COLLEGIATE BOARD RESOLUTION – RDC NO. 750 OF 6 SEPTEMBER 2022

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Establishes the temporary optimized analysis procedure, which uses the assessments carried out by an Equivalent Foreign Regulatory Authority for the verified analysis of applications for marketing authorization and post-marketing authorization for medicinal products, biological products, and their inputs, as well as the active pharmaceutical ingredient dossier adequacy letter (CADIFA, in Portuguese), submitted to Anvisa after Law no. 13,411 of 28 December 2016 entered into force.

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 in Article 187, item VI, and paragraphs 1 and 3 of Anvisa Regulation approved pursuant to Collegiate Board Resolution – RDC no. 585 of 10 December 2021, adopts the following Resolution, as decided upon in a meeting held on 31 August and 1 September 2022, and I, Director-President, determine its publication.

CHAPTER I

INITIAL PROVISIONS

Section I

Objectives and Scope

Article 1. This Resolution establishes the criteria and temporary procedures for the purposes of analysis and decision making with regards to applications for marketing authorization and post-marketing authorization for medicinal products and biological products and their active substances, as well as the active pharmaceutical ingredient dossier adequacy letter (CADIFA, in Portuguese), by using the analyses carried out by an Equivalent Foreign Regulatory Authority (EFRA), submitted to Anvisa after Law no. 13,411 of 28 December 2016 entered into force.

Article 2. The temporary optimized analysis procedure is applicable to active pharmaceutical ingredients (APIs), medicinal products, and biological products approved by an EFRA.

Sole paragraph. This Resolution does not apply to applications regarding:

I – marketing authorization for vaccines;

II – medicinal products and biological products, and their active substances, submitted with a safety and efficacy report including clinical studies completed up to phase II or with phase III in progress, still without a final analysis of primary endpoints.

Article 3. The temporary optimized analysis procedure is applicable to requests for marketing authorization and post-marketing authorization for medicinal products and biological products and their active substances, as well as the related CADIFA, which are under analysis or awaiting for analysis, and to the applications that shall be submitted to Anvisa during the effect of this Resolution.

Paragraph 1. The procedure set forth in the caption of this article is applicable to part of the marketing authorization or post-marketing authorization dossier that has not yet been object of technical requirement.

Paragraph 2. For the applications that had their analyses started before the submission of the addition provided for in this Resolution, Anvisa may adopt the temporary optimized analysis procedure for the part of the process that has not yet started to be analyzed.

Paragraph 3. In the case provided for in Paragraph 2, when the temporary optimized analysis procedure is not adopted, the application shall be analyzed through the ordinary analysis.

Section II

Definitions

Article 4. For the purposes of this Resolution, the following definitions are adopted:

I – Equivalent Foreign Regulatory Authority (EFRA): foreign regulatory authority or international organization with regulatory practices aligned with Anvisa's, which is responsible for ensuring that the products authorized for distribution were appropriately assessed and meet recognized standards of quality, safety, and efficacy, and which shall be considered by Anvisa in a practice of regulatory reliance;

II – Verified analysis: assessment of a regularization petition based on observing the applicability of results from an EFRA's assessment, for regulatory decision making in the Brazilian context, including analyses related to legal and regulatory matters, risk-benefit assessment, comorbidities, unmet medical needs, risk management plans, and any quality specificities. The documents and studies that are specific for the Brazilian context, including evidence related to differences in the target population, epidemiology, and other characteristics of the disease, medicinal products used concomitantly, and other factors that may significantly affect the risk-benefit profile of a product, as well as specific quality parameters, are submitted to ordinary analysis;

III – Essential characteristics: attributes of the medicinal product and of the biological product that include their manufacturers, qualitative and quantitative composition, concentration, pharmaceutical form, therapeutic indications, contraindications, posology, target population, administration route, usage, specifications, manufacturing process and the respective production plants involved, API manufacturers, and API and excipient quality levels;

IV – Regulatory documentation: reports, opinions, or technical/ legal documents of decision-making, auxiliary, or opinionative nature provided for in the Equivalent Foreign Regulatory Authority's own regulatory instrument, which can be used by Anvisa in the temporary optimized analysis procedure;

V – Active pharmaceutical ingredient (API): any substance introduced into the formulation of a pharmaceutical form that, when administered to a patient, acts as an active ingredient, and may exert pharmacological activity or another direct effect on the diagnosis, cure, treatment, or prevention of a disease, and may also affect the structure and functioning of the human organism;

VI – Temporary optimized analysis procedure: technical assessment mechanism facilitated by regulatory reliance practices, which uses the regulatory documentation issued by an Equivalent Foreign Regulatory Authority, established in this Resolution on a temporary basis, until a definitive optimized analysis procedure is established;

VII – Active substance: biological active pharmaceutical ingredient that can be subsequently formulated for the manufacture of a particular biological product;

VIII – Ordinary analysis: assessment of a regularization application based on the requirements provided for in the applicable Collegiate Board Resolutions – RDCs, without the systematized use of regulatory documentation issued by an EFRA;

IX – Regularization: authorization for an API, medicinal product, or biological product to be manufactured, distributed, commercialized, dispensed, and consumed. Health regularization occurs through health marketing authorization or issuance of CADIFA, and includes the alterations made after the initial approval.

CHAPTER II

RECOGNIZED EFRAs

Article 5. For the purposes of adoption of the temporary optimized analysis procedure, the following EFRAs are considered:

I – European Medicines Agency – EMA (centralized analyses processes): applicable to medicinal products and biological products;

II – Health Canada: applicable to medicinal products and biological products;

III – World Health Organization – WHO: applicable to APIs and medicinal products;

IV – European Directorate for the Quality of Medicines & HealthCare – EDQM: applicable to APIs;

V – Swiss Agency for Therapeutic Products – Swissmedic: applicable to medicinal products;

VI – Medicines and Healthcare Products Regulatory Agency – MHRA, United Kingdom: applicable to medicinal products and biological products;

VII – US Food and Drug Administration – FDA: applicable to medicinal products and biological products.

CHAPTER III

GENERAL REQUIREMENTS FOR THE ADOPTION OF THE TEMPORARY OPTIMIZED ANALYSIS PROCEDURE OF APPLICATIONS

Article 6. For the purposes of assessment and decision making on the regularization of APIs, medicinal products, biological products, and their active substances, the temporary optimized analysis procedure may be used, as long as:

I – the requesting company presents the regulatory documentation issued by the EFRA, in accordance with Article 8 of this Resolution;

II – the requesting company presents a statement signed by its legal and technical responsible officers, in the terms of Annex I or Annex II of this Resolution;

III – all conditions established in this Resolution and its annexes are complied with.

Article 7. The temporary optimized analysis procedure for APIs, medicinal products, biological products, and their active substances may be used for regularization applications that meet the following requirements:

I – the API, medicinal product, or biological product and their active substances must not have been object of recall, cancellation of marketing authorization or regularization, suspension of manufacturing, or suspension of commercialization in the countries where the product is regularized, in the last 3 (three) years, in accordance with the statement presented in Annex I or Annex II of this Resolution;

II – the API, medicinal product, or biological product and their active substances must have been approved by at least one of the EFRAs listed in Article 5 of this Resolution;

III – the API, medicinal product, or biological product and their active substances must not have been rejected by any of the EFRAs listed in Article 5 of this Resolution;

IV – the regulatory documentation issued by the recognized EFRA must include enough technical and scientific information for the assessment of the API, medicinal product, or biological product and their active substances in the terms of this Resolution;

V – the manufacturers must not have a history of interdiction by the health authority of their country due to incompliance with health requirements, or of restrictive measures by Anvisa or the regulatory authorities listed in Article 5 of this Resolution, in the last 3 (three) years, in accordance with the statement presented in Annex I or Annex II of this Resolution;

Sole paragraph. If the quality assessment of the product has already been approved by Anvisa, item V shall not be required.

Article 8. The EFRA regulatory documentation submitted to support the regularization application for the API, medicinal product, or biological product and their active substances at Anvisa through the temporary optimized analysis procedure must:

I – include updated data and information that ensure the medicinal product or biological product and their active substances have essential characteristics equivalent to the ones approved by the EFRA, also regarding their quality aspects;

II – have been developed in accordance with standards equivalent to the ones adopted by Anvisa, in order to ensure it has the same scope;

III – be able to identify the quality level of the API, medicinal product, or biological product;

IV – be submitted in its entirety, without any essential information for Anvisa’s analysis being censored or omitted;

V – not be subject to use restriction by Anvisa;

VI – allow to conclude that the manufacturing process assessed by the EFRA is equivalent to the one being submitted to Anvisa;

VII – describe the data from clinical and non-clinical evidence supporting the EFRA's decision, in a way to allow for the conclusion that it is the same evidence presented to Anvisa; and

VIII – include the insert package text approved by the EFRA.

Paragraph 1. Eventual differences among non-essential characteristics of the API, medicinal product, or biological product and their active substances in relation to the one approved by the EFRA must be identified and technically justified, and the potential impact on the product's safety, efficacy, and quality must be assessed by the company.

Paragraph 2. In the cases where the justification referred to in Paragraph 1 is presented, Anvisa shall decide if the temporary optimized analysis procedure may be applied to the request.

Article 9. In the cases where the API, medicinal product, or biological product is approved by more than one of the EFRAs listed, the applicant may designate the EFRA to be used as reference for the temporary optimized analysis procedure.

Paragraph 1. The regulatory documentation issued by the designated EFRA must be enough to confirm the provisions in Article 8.

Paragraph 2. The regulatory documentation issued by another EFRA may be partially or totally submitted to Anvisa for the purposes of complementing the confirmation referred to in Paragraph 1 of this Article.

Paragraph 3. In case of differences among the use conditions (indication, dosage, route of administration, and target population) approved by the EFRAs, the applicant must discuss the differences on a technical basis and justify the designation of the EFRA used as reference.

CHAPTER IV

ASSESSMENT THROUGH THE TEMPORARY OPTIMIZED ANALYSIS PROCEDURE

Section I

General requirements

Article 10. The application for regularization of an API, medicinal product, or biological product and their active substances through the temporary optimized analysis procedure must be submitted with all documents and information established in the specific regulation in force for its respective regulatory category.

Article 11. In the cases where the applicant does not have access to the regulatory documentation, the company may request the EFRA to send the pertinent regulatory documentation to Anvisa.

Paragraph 1. The applicant is exclusively responsible for the actions provided for in the caption of this article.

Paragraph 2. If the pertinent documentation is not sent by the EFRA, the documentation submitted shall be assessed through ordinary analysis.

Article 12. Anvisa may issue a technical requirement requesting clarifications on the documents and information submitted by the applicant.

Section II

Specific addendum

Article 13. For the purposes of adopting the temporary optimized analysis procedure, the applicant must attach a specific addendum to the application, including the following:

I – copy of the checklist completed, available in Annex I of this Resolution, when related to medicinal products or biological products;

II – copy of the checklist completed, available in Annex II of this Resolution, when related to APIs;

III – proof of regularization granted by the EFRA, in force at the moment of the application;

IV – list containing all documents submitted in the initial application and the specific addendum, differentiating the ones previously assessed by the EFRA from those produced for the Brazilian context;

V – regulatory documentation in compliance with the provisions of Article 8; and

VI – report including the documentation assessment provided for in Article 8 and also confirming that the medicinal product or biological product and their active substances, object of the regularization application, have essential characteristics equivalent to the ones approved by the EFRA.

Paragraph 1. The report referred to in item VI of the caption of this article, developed by the company, shall be considered public.

Paragraph 2. The applicant must identify the parts of the report referred to in item VI of the caption of this article that contain restricted information, as provided for in Law no. 12,527 of 18 November 2011.

Paragraph 3. The company's technical assessment report must be presented in Portuguese, through electronic petitioning, in editable format, in a way to allow for text search and copy.

Article 14. The applications with specific addendum for the adoption of the temporary optimized analysis procedure, and which comply with the criteria established in this Resolution, shall be submitted to verified analysis by Anvisa.

Paragraph 1. Anvisa, when analyzing the regulatory documentation issued by the EFRA, may choose to apply the ordinary analysis procedure to part of the documents submitted or the whole documentation presented.

Paragraph 2. Anvisa's technical units responsible for analyses, when having access to documents and reports issued by the EFRA, may choose to apply the temporary optimized analysis procedure to assess applications already submitted, recording the adoption of such approach in the respective process.

Article 15. In order to request the adoption of the temporary optimized analysis procedure, the company must attach a specific addendum to the regularization application, including the documents listed in Article 13.

Paragraph 1. The temporary optimized analysis procedure shall be applied to all applications that have the specific addendum submitted up to the date this Resolution becomes ineffective and that comply with the requirements accordingly.

Paragraph 2. A list with the regularization applications with specific addenda submitted, referred to in the caption of this article, shall be published on a monthly basis.

Paragraph 3. Adoption of the temporary optimized analysis procedure shall not imply an alteration of the chronological order of applications.

CHAPTER V

MONITORING

Article 16. Anvisa's areas responsible for regularization, inspection, and pharmacovigilance of medicinal products and biological products may adopt additional strategies to monitor the APIs, medicinal products, biological products, and their active substances approved through the temporary optimized analysis procedure.

Sole paragraph. The following are considered monitoring strategies: process audits, follow-up of information referring to safety profile, based on national and international warnings, amongst other measures that may contribute towards maintaining the conditions approved in the marketing authorization.

Article 17. The applications that are object of the temporary optimized analysis procedure, in the terms of this Resolution, may be assessed in their entirety by Anvisa at any time, which may result in alteration of decision, request of additional evidence, recall of batches, suspension of manufacturing and/ or commercialization, and cancellation of API regularization, or cancellation of the marketing authorization for the medicinal product or biological product, as well as other legal applicable measures.

CHAPTER VI

FINAL AND TRANSITIONAL PROVISIONS

Article 18. Failure to comply with the provisions contained in this Resolution constitutes a health infraction, and the offender is subject to lawsuit and penalties provided for in Law no. 6,437 of 20 August 1977, or legal instrument substituting it, without prejudice to the applicable criminal and civil liabilities.

Article 19. The temporary optimized analysis procedure established in this Resolution maintains Anvisa's decision-making autonomy, the decisions of which may be taken regardless of the decisions and conditions approved by the EFRAs.

Article 20. A conditional approval shall be published referring to the post-marketing authorization application in the following conditions:

I – if there is the specific addendum provided for in this Resolution approved by the technical area;

II – if the period and period extension, established in Law no. 13,411 of 28 December 2016, are overdue; and

III – if there is no manifestation by Anvisa within 90 (ninety) days, after the submission of the addendum provided for in item I of this Article.

Sole paragraph. The conditional approval referred to in the caption of this article may be reversed automatically, at any time, and in case of rejection of post-marketing authorization alteration.

Article 21. The areas responsible for the marketing authorization of medicinal products and biological products must publish Resolutions regarding the arrangements and issues decided upon in the terms of this Resolution.

Article 22. In up to 60 days, the General-Office for Medicinal Products must start the analysis, based on risk criteria, of applications for marketing authorization and post-marketing authorization for innovative, generic, similar, herbal, and specific medicinal products.

Sole paragraph. The criteria referred to in the caption of this article must consider at least the product's intrinsic risk and the company's history of compliance with the health regulations issued by Anvisa.

Article 23. The temporary optimized analysis procedure may be applied only to the applications that comply with the requirements in this Resolution.

Article 24. When the period established to submit the specific addendum is finished, or in the cases where it is not possible to use the optimized analysis procedure, Anvisa shall assess the applications through ordinary analysis.

Article 25. This Resolution is valid for 180 (one hundred and eighty) days counting from the date it comes into force.

Article 26. This Resolution comes into force on 19 September 2022.

ANTONIO BARRA TORRES

ANNEX I

ASSESSMENT OF ANALYSIS ELIGIBILITY OF APPLICATIONS OF MEDICINAL PRODUCTS AND BIOLOGICAL PRODUCTS FOR THE TEMPORARY OPTIMIZED ANALYSIS PROCEDURE

GENERAL INFORMATION	
Marketing authorization process number	
Number(s) of the file(s) the temporary optimized analysis procedure is applied for	
Subject of the application(s)	
Name of the product	
Active pharmaceutical ingredient(s) (API), when it is the case of synthetic or semi-synthetic medicinal products	
Inform the Regulatory Authority(ies) that approved the regularization application being submitted	

CRITERION	**CHECKLIST**
Administrative information (Applicable to all processes)	
General	
Is the regulatory documentation issued by an equivalent foreign regulatory authority (EFRA) designated by Anvisa?	☐ **Yes.** Inform the name of the EFRA chosen as reference: Name of the EFRA:_____ ☐ **No.** The application is not eligible for the temporary optimized analysis procedure.
Is there any complementary information issued by another EFRA, which has been attached to the application?	☐ **No.** Informative item. ☐ **Yes.** Inform the name of the EFRA chosen as reference: Name of the EFRA:_____
Does the applicant belong to the same corporate group as the company responsible for the documentation regarding the marketing authorization approved by the EFRA?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** It is necessary to attach an authorization letter from the marketing authorization holder confirming that the applicant acts in accordance with the rights deriving from the marketing authorization holder and the holder agrees with applying for regularization in Brazil.
The regulatory documentation issued by the EFRA refers to an assessment for a definitive approval for the commercialization of the medicinal product, that is, it was not provisionally or conditionally approved.	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** The application is not eligible for the

	temporary optimized analysis procedure.
The regulatory documentation issued by the EFRA complies with the requirements in this Resolution, and is in Portuguese, English, or Spanish, and no information essential for Anvisa's analysis has been censored or omitted.	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** The application is not eligible for the temporary optimized analysis procedure.
Was an application for the marketing authorization for the medicinal product or biological product object of this application denied, rejected, refused, or withdrawn, or is it commercialized with a court order in any country?	☐ **No.** The application is eligible for the temporary optimized analysis procedure. ☐ **Yes.** Inform the country and attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure. Country: _____
Was there a withdrawal of application for marketing authorization for the medicinal product or biological product in any of the EFRAs designated by Anvisa?	☐ **No.** The application is eligible for the temporary optimized analysis procedure. ☐ **Yes.** Inform the EFRA and attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure. Country: _____
International alignment of directives	
Does the quality regulatory documentation issued by the EFRA refer to or was it elaborated in accordance with the guides published by the ICH or the WHO?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** It is necessary to attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure. If eligible, additional assessment shall be carried out.
Does the regulatory documentation issued by the EFRA refer to or was it elaborated in accordance with non-clinical directives published by the ICH or the WHO?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** It is necessary to attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure.
Does the regulatory documentation issued by the EFRA refer to or was it elaborated in accordance with the safety and efficacy directives published by the ICH or the WHO?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** It is necessary to attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure.
	☐ **No.** The application is eligible for the temporary optimized analysis procedure.

Does the report refer to specific directives or guides different from ICH or WHO references?	☐ **Yes.** It is necessary to attach clarifications to identify and justify the divergences between the directives or guides adopted by the EFRA and ICH or WHO directives. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure.
Quality	
Characteristics of the medicinal product or biological product object of the application	
Does the Medicinal Product or Biological Product object of the application have essential characteristics equivalent to the characteristics of the one approved by the EFRA and described in the EFRA regulatory documentation presented, regarding the criteria described below? 1 – Dosage; 2 – Concentration; 3 – Formulation (active substance and excipients); 4 – Manufacturers (API, intermediate product, medicinal product, and package); 5 – Manufacturing process (intermediate product and finished product); 6 – Specifications of release of the finished product and stability of the finished product; 7 – Cell and viral banks, in case of biological products; 8 – Molecular characterization, in case of biological products; 9 – Specifications of release and stability of the active substance, in case of biological products.	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** The application is not eligible for the temporary optimized analysis procedure.
Was the generic/ similar medicinal product developed based on the reference medicinal product elected by Anvisa and commercialized in Brazil?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** The application is eligible for the temporary optimized analysis procedure, but additional assessment shall be carried out. ☐ **Not applicable.** It is not a generic medicinal product.

Additional manufacturing sites	
Are additional manufacturing sites (that is, not included in the dossier sent to the EFRA) indicated in this submission to Anvisa?	☐ **No.** The application is eligible for the temporary optimized analysis procedure. ☐ **Yes.** It is necessary to attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure.
Is the additional site solely for the stages of labeling, secondary packaging, or release of batches for distribution?	☐ **Not applicable.** There are no additional manufacturing sites. ☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** Other stages are carried out at the additional sites. It is necessary to attach clarifications describing the additional stages. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure. If eligible, additional assessment shall be carried out.
Have validation data, including batch analyses, been provided for the additional sites?	☐ **Not applicable.** There are no additional manufacturing sites. ☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** The application is not eligible for the temporary optimized analysis procedure. Note: additional assessment may be necessary.
Good Manufacturing Practices (GMP)	
Do all manufacturing sites indicated have a valid Good Manufacturing Practices Certificate (GMPC) issued by Anvisa?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** The application is eligible for the temporary optimized analysis procedure, but analysis conclusion is conditioned to the GMPC publication by Anvisa. ☐ **Not applicable.** The GMPC issued by Anvisa is not required by the legislation in force. It is necessary to attach the documentation issued by the EFRA, confirming the production plant's regular status at the EFRA with regards to the Good Manufacturing Practices.
Stability, shelf life, and packaging	
	☐ **Yes.** The application is eligible for the

Were the stability studies assessed by the EFRA for granting shelf life conducted according to the climate zone (IVb)?	temporary optimized analysis procedure. ☐ **No**, because the medicinal product or biological product object of the application must not be stored in environment temperature (e.g., storage and transportation in controlled temperature). The application is eligible for the temporary optimized analysis procedure. ☐ **No**, but the applicant is sending zone IVb stability studies. The application is eligible for the temporary optimized analysis procedure, but additional assessment shall be carried out. ☐ **No**, although the product is stored in environment temperature. The application is not eligible for the temporary optimized analysis procedure.
Are the proposed shelf life, the shelf life in use, and the storage conditions identical to the ones accepted by the EFRA?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** It is necessary to attach clarifications on the specific shelf life proposed. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure. If eligible, additional assessment shall be carried out.
Information on the API regularization	☐ **Not applicable (check this option if the product object of analysis does not have a synthetic or semi-synthetic API liable to regularization).**
Will the API regularization be carried out through the temporary optimized analysis procedure?	☐ **Yes.** The DIFA holder must complete Annex III and submit it in the API regularization process. ☐ **No.** Include a copy of CADIFA (or present "CADIFA Process Notification") and the additional information in the medicinal product marketing authorization process.
Safety and efficacy	
Indications and use instructions	
Are the proposed use conditions equivalent to the ones approved by the EFRA, considering therapeutic indications, contraindications, posology, target population, route of administration, and mode of use?	☐ **No.** The application is not eligible for the temporary optimized analysis procedure. ☐ **Yes.** Inform the hyperlink to access the EFRA's approval public report: _____
	☐ **Yes.** The application is eligible for the

Are the proposed indications identical to the approved indications of the reference medicinal product or comparator product in Brazil?	temporary optimized analysis procedure. ☐ **No.** It is necessary to attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure. ☐ **Not applicable.** It is not a generic medicinal product or a biossimilar product.
Package leaflets	
Does the EFRA's regulatory documentation provide the safety and efficacy information required for the elaboration of the Brazilian package leaflet text, considering the requirements in RDC 47/2009?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** The application is not eligible for the temporary optimized analysis procedure.
Clinical studies	☐ **Not applicable (check this option if clinical studies have not been conducted for the product object of analysis (e.g., generic and similar medicinal products)).**
Did the medicinal product have a clinical study, or part of it, conducted in Brazil?	☐ **No.** ☐ **Yes.** Inform which study phase was conducted.
Are there updates for main studies or support studies available that were not considered in the EFRA's approval and support the proposed indication?	☐ **No.** The application is eligible for the temporary optimized analysis procedure. ☐ **Yes.** It is necessary to inform details, such as notes on the proposed package leaflet with references to relevant documentation. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure.
Is there any additional information available relevant to the risk-benefit ratio of the indication approved by the EFRA (for example, additional Periodic Risk-Benefit Assessment Report or long-term safety study available since the approval)?	☐ **No.** The application is eligible for the temporary optimized analysis procedure. ☐ **Yes.** It is necessary to submit the additional information. The application is eligible for the temporary optimized analysis, but additional assessment shall be carried out.
Have new clinical studies been conducted or has new clinical evidence been obtained since the medicinal product or biological product was assessed by the EFRA?	☐ **No.** The application is eligible for the temporary optimized analysis procedure. ☐ **Yes.** The application is not eligible for the temporary optimized analysis procedure.
Are there bridging studies designed to adjust the medicinal product or biological product to the Brazilian population?	☐ **No.** The application is eligible for the temporary optimized analysis procedure. ☐ **Yes.** Only the quality aspects are eligible for the temporary optimized analysis

	procedure.
Generic and Similar Medicinal Products	☐ **Not applicable (check this option if the product object of analysis is not a generic or similar medicinal product).**
Was the reference medicinal product used in the comparability studies presented to the EFRA the medicinal product elected as reference in Brazil?	☐ **No.** Informative item. ☐ **Yes.** Inform the marketing authorization number in Brazil. Marketing authorization number: _____
Did the dossier submitted to the EFRA contain bioequivalence and bioavailability (biopharmaceutical) data?	☐ **Yes.** Informative item. ☐ **No.** It is necessary to attach clarifications on the lack of biopharmaceutical data in the dossier submitted to the EFRA.
Was a reference medicinal product granted marketing authorization in Brazil used in bioequivalence and bioavailability (biopharmaceutical) studies?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** The application is not eligible for the temporary optimized analysis procedure. ☐ **Not applicable.** The product is bio-exemptible, in accordance with the Brazilian legislation in force. It is necessary to attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure. ☐ **Not applicable.** The reference medicinal product considered by the EFRA and the reference medicinal product in Brazil are manufactured in a single location for global distribution. It is necessary to attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure. If eligible, additional assessment shall be carried out.
Biosimilar medicinal products	☐ **Not applicable (check this option if the product object of analysis is not a biosimilar medicinal product).**
Is the comparator product representative of the Brazilian product?	☐ **Yes.** Inform the marketing authorization number in Brazil. Marketing authorization number: _____ ☐ **No.** The application is not eligible for the temporary optimized analysis procedure.
Risk Management Plan (RMP)	☐ **Not applicable (check this option if the Risk Management Plan (RMP) is not required in accordance with the Brazilian legislation in force).**
	☐ **No.** The application is eligible for the

Are there issues related to risk management, specific to the Brazilian scenario, included in the application submitted to Anvisa?	temporary optimized analysis procedure. ☐ **Yes.** It is necessary to attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure.
Is the risk management plan proposed for Brazil equivalent to the one approved by the EFRA?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** It is necessary to attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure.
Does the EFRA's report include an assessment of an RMP, proposing a risk management system equivalent to the one proposed for Brazil (including equivalent pharmacovigilance and risk minimization activities, as well as considerations on the adequacy of an equivalent summary of safety concerns)?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** It is necessary to attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure.
Conclusion	
In any of the questions in this checklist, was an answer checked indicating the application is not eligible for the temporary optimized analysis procedure?	☐ **Yes.** The process is not eligible for the temporary optimized analysis procedure. ☐ **No.** Answer the next question.
In any of the questions in this checklist, was an answer checked informing that an additional assessment may be carried out?	☐ **Yes.** Eligibility assessment depends on analysis of the documents attached to this checklist. ☐ **No.** The process is eligible for the temporary optimized analysis procedure.

Based on the checklist above, I hereby request analysis of the aforementioned application(s) through the temporary optimized analysis procedure.

I am aware that Anvisa may, in accordance with the technical assessment of the information provided, adopt the ordinary analysis.

I hereby declare that I have complied with the provisions of health regulations on medicinal products and biological products, according to the regulatory category established in Brazil, regarding the documentation, the conduction of studies, and the obtention of evidence required at the time of submission of the application, and also declare that I am committed to maintain continuous pharmacovigilance and monitoring with respect to ensuring the maintenance of quality, efficacy, and safety attributes of the medicinal product or biological product.

Additionally, I hereby declare that the medicinal product or biological product, during the last three years, was not object of recall, cancellation of marketing authorization, suspension of manufacturing, or suspension of commercialization due to quality deviations (applicable in

cases where the quality analysis has not yet been carried out) or issues related to safety or efficacy (applicable in cases where the safety or efficacy analysis has not yet been carried out) in the countries where the marketing authorization is valid, and also declare that the company(ies) responsible for manufacturing the active pharmaceutical ingredient and the finished product has (have) not been subjected to interdiction or precautionary measure due to incompliance with quality requirements and the good manufacturing practices established in health regulations. I also inform that the medicinal product or biological product, object of analysis, has not been rejected by any of the EFRAs listed in Article 5 of this Resolution.

I hereby declare that I have authorization from the EFRA(s) to submit to Anvisa all the regulatory documentation comprising this protocol.

By completing and signing this form, I authorize Anvisa, if necessary, to contact the EFRA and exchange the information relating to my application.

The company, represented by its legal and technical responsible officers, ensures and accounts for the veracity and reliability of the information provided herein, and is aware that it is responsible for the quality, safety, and efficacy of the medicinal products it has been granted marketing authorization for, ensuring that they are adequate to their intended purposes, comply with the requirements established in their marketing authorization, and do not put patients at risk by presenting inappropriate safety, quality, or efficacy, and that eventual inconsistencies among the information provided herein and the marketing authorization process of the medicinal product may lead to decision alteration, batch recall, manufacture and/ or commercialization suspension, marketing authorization cancellation, and other penalties established in Law no. 6,437 of 20 August 1977 and its updates, without prejudice to other penalties provided for in the legislation in force.

Date: __/__/____

Name: _____

Signature (Technical Responsible Officer): _____

Signature (Legal Responsible Officer): _____

ANNEX II

ASSESSMENT OF ANALYSIS ELIGIBILITY OF APPLICATIONS OF DIFA FOR THE TEMPORARY OPTIMIZED ANALYSIS PROCEDURE

GENERAL INFORMATION	
Application process number:	
Number(s) of the file(s) the temporary optimized analysis procedure is applied for	
Subject(s) of the application(s)	
Name of the API	
Name of DIFA Holder	

CRITERION	**CHECKLIST**
General	
Was the submitted regulatory documentation issued by an equivalent EFRA designated by Anvisa?	☐ **No.** The application is not eligible for the temporary optimized analysis procedure. ☐ **Yes.** Inform the name of the EFRA and the date it was approved by Anvisa. Name of the EFRA:_____ If applicable, present a letter authorizing the exchange of regulatory documentation by the EFRA with Anvisa.
Does the EFRA's regulatory documentation meet the following general application criteria? I – The regulatory documentation refers to an assessment for a definitive regularization of the API (that is, it is not a provisional or conditional approval). II – The regulatory documentation is complete, in Portuguese, English, or Spanish, and it was not edited or censored.	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** The application is not eligible for the temporary optimized analysis procedure.
Was the application for regularization of the API object of this petition denied, rejected, refused, or withdrawn, or is it commercialized with a court order in any country?	☐ **No.** The application is eligible for the temporary optimized analysis procedure. ☐ **Yes.** Inform the country and details on the case: _____ Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure.
Was there a withdrawal of application for marketing authorization for the medicinal	☐ **No.** The application is eligible for the temporary optimized analysis procedure.

product or biological product in any of the EFRAs designated by Anvisa?	☐ **Yes.** Inform the EFRA and attach clarifications. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure. Country: _____
Active Pharmaceutical Ingredient Dossier (DIFA, in Portuguese)	
Is the DIFA approved by an EFRA?	☐ **No.** The application is not eligible for the temporary optimized analysis procedure. ☐ **Yes.** Inform the name of the EFRA and the date of approval by the EFRA. In addition, inform the Version of the DIFA submitted to the EFRA. Name of the EFRA: _____ Date of approval: _____ Version of the DIFA submitted to the EFRA: _____
Is there a copy attached of: I – the latest approved version of a valid Certificate of Suitability to the monographs of the European Pharmacopoeia (CEP), issued by EDQM, completed by its holder in the name of the medicinal product marketing authorization/ post-marketing authorization applicant; or II – the latest approved version of a valid Confirmation of API prequalification (CPQ), issued by the WHO, completed by its holder in the name of the medicinal product marketing authorization/ post-marketing authorization applicant; or III – equivalent document confirming the approval by an EFRA.	☐ **Yes.** Inform the document version and its respective issuer. Document version: _____ Issuer: _____ ☐ **No.** The application is not eligible for the temporary optimized analysis procedure. ☐ **Not applicable.** The API temporary optimized analysis procedure shall not use such documents.
Are the quality information of the DIFA submitted to Anvisa (part 3.2.S) identical to the quality information of the DIFA currently approved by the EFRA?	☐ **Yes.** The application is eligible for the temporary optimized analysis procedure. ☐ **No.** In case this option is checked, indicate on the list below the sections with identical information, if any. Subject to assessment by Anvisa of the eligibility for the temporary optimized analysis procedure. If eligible, additional assessment may be carried out.

	General Information (3.2.S.1) ☐ Nomenclature (3.2.S.1.1) ☐ Structure (3.2.S.1.2) ☐ General Properties (3.2.S.1.3) Manufacture (3.2.S.2) ☐ Manufacturer(s) (3.2.S.2.1) ☐ Description of the Manufacturing Process and In-process Controls (3.2.S.2.2) ☐ Control of Raw Materials (3.2.S.2.3) ☐ Control of Critical Stages and Intermediates (3.2.S.2.4) ☐ Process Validation (3.2.S.2.5) ☐ Manufacturing Process Development (3.2.S.2.6) ☐ Characterization (3.2.S.3) Structure Elucidation and Other Characteristics (3.2.S.3.1) ☐ Impurities (3.2.S.3.2) API Quality Control (3.2.S.4) ☐ Specification (3.2.S.4.1) ☐ Analytical Methods (3.2.S.4.2) ☐ Validation of Analytical Methods (3.2.S.4.3) ☐ Analysis of Batches (3.2.S.4.4) ☐ Justification for Specification (3.2.S.4.5) ☐ Materials and Reference Chemical Substances (3.2.S.5) ☐ Packaging (3.2.S.6) Stability (3.2.S.7) ☐ Stability Summary (3.2.S.7.1) ☐ Protocols and Post-submission Commitments (3.2.S.7.2) ☐ Stability Data and Reports (3.2.S.7.3) For unchecked sections, present Comparative Table (Annex 8 of the CADIFA Request Application Form), for assessment of the eligibility for the temporary optimized analysis procedure.
Conclusion	
In any of the questions in this checklist, was an answer checked indicating the application	☐ **Yes.** The process is not eligible for the temporary optimized analysis procedure.

is not eligible for the temporary optimized analysis procedure?	☐ **No.** Answer the next question.
In any of the questions in this checklist, was an answer checked informing that an additional assessment may be carried out?	☐ **Yes.** Eligibility assessment depends on analysis of the documents attached to this checklist. ☐ **No.** The process is eligible for the temporary optimized analysis procedure.

Based on the checklist above, I hereby request analysis of the aforementioned application(s) through the temporary optimized analysis procedure.

I am aware that Anvisa may, in accordance with the technical assessment of the information provided, adopt the ordinary analysis.

I hereby declare that the API approved by the EFRA has the same quality level as the API in this application, including the following:

1. Manufacturing process (including parameters and in-process controls);

2. Manufacturing sites;

3. Specification of raw materials, including the specification of start materials;

4. Suppliers and route for obtention of start materials;

5. Specification and analytical methods of intermediate products;

6. Specification and analytical methods of APIs;

7. API solid phase properties;

8. Packaging;

9. Stability data;

10. Information level (open part) available to the applicants;

11. Any other parameters that may have a potential impact on the API quality.

I hereby declare that the DIFA meets the international quality guidelines adopted by Anvisa, particularly the following:

I – ICH Q1A – Stability Testing of New Drug Substances and Products;

II – ICH Q1B – Stability Testing: Photostability Testing of New Drug Substances and Products;

III – ICH Q1D – Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products;

IV – ICH Q1E – Evaluation for Stability Data;

V – ICH Q2(R1) – Validation of Analytical Procedures;

VI – ICH Q3A(R2) – Impurities in New Drug Substances;

VII – ICH Q3C(R6) – Impurities: Guideline for Residual Solvents;

VIII – ICH Q3D(R1) – Guideline for Elemental Impurities;

IX – ICH Q6A – Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances;

X – ICH Q11 – Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/ Biological Entities); and

XI – ICH M7(R1) – Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk.

I hereby declare that I have complied with the provisions of health regulations on APIs at the time of submission of the application.

Additionally, I hereby declare that the API, during the last three years, was not object of recall, cancellation of marketing authorization or regularization, suspension of manufacturing, or suspension of commercialization due to quality deviations or issues related to safety or efficacy in the countries where the API is approved, and also declare that the company(ies) responsible for manufacturing the active pharmaceutical ingredient has (have) not been subjected to interdiction or precautionary measure due to incompliance with quality requirements and the good manufacturing practices established in health regulations. I also inform that the API, object of analysis, has not been rejected by any of the EFRAs listed in Article 5 of this Resolution.

I hereby declare that I have authorization from the EFRA(s) to submit to Anvisa all the regulatory documentation comprising this protocol.

By completing and signing this form, I authorize Anvisa, if necessary, to contact the EFRA and exchange the information relating to my application.

The company, represented by its legal and technical responsible officers, ensures and accounts for the veracity and reliability of the information provided herein, and is aware that it is responsible for the quality and safety of the active pharmaceutical ingredient regularized by it, ensuring that it is adequate to its intended purpose, complies with the requirements established in its regularization, and do not put patients at risk by presenting inappropriate safety and quality, and that eventual inconsistencies among the information provided herein and the regularization process of the active pharmaceutical ingredient may lead to decision alteration, batch recall, manufacture and/ or commercialization suspension, regularization cancellation, and other penalties established in Law no. 6,437 of 20 August 1977 and its updates, without prejudice to other penalties provided for in the legislation in force.

Date: __/__/____

Name: _____

Signature (Technical Responsible Officer): _____

Signature (Legal Responsible Officer): _____