الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Regulatory Framework for Rare Diseases Drugs

The New Accelerator Program for Drugs in Rare Diseases (NADR)

Version 1.0

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Saudi Food & Drug Authority

Drug Sector

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Saudi Food and Drug Authority

Vision and Mission

Vision

To be a leading international science-based regulator to protect and promote public health

Mission

Protecting the community through regulations and effective controls to ensure the safety of food, drugs, medical devices, cosmetics, pesticides and feed

Document Control

Version	Author	Date	Comments
Version 1.0	Executive Directorate for Regulatory Affairs	05 August 2026	-

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1. INTRODUCTION

Rare diseases pose a significant public health challenge despite their low individual prevalence. Recognizing this, the Saudi Food and Drug Authority (SFDA) has taken proactive and forward-looking steps to foster a regulatory environment that supports the development and timely access to innovative medicines, particularly for serious and life-threatening conditions.

As part of its mandate to protect and promote public health, the SFDA is launching a new Program, the New Accelerator Program for Drugs for Rare Diseases (NADR)[1], focused on enhancing access to such therapies for patients with rare diseases. Aims to further optimize regulatory processes, strengthen stakeholder engagement, and support the development of treatments targeting areas of high unmet medical need.

1.1.Rare Diseases: Definition and Situation in Saudi Arabia

In Saudi Arabia, a disease is considered rare when it affects fewer than 1 in 2,000 people in the community. More than 10,000 types of rare diseases are estimated to exist worldwide, including chromosomal, cardiovascular, and endocrine disorders. To date, approximately 350 million people live with rare diseases worldwide, including more than 370,000 people living with rare diseases in Saudi Arabia, which has the highest prevalence in the Middle East and Africa region.

Rare diseases are often chronic, progressive, degenerative, and life-threatening. Approximately 80% of rare diseases have a genetic cause, and their frequency is also more prominent in populations with high consanguinity, as published evidence from Saudi Arabia found. Almost 70% of these are present in childhood, and about 30% of children with a rare disease die before age of five. The average time for an accurate diagnosis is 5 years, and about 95% of known rare diseases lack satisfactory treatment options. Some rare diseases arise from acquired infections, environmental changes, or dysregulation of the immune response.

[1] The name "NADR نادر" reflects the essence of addressing rare diseases, symbolizing regulatory program specialized for orphan drugs.

Individuals with rare diseases face multiple challenges, including delayed or imprecise diagnosis, insufficient healthcare support, and limited treatment options, which consequently result in increased disease severity and a reduced quality of life (Saudi Ministry of Health, 2024).

A collective approach is needed to prioritize addressing the unmet needs of patients with rare diseases, calling for the combined support of government, industry, voluntary organizations, and others concerned with health care.

1.2.Scope

This framework applies to all drugs, which encompass both pharmaceuticals and biologics, intended for the prevention or treatment of rare diseases.

1.3.Related documents

This document should be read in conjunction with the following:

- Guidance for Orphan Drug Designation
- Breakthrough Medicine Program
- Research and Investigational Drugs (RAID) Designation
- Conditional Approval for Medicinal Products for Human Use
- Guidance for Priority Review
- Data Requirements for Human Drugs Submission
- Meeting Requirements Between Drug Sector and Applicants

2. Existing Regulatory Programs

The established SFDA regulatory framework for drug approval already exists to support the authorization of drugs for rare diseases, including designation programs, incentives, and flexible approval pathways designed to accelerate the development and access of such drugs. In addition to the regular registration pathway, the table below provides an overview of SFDA's regulatory programs applicable to rare disease drugs.

Table 1: Overview of regulatory framework for approval and designation programs of drugs for rare diseases.

Regulatory procedure	Nature of procedure	Eligibility criteria	Stage of submission	Features
Orphan Drug Designation (ODD)	Designation	A drug must meet the following criteria: 1. for the treatment, prevention or diagnosis of a life-threatening or serious disease. 2.The disease must affect fewer than 5 in 10,000 individuals in Saudi Arabia, 3. Under development, at an early or late stages, for this orphan condition. 4. No satisfactory available alternative.	At any stage of development (pre-submission of marketing authorization application (MAA))	pre-submission meetings, priority review, scientific and regulatory advice
Research and Investigational Drugs (RAID) Designation	Designation	Eligible drugs for rare disease must meet all criteria: 1.under clinical development and not yet authorized by any regulatory authority; 2.address an unmet medical need; and 3. Committed to conducting clinical trials in Saudi Arabia.	At any clinical phase (Phase I, II, or III) of drug development.	Pre- designation meeting. Scientific guidance and regulatory support throughout drug development.
Breakthrough Medicines Program (BMP)	Designation	Eligible drugs for rare disease must meet all criteria: 1.targeting serious, debilitating, or life-threatening conditions with unmet medical need; 2.offering a major advantage over current methods; 3.a positive benefit/risk balance, and 4. Not yet registered with any regulatory authority.	Request should be submitted by the end of phase 2 or at any time after. Submission of MAA	Regulatory support, meetings, and scientific advice to accelerate development and review. Pre-designation meeting. Fast medicines access

Priority review	Registration pathway	Eligible drugs for rare disease must fall into one of the following: 1. New drugs and biologics for treating serious or life-threatening conditions with an unmet medical need. 2.The first biosimilar to the innovative product, or 3. Unavailable drugs that are listed in the unregistered or unavailable products.	Submission of MAA	Accelerated review timelines
Conditional Approval	Approval subject to obligations	Eligible drugs for rare disease must fall into one of the following: 1.Serious or life-threatening diseases, or 2. Emergency situations.	Submission of MAA	Authorization before availability of comprehensive data, ensuring timely access while balancing safety and efficacy through post-approval obligations. Rolling submission.

2.1 Named Patient and Special Access program

Furthermore, other established regulatory approaches, the Named Patient Program (NPP) and Special Access Program (SAP), facilitate access to therapies for patients with unmet medical needs, including patients affected by rare diseases, in accordance with applicable regulatory requirements.

3. The New Accelerator Program for Drugs for Rare Diseases (NADR)

The central feature of the rare disease drugs regulatory framework is the introduction of the NADR designation, which is specifically intended for products targeting rare diseases with unmet medical needs. NADR designation is an official designation granted by SFDA to a drug confirming its eligibility for the NADR program and entitling the product to all associated incentives and obligations under the program.

3.1 Eligibility Criteria:

To qualify for the NADR program, a drug must meet all the following criteria:

- **Criterion 1: Orphan condition**

The product is intended to prevent or treat a rare, life-threatening, or seriously debilitating disease, as defined by a prevalence of fewer than 5 in 10,000 persons in Saudi Arabia. The condition must align with the definition set out in the SFDA Guidance for Orphan Drug Designation.

- **Criterion 2: Unmet medical need**

Either no satisfactory treatment exists in Saudi Arabia, or the product offers significant clinical benefit, such as improved safety, efficacy, or patient outcomes, over currently available therapeutic options.

- **Criterion 3: Product developmental and regulatory status**

The product could be under active development at any stage (from pre-clinical through to Phase III) or already authorized by any regulatory authority but not yet registered in Saudi Arabia for the proposed indication.

3.2 NADR Program Incentives

With the NADR program, drugs will benefit from SFDA incentives tailored to each stage of submission, which will address regulatory and scientific challenges to support the development and authorization of rare disease drugs through:

A. Regulatory and scientific support

SFDA offers a range of tools supporting development and expediting patient access to drugs for rare diseases, which may include conditional approval, priority review, rolling submission, and scientific advice to help applicants align their development strategies with SFDA requirements. Furthermore, there are opportunities for frequent interactions with SFDA, including a dedicated SFDA Product Manager (PM) assigned to guide applicants through the process and formal meetings throughout product development.

B. Adaptive and Innovative Evidence Generation

Recognizing that traditional randomized controlled trials (RCTs) are frequently not feasible or ethical in rare disease populations, the SFDA will accept a broader evidence base for rare disease submissions, including:

- **Novel and advanced trials**: Adaptive trial designs including Bayesian adaptive, N-of-1, basket, umbrella, and platform trials that maximize information yield from small patient samples.
- **Natural History Data**: Natural history studies as acceptable external comparators when concurrent control is not feasible,
- **New Approach Methodologies (NAMs)** including AI/ML and In Silico Modeling. Recognizing that artificial intelligence (AI), machine learning (ML), and in silico computational models are integral components of NAMs, the SFDA will accept data derived from these advanced methodologies alongside in vitro biological models (e.g., organ-on-a-chip). Under a 'weight of evidence' principle, sponsors may utilize these unified tools for toxicity prediction, pharmacokinetic/pharmacodynamic (PK/PD) modeling, and efficacy assessment. This integrated approach compensates for the limitations and ethical challenges of utilizing traditional animal models in rare diseases, provided the models are validated and transparently documented. Dedicated SFDA guidance on NAMs is anticipated within 2026-2027.

- **Modeling and simulation:** Recognizing modelling and simulation outputs (such as PK/PD, PBPK, Dose-Response, QSP, etc.) as an acceptable source of evidence within the benefit–risk assessment of orphan (rare disease) medicines, provided that ICH – M15 requirements are met.

- **Surrogate/Biomarker Endpoint Framework**: In rare diseases settings it is acceptable to utilize surrogate endpoints for primary efficacy estimation when non-clinical and clinical endpoints are not feasible

- **Platform Technology**: Leverages prior knowledge of an established platform technology, allowing data from related products or manufacturing processes to support regulatory submissions for new medicines developed using the same platform, particularly for ultra-rare diseases.

- **Saudi Genomic Data**: Saudi Human Genome Program data and biobank-derived population genomics data as supporting evidence for precise disease characterization.

- **Proportionate Nonclinical Safety Requirements**: The SFDA will accept a proportionate, risk-based nonclinical safety package scaled to the indication, the seriousness of the condition, the intended population, the proposed clinical exposure, and prior knowledge of the molecule, class, or platform. The detailed considerations governing this proportionate nonclinical approach are set out in Annex 4.

The SFDA will apply a risk-proportionate, disease-severity-calibrated approach to evidence requirements. For instance, a therapy for a rapidly fatal childhood disorder with no treatment alternative may, on a case-by-case basis subject to SFDA scientific assessment, be evaluated against different, and appropriately lower, pre-approval evidence thresholds than one targeting a condition with existing treatment options, provided robust post-approval monitoring obligations are accepted.

C. Exemption from CMC Requirements

This incentive aims to facilitate and expedite the registration of drugs for rare diseases under the NADR program by applying a flexible, science- and risk-based approach for Chemistry, Manufacturing, and Controls (CMC) data requirements. Annex 2 outlines the procedures to request exemptions for CMC requirements, where scientifically justified and where product quality can be adequately assured at time of approval.

D. Inspection (GMP)

The program provides flexibility measures in manufacturing site registration for rare disease products through risk-based approaches to facilitate and expedite the registration processes. Key incentives include:

- If the product manufacturing site is not registered at SFDA and located in one of the following countries: USA, UK, Canada, Australia, Japan, Switzerland, Germany, France, Ireland, Italy, Spain, Portugal, Finland, Sweden, Norway, Denmark, Belgium, Netherlands, Austria or Singapore, site inspection will not be a barrier for the product registration. SFDA will take the necessary actions to facilitate the registration within the timeframe. The following requirements need to be prepared and submitted to accelerate the site registration process:
    - Proof of payment of inspection fees,
    - Valid GMP certificates from the local authority and other international authorities,
    - A copy of Site Master File (SMF),
    - List of all products that manufactured at the site and supplied to Saudi Arabia,
    - Last Inspection Report - in English - from the local authority,
    - If available, last Inspection Report - in English - from other international authorities.
- Provide priority for on-site inspection, if an inspection is required

E. Pharmacovigilance Obligations

The SFDA will apply a proportionate evidence approach for PSURs and Registries, tailoring requirements to the specific patient population size to ensure technical feasibility and encourage industry compliance.

3.3 Applying for NADR designation

Applicants seeking NADR designation shall submit a completed application form (see Annex1), with supporting documents indicating how the product fulfils the criteria for designation.

Timing of application:

The applicant can apply for NADR designation at any stage of the product's development before the application for marketing authorization.

Submission Process

1. **Submission**: In order to apply for the NADR program, the applicant should submit a request to SFDA through email (Designation.Drug@sfda.gov.sa), accompanied by the designation application form and details showing that the product is within the scope of the eligibility criteria and satisfies the requirements.
    - Applicants are advised to organize a pre-submission meeting with SFDA to discuss planned applications for NADR program.
    - **Parallel ODD Submission:** If the product does not already hold an Orphan Drug Designation, applicants may submit the ODD request in parallel with the NADR program.
2. **Evaluation**: SFDA evaluates the designation request and supporting documentation, and then provides the applicant with SFDA's opinion via e-mail on whether the request is accepted or not.
    - **Review Timeline:** Review of the NADR program eligibility and the Orphan Drug Designation (ODD) request will be completed within 20 working days from the date of a complete submission.

- If deficiencies, comments, or additional information related to the application are raised during the evaluation, the applicant will be notified via email to address them and update the application.
- Applicants are allowed to request a timeframe extension by email to address deficiencies if needed.

3. **Decision on designation**: Once the evaluation is complete, the SFDA will issue a final decision letter through Designation.Drug@sfda.gov.sa

Following the decision to grant the NADR designation, the applicants should submit the marketing authorization application via the Saudi Drug Registration (SDR) System using the electronic common technical document (eCTD) format within 6 months from the date of the designation decision.

- If it is not possible to comply with the eCTD format submission in case of the rolling submission, applicants can request an exception through SDR.drug@sfda.gov.sa

Annex 1: NADR designation application form

Please send a completed form to Designation.Drug@sfda.gov.sa. All fields are mandatory. If any field is not applicable or no information is to be provided, write 'Not applicable' or 'N/A'.

Date of request: (dd/mm/yyyy)	
Applicant contact information:	
Applicant	Name: Address:
Marketing Authorization Holder/ Study Sponsor	Name: Address:
Authorized Contact Person	Name: Title: Phone Number: Email Address:
Section I: Drug Information	
Drug Type	○ Biologic (Specify) ○ Pharmaceutical/Drug (Specify)
Name of Drug	Include all available names: Trade, Chemical, or Code
ATC code	
Strength(s)	
Dosage Form(s)	
Route(s) of Administration	
Mechanism of Action	
Proposed Indication	
Dosing Regimen, Including Concentration, Amount Dosed, And Frequency and Duration of Dosing If Known	
Drug Substance Manufacturer(s)	
Drug Product Manufacturer(s)	
Description and Composition of Drug Product	
Regulatory Status outside Saudi Arabia	**Details of current regulatory status and marketing history in other regulatory authorities, especially stringent regulatory authorities (SRAs), of the product for the proposed indication, for example:** - Application in other global expedited pathways and designation (e.g. PRIME, Breakthrough designation, Fast track designation, ODD) - Compassionate/specials usage - Pending and refused marketing authorization applications - Granted marketing authorizations

Regulatory status in Saudi Arabia	**Is the drug authorized or under registration process in Saudi Arabia?** ○ Yes (with evidence) ○ No
	Has this drug been granted an SFDA Orphan Drug Designation for the same indication? ○ Yes (with evidence) ○ No ○ For parallel ODD Submission
	Previously designated as an orphan drug for a different indication? ○ Yes (with evidence) ○ No
Proposed MAA pathway	
Is this indication for a rare disease (prevalence of fewer than 5 in 10,000 individuals in Saudi Arabia)?	○ Yes (with evidence) ○ No
Description of the condition: Definition: Aetiology: Specific characteristics; pathophysiological, histopathological, clinical characteristics:	
No satisfactory treatment exists in Saudi Arabia, or the product offers a significant clinical benefit, such as improved safety, efficacy, or patient outcomes, over currently available options?	○ Yes (with evidence) ○ No
Detailed scientific rationale for why such a drug is needed. Justification as to why available treatments/methods are not satisfactory, if applicable. Justification of significant benefit over available options, if applicable.	

Description of the stage of development
Summary of the development of the product Quality aspects, non-clinical aspects, proof-of concept in relevant model, pharmacology, pharmacokinetics, toxicology, clinical aspects, pharmacokinetics, pharmacodynamics, clinical efficacy, dose-response studies and main clinical studies, clinical studies in applied condition, planned clinical studies, clinical safety, adverse events, serious adverse events and deaths.

Annex 2: Exemption from CMC Requirements for Rare Disease Drugs

The annex outlines the procedures to request exemptions for CMC requirements to support efficient preparation and submission of Module 3 (Quality) of Common Technical Document (CTD) for marketing authorization applications of drugs for rare diseases, while ensuring that sufficient evidence is provided to demonstrate quality of product.

1. Procedure for Requesting CMC Exemptions

- **Step 1: Submission of Request**

Following the granting of orphan drug designation, the applicant can submit a request for exemption from certain CMC requirements to Designation.Drug@sfda.gov.sa; with the subject line: "**Request for CMC Exemptions**".
The request shall include:

a) A copy of the NADR designation.
b) A complete Submission Plan Form, including the required information (justification and supported data) for each requested CMC exemption (see Annex 3).

- **Step 2: SFDA Review**

The SFDA will review the submitted request and assess the proposed exemptions based on the provided information.

- **Step 3: SFDA Response**

The SFDA will provide its response within 20 working days of receiving a complete request.
Where the submitted justification or supporting data are considered insufficient, the review timeline may be extended. In such cases, the SFDA may request additional information and/or a meeting with the applicant to further discuss the request.

2. Meeting Request

Upon receipt of the SFDA response, the applicant may request a meeting with SFDA to discuss the outcome of the exemption request. Meeting requests shall be submitted in accordance with the SFDA Guidance on Requirements for Formal Meetings between the Drug Sector and Applicants.

Annex 3: Submission Plan Form

This form shall be used by the applicant to request exemption for Chemistry, Manufacturing, and Controls (CMC) requirements, prior to the official submission of marketing authorization application of rare disease drug to the SFDA.

1. Product Information:

Trade Name	
Active substance	
Marketing Authorization Holder	
NADR Designation Date	
Orphan Indication	

2. Check List for CMC Data (Module 3):

Notes:

- Where CMC data are partially available, unavailable, or proposed for waiver, the applicant shall provide a scientific justification with supportive data and expected submission date (when applicable) to facilitate SFDA assessment of the proposed CMC package.
- For each requested exemption, the required information shall be clearly identified and referenced to the relevant CTD Module 3 section.

Section	Description	Data Availability Status	Request Exemption	Expected Submission Date (If partial/not available)	Justification and supportive data provided
3.2.S	**Active Substance**				
3.2.S.1	**General Information**				
3.2.S.1.1	Nomenclature	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.1.2	Structure	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.1.3	General Properties	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.2	**Manufacture**				

3.2.S.2.1	Manufacturer(s)	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.2.2	Description of Manufacturing Process and Process Controls	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.2.3	Control of Materials	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.2.4	Controls of Critical Steps and Intermediates	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.2.5	Process Validation and/or Evaluation	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.2.6	Manufacturing process development	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.3	**Characterization**				
3.2.S.3.1	Elucidation of Structure and Other Characteristics	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.3.2	Impurities	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.4	**Control of Drug Substance**				
3.2.S.4.1	Specifications	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.4.2	Analytical Procedures	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.4.3	Validation of Analytical Procedures	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.4.4	Batch Analysis	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.4.5	Justification of Specifications	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.5	**Reference Standards or Materials**	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.6	**Container Closure System**	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.7	**Stability**	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.7.1	Stability summary and	☐ Complete	☐ Yes	DD-MM-YYYY	☐ Yes

	conclusion	☐ Partial ☐ Not available	☐ No		☐ No
3.2.S.7.2	Post-Approval Stability Protocol and Stability Commitment	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.S.7.3	Stability Data	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P	**Finished Product**				
3.2.P.1	**Description and Composition of the Drug Product**	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.2	**Pharmaceutical Development**				
3.2.P.2.1	Components of the Drug Product	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.2.1.1	Drug substance	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.2.1.2	Excipients	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.2.2	Drug Product	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.2.2.1	Formulation Development	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.2.2.2	Overages	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.2.2.3	Physiochemical and Biological Properties	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.2.4	Container Closure System	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.2.5	Microbiological Attributes	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.2.6	Compatibility	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.3	**Manufacture**				
3.2.P.3.1	Manufacturer(s)	☐ Complete ☐ Partial	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No

		☐ Not available			
3.2.P.3.2	Batch Formula	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.3.3	Description of Manufacturing Process and Process Controls	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.3.4	Control of Critical Steps and Intermediates	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.3.5	Process Validation and/or Evaluation	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.4	**Control of Excipients**				
3.2.P.4.1	Specifications	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.4.2	Analytical Procedures	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.4.3	Validation of Analytical Procedures	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.4.4	Justification of Specifications	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.4.5	Excipients of human or animal origin	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.4.6	Novel excipients	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.5	**Control of Drug Product**				
3.2.P.5.1	Specifications	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.5.2	Analytical Procedures	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.5.3	Validation of Analytical Procedures	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.5.4	Batch Analysis	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.5.5	Characterization of Impurities	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.5.6	Justification of Specifications	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No

3.2.P.6	**Reference Standards or Materials**	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.7	**Container Closure System**	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No

3.2.P.8	**Stability**				
3.2.P.8.1	Stability Summary and Conclusion	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.8.2	Post-Approval Stability Protocol and Stability Commitment	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.P.8.3	Stability Data	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.A	**Appendices**				
3.2.A.1	Facilities and Equipment	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.A.2	Adventitious Agents Safety Evaluation	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.A.3	Excipients	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No
3.2.R	**Regional information**	☐ Complete ☐ Partial ☐ Not available	☐ Yes ☐ No	DD-MM-YYYY	☐ Yes ☐ No

Annex 4: Proportionate Nonclinical Safety Requirements for Rare Disease Drugs

Recognizing that conventional nonclinical programs may be neither feasible nor scientifically informative for many rare disease products, the SFDA will accept a proportionate, risk-based nonclinical safety package scaled to the indication, the seriousness of the condition, the intended population, the proposed clinical exposure, and prior knowledge of the molecule, class, or platform. The objective of the nonclinical package is to characterize the principal safety risks needed to support first-in-human or pivotal dosing and to inform the benefit–risk assessment, rather than to satisfy a fixed checklist of studies.

In applying this proportionate approach, the SFDA will consider, on a case-by-case basis and following early engagement with the relevant review division, the following flexibilities:

- **Read-across and prior knowledge**: Existing nonclinical and clinical data from the same active substance, pharmacological class, vector, or technology platform may be leveraged to reduce or replace de novo studies, consistent with the platform technology and prior-knowledge principles described above.

- **Proportionate study design:** General toxicology in a single relevant (pharmacologically responsive) species may be acceptable where scientifically justified; study duration, recovery arms, and the scope of safety pharmacology, genotoxicity, and reproductive and developmental toxicity assessments may be tailored to the indication, the intended duration of treatment, and the target population. Staggered or deferred conduct of chronic, carcinogenicity, or juvenile studies may be accepted, with completion as a post-approval commitment where justified by disease severity and unmet need.

- **New Approach Methodologies (NAMs):** Where a non-animal method is scientifically suitable, validated, and fit for purpose, the SFDA encourages its use to replace, reduce, or refine animal testing for hazard identification, target-organ toxicity, and PK/PD

characterization, consistent with the NAMs provisions of this framework and the weight-of-evidence principle.

- **Biomarker bridge:** Biomarkers intended to serve as surrogate or accelerated-approval endpoints should be mechanistically linked to the disease in the nonclinical model, where that link is first established, so that the nonclinical program also supports the proposed efficacy-evidence strategy.

Any reduction in the nonclinical package should be agreed with the SFDA in advance through scientific advice or a pre-submission meeting, and supported by a clear scientific justification and, where applicable, a post-approval plan to generate the outstanding nonclinical data.