GUIDELINES ON

Emergency Use Approval

2022

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1. Introduction

Based on the ministerial decrees for registration & marketing authorization of biological products (343/2021) & human pharmaceutical products, Egyptian Drug Authority EDA issues this guideline for emergency use application & approval (EUA) including details on regulatory requirements in public health emergency cases. This guideline is intended to clarify these details for industry & other stakeholders as regulatory main tool for readiness & preparedness in such cases.

2. Scope

- This guideline is applicable for public health emergency cases.
- The EUA is a risk-based procedure for assessing unlicensed biological products and medicines for use during public health emergency cases. It is intended to provide a time-limited approval for unlicensed biological & medicinal products in an emergency context when limited data are available and the products are not yet ready for application for licensure through the normal marketing authorization pathways.
- The goal of this guideline is to define & illustrate the steps & key consideration that satisfy the regulatory requirements to give an EUA for an unlicensed biological products & medicines.

3. Definitions

Emergency: Is a situation that poses an immediate risk to health, life, property or environment. An incident, to be an emergency, conforms to one or more of the following:

- Poses an immediate threat to life, health, property, and environment.
- Has already caused loss of life, health detriments, property damage or environmental damage.
- Has a high probability of escalating to cause immediate danger to life, health, property or environment.

A pandemic: Is an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people. The classical definition includes nothing about population immunity, virology or disease severity.

An epidemic: Is the rapid spread of disease to a large number of people in a given population within a short period of time.

Good clinical practice (GCP): A standard for clinical studies which encompasses the design, conduct, monitoring, termination, audit, analysis, reporting and documentation of the studies and which ensures that the studies are scientifically and ethically sound and that the clinical properties of the pharmaceutical product (diagnostic, therapeutic or prophylactic) under investigation are properly documented.

Good manufacturing practice (GMP): That part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.

Stringent regulatory authority (SRA): A regulatory authority which is: (a) a member of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), being the European Commission, the US Food and Drug Administration and the Ministry of Health, Labour and Welfare of Japan; or (b) an ICH observer, or (c) a regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement.

Adverse drug reaction (ADR): Is an unwanted, undesirable effect of a medication that occurs during usual clinical use.

The Egyptian pharmaceutical vigilance center (EPVC): The center responsible for the collection, evaluation and assessment of information about the safety of pharmaceutical products and Medical Devices marketed in Egypt.

Periodic benefit risk evaluation report (PBRER): Is an analysis of the safety,efficacy, and efficiency of a drug, once it is already in the market. The PBRERsubmission is intended to present a periodic, comprehensive, brief and

critical evaluation of new or emerging information on the risks of the health product and the product's overall benefit-risk profile.

Pharmacovigilance system master file (PSMF): Is a comprehensive document containing the detailed description of a Marketing Authorization Holders' (MAH's) pharmacovigilance (PV) system ensuring the safety of their products.

Risk assessment: A systematic process of organizing information to support a risk decision to be made within a risk management process. It consists of the identification of hazards and the evaluation of risk associated with exposure to those hazards.

Risk management plan (RMP): A document submitted as part of the marketing authorization dossier that is evaluated by regulatory authorities before a medicine can be authorized and which is regularly updated as new information becomes available. RMPs include information on a medicine's safety profile and explain the measures that are taken in order to prevent or minimize the medicine’s risks in patients.

4. Procedures

4.1. Eligibility Criteria of the candidate products

The two product streams (biological & medicines) each have specific requirements for products to be eligible for evaluation under the EUA

procedure. In order to qualify for assessment under this procedure, the following criteria must be met:

a. Serious or life-threatening disease or condition, which has the potential of causing an outbreak, epidemic or pandemic, e.g., there are no licensed products for the indication or for a critical subpopulation (e.g., children).

b. Existing products have not been successful or effective in eradicating the disease or preventing outbreaks (in the case of vaccines and medicines).

c. The product may be considered for an emergency use authorization if the EDA determines that the known and potential benefits of the product, when used to diagnose, prevent, or treat the identified disease or condition, outweigh the known and potential risks of the product.

d. The product is manufactured in compliance with current GMP.

e. The applicant undertakes to complete the development of the product and apply for marketing authorization once the product is approved for emergency use. For that purpose, the remaining clinical trials and other testing needed to complete the development of the product must already be underway at the time of the application for a EUA.

f. In case of imported products, the product must have been granted an EUA and is in market of the country of origin or the product is listed by the WHO / SRA for emergency use.

g. The product should be included in the treatment protocols for such pandemic or epidemic situation which is approved by the WHO or the Egyptian governmental health authorities.

h. In case of EUA for generic medicinal product, it should rely on an innovator product which has been at least granted an EUA approval or has a well-established approved indication for treating such epidemic or pandemic situation, for instance by the WHO, EMA, FDA, or Japan.

4.2. EUA for biological products:

4.2.1. Termination and renewal of EUA:

- After granting the emergency use license, the product is evaluated in terms of its registration procedures and completion of the remaining studies. Based on the evaluation, a decision is made for renewal or the withdrawal of the emergency use license or to continue its circulation until the completion of the registration procedures license.
- The applicant apply for renewal of EUA license to the EUA committee who will take the decision for the renewal of EUA license.
- The applicant must take into consideration that the renewal file must contain the most updated stability data
- The marketing authorization department will submit the list of EUA products approval to the Directorate of Importation and customs Release of Pharmaceutical products
- EUA is terminated for certain product or indication when the EDA declared that the circumstances that precipitated the authorization have ceased or a change in the approval status of the product such that the authorized use(s) of the product are no longer unapproved.

4.2.2. Pre-submission activity

- Before submission of EU application, early engagement between applicants with EDA through scientific advice pathways is preferred.
- Based on the submitted data to EDA technical experts & the answers to their questions, EU approval procedure moves forwards.
- Pre-submission activity doesn't substitute the applicant effort to develop the product toward approval as the applicant should submit the registration file upon completion.

4.2.3. Recommendations for included data

- An annex is attached with this guideline for all data required during the submission and release of EUA license.

4.2.3.1. Administrative Requirements

All administrative requirements are mentioned in annex listed below.

4.2.3.2. Chemistry, Manufacture & Control:

-For imported products, complete CTD file should be submitted (considering ongoing development & stability parts), while for local products, CMC may be accepted.

-The application needs to be submitted with detailed information on chemical, manufacturing and controls; manufacturing site(s) where the product, if registered, is or would be manufactured and the current status

of the manufacturing site(s) with respect to current Good Manufacturing Practice (cGMP) requirements and relevant information regarding the product supply chain.

- Any manufacturing and process control data that will not be available at the time of submission of an EUA request should be clearly discussed with EDA and identified in the submission with sufficient justification, and a plan must be presented to address the data gaps with commitment to supply this information whenever it's available.

4.2.3.3. Non-clinical

- Non-clinical data demonstrating acceptable safety and efficacy in the most appropriate animal model. The choice of animal model shall be justified. If the non-clinical package is not complete at the time of submission; the applicant must submit adequate justification for the lack of complete data and a plan and timeline for submitting those data.

4.2.3.4. Clinical data

- Products- specific international guidelines are considered on case-by-case basis.
- In certain cases, approval of phase I and phase II shall be performed, the applicant must submits the results of phase II study by time of the end-of-phase II, and before initiation of the clinical trial(s) intended to serve as the primary basis for demonstration of efficacy; the applicant should submit phase III clinical study protocols with its evidence of ethical approval & GCP compliance.

4.2.3.5. Facilities and inspection

- Manufacturing data for drug substance and drug product should be submitted to support EDA regulatory decisions regarding compliance with GMP.
- Assessment of GMP compliance of facilities will be according to WHO GMP Guidelines, and any subsequent updates.
- For foreign manufacturer, desk assessment of inspection information from national authorities, SRA/reference country & WHO will be done.
- The desk assessment process involves submission of documentary evidence by the applicant, usually a manufacturer or representative, to the NRA to demonstrate the conformity of all sites involved in DS & DP manufacturing, or of an outsourced quality control laboratory (QCL) to GMP & Good Laboratory Practice (GLP).
- Based on risk-based approach, a decision will be taken based on reviewing submitted documents & evidence to perform a further on-site inspection or not.
- If onsite-inspections of manufacturing sites are considered for approval; In case of public health emergency, EDA will utilize all available tools, resources and sources of information to support regulatory decisions on applications that include sites impacted by EDA's ability to inspect due to emergency, Providing that the inspection will be undertaken as soon as the conditions preventing it are over.

4.2.3.6. Pharmacovigilance requirements

- Brief description of the company's pharmacovigilance system (Pharmacovigilance System Summary (PVSS) including the Adverse Drug Reaction (ADR) reports management procedures and safety risks assessment and management.

- If the applicant is an agent company, there should be a PV agreement between the global MAH and the local company including:

- The responsibility of each party regarding all the PV activities (global & local).
- The Signature of all involved parties
- Authorized agreement regarding the local part and Embassy legalization regarding the global part(s) /or (official declaration to submit the legalized copy within specific timeline) with the signed agreement

4.2.4. Process flow

Pre-submission activities / meetings

If considered necessary or desirable by the applicant and EDA, scientific advice request may be performed and a discussion may be held before the actual evaluation process starts.

Submission of applications

- The applicant must submit an application letter to EDA Registration directorate.

- The application letter should include details of country and sites of

manufacture, as well as the presentations proposed for the product.

Assessment of information received

- Once the product has been considered eligible for assessment under the EUA procedure, a product evaluation team is established within 2 WD.
- The product evaluation team will perform the screening of the submission to ensure that sufficient information is available to initiate the assessment based on the essential data requirements within 7 WD.
- Rolling submissions procedure is followed for evaluation of data & EDA requirements / reports are continuously sent to applicants as an outcome for each roll, rolling evaluation is performed within 20 WD. In practice, where there is an urgent public health need, assessment timelines will be reduced to the absolute minimum
- Applicants should promptly submit any additional information on the development of the product to EDA particularly if it may affect the product's benefit/risk assessment.

Requirements for batch release:

- Each lot of biological products is subjected to lot release procedure before marketing in Egypt by EDA through applying risk based approach.
- The assessment and testing of biologicals is based on the degree of risk associated with the product.
- There are technical and logistic issues for pandemic emergency which could affect the EDA lot release policy for biologicals.
- Biological products received for batch release in Egypt should be

produced in compliance with GMP and tested for quality and safety by the manufacturer.

- For emergency situations, first priority in lot release procedures should be given to review of the manufacturer's protocol and should always be part of the lot release by EDA.
- Protocol review: A summary protocol should be submitted to the EDA. It should be complying with the national and international regulations, as well as literature to support scientific consensus on aspects related to the specific type of product.
- Sample testing: In case of emergency, biological product could be released into the market after performing the minimum testing items that assure safety and quality of the product based on risk assessment in accordance to each product type and laboratories capabilities.

Assessment and issuance of the EUA

- The product evaluation team prepares a technical assessment report for submission to the emergency committee who will give the recommendation regarding issuing EUA for the product submitted.
- The conditional time-limited EUA is issued from the relevant Central Administration after the recommendation of EDA chairman deputy recommendation and endorsement of EDA chairman.

4.2.5. Post EUA obligations after EUA

After the emergency approval, any process changes &/or any intended changes for scale up, if any, should be submitted for evaluation of impact of these changes on the quality, efficacy and safety of the product.

Pre-clinical data

A final study report, if available, for a developmental and reproductive toxicology (DART) study, or the timeline for study completion and submission of the final study report, should be provided in order to inform potential emergency use of the vaccine in pregnant women.

Clinical data

-The EUA holder is required to complete specific obligations (ongoing or new studies, and in some cases additional activities) with a view to providing comprehensive data confirming that the benefit-risk balance is positive.

- Post authorization efficacy study (phase 3) to ensure efficacy and safety of the product.

PV and post marketing data

- Allocation of reporting channels for ADRs, communicate it with HCPs and informing EPVC, and spread awareness for HCPs about these channels.

- Submission adverse events reports to EPVC in an expedited manner according to PV requirement whether they are classified as serious or not.

- Mandatory ICSR follow up using targeted follow up questionnaire.

- Reporting Pregnancy exposure and off-label use without an associated adverse event using Pregnancy exposure and off label use reports.

- Submission of Global monthly safety report including: (narrative summary and analysis of ADR, newly identified safety concerns and actions taken for safety reasons during this interval, etc.).

*For local products, national monthly safety report will be requested.

- Submission of PBRER of periodicity determined by EPVC (e.g., 6 months for vaccines).

Post approval Monitoring

- After a product has been approved for emergency use, it will be put on the national market surveillance plan as a high risk product. Where, intense monitoring & sampling from the market and throughout the supply chain will be conducted.
- EDA will monitor the emergency situation for renewal of the EUA license or terminating it.

Lot release

- Each batch (local or imported) will be subject to lot release procedures before being released into the Egyptian market.
- Biological products used in case of emergency crisis will have a priority release schedule.

1. Products with WHO prequalified, listed under WHO EUL or approved by SRAs

- Products with overseas certification as evidence that the batch has already undergone independent testing and assessment by a recognized National Control Laboratory, such as the Official Control Authority Batch Release (OCABR) process in Europe, the release will be done quickly and through the review of the minimum documents and performing minimum test items.

2. Locally produced or self-procured biological products

In this case release of the biological product is based upon EDA review of the manufacturing summary protocol and /or submitted documents in addition to shipping information and testing in the EDA Laboratories.

Road to granting licensing of EU approved vaccine:

Full data concerning the drug substance and drug product should be submitted upon completion for the registration process of the product.

4.3. Emergency Use Approval for medicines

- Emergency use approval for medicines (generic products);

4.3.1. Reviewing quality aspects to grant preliminary approval:

- The applicant should submit the following documents for evaluation by EDA to grant a preliminary quality approval to be able to proceed to the manufacturing process of the drug product within 3 month starting from the approval of the registration request:

- Specifications & certificate of analysis for the drug substance.
- Composition of the drug product.
- Specifications of the drug product.
- Container closure system of the drug product.

Notes:

1. Generic products subjected to EUA must have the same pharmaceutical form, composition, specifications of the drug substance and drug product, and container closure system of the innovator product.
2. EDA has the right to request full data for drug substance and/or drug product in accordance with the most updated guidelines for assessing quality module 3 according to WHO or ICH guidelines.
3. The manufacturer will be allowed to produce commercial batches instead of primary batches to be able to perform Bioequivalence studies when applicable and accelerated stability testing for 6 months with a commitment to submit long term stability data when requested by EDA.
4. The drug substance and the commercial batches will be analyzed at EDA labs or at the manufacturing site by EDA labs analysts, the analysis results for the commercial batches will be considered a zero time for the stability study.
5. Results of accelerated stability study will be reviewed and assessed by EDA at 1st, 3rd and 6th month.
6. Excessive follow up for the accelerated stability study should be performed by the manufacturer at 2nd, 4th & 5th month, any out of

specification results should be reported to EDA within 10 days.

4.3.2. Manufacturing process:

1. The manufacturer must have a valid preliminary quality approval on for the drug substance and drug product.
2. The manufacturer should comply with the current GMP regulations.
3. The commercial production batches must be produced under the responsibility of the manufacturer in the presence of EDA inspectors to attend and monitor all manufacturing process to assure compliance with the requirements of the preliminary quality approval.
4. EDA inspector should confirm that required stability studies have been started.
5. The manufacturer must commit to continue the process validation study on the upcoming batches and the results of the validation should be submitted to EDA for assessment and evaluation.

4.3.3. Pharmacovigilance

As explained in biological products.

4.3.4. EU License for 8 months

The applicant should submit the following essential documents to grant the EU License:

- Preliminary approval of quality aspects.
- EDA labs analysis report for the drug substance & drug product.

- Inspection report for the manufacturing process and compliance to the preliminary quality approval.
- Bioequivalence study approval. (If applicable)
- Preliminary stability approval.
- Preliminary pricing certificate. (If available)
- Medical Insert.
- Inner and outer artwork.
- Initial Pharmacovigilance report.

Notes:

1. After receiving the EU license, the commercial batches are allowed to be released gradually according to urgent necessity and consumption rates to the entities specified by the Egyptian governmental health authorities & the Egyptian Drug Authority according to a specific and restricted drug tracking and tracing system and monitoring.
2. If the time of release of the batches intersected by the 1st or 3rd or 6th month of the accelerated stability studies, the batches will not be released till EDA approves the stability data for the intersected time interval.

4.3.5 Final License

The applicant should submit the following documents to have the Final License:

- Final Pricing Certificate.

- Results of accelerated stability study for 6 months.
- Results of long term stability study (when needed).
- Final Pharmacovigilance report.

Notes: Full data concerning the drug substance and drug product (after production of 3 consecutive commercial batches) in accordance with the most updated guidelines WHO or ICH should be available upon request by EDA for assessing quality module.

5. Glossary:

ADRs: Adverse drug reactions

BLA: Biologics License Applications.

DP: Drug Product

DS: Drug Substance

EMA: European Medicine Agency

EPVC: The Egyptian Pharmaceutical Vigilance Center.

EU: European Union

EUA: Emergency Use Approval WHO: World Health Organization

FDA: Food & Drug Administration

GCP: Good Clinical Practice

GMP: Good Manufacturing Practice

HCP: Healthcare professional.

ICH: International Conference of Harmonization EDA: Egyptian Drug Authority

ICSR: Individual case safety report.

MAH: Marketing authorization holder

NRA:	National Regulatory Authority
PBRER:	Periodic benefit-risk evaluation report
PSMF:	Pharmacovigilance system master file
PSSF:	Pharmacovigilance sub-system files (on national level)
RMP:	Risk management plan
PV:	Pharmacovigilance
SRA:	Stringent Regulatory Authority

6. References:

Development & Licensure of Vaccines to prevent COVID-19, FDA, June 2020

WHO emergency use listing procedure, EUL, Jan. 2020

7. Annexes

Annex I: Check list for EUA approval

Annex I

Check list for EUA approval

I. Administrative requirements:

No.	Requested item	Yes	No
1	Company profile		
2	Covering letter on applicant head letter signed and stamped for file submission for EUA.		
3	Emergency use Approval from country of origin (or proof of submission for emergency use approval).		
4	C.D. containing all content of the files (if applicable).		
5	Copy of Authorization letter for the person responsible for communication on behalf of applicant during the procedure and this letter should be certified as truly signed.		
6	Payment receipt (according to last update of fees decree).		
7	In cases of imported bulk products and filling in local manufacturing site: The filling contract between the foreign manufacturing company and the local filling site should submit		
8	In case of Toll manufacturing: The manufacturing contract specifying the intended product should be submitted certified as truly signed.		
9	Outer and inner labels of the Product.		
10	Package insert.		

11	Official declaration (from scientific office or from manufacturer) stating the type of the submitted pack (COO pack, country-specific pack, international pack …..etc.) with differences.		
12	Copy of Agency or distribution contract that should be notarized from the chamber of commerce or its equivalent in the country of origin and Authenticated from the Egyptian embassy abroad & submit original for review.		
13	In case of imported bulk naked vial that manufactured abroad and secondary packed locally: Copy of packaging contract between the importing company & local manufacturing.		
14	Copy of technology transfer contract (if available).		
15	If the excipient is plasma derived product used the company submit: plasma source certificate, HIV-1, HIV-2, HBsAG, HCV freedom certificate for the plasma.		
16	If the product is plasma derived, the following will be presented: - Plasma Master file that contain information of plasma source starting from collection passing all production process & in-process control & Viral safety - Official certificates declaring plasma source (legalized in case of		

	blood products active substance). - HIV-1, HIV-2, HBsAG, HCV freedom legalized certificate for the plasma. - Copy of Certificate of release from Health authority (Drug substance only).		

II. Chemistry, Manufacture & Control:

Detailed description of the manufacturing process and controls

No.	Requested item	Yes	No
	a. Manufacturing		
1	Critical process parameters.		
2	Critical quality attributes.		
3	Batch records, defined hold times.		
4	In-process testing scheme.		
5	Justified specifications for each critical parameter (Starting, intermediates, and final product).		
6	Validation data from the manufacture (validation protocol – study – reports of all critical process).		
7	Process validation (based on quality risk assessment for the development stage).		
8	Data on clinical batches with a commitment to complete validation on production batches.		
9	Validation data from the manufacture of platform-related products.		

10	Data for biological product storage, shipping and distribution at required temperatures.		
11	Any process changes &/or any intended changes for scale up after EUA.		
	b. Control of drug substance and drug product		
1	Full characterization of cell banks, master and working seed organism(s), based on reference to the most appropriate WHO Technical Report Series 978 (TRS 978), and any subsequent updates.		
2	History and qualification of cell banks, history and qualification of virus banks, and identification of all human or animal derived materials used for cell culture and virus growth.		
3	An evaluation and mitigation plan for potential adventitious agents.		
4	Data to demonstrate that the drug substance (DS) is sufficiently characterized in order to identify and understand the critical properties that impact performance and stability.		
5	The manufacturing process and process controls should be adequately described (A flow chart of all successive steps including relevant process parameters and in-process-testing should be given).		
6	Storage conditions, including the container-closure integrity, should be validated and this information should be provided for DS and drug product (DP).		

7	A stability plan including safety and stability-indicating tests and available stability data from all developmental, clinical, and commercial lots.		
8	Data to support short-term stability, reflecting storage conditions during transport and distribution and in clinics and covering the time from dose preparation to administration expected for DS and DP.		
9	The stability data should be submitted to cover the scale to be supplied in the field.		
10	The stability and expiry date of the biological's products in its final container, when maintained at the recommended storage temperature, should be demonstrated using final containers from at least three final lots made from different bulks.		
11	The DP must have been shown to maintain its quality especially the potency of biological products for a period equal to that from the date of release to the expiry date.		
12	Post marketing commitments to provide full shelf life data may be acceptable with appropriate justification.		
13	Analytical methods and qualification/validation data for all quality-indicating assays including key tests for vaccine purity, identity and potency, should be validated and shown to be suitable for the intended purpose.		
14	If novel test methods have been developed, full description of the test development and qualification must be presented. Validation data for assays used to evaluate critical		

	vaccine qualities such as purity, identity, and potency.		
15	A tabular listing of all clinical studies and DP lot numbers used in each study including DS lot genealogy, manufacturing processes used, and the manufacturing site, as well as the certificates of analysis (COAs) for all clinical lots used in clinical studies and information on any lots that were initiated but not accepted for release.		
16	Report(s) from the responsible stringent regulatory authority (SRA) or WHO listed authority (Summary basis for the emergency use approval or equivalent), and the release certificates of the SRA for the phase 1, 2, 3 and EUA lots (if available).		

III. Facilities and Inspections

No.	Requested item	Yes	No
1	List of each site where the product (DS and DP), if authorized, is or would be manufactured.		
2	Update Site Master File whose approval date was not more than one year ago including relevant layouts, premises & utilities information about each site including in production of the product required to issue an emergency use license and the current status of the manufacturing site(s) with respect to current GMP requirements.		
3	List of all equipment used for manufacturing DS and DP.		

4	Information about quality control unit and any outsourcing activities.		
Essential submitted documentary evidence for desk assessment			
1	Copy of the manufacturing authorization granted by national authorities (certified translation in English).		
2	A site master file whose approval date was not more than one year ago, and anyforecast modifications, together with: i. List of each site where the product (DS & DP), if authorized, is or would be manufactured. ii. Facility layout & personnel & materials flowchart for production workshops are required. iii. Legible color printouts of water treatment and air-handling systems, including pipeline and instrumentation drawings in A3 or A2 format. iv. List of all equipment used for manufacturing DS and DP should be submitted. Information about Quality control unit and any outsourcing activitiesshould be available.		
3	A list of all the products and dosage forms manufactured on-site.		
4	Cleaning validation for manufacturing line.		
5	Last qualification report of clean area		
6	A copy of the last inspection report issued by the national regulatory authority (NRA) and GMP certificate (production-line specific); (a		

	certified translated copy in English).		
7	List of all regulatory inspections performed in the last 3 years and their outcomes.		
8	Most recent product quality reviews (PQRs) of the concerned product (if available).		
9	The completed batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant product(s).		
10	Master batch manufacturing and packaging record(s) of the product(s) of interest.		
11	A list of any recalls in the past three years related to products with quality defects.		
12	Confirmation by the senior quality assurance representative that a full self- inspection or external audit dedicated to the product(s) has been performed and all matters dealt with (if applicable).		
13	Copy of any warning letter, or equivalent regulatory action, issued by any authority to which the site provides or has applied to provide the product.		

IV. Non-Clinical data

No.	Requested item	Yes	No
1	All relevant in vitro and in vivo pharmacodynamics data, e.g., on microbiologic / virology activity (including any modeling performed).		
2	Data on efficacy and safety in in-vitro tests and in animal model(s) under well controlled		

	and documented conditions. The preferred model depends on the disease and may vary according to the medicine's mechanism of action. The applicant must justify the choice of animal model.		
3	Evidence of efficacy should include improved survival and/or reduced morbidity of animals in the preferred model under relevant conditions. Surrogate markers, validated or reasonably expected to predict efficacy, would be supportive.		
4	All available evidence of the medicine's activity in vitro and in other animals, together with pharmacokinetics and efficacy in humans, also against other diseases should be submitted.		
5	A rationale should be provided for the proposed dosing in humans, with reference to drug exposures shown to be safe and effective in suitable models. Ideally, human pharmacokinetic data should be available, demonstrating similar levels of the drug following administration at the proposed dose, compared to blood levels found to be safe and efficacious in the relevant animal model.		
	Note: If human pharmacokinetic trials or studies in other indications at the exposure level proposed for treatment of the public health emergency disease have been conducted, assessment of safety using standard parameters (e.g., adverse events, clinical laboratory monitoring, etc.) will be done. This safety evaluation may be supplemented by any other nonclinical and clinical data at different exposure levels.		

V. Clinical data

No.	Requested item	Yes	No
1	Comprehensive data		
2	Reports of the on-site GCP inspections conducted by the other NRAs		
3	Available safety and effectiveness information for the product		
4	Any advisory committee reports by other NRAs		
5	Preliminary clinical evidence demonstrating that the drug may represent a substantial improvement over available therapy should involve a sufficient number of patients to be considered credible		
6	Justification for why the endpoint or other findings should be considered clinically significant		

VI. Pharmacovigilance

No.	Requested item	Yes	No
	a. For Local products		
1	The most updated “Risk Management Plan (RMP)" of the product.		
2	The most updated Pharmacovigilance System Master File (PSMF)/ PV system approval letter along with Summary PSMF of the MAH.		
	b. For Imported products		
1	The most updated "EU/Global/Core -Risk Management Plan (RMP)"		

2	The most updated Egyptian Display of RMP		
3	Periodic Benefit Risk Evaluation Report PBRER (If applicable)		
4	The most updated Pharmacovigilance System Master File (PSMF)/PVsystem approval letter along with Summary PSMF of the Global MAH		
5	The national Pharmacovigilance Sub-System File (PSSF) for local office/PV system approval letter or PSMF of the agent / PV system approval letter along with Summary of PSMF/ PSSF.		

VII. Supply Chain

No.	Requested item	Yes	No
1	Importation approval		
2	Customs invoice		
3	Cold chain		
4	CoA		
5	Any requirements mentioned in importation approval		

VIII. Lot release

No.	Requested item	Yes	No
1	CoA		
2	Summary protocol (if applicable).		
3	For imported Biological products: The manufacturer national regulatory authority's release certificates for the EUA lots should be submitted per batch. (in case of vaccine and plasma derived products)		