPTER II

SPECIFIC CRITERIA AND PROCEDURES TO DEFINE AN EQUIVALENT FOREIGN REGULATORY AUTHORITY AND LEVELS OF REGULATORY RELIANCE

Section I

EFRA DESIGNATION BY ANVISA

Article 3. Foreign authorities or entities are established as EFRAs, for the purposes of health inspection and Good Manufacturing Practices Certification (GMPC) of active pharmaceutical ingredients (APIs), Cannabis products for medicinal purposes, medicinal products, and biological products, provided they meet the following requirements:

I – to be regulatory authorities or entities members of the Pharmaceutical Inspection Cooperation Scheme (PIC/S); and

II – to be regulatory authorities or entities members of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

Sole paragraph. The European Medicines Agency (EMA), in the position of PIC/S Associated Partner Organization, with Guides recognized as equivalent, shall be considered as PIC/S member for the purposes of this Normative Instruction.

Article 4. The designation of EFRA with Mutual Recognition Regulatory Reliance shall be decided by Anvisa Collegiate Board, which shall consider the reports developed by the technical area officially responsible for inspecting and issuing the Good Manufacturing Practices Certification, as well as by Anvisa International Affairs Office.

Paragraph 1. The EFRAs with Mutual Recognition Regulatory Reliance approved by Anvisa Collegiate Board are listed in the Annex of this Normative Instruction.

Paragraph 2. The Annex referred to in Paragraph 1 shall be updated in accordance with the regulatory flow and procedures for regular update issues.

Article 5. Anvisa Collegiate Board may, at any time, revise and/ or revoke the designation of EFRAs with Mutual Recognition Regulatory Reliance of any foreign regulatory authority, based on a report by the technical area responsible for issuing the Good Manufacturing Practices Certification.

Sole paragraph. The technical area responsible for issuing the Good Manufacturing Practices Certification shall make qualified inspectors available to participate in the process to reassess the PIC/S member designated as EFRA, which Anvisa has a Mutual Recognition Agreement with, in the scope of PIC/S Reassessment Program.

Section II

Levels of Regulatory Reliance

Article 6. For the purposes of applying the optimized analysis procedure to Good Manufacturing Practices Certification, the following levels of regulatory reliance may be adopted:

I – partial;

II – full; and

III – mutual recognition.

Paragraph 1. The Partial Regulatory Reliance established in item I is the optimized analysis procedure, in which the decision for the purposes of compliance with the GMP is based on the complete review of the inspection report or on other information from another EFRA, and it may be adopted unilaterally by Anvisa, in accordance with specific internal procedures.

Paragraph 2. The Full Regulatory Reliance established in item II is the optimized analysis procedure, in which the decision for the purposes of compliance with the GMP is based on the simplified review of the inspection report or on the acceptance of part or the whole of the GMP certificate originated from another EFRA, and it may be adopted unilaterally by Anvisa, in accordance with specific internal procedures.

Paragraph 3. The Mutual Recognition established in item III is the practice of regulatory reliance, in which the decision of another regulatory authority or international entity is automatically adopted by Anvisa based on the GMP certificate or on the inspection report originated from another EFRA. It must be adopted bilaterally by Anvisa and the EFRA through a MRA signed after the Regulatory Reliance Building Program is completed.

Section III

Regulatory Reliance Building Program

Article 7. The Regulatory Reliance Building Program is comprised of the following stages:

I – sharing of information on the work process related to health inspections;

II – conduction of concomitant parallel inspection; and

III – planning of periodic joint inspections.

Paragraph 1. The technical area responsible for issuing the GMPC may decide to remove stages from, or include stages in the program, due to the bilateral relationship with the foreign regulatory authority at issue.

Paragraph 2. At the end of each program, the technical area responsible for issuing the GMPC must elaborate a technical report including the process report and conclusion on the equivalence of the health inspection process.

Paragraph 3. The concomitant parallel inspection may be replaced by the participation of qualified inspectors in the process to reassess the PIC/S member applying to the status of EFRA for the Mutual Recognition level, in the scope of PIC/S Reassessment Program.

Section IV

Mutual Recognition Agreements

Article 8. The practice of regulatory reliance at a Mutual Recognition level must be formalized through the signature of an MRA between Anvisa and the EFRA.

Article 9. The mutual regulatory reliance agreements must provide for:

I – prohibition of the regulatory reliance practice of EFRA decisions based on regulatory reliance with third parties;

II – acceptance of inspections carried out by Brazilian Health Surveillance System entities and PIC/S members in Brazilian and foreign territories; and

III – agreement scope, protection of confidential information, points of contact for the exchange of information and documents between the parties, safeguard for inspections, provisions on entry into force, review, and termination of the agreement.

CHAPTER III

OPTIMIZED ANALYSIS PROCEDURE

Article 10. The optimized analysis procedure is based on the assessment of inspection reports or GMP certificates, as well as on the whole regulatory documentation issued by the EFRAs.

Article 11. The optimized analysis procedure provided for in this Normative Instruction is optional and must be applied for with a specific subject code.

Paragraph 1. Applications for GMPC through the optimized analysis procedure must be submitted with the documents established in the specific subject code.

Paragraph 2. The manufacturing establishment applying for certification is allowed to submit directly to Anvisa the documents it acknowledges as confidential.

Paragraph 3. The period to submit the documents provided for in Paragraph 2 is up to 30 (thirty) days after the date the certification application was submitted.

Paragraph 4. The non-submission of the regulatory documents provided for in the subject code shall lead to rejection of the application.

Paragraph 5. The company is not allowed to apply for subject code alteration from optimized analysis procedure to ordinary analysis.

Paragraph 6. Anvisa may adopt the optimized analysis procedure in situations where it has access to the regulatory documentation issued by the EFRAs.

CHAPTER IV

FINAL PROVISIONS

Article 12. Anvisa technical area responsible for issuing the GMPC shall decide on the certification.

Article 13. Anvisa technical area responsible for issuing the GMPC may, at any time, carry out a routine health inspection or a health inspection for the purposes of investigation of a complaint or possible irregularities in any manufacturer of APIs, Cannabis products for medicinal purposes, medicinal products, and biological products used in Brazil, regardless of the certification process and level of regulatory reliance.

Sole paragraph. Refusal to receive Anvisa's inspectors may result in alteration of decision, request of additional evidence, and any other health measure necessary, without prejudice to the other applicable legal measures.

Article 14. The provisions in this Normative Instruction do not hinder the adoption of other regulatory reliance practices already established by previous normative rules or collaborative work based on agreements already signed or agreements in progress.

Article 15. This Normative Instruction enters into force on 3 June 2024.

RÔMISON RODRIGUES MOTA

Acting Director President

ANNEX

EQUIVALENT FOREIGN REGULATORY AUTHORITY FOR THE PURPOSES OF HEALTH INSPECTION AND GOOD MANUFACTURING PRACTICES CERTIFICATION (GMPC)

Jurisdiction and Authority

1. Austria – Austrian Federal Office for Safety in Healthcare;

2. Belgium – Federal Agency for Medicines and Health Products;

3. Bulgaria – Bulgarian Drug Agency (BDA);

4. Canada – Heath Canada (HC);

5. Croatia – Agency for Medicinal Products and Medical Devices of Croatia (Halmed);

6. Cyprus – Pharmaceutical Services (CyPHS);

7. Czech Republic – State Institute for Drug Control (SÚKL) and Institute for State Control of Veterinary, Biologicals and Medicines (ISCVBM);

8. Denmark – Danish Medicines Agency (DKMA);

9. Estonia – State Agency of Medicines (SAM);

10. European Union – European Medicines Agency (EMA);

11. Finland – Finnish Medicines Agency (FIMEA);

12. France – French National Agency for Medicines and Health Products Safety (ANSM) and Agency of Food, Environmental & Occupational Health Safety (ANSES);

13. Germany – Federal Ministry of Health (BMG) and Central Authority of the Laender for Health Protection regarding Medicinal Products and Medical Devices (ZLG);

14. Greece – Greek National Organisation for Medicines (EOF);

15. Hungary – National Center for Public Health and Pharmacy (NCPHP);

16. Iceland – Iceland Medicines Agency (IMA);

17. Ireland – Health Products Regulatory Authority (HPRA);

18. Italy – Italian Medicines Agency (AIFA);

19. Japan – Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA);

20. Latvia – State Agency of Medicines (ZVA);

21. Liechtenstein – Office of Healthcare (AG);

22. Lithuania – State Medicines Control Agency (SMCA);

23. Malta – Malta Medicines Authority (MMA);

24. Mexico – Federal Commission for the Protection Against Sanitary Risks (COFEPRIS);

25. Norway – Norwegian Medical Products Agency (NOMA);
26. Poland – Chief Pharmaceutical Inspectorate (CPI);
27. Portugal – National Authority of Medicines and Health Products, IP (Infarmed, IP);
28. Romania – National Agency for Medicines and Medical Devices of Romania (NAMMDR);
29. Saudi Arabia – Saudi Food and Drug Authority (SFDA);
30. Singapore – Health Sciences Authority (HSA);
31. Slovakia – State Institute of Drug Control (SIDC);
32. Slovenia – Agency for Medicinal Products and Medical Devices (JAZMP);
33. South Korea – Ministry of Food and Drug Safety (MFDS);
34. Spain – Spanish Agency of Medicines and Medical Devices (AEMPS);
35. Sweden – Swedish Medical Products Agency (MPA);
36. Switzerland – Swiss Agency for Therapeutic Products (Swissmedic);
37. Taiwan – Taiwan Food and Drug Administration (TFDA);
38. The Netherlands – Health and Youth Care Inspectorate (IGJ);
39. Turkey – Turkish Medicines and Medical Devices Agency (TMMDA or TITCK);
40. United Kingdom – Medicines & Healthcare Products Regulatory Agency (MHRA);
41. United States of America – US Food and Drug Administration (US FDA); and
42. Ukraine – State Service of Ukraine on Medicines and Drugs Control (SMDC).