

COVID-19

Recommendations on Regulatory Processes and Aspects related to the Introduction of Vaccines during the COVID-19 Pandemic and Other Emergencies

Introduction

The objective of this document is to identify the main gaps in readiness for the introduction of COVID-19 vaccines and to propose the regulatory procedures needed to manage and reduce these gaps, which were detected through a situation analysis of the emergency regulatory procedures implemented by national regulatory authorities (NRAs) in the Americas and based on the available information regarding existing regulatory frameworks in the Region.

NRAs are responsible for establishing the requirements, procedures, and timeframes for vaccine introduction and use at the national level (1). During emergency situations, the World Health Organization (WHO) recommends that NRAs adopt agile and efficient regulatory pathways to evaluate the quality, safety, and efficacy of new vaccines, which should be based on risk-benefit assessments. It also recommends that, for each authorized vaccine, pharmacovigilance activities should be implemented, based on risk management plans (2).

As noted in previous documents and recommendations, countries should have national emergency preparedness and response plans that include streamlined regulatory pathways that allow new vaccines to be introduced following legal and orderly processes (1-4). This regulatory preparedness is key to achieving a rapid response that does not obstruct or delay the availability of vaccines.

Results of regulatory preparedness for the introduction of COVID-19 vaccines in the Region of the Americas

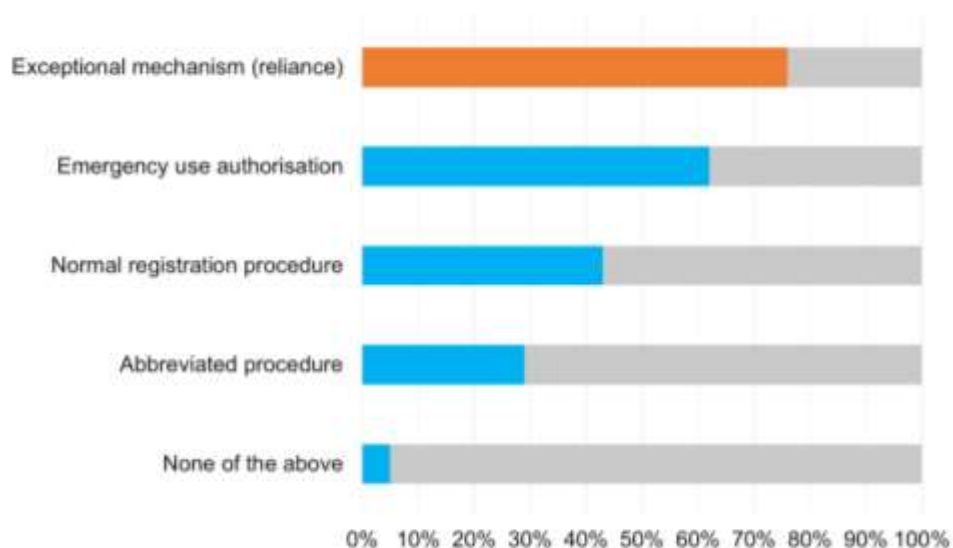
In response to the COVID-19 pandemic, WHO recommends that vaccines be introduced subject to the development and implementation of a national deployment and vaccination plan (3). This plan should include the implementation of appropriate and streamlined regulatory mechanisms to facilitate timely access to vaccines without compromising proper quality, safety, and efficacy assessments.

In April 2020, the Pan American Health Organization (PAHO) formed a network of NRA focal points to identify regulatory obstacles related to the COVID-19 pandemic and provide guidance on how these might be overcome, as well as promoting the timely exchange of information among NRAs in the Region. Also in November 2020, this network participated in submitting data to PAHO on existing regulatory mechanisms for the COVID-19 response in the Region. This information, together with the regulatory aspects included in the updated COVID-19 Vaccine Introduction Readiness Assessment Tool (VIRAT/VRAF 2.0), 3 December 2020 (5) and the national regulations of participating countries, was used to characterize and analyze the current regulatory systems for emergency situations across the Region.

For this analysis, the regulatory processes considered were: authorization, importation, and lot release of vaccines for the national immunization program (NIP), and post-introduction surveillance of COVID-19 vaccines. The following results were compiled from 21 of 25 NRAs consulted:¹

- 1) **NRAs' knowledge of the VIRAT/VIRAF tool:** The self-assessment tool aims to provide assistance to countries in assessing their readiness for the introduction of COVID-19 vaccines, identifying obstacles and establishing priority actions in 10 specific areas, including regulatory preparedness. In November 2020, 43% of NRAs indicated that they had not participated in the consolidation of the information outlined in the VIRAT/VIRAF tool in their countries.
- 2) **COVID-19 vaccine authorization process:** There are at least four different vaccine authorization mechanisms within the regulatory frameworks of the countries of the Region (Figure 1). It is important to note that, in some cases, more than one authorization mechanism is permitted under current legislation, depending on the vaccine procurement route.

Figure 1. Regulatory mechanisms for COVID-19 vaccine approval used by the national regulatory authorities of 21 countries of the Region of the Americas, November 2020



Sources: Pan American Health Organization. Guidance on developing a national deployment and vaccination plan for COVID-19 vaccines (v.2), 4 June 2021. Washington, DC: PAHO; 2021.; Pan American Health Organization. COVID-19 Vaccine Introduction Readiness Assessment Tool (VIRAT). Washington D.C.: PAHO, 2020; and national regulations of the countries analyzed.

The following are the four mechanisms reported (Figure 1):

- **Exceptional approval mechanism based on reliance on regulatory decisions issued by other entities of reference:** 76% of the NRAs indicated that they would use this route for the approval of COVID-19 vaccines.² However, it is unclear in some cases how this will be implemented. There is no legislation

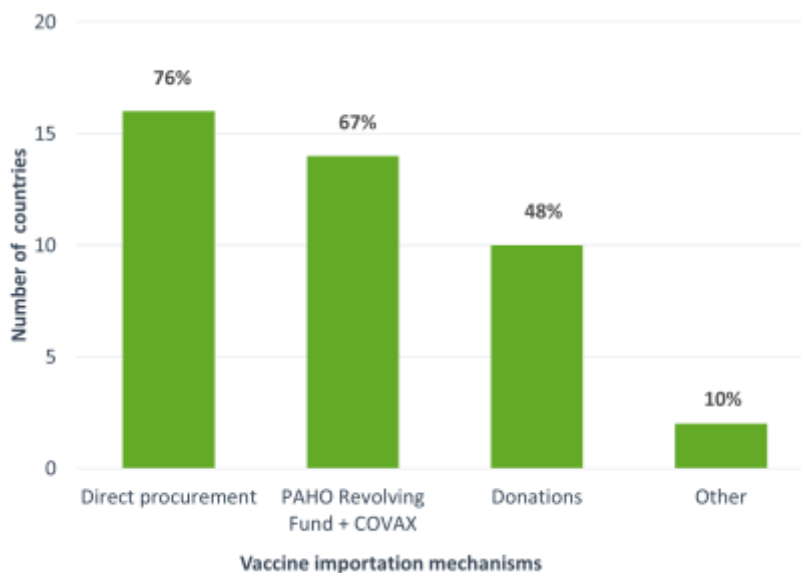
¹ The NRAs of the following countries were consulted: Argentina, Belize, Bolivia (Plurinational State of), Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Trinidad and Tobago, United States of America, Uruguay, and Venezuela (Bolivarian Republic of).

² The entities of reference are the WHO Prequalification Programme, the PAHO Revolving Fund for Vaccine Procurement, NRAs of regional reference, and Stringent Regulatory Authorities.

stipulating what documentation is required, whether the decision is automatic, or who is responsible for submitting the information.

- **Emergency Use Authorization (EUA):** 62% of NRAs indicated that they would use an EUA, although the name varies from country to country. On reviewing the various requirements and regulatory frameworks, it became clear that the EUA does not always entail a fast-tracked authorization procedure, and that there is also a lack of uniformity in the requirements defined by each country for this option.
 - **Normal registration procedure:** 43% of the NRAs indicated that they would follow the normal registration pathway. It is not known if this is applicable in an emergency situation. It is important to note that, of all the mechanisms notified, this is the only one that does not imply a possible waiving of requirements or streamlining of processes.
 - **Streamlined procedure:** 24% of NRAs reported having streamlined procedures for the authorization of the COVID-19 vaccines. In these cases, there are no regulations that clearly establish how the requirements or timelines may differ from the other mechanisms described above. Furthermore, the review of the relevant legislation indicated that some NRAs in the Region make no clear distinction between 1) procedures applicable to cases of reliance or exceptions to registration processes, and 2) procedures applicable to EUA.
- 3) **COVID-19 vaccine import authorization in the context of a pandemic emergency:** Participants were asked about three hypothetical frameworks regarding practices followed in the Region for the control of imports and customs clearance: 1) direct procurement of vaccines by the ministry of health; 2) procurement through the PAHO Revolving Fund for Vaccine Procurement and the Global Access Fund for COVID-19 Vaccines (COVAX); and 3) supplies received through donations (Figure 2). As in the case of COVID-19 vaccine authorization processes, national legislations also establish more than one mechanism by which vaccines can be introduced at the national level in emergency situations. In some cases, importation permits do not fall under the competencies of the NRAs of the countries participating in the consultation but are granted by other actors who may or may not belong to the ministry of health.

Figure 2. Vaccine import scenarios according to procurement pathways



Seventy-six percent of the laws of the countries consulted have requirements for the issuance of importation permits, authorizations, and customs clearance when vaccines are purchased directly. Likewise, 67% of the laws have requirements when vaccines are imported following procurement through the PAHO Revolving Fund and COVAX, and in 48% of cases when they are imported via donations. In addition, 10% of NRAs report that they have no specific requirements in their regulations for any of the procedures described above. Furthermore, the regulatory frameworks in most countries that routinely purchase vaccines through the PAHO Revolving Fund do not reflect the expedited mechanisms they use to import or license vaccines obtained this way, which includes waiving authorization prior to importation and requesting minimal authorization requirements.

With regard to the timeframes for granting import permits and customs clearance, 71% of the NRAs that participated in the consultation indicated that, in response to the pandemic, this process takes less than five days, as established by the VIRAT/VIRAF tool (5); however, it should be noted that this timeframe could not be corroborated in the current regulations of those countries.

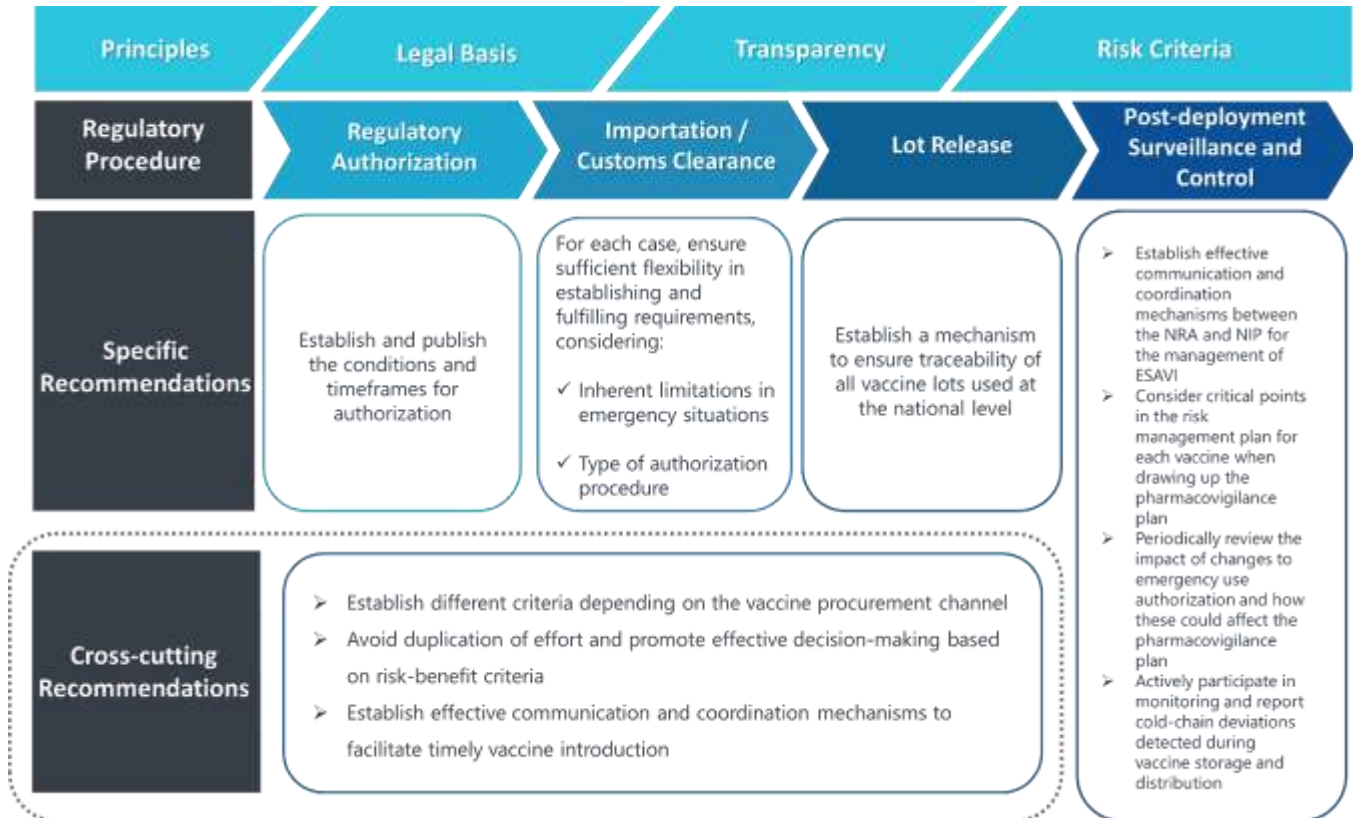
- 4) COVID-19 vaccine lot release procedure:** Participants were asked about the mechanisms used for this regulatory activity in the context of the COVID-19 pandemic. It should be noted that, according to the risk criteria established by the NRA, any of the first two procedures described below can be applied at the national level:
- Forty-three percent of NRAs indicated that they would recognize lot release certificates already issued by the corresponding NRA (from the country of manufacture or reference), without the need to duplicate this process at the national level.
 - In 57% of the countries consulted, the NRA evaluates the summary protocols for manufacturing and control, and then issues its national release certificate. Furthermore, 10% of these NRAs indicated that their regulations grant them the power to carry out further laboratory analyses as deemed necessary, in addition to reviewing the aforementioned documentation, before issuing a national release certificate. From the responses received, it was not possible to determine how they would address comments or doubts that may arise during the review of these documents, or deviations in laboratory results, nor how timelines for such cases could affect the availability of COVID-19 vaccines.
 - Finally, 19% of NRAs do not carry out lot release activities, or do not require them.
- 5) Cold chain verification mechanism:** The majority (71%) of the responding NRAs indicated that they participate in the cold chain verification process for vaccines entering their respective countries. In cases where NRAs are not involved in this activity, they rely on notifications made by third parties for subsequent decision-making.
- 6) Evaluation and reporting of adverse Events Supposedly Attributable to Vaccination or Immunization (ESAVI):** 90% of the NRAs consulted indicated that they participate in the evaluation and reporting of ESAVI. The remaining NRAs reported that they did not have the capacity to perform this activity, or that they were now in the process of developing this activity. This could mean that the NRAs are unaware of the possible adverse events attributable to the COVID-19 vaccines used in their country.

Recommendations on emergency regulatory procedures for the introduction of new vaccines

To support the implementation of effective mechanisms for the timely incorporation of vaccines into health systems in an emergency situation, and considering the findings described above, recommendations are provided here for NRAs in the Region (summarized in Figure 3). The implementation of these recommendations should be

assessed in light of the particular circumstances of each country and the procurement mechanisms established by the ministry of health in response to the emergency.

Graph 3. Aspects to consider when establishing effective regulatory mechanisms for the incorporation of vaccines into health systems in emergency situations



Recommendations on the basic elements and principles of regulatory processes associated with emergency situations

In view of the diversity of mechanisms and environments in which NRAs carry out their activities and make their decisions, the following universal principles must be upheld to guide and inform their decisions (6):

- **Transparency:** Regulatory processes and their implementation schedules must be made available. In addition, regulatory decisions, as well as their timeframes, implementation dates, and any elements used to inform such decisions, should be duly documented.
- **Legal basis:** Decisions reached by regulatory authorities must be consistent with the national legal framework and be based on clear mandates and rules aimed at efficient implementation. Any documentary or regulatory requirements for emergency mechanisms must not undermine the advantages gained with the implementation of such mechanisms.
- **Consider establishing risk criteria when applying regulatory procedures:** In both emergency and non-emergency situations, NRA decisions should be supported by reliable information on the quality, safety, and efficacy of these products; however, given the timeframes and mechanisms required for a timely response in an emergency situation, a less stringent risk approach may be tolerated compared to that used in normal situations. Both the nature of the product under evaluation and its origin (manufacture and procurement

pathway) should be considered when defining the risk factors for regulatory decision-making and establishing differentiated mechanisms according to these parameters.

General recommendations

As summarized in Figure 3, the regional analysis produced two recommendations common to more than one regulatory function: 1) establish differentiated criteria based on the vaccine procurement pathway; and 2) avoid duplication of efforts and improve efficiency in decision-making based on risk-benefit criteria. Further details on these recommendations are provided below:

1) Establish differentiated criteria based on the vaccine procurement pathway:

- Authorization processes:** NRAs are expected to define the requirements, procedures, and evaluation times based on the procurement mechanisms envisaged by ministries of health to ensure timely access to vaccines in emergency situations. There are a number of elements that can guide NRAs when defining their own regulatory requirements: knowledge of the criteria and terms of the procurement or donation agreements to verify the origin, quality, safety, and efficacy of the vaccines; or the feasibility of accessing key product information (publicly available, under confidentiality agreements signed with other entities, or through the manufacturer in certain cases). For example, COVID-19 vaccines purchased through the COVAX mechanism must be included in the WHO emergency use list (EUL) or be prequalified. WHO has drawn up a confidentiality agreement that allows NRAs to access documentation submitted by manufacturers, as well as the corresponding assessment reports.
- Importation and custom clearance processes:** In the case of imported products, the NRAs must establish agile emergency procedures that allow them to issue the respective permits faster than usual, but without compromising the procedures required to verify the origin and quality of the product received. All medical products must be imported in accordance with national legislation (2). The WHO guidelines state that regulatory frameworks should have documented mechanisms so that NRAs can waive requirements for expedited importation in emergency situations (7). This is of particular importance as certain documents that traditionally form part of import requirements (such as apostilled and translated certificates of pharmaceutical products or over-the-counter medicines) may not be available when applying for an import authorization during an emergency. Therefore, local authorities should consider measures that would facilitate import licensing taking into account such limitations. All these procedures should be duly documented to ensure that they are consistently replicated over time, regardless of who is responsible for the authorization. For example, most countries in the Region of the Americas purchase the vaccines used in their NIPs through the PAHO's Revolving Fund for Vaccine Procurement. Knowing the procurement criteria used by this mechanism has allowed most countries to acquire these products without the need to carry out their own registration processes or emergency use authorizations. While this has been standard practice, it is important that national regulatory frameworks reflect the expedited mechanisms for the importation and authorization of vaccines obtained through this channel, such as waiving of pre-import authorization and establishing minimum authorization requirements.
- Lot release at the national level:** These procedures should take into account the risk-benefit assessment depending on the origin of the product (domestically manufactured or imported) and the procurement pathway. NRAs must ensure that such procedures can be repeated over time, regardless of the personnel in charge of the lot release process. Also, in countries where there is no legislation governing lot release processes, other mechanisms should be devised to record the details of all lots entering the country and ensure the traceability of these in an emergency context.

2) Avoid duplication of efforts and improve decision-making based on risk-benefit criteria:

- **Authorization procedures:** NRAs must implement emergency regulatory procedures that allow them to properly evaluate the available information related to the quality, safety, and efficacy of the vaccines and to conduct risk-benefit analyses so these products can be authorized. It is important that NRAs establish a clear distinction between these emergency use authorization procedures and those which rely on decisions of other jurisdictions or registration waivers. Table 1 outlines some of the characteristics of emergency mechanisms, as well as suggestions and considerations to take into account when applying them.
- Relying on decisions made by other trusted or reference authorities is a widely used tool, not only in emergency situations. This strategy allows NRAs to focus their human resources, time, and funds on vaccines that require more detailed evaluation. This allows for more efficient and timely responses, for example, in the case of vaccines that are nationally manufactured or for which no prior authorization has been issued by a reference entity—where regulatory decisions may involve greater or unknown risks. In this regard, it is recommended to consult other sources (3) that describe the guidelines to be considered when applying this type of authorization. It is also important to remember that in order to adopt decisions made by regulatory authorities of other jurisdictions, there must be a legal basis for this in the country's legislation. The decision must be documented as part of good review practices and it is necessary to uphold the principles of transparency and consistency when applying the rules and processes. Mechanisms for the exchange of information with such entities to facilitate the authorization process should also be established (6). In some cases, subregional mechanisms provide a single point of entry to expedite EUAs in several countries, particularly those without formal regulatory entities. These mechanisms are therefore essential to minimize the time it takes for a product to be authorized for emergency use or procurement.

Table 1. Characteristics of authorization procedures granted in emergency situations: emergency use authorization and mechanisms for exemptions or reliance on decisions of other authorities

Emergency Use Authorization	Exemptions and reliance on decisions of other authorities or jurisdictions
<ul style="list-style-type: none"> • Authorization is granted based on a risk-benefit analysis of the limited quality, safety, and efficacy data available at the time of authorization. • This is a rolling review process carried out continuously as the manufacturer submits the information. 	<ul style="list-style-type: none"> • These authorizations are granted on an exceptional basis by the NRA, or by ministerial decree, without the intervention of the NRA: <ul style="list-style-type: none"> ○ Sometimes, a formal evaluation by the NRA may not be necessary, according to the decisions established in ministerial decrees (hence their exceptional nature). ○ These mechanisms are often used in situations where there is a risk of shortages in the national market, and not only in emergency situations. • Irrespective of who may grant this exemption, it is imperative that the competent authorities ensure that they have information certifying that the product is made using the same process, same manufacturing sites, and same supply chain authorized by the respective reference body.
<ul style="list-style-type: none"> • The information must be submitted by the interested party, usually the manufacturer. • Authorization is granted subject to specific conditions (case by case). These conditions include: <ul style="list-style-type: none"> ○ Authorization is only valid for the duration of the emergency. ○ The product is administered by institutions at the national level. ○ Indications are often restricted to high-risk groups. ○ Periodic updating of risk management plans. ○ Mandatory safety notifications following vaccine introduction. 	<ul style="list-style-type: none"> • Such interventions are requested or authorized through the ministries of health. • In general, the NRA or the ministry of health adopts the conditions under which the other NRA granted the initial marketing authorization. However, it is recommended that NRAs document their decisions based on the information used and establish vaccine surveillance and monitoring mechanisms.
<ul style="list-style-type: none"> • The conditions of authorization are subject to review as up-to-date information on the quality, safety, and efficacy of vaccines becomes available. • Manufacturers are legally bound to submit the information established under the terms of the EUA. • The NRA must have legal mechanisms in place that allow it to revoke the EUA in case of non-compliance with the conditions and agreements established in the authorization. 	<ul style="list-style-type: none"> • Although not always envisaged, it is recommended to keep a national-level record of the lots used and to strengthen the quality, safety, and efficacy monitoring and surveillance processes for vaccines authorized via this mechanism.

NRA: national regulatory authority, EUA: emergency use authorization.

- **Importation and customs clearance processes:** WHO guidelines state that regulatory frameworks should have documented mechanisms whereby NRAs may grant exemptions to some requirements for expedited importation in emergency situations (7). Measures should be considered that would allow import permits to be issued prior to the arrival of the vaccine, and for customs clearance processes to take less than five days (5).
- **Batch release at the national level:** WHO also recommends that imported vaccines purchased from reliable sources (e.g., through UN procurement agencies or, in the case of COVID-19 vaccines, the COVAX Facility) should be exempted from additional quality control in recipient countries (2). To expedite lot release in the country (i.e., in less than two days), lot release certificates issued by other NRAs should be recognized, or the possibility of legislating or granting special exemptions in the case of emergencies should be explored (2, 8, 9). Also, in countries with no legislation governing lot release activities, other mechanisms should be devised to record data on the lots entering the country and facilitate their traceability in an emergency context.

Specific recommendations

Regulatory authorization processes

In general, NRAs must have mechanisms and processes in place that would enable them to evaluate the information submitted by manufacturers on an ongoing basis and to prioritize activities in accordance with the emergency situation. NRAs should also establish legal mechanisms to ensure that manufacturers submit critical information in a timely manner as part of their responsibility under the terms of the EUA. The following are other specific recommendations to consider for authorization processes in emergency situations:

- **Establish and publish the terms and conditions of authorizations issued during the emergency:**
 - **EUA validity:** A key aspect to consider in the case of EUA is that they are only valid for the duration of the emergency. Countries must have clearly defined regulatory mechanisms and frameworks for declaring the beginning and end of an emergency.
 - **Specific conditions for authorization:** The specific conditions under which each vaccine is authorized (e.g., its exclusive use in certain population groups) will be based on risk-benefit analyses, post-authorization safety notifications, additional information that manufacturers are obliged to submit as it becomes available, and the respective risk management plans. This will allow the conditions of authorization to be updated accordingly (3, 6). All information related to the authorizations issued, as well as the specific conditions of use, must be made available to the different actors involved in the use of the vaccines, both in the country and internationally.
 - **Revocation of a EUA or EUL:** An authorization may be revoked if the manufacturer fails to comply with the conditions established in the authorization; once the emergency is over and use of the product is no longer required; or if the risks are deemed to be greater than the benefits (based on the data on the use of the vaccine) and its use is suspended.
 - When necessary and **on an exceptional basis, accepting information on vaccines in languages other than local one should be considered.** Support should be provided for local authorities to draw up fact sheets to be included in the health programs defined by the ministry of health. In some

- situations, NRAs may choose to adapt public information developed by other reference NRAs, which may be available in their country's language.³
- **Updates to the conditions of authorization:** Updates also apply when EUAs are granted on the basis of reliance on decisions by other jurisdictions. It is, therefore, recommended to constantly monitor the information from the reference entity in order to update the established conditions accordingly. Here are some examples that could affect or modify the decisions issued by NRAs:
 - **Changes in conditions or characteristics originally included in the EUA or EUL:** As EUAs are based on the progressive generation of information, some characteristics of a vaccine may need to be modified during the emergency period, hence requiring updates (e.g., shelf life, stability under different storage conditions, incorporation of alternative manufacturing sites, among others).
 - **Transition from a EUA to a marketing authorization, or from the EUL to prequalification:** When the manufacturer has provided sufficient data to confirm an adequate risk-benefit balance for the use of the vaccine and a drug registration or marketing authorization is granted to replace the previous EUA; or, in the case of EUL, when it has been included in the WHO list of prequalified products.

Importation process (custom clearance) in emergency situations

Establish communication and coordination mechanisms between the different actors involved: Medical products, including vaccines, are usually imported with the supervision and participation of various actors such as NRAs, customs authorities, and port control authorities, among others. All participating agencies should coordinate their actions in order to improve and expedite clearance and importation (2).

Lot release process during emergencies

Maintain an up-to-date record of vaccine lots deployed at the national level: Regardless of the criteria and lot release mechanism used, the NRA should maintain a record of how vaccine lots entering the country are distributed, enabling tracking of different lots/units of the same vaccine obtained through different procurement routes. This information is critical for compensation clauses and for pharmacovigilance activities in response to the COVID-19 pandemic.

Post-introduction vaccine monitoring and surveillance process

- 1) **Strengthen COVID-19 vaccine post-introduction surveillance and monitoring activities:** Whatever procurement pathways or authorization criteria may be used, these surveillance activities cannot be delegated to other regulatory authorities or reference entities.
- 2) **Establish a pharmacovigilance plan taking into account the critical points of the risk management plans defined by the manufacturer of each vaccine** in order to strengthen the monitoring and ongoing risk-benefit assessments of the authorized vaccine.

³ For example, the fact sheets for the Pfizer-BioNTech COVID-19 vaccine[®] published in several languages by the NRA in the United States of America and the European Medicines Agency can be consulted on their respective websites at:

<https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine>;
Comirnaty, INN-COVID-19 mRNA Vaccine (nucleoside-modified) (europa.eu).

- 3) **Establish information exchange mechanisms with other NRAs** in the Region and with trusted or reference regulatory authorities to strengthen COVID-19 vaccines surveillance activities, particularly with regard to the detection of possible substandard or falsified products.
- 4) **Maintain an integrated and coordinated regulatory system** that allows mechanisms to be established for the exchange of information between those responsible for reviewing and updating EUA conditions and those responsible for pharmacovigilance (including the NIP) for the notification, identification, and evaluation of ESAVI. Surveillance plans may need to be updated as more information is received from manufacturers through Periodic Safety Update Reports or by monitoring the status of the EUA issued by other jurisdictions of reference.
- 5) **Cold chain verification:** As part of the vaccine post-introduction surveillance activities, it is important that NRAs support ministries and other entities in aspects related to the proper storage of vaccines, depending on the specific nature of each vaccine, and in resolving issues such as possible breaks in the cold chain. This would reduce the likelihood of administering vaccines with compromised efficacy or safety due to the fluctuations in storage temperatures and of unnecessary wastage of vaccine doses.

Conclusions and lessons learned on emergency regulatory processes in the Region

The results of the regional mapping on the regulatory procedures deployed in the context of the COVID-19 emergency indicate that most NRAs in the Region have maintained a traditional approach. They have responded to the emergency by adapting regulations and procedures as required rather than adopting a more proactive approach based on lessons learned in similar emergency situations, such as the swine flu pandemic, and on the recommendations set out by WHO in the *Guidelines on regulatory preparedness for provision of marketing authorization of human pandemic influenza vaccines in non-vaccine-producing countries* (4).

It is important that the countries of the Region proactively establish a regulatory framework for emergency situations with laws or policies that enable them to address the situation. These should include approval mechanisms—based on the procurement channels and the respective risks—for the authorization, importation, and lot release of vaccines as well as post-introduction surveillance. Specific requirements and response times should be established for each procurement channel, based on the recommendations issued by PAHO. This will help to prepare countries for possible similar emergencies in the future.

When establishing a regulatory framework for emergencies, the general universal principles that should guide and inform NRAs decisions should also be considered. These include transparency, decision-making consistent with national legislation, and the establishment of procedures based on potential risks. Consideration should also be given to the implementation of measures that would enable NRAs to improve their performance with decision-making processes based on specific risk-benefit criteria for each of the vaccine procurement channels, as well as mechanisms to avoid duplication of regulatory actions already carried out by other NRAs or reference entities.

This would allow NRAs to focus their efforts on activities they must perform regardless of the procurement channel or vaccine authorization criteria, and that cannot be delegated to other regulatory authorities or reference entities: post-introduction surveillance and monitoring of vaccines, continuous risk-benefit assessments on the use of vaccines introduced in emergency situations, and timely detection of possible substandard or falsified vaccines.

References

1. Pan American Health Organization. Questions and answers (Q&A) on regulatory matters related to the introduction and pharmacovigilance of COVID-19 vaccines. 19 January 2021. Washington, DC: PAHO; 2021. Available from: <https://iris.paho.org/handle/10665.2/53229>.
2. Pan American Health Organization. Guidance on developing a national deployment and vaccination plan for COVID-19 vaccines (v.2), 4 June 2021. Washington, DC: PAHO; 2021. Available from: <https://www.paho.org/en/documents/guidance-developing-national-deployment-and-vaccination-plan-covid-19-vaccines-v2>.
3. Pan American Health Organization. Reliance for Emergency Use Authorization of Medicines and Other Health Technologies in a Pandemic (e.g. COVID-19) (paho.org). Washington, DC: PAHO; 2020. Available from: <https://iris.paho.org/handle/10665.2/52027>.
4. World Health Organization. Annex 7: Guidelines on regulatory preparedness for provision of marketing authorization of human pandemic influenza vaccines in non-vaccine-producing countries. WHO Technical Report Series, No. 1004, 2017. Geneva: WHO; 2017. Available from: <https://apps.who.int/medicinedocs/documents/s23326en/s23326en.pdf>.
5. World Health Organization. COVID-19 Vaccine Country Readiness Assessment Tool, updated (VIRAT/VRAF 2.0), 3 December 2020. Geneva: WHO; 2020. Available from: <https://www.paho.org/en/documents/covid-19-vaccine-country-readiness-assessment-tool-virat>.
6. Pan American Health Organization. Regulatory Reliance Principles: Concept Note and Recommendations. Ninth Conference of the Pan American Network for Drug Regulatory Harmonization (PANDRH). San Salvador, 24 to 26 October 2018 Washington, DC: PAHO; 2019. Available from: https://iris.paho.org/bitstream/handle/10665.2/51549/PAHOHSS19003_eng.pdf.
7. World Health Organization. Annex 5: Guidelines on import procedures for medical products. Fifty-third Report. Geneva: WHO; 2019. Available from: https://www.who.int/medicines/areas/quality_safety/quality_assurance/WHO_TRS_1019_Annex5.pdf.
8. World Health Organization. Annex 2: Guidelines for independent lot release of vaccines by regulatory authorities. Sixty-first report. Geneva: WHO; 2013. Available from: https://www.who.int/biologicals/TRS_978_Annex_2.pdf.
9. World Health Organization. Operational tool for efficient and effective lot release of SARS-CoV-2 (Covid-19) vaccines. Geneva: WHO; 2021. Available from: https://extranet.who.int/pqweb/sites/default/files/documents/WHO_OperationalTool_EfficientLotRelease_v20Jan2021.pdf.

PAHO/HSS/MT/COVID-19/21-0011

© Pan American Health Organization, 2021. Some rights reserved. This work is available under license [CC BY-NC-SA 3.0 IGO](https://creativecommons.org/licenses/by-nc-sa/3.0/).