National Agency for Food & Drug Administration & Control (NAFDAC)

Guidance on Regulatory Preparedness for Licensing or Access to COVID-19 Vaccines

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Abbreviations

CTD	Common Technical Document
GMP	Good Manufacturing Practice(s)
ML	Maturity Level
NCL	National Control Laboratory
NRA	National Regulatory Authority
WHO	World Health Organisation

Acknowledgments

This guidance document is technically and structurally inspired by theWorld Health Organization (WHO) Technical Report Series, No. 1004. Annex 7 Guidelines on regulatory preparedness for provision of marketing authorization of human pandemic influenza vaccines in non-vaccine-producing countries and US-FDA's Development and Licensure of Vaccines to Prevent COVID-19: Guidance for Industry.

1. Introduction

There is currently an outbreak of respiratory disease caused by a novel coronavirus. The virus has been named "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). On 11th Marchof 2020 the World Health Organization (WHO) declared the COVID- 19 outbreak as a pandemic.

The SARS-CoV-2 pandemic presents an extraordinary challenge to global health. There are currently no licensed vaccines to prevent COVID-19. Commercial vaccine manufacturers and other entities are developing COVID-19 vaccine candidates using different technologies including RNA, DNA, protein, and viral vectored vaccines.

These Guidance provide applicants and vaccine manufacturers with:

1.1. Guidance regarding regulatory pathways for approving COVID-19 vaccines;

1.2. The regulatory considerations to take into account when evaluating the quality, safety and efficacy of candidate vaccines;

1.3. Guidance on effective post-marketing surveillance of COVID-19 vaccines.

The Guidelines were developed in the context of the Pandemic COVID-19 Preparedness Framework for regulatory capacity-building and strengthening of pandemic preparedness and response.

2. Purpose and scope

This guidance provides guidance on the regulatory oversight of COVID-19 vaccines for use in public health emergencies.

This guidance is aimed to prepare and put in place a regulatory process for COVID-19 vaccines in advance of vaccines that are being developed for that purpose. Such a process would enable NAFDAC toexpedite the provision of marketing authorization and lot release of COVID-19 vaccines in response to this pandemic emergency.

The document specifically provides the general principles for evaluating COVID-19 vaccines and establishing basic emergency procedures for regulating COVID-19 vaccines. A strong emphasis is placed on the decision-making processes that have been put in place which minimize duplication and make much-needed vaccines available for use without unnecessary delay during pandemic emergencies.

Other relevant NAFDAC vaccine guidelines should also be consulted as appropriate.

3. General considerations for regulatory preparedness forCOVID-19 vaccines

The guidance provides for a risk-based approach that: (a) enables a more flexible response to different scenarios; (b) uses a simplified pandemic phase structure (pandemic and post pandemic) phases.

NAFDAC has reviewed the options available during this public health emergency and has chosen the appropriate procedures to fit the situation. The emergency procedures include processes for ensuring information management, effective communication and cooperation between different Directorate of the Agency and relevant stakeholders such as public health authorities.

Plans have been developed to address the need for official communication from NAFDAC relevant to specific audiences – such as the public, health-care workers, national and subnational authorities and international collaborators when needed. Existing communication and information-sharing systems will be used.

The submission of a Risk-management plan which is part of marketing authorization to monitor the safety and efficacy of COVID-19 vaccines used during a pandemic is necessary.

3.1 Considerations for national regulatory preparedness

NAFDAC is responsible for developing the following procedures and plans to support the national pandemic COVID-19 preparedness plan and vaccine deployment plan:

i) Suitable regulatory pathways for COVID-19 vaccinesduring the emergency;
ii) Appropriate vaccine lot release procedures for emergency use;
iii) Post-marketing safety surveillance plans.

NAFDAC's preparedness procedures for facilitating the rapid availability of COVID-19 vaccines include:

3.1.1. Designated contact point for communications with WHO and other stakeholders on public health/regulatory issues;
3.1.2. Allocation of resources to be used when this pandemic alert was declared by WHO;
3.1.3. A public risk-communications plan summarizing the basis for decision-making;
3.1.4. An existing National Advisory Committee on Vaccines and Biologics (NACVB) for COVID-19 vaccines that:
3.1.4.1. Include appropriate regulatory and programmatic expertise;
3.1.4.2. Prepare procedures for evaluation of applications for COVID-19 vaccine;
3.1.4.3. Define the dossier and supporting documentsneeded for evaluation;
3.1.4.4. Evaluate and recommend marketing authorization of suitable vaccines to the agency; and

3.1.5. Procedures for interactions (including discussion of options for appropriate sources of vaccine) with the public health agencies that will procure, deploy andadminister the vaccines;

3.1.6. A system to accelerate the licensure and lot release of COVID-19 vaccine including recognition of the decisions, or reliance upon the expertise, of supporting NRAs, and the optimizing of available resources in response to the pandemic;

3.1.7. Procedures and requirements for lot release of COVID-19 vaccines by the agency during the pandemic (oremergency situation).

The following steps are included in the regulatory preparedness procedures:

3.1.8. A working procedure for marketing authorization of COVID-19 vaccine.

3.1.9. Preparation of a template emergency risk–benefit consideration and assessment report;

3.1.10. procedure for emergency approval of the NRA recommendation, as appropriate;

3.1.11. A process to expedite marketing authorization through the WHO collaborative procedure for prequalified vaccines, when appropriate;

3.1.12. Preparation of an outline post-marketing surveillance plan which includes special provisions for post- marketing surveillance of the COVID-19 vaccine in use.

3.2 Reliance on the decisions and expertise of other regulatory authorities

Mechanisms have been put in place to consider reliance on the product evaluation decisions made by other NRAs in vaccine-producing countries. NAFDAC has established mechanisms and procedures for recognizing the marketing authorization decisions of the NRA of the country producing the vaccine, or of other NRAs with WHO ML 3 and above as appropriate, when considering the licensing of a COVID-19 vaccine. The Agency may rely on the assessment report of such NRAs.

Mechanisms and procedures may include recognition, including an information-sharing agreement between NAFDAC and the selected NRAs, reliance on assessment report.

The assessment reports (summary basis for decision) from other NRAs may provide valuable information and insight into the decision-makingprocesses of these NRAs but may not be readily available during the pandemic. In this case communication with the relevant NRA regardingthe licensure will be pursued.

In addition, NAFDAC may participate in joint reviews and the report will form the basis for a national decision.

It is expected that COVID-19 vaccines prequalified by WHO will include a summary assessment report outlining the basis for prequalification that will be available to countries intending to import, grant marketing authorization for and use these vaccines to mitigate COVID-19 pandemic.

4. Regulatory evaluation processes

The following regulatory procedures have been put in place granting timely marketing authorization or emergency approval and lot release of a COVID-19 vaccine in an emergency situation:

4.1. NAFDAC policies and procedures for:

4.1.1. NAFDAC evaluation of COVID-19 vaccine applications;

4.1.2. Procedures and criteria for rapid identification of suitable experts for regulatory evaluation of COVID-19 vaccine applications (NACVB);

4.1.3. Consideration of a joint review (global or regional); and

4.1.4.Recognition of the marketing authorization decisions of other NRAs and the WHO prequalification decision;

4.2. Depending on the pandemic phase and the source of the vaccine, the following regulatory approaches could befollowed:

4.2.1. Full review – a standard review process to authorize a product licensure that can include fast-track review.

4.2.2. Fast-track review of basic documentation – a fast-track review process based on basic available information for emergency authorization.

4.2.3. Reliance – a process to review the marketing authorization report/ decision issued by an NRA with WHO ML 3 and above or WHO prequalification.

4.2.4. Recognition – recognition of the marketing authorization decision of another NRA or WHO prequalification without further evaluation.

4.3. Expected basic documentation according to the source of COVID-19 vaccine

COVID-19 vaccines for programmatic use are expected to be from different sources, including a United Nations agency, a donation from a company or other source, or through national procurement. In general, full dossiers are required for evaluation of the quality, safety and efficacy of vaccines – however, in the current emergency situationthe accompanying documentation dossier may be provided in sectionsas it becomes available.

Under these circumstances, at least the following documents should bemade available for evaluation to ensure the quality, safety and efficacyof vaccines from each source:

4.3.1. United Nations agency supply (WHO-prequalified vaccines)

4.3.1.1. Evidence/certificate of WHO prequalification with assessment report.

4.3.2. Donation from a company or other source

4.3.2.1. If the vaccine has been prequalified by WHO the Common Technical Document (CTD) Module-2 and prequalification assessment report should be provided.

4.3.2.2. If the vaccine has been licensed by an NRA with WHO ML 3 and above, the CTD Module-2 and assessment report by the NRA, if available, should be provided.

4.3.2.3. Where the vaccine has been licensed by an NRAother than an NRA with WHO ML 3 and above the full dossier for marketing authorization and the assessment report by the NRA, if available, should be provided.

4.3.2.4. In the case of a vaccine that has not previously been licensed a full dossier for marketing authorization should be provided by the manufacturer. The procedures and requirements in the Guidance Document for Submission of Application in CTD Format - Vaccines for Human Use should be followed. Clinical trial study conducted in Nigeria shall be required andsupport may be sought from the NRA of the producing country. NAFDAC guidelines on donations of medicines should also be followed.

4.3.3. National procurement

4.3.3.1. If the vaccine has been prequalified by WHO theCTD Module-2 and prequalification assessment report should be provided.

4.3.3.2. If the vaccine has been licensed by an NRA with WHO ML 3 and above, the CTD Module-2 and assessment report by the NRA,if available, should be provided.

4.3.3.3. Where the vaccine has been licensed by an NRAother than an NRA with WHO ML 3 and above the full dossier for marketing authorization and the assessment report by the NRA, if available, should be provided.

4.3.3.4. In the case of a vaccine that has not previously been licensed, a full dossier for marketing authorization should be provided by the manufacturer. The procedures and requirements of NAFDAC's Guidance Document for Submission of Application in CTD Format -Vaccines for Human Use should be followed.

Clinical trial study conducted in Nigeria shall be required and support may be sought from the NRA of the producing country.

4.4. Possible regulatory review processes in the pandemic emergency

Even in the midst of the COVID-19 pandemic, NAFDAC will conduct an appropriate review of the documentation submitted that covers the components set out below, and will document the extent of the available evidence on which the recommendation to authorize, approveor reject will be based.

NAFDAC will accept a Rolling Submission and conduct a Rolling Review as it understands that in the pandemic emergency, it is possible that not all documentation for a vaccine will be available at the time of application, and the Agency shall accept that applicants will submit theevidence as it becomes available. It would be expected that the sections on manufacturing, specifications and controls would be available, together with evidence of consistency of manufacture. For nonclinical safety studies, preliminary results should be available. An abridged clinical study to generate data for target population may be required. The results of stability studies would be delayed as would any results from clinical studies. However, this may not be applicable to vaccinesmanufactured using novel construct or formulation.

Where possible Participation in a joint review at the regional or globallevel is acceptable.

Depending on the pandemic phase and the source of the vaccine, review activities may include one or more of the following procedures (see also Fig 1):

- Full review;
- fast-track review of basic documentation;
- Reliance;
- Recognition;

4.4.1. Full review

This is the standard process of review of the full dossier in a fast-trackreview process (as normally conducted) for vaccines that are new applications or previously licensed by NRAs other than an NRA with WHO ML 3 and above.

4.4.1.1. *Available documentation*: the documentation should be complete, as required and stated in theNAFDAC's Guidance Document for Submission of Application in CTD Format -Vaccines for Human Use.

4.4.1.2. *Applicability*: this procedure would apply to licensed vaccines in the post pandemic phase.

This would require evaluation of the documentation of product qualityand of the results of nonclinical and clinical studies to demonstrate safety and efficacy in the target population. The documentation should be as legally required in each country.

During the post pandemic phase, NAFDAC may conduct a full COVID-19 vaccine dossier review to ensure familiarity with the characteristics of such vaccines.

4.4.2. Fast-track review of basic documentation

This is a fast-track review process in which marketing authorization isbased upon the information available at the time. In the event that a fast-track review is deemed appropriate (as defined in the NAFDAC pandemic emergency procedures) the following documents from the manufacturer and the responsible NRA and/or WHO should be reviewed. The full application dossier may be provided when available.

4.4.2.1. *Available documentation*:

4.4.2.1.1. Assessment reports of the responsible NRA;

4.4.2.1.2. Evidence of quality (certificate of analysis or lot release) and good manufacturing practices (GMP) compliance (GMP certificate);

4.4.2.1.3. CTD Module-2 quality, nonclinical and clinical overviews (if available).

4.4.2.2. *Applicability*: this procedure would apply during the pandemic and post pandemic phase for a COVID-19 vaccine licensed by an NRA other than an NRA with WHO ML 3 and above.

4.4.3. Reliance

This is the process of reviewing the decisions of other competent NRAs with which there has been an agreement for support. Where it has been agreed that the decision of another NRA can be considered and used as the basis of a recommendation for marketing authorization, this approach would involve acceptance on the basis of the already agreed conditions and limitations on the use of the vaccine.

4.4.3.1. Available documentation required:

4.4.3.1.1. Certificate of the responsible NRA's marketing authorization decision

4.4.3.1.2. Assessment reports of the responsible NRA.

4.4.3.2. *Applicability*: this procedure would apply during the pandemic and post pandemic for the COVID-19 vaccine licensed by an NRA with WHO ML 3 and above.

4.4.4. Recognition

This is the process of recognizing the WHO prequalification decision or the decision of an NRA with WHO ML 3 and above. Where it has been agreed that the decision of an NRA with WHO ML 3 and above can be used as the basis for a recommendation for marketing authorization, this approach would involve acceptance on the basis of the already agreed conditions and limitations on the use of the vaccine.

4.4.4.1. A*vailable documentation required*: Certificate of the responsible NRA's marketing authorization decision or WHO prequalification assessment report.

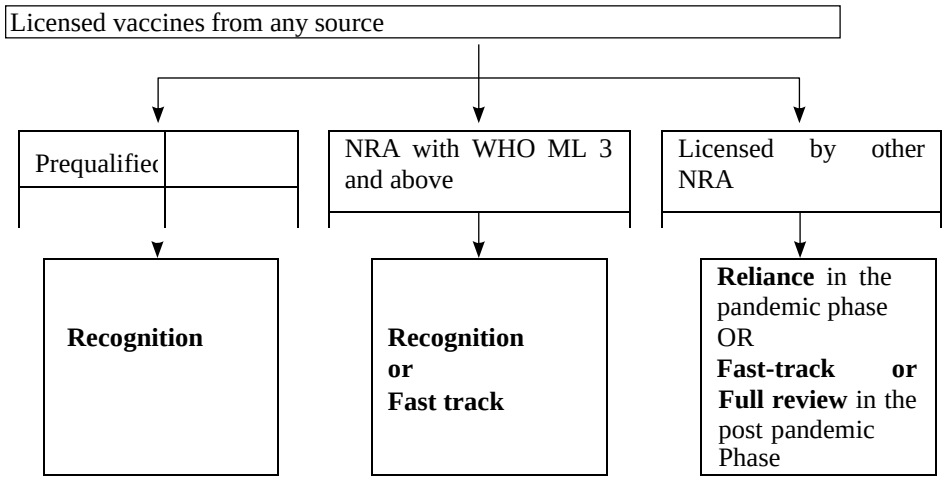
4.4.4.2. *Applicability*: this procedure would apply during the pandemic phase and Post pandemic phase for

COVID-19 vaccine licensed by an NRA with WHO ML 3 and above or prequalified by WHO.

4.4.5. WHO collaborative procedure for prequalified vaccines

Apart from the regulatory procedures for marketing authorization of COVID-19 vaccines, expedited licensure through the WHO collaborative procedure for prequalified vaccines may also be used forsuitable COVID-19 vaccines as appropriate. For this procedure, this NAFDAC guideline:
Guidelines for Registration of Drugs Vaccines IVDs Under Collaborative Registration Procedure should be followed

Fig.1
Regulatory pathways relative to the status of the vaccine and thecontinuum of pandemic phases[a]



[a] pandemic and post pandemic phases.

4.5. Final evaluation

Before a regulatory decision to recommend marketing authorization ofa COVID-19 vaccine is taken a final evaluation of the available

documentation will be conducted to ensure that the COVID-19 vaccine presentation is suitable for use in Nigeria.

Provided the necessary procedures outlined in this guidance are followed final evaluation can be conducted rapidly (for example, in aslittle as one day depending on circumstances and COVID-19 vaccine marketing authorization status) with a risk– benefit consideration and recommendation for marketing authorization. The Agency will ensurethat the following conditions are met:

4.5.1. An adequate document package is provided. A post-marketing commitment by the manufacturer to provide any outstanding information will be considered.
4.5.2. There is a local agency responsible for supply of the product (that is, an "applicant" or state body that is a defined responsible legal entity).
4.5.3. Packaging, label and package insert are nationally acceptable.
4.5.4. The vaccine is compatible with the national COVID-19 pandemic preparedness plan.

This evaluation may need to be based upon minimal and incomplete documentation, and this will be acknowledged in the approval.

An evaluation report should be produced will be produced by the Agency.

4.6. Emergency approval

During the pandemic period, emergency approval procedures may be used. Approval may be based upon limited clinical data or quality data (for example, on stability) and upon expedited evaluation of the available evidence. Therefore, the approval may include one or more special conditions for use. These can include post-marketing safety reporting requirements, and limitations such as:

4.6.1. Use only during the pandemic period
4.6.2.Use only by certain agencies
4.6.3.Use only in certain listed groups at high risk 4.6.4.Special conditions for post-marketing safety reporting.

4.7 Post-marketing risk management and surveillance

The applicant is to provide an outline of the post-marketing pharmacovigilance plan (PVP) for the product or Risk Management Plan (RMP).

The PVP should include actions designed to address all important identified risks, important potential risks or important missing information. Pharmacoepidemiologic studies or other actions to evaluate notable potential risks, such as vaccine-associated Enhanced respiratory disease (ERD), transverse myelitis and some reactogenic illnesses, should be considered. NAFDAC may recommend one or more of the following as components of a PVP for a COVID-19 vaccine:

4.7.1 Submission of reports of specific adverse events of interest in an expedited manner beyond routine requiredreporting;

4.7.2 Submission of adverse event report summaries at more frequent intervals than specified for routine required reporting;

4.7.3 Ongoing and/or extended safety follow-up for vaccine associated ERD of subjects enrolled in pre-licensure clinical studies;

4.7.4 A pharmacoepidemiologic study to further evaluate (an) important identified or potential risk(s) from the clinical development program, such as vaccine associated ERD or other uncommon or delayed-onset adverse events of special interest;

4.7.5 A pregnancy exposure registry that actively collects information on vaccination during pregnancy and associated pregnancy and infant outcomes

National systems for post-marketing surveillance and reporting of adverse events following immunization shall be in place.

4.8. Traceability

Mechanisms are being put in place to ensure that effective traceability solutions can be deployed to support the distribution of a COVID-19 vaccine.

Applicants are therefore expected to deploy Serialisation Technology which are based on proven international global standards. This will enable the achievement of safe and effective distribution and delivery of COVID-19 vaccines.

The Technology will also ensure that falsified products can be easily detected along the supply chain and also facilitate the conduct of activepost marketing surveillance and pharmacovigilance activities of the COVID-19 vaccines.

5. Quality control preparedness

Lot release and quality control of COVID-19 vaccines will be handled by National Control Laboratory for Vaccines and other Biologicals (NCLVB).

Vaccines should be produced in compliance with GMP and tested for quality and safety by the vaccine manufacturer. Such vaccines should also be subjected to quality control testing (with certificate of analysis issued) and released by the responsible NCL in accordance with the WHO's *Guidelines for independent lot release of vaccines by regulatory authorities* (and should be accompanied by lot release certificate). For vaccines supplied through United Nations agencies further release by the NCLVB shall not be performed because such products are prequalified by WHO and released by the responsible NRA/NCL. Likewise, WHO prequalified vaccines are normally released by the responsible NRA/NCL and as such will not be subjected to further lot release. The lot release certificate of the responsible NRA/NCL of the producing country shall be duly recognized.

For non-WHO-prequalified COVID-19 vaccines, the NCLVB of NAFDAC will conduct lot release. The need for further Laboratory testing will be determined on a case by case bases guided by outcomes of risk-based assessment.

The procedures adopted shall be to ensure the deployment of vaccines without undue delay.