

INDICATIVE LIST OF TRADE-RELATED BOTTLENECKS AND TRADE-FACILITATING MEASURES ON CRITICAL PRODUCTS TO COMBAT COVID-19

INFORMATION NOTE¹

1. INTRODUCTION

This information note seeks to facilitate access to information on possible trade-related bottlenecks and trade-facilitating measures on critical products to combat COVID-19, including inputs used in vaccine manufacturing, vaccine distribution and approval, therapeutics and pharmaceuticals, diagnostics and medical devices. It is not meant to be an exhaustive list of all specific trade barriers, nor does it make any judgement on the existence or importance of bottlenecks, nor on the desirability of implementing any of the suggestions on trade-facilitating measures.²

The indicative list is based on issues identified and suggestions made by speakers at the WTO webinar Regulatory Cooperation during the COVID-19 Pandemic, on 2 June 2021, and the WTO symposium COVID-19 Vaccine Supply Chain and Regulatory Transparency, on 29 June 2021.³ Entries under each subheading are presented in no particular order. One common theme that emerges is that essential goods and inputs need to flow efficiently and expeditiously to support the rapid scaling up of COVID-19 production capacity worldwide. The delay of a single component may significantly slow down, or even halt, vaccine production given the globally integrated supply chains that underpin COVID-19 vaccine manufacturing.

The information note is intended to be a living list. Comments, clarifications, modifications and improvements are actively sought. To contribute with inputs that may be incorporated in future updates, please contact Mr Roy Santana (Roy.Santana@wto.org) or Mr Devin McDaniels (Devin.McDaniels@wto.org).

2. TRADE-RELATED BOTTLENECKS

The following trade-related bottlenecks were identified by speakers at the Regulatory Cooperation during the COVID-19 Pandemic Webinar and the COVID-19 Vaccine Supply Chain and Regulatory Transparency Symposium.⁴ They are compiled here for ease of reference. Entries under each subheading are presented in no particular order, and no judgement is made on the existence or importance of these bottlenecks.

¹ This document has been prepared under the WTO Secretariat's own responsibility and is without prejudice to the positions of WTO members or to their rights and obligations under the WTO.

² In the context of the Trade Monitoring Exercise, the WTO Secretariat maintains a list of trade and trade-related measures taken in the context of the COVID-19 pandemic: see

https://www.wto.org/english/tratop_e/covid19_e/trade_related_goods_measure_e.htm.

³ See https://www.wto.org/english/news_e/news21_e/trip_28may21_e.htm and https://www.wto.org/english/tratop_e/trips_e/technical_symposium_2906_e.htm.

⁴ *Ibid.*

2.1. Vaccine manufacturing and its inputs⁵

- There is an absence of expedited procedures for vaccine inputs. Trade in vaccine inputs is subject to standard import and export procedures, which include rigorous documentation requirements and frequent renewal of licences and certificates. They do not benefit from “green channels” or other simplified or expedited procedures put in place for certain critical products to combat COVID-19 (e.g. procedures for personal protection equipment (PPE), medical equipment and vaccines).
- Vaccine manufacturers may find it difficult to send non-commercial samples for testing and quality control purposes to specialized laboratories located abroad, which is a time-sensitive operation. These samples are subject to the same import and export procedures as commercial shipments, including export restrictions, which can delay or prevent the release of manufacturing batches for distribution.
- The lack of predictability in the administration of import and export restrictions makes it difficult for vaccine manufacturers to plan and execute the sourcing of critical inputs, resulting in suboptimal supply-chain decisions and accretion of sourcing delays.
- Exports by vaccine manufacturers to foreign fill and finish sites can be subject to export restrictions, both for sites owned by the manufacturer and the contract development and manufacturing organizations (CDMOs) with which vaccine originators may have partnered.
- Since donations of supplies and vaccines (e.g. to COVAX) are not commercial transactions, they can be subject to more stringent controls and may result in tariffs and internal taxes (e.g. VAT) or longer exemption processes, which can cause delays and increased costs.
- Some embassies and consulates (remain) closed as a result of lockdowns, making it impossible to complete consular transactions (sometimes referred to as legalization or consularization) or to submit documents needed for cross-border trade of vaccine inputs.
- Applied tariffs can remain high for certain inputs in some manufacturing countries, which can have a cumulative effect on manufacturing cost, most notably on CDMOs in developing countries.
- Complicated visa entry requirements and the consequences of health regulations on the openness of borders mean that highly qualified personnel can find it difficult to move across borders to support vaccine manufacturing in other countries.

2.2. Vaccine regulatory approval

- Differences between countries in terms of regulatory frameworks, procedures and timelines adds complexity for manufacturers.
- Significant variation among registration regime requirements across different regions can make it onerous for manufacturers to apply for registration in multiple locations.
- Some national regulatory authorities (NRAs) require local retesting of vaccines (instead of reliance on the releasing country), which can lead to delays and spoilage.
- The rapid development of COVID-19 vaccines has led to additional challenges and burdens for vaccine manufacturers following the initial emergency use authorization (EUA), such as gathering data and optimizing processes.
- Some NRAs have not established accelerated pathways for post-approval changes to vaccines under EUA, which could hinder availability due to delays in approval.
- Local NRAs may require small bridging clinical trials to be approved by the reference NRA that first approved the vaccine, which can lead to delays.
- There can be uncertainty about when EUA will expire and the accompanying processes to move to regular approval and registration of vaccines (including against new coronavirus variants). A particular concern is that rules and accompanying data and legal requirements will differ between regulatory agencies.

2.3. Vaccine distribution

- Few challenges in the distribution and border clearance of COVID-19 vaccines have been identified. COVID-19 vaccine shipments have frequently become media events, with deliveries often being received by high level officials or are sent through government

⁵ Examples of vaccine inputs include active ingredients, inactive ingredients, flasks, vials, bags, instruments and equipment: see *Joint Indicative List of Critical COVID-19 Vaccine Inputs for Consultation*, available at https://www.wto.org/english/tratop_e/covid19_e/vaccine_inputs_report_e.pdf.

channels. Border clearance conditions for ancillary immunization products (e.g. syringes, refrigerators) needed for administering vaccines can be quite different. As the number of doses of COVID-19 vaccine delivered worldwide grows, it is unclear whether these expedited border clearance processes will remain in place.

2.4. Therapeutics and pharmaceuticals

- Different technical requirements on the same product between countries (e.g. the more common fill volume of 3.5 ml versus 3.51 ml in some countries; the sterilization of injectable products required by terminal sterilization in some countries versus by aseptic processing in other countries) require vaccine manufacturers to establish separate production lines, which increases manufacturing cost and compromises access, affordability and speed of delivery, especially for low volume products.
- Post-approval change requirements vary across markets. NRAs request different process changes to approved products in an uncoordinated manner, which requires manufacturers to carry multiple manufacturing processes. This can lead some manufacturers to exit some markets, especially those in countries with low levels of consumption.
- Some NRAs require local population-based studies for medicines with no evidence of ethnic pharmacokinetic differences, which increases the time required to bring the product to market.
- Applied tariffs can remain high in many countries, thereby making it costly to import essential therapeutics to treat COVID-19 patients.

2.5. Diagnostics and other medical devices

- Divergent regulations and barriers to accessing viral samples that are needed to develop effective diagnostic tests.
- Some NRAs may still require a consularized apostille of the original paper document to confirm information already provided to the NRA and available online.
- Duplication of rigorous local testing can lead to delays and uncertainty for suppliers.
- An unclear process for regulatory approval of diagnostics can lead to diagnostics of varying quality. Inefficient and overly complex regulatory systems slow down activation of clinical trials and hamper the adoption of results.

2.6. Other issues

- Duplication of standards and multiple regulatory authorities responsible for medical goods can increase complexity and drive up costs, including for developing country CDMOs.
- A lack of coordination among border agencies can lead to unnecessary delays, in particular for transit through third countries.
- Many administrations recognize (international) transport workers as essential and have taken measures to expedite their border entry and exit. Difficulties remain, however, that could cascade through into manufacturing delays. The sanitary entry protocols developed by the International Civil Aviation Organization (ICAO), the International Road Transport Union (IRU), the World Health Organization (WHO) and other relevant bodies are pertinent in this context.

3. POSSIBLE TRADE-FACILITATING MEASURES

The following suggestions were raised by speakers at the Regulatory Cooperation during the COVID-19 Pandemic Webinar and the COVID-19 Vaccine Supply Chain and Regulatory Transparency Symposium.⁶ They are compiled here for ease of reference. Entries under each subheading are presented in no particular order, and no judgement is made on the desirability of implementing any of these suggestions.

⁶ See https://www.wto.org/english/news_e/news21_e/trip_28may21_e.htm and https://www.wto.org/english/tratop_e/trips_e/technical_symposium_2906_e.htm.

3.1. General import, export and transit procedures

- Implementation of the provisions in the Trade Facilitation Agreement (TFA), such as those concerning pre-arrival procedures, could help to expedite the movement of essential products to combat COVID-19, as delays may have a detrimental impact on public health. Where possible, implementation of the provisions in the TFA should be accelerated.
- Enhanced cooperation among governments, international organizations and the private sector is critical to ensure that all relevant stakeholders have sufficient information to make decisions.
- Where possible, digitalization and simplification of import, export and transit procedures (e.g. paperless trade) should be accelerated.
- An examination of best practices by WTO members can help to identify solutions to bottlenecks and new trade-facilitating measures, which could further expedite trade in these products.⁷ Where possible, existing tools and international standards can be used.
- Identification of relevant Harmonized System (HS) codes for medical goods essential for the treatment of COVID-19 by the World Customs Organization (WCO) and the WHO greatly assists members and other stakeholders in identifying the relevant products in global trade and their tariff classification, and enables the establishment of expedited procedures for border clearance.

3.2. Vaccine manufacturing and its inputs

- Transparent and predictable inward investment regimes facilitate planning and executing vaccine production plans.
- Bilateral and regional agreements could ease import and export restrictions on input supplies of key routes.
- To obtain clear and reliable information a communication channel can be established between vaccine manufacturers and other relevant stakeholders to raise awareness about bottlenecks at domestic and regional levels (e.g. a national committee on trade facilitation).
- A national dialogue with manufacturers and other relevant stakeholders could be established to understand the current conditions for trade in critical vaccine inputs.
- Predictable tariff classification in the HS is in itself a trade-facilitating measure, but it may not be sufficiently clear for the wide range of critical inputs used in vaccine manufacturing. Members could engage in the Harmonized System Committee of the WCO to identify the relevant products and to agree on the appropriate classification.

3.3. Vaccine regulatory approval

- Measures can include the facilitation of EUA based on the prequalification procedure of the WHO Emergency Use Listing or approval by WHO-recognized stringent regulatory authorities (SRAs) (e.g. WHO prequalification collaborative registration procedure, SRA collaborative registration procedure) and regional networks (e.g. African Medicines Regulatory Harmonisation (AMRH), harmonized requirements for drug registration of the Association of Southeast Asian Nations (ASEAN)). WHO special procedures can be used to share regulatory dossiers under confidentiality agreements and to promote the use of reliance to allow low- and middle-income countries to authorize emergency use of vaccines quickly and efficiently.
- NRAs could activate (or create) national EUA pathways. Authorization of COVID-19 vaccines could be fast tracked.
- NRAs can allow restricted emergency use of foreign-produced vaccines with EUA by SRAs, under the condition of a post-approval parallel-bridging trial.
- Where appropriate, batch release testing from NRAs or national control laboratories (NCLs) of the releasing country (through the WHO-National Control Laboratory Network for Biologicals) could be relied upon.
- Early interaction of NRAs with vaccine developers could expedite approval.
- Scientific advice from NRAs could be provided to developers and manufactures to speed up development of COVID-19 vaccines.
- Rapid approval of clinical trials (phases undertaken in parallel in real time) could expedite approval of vaccines.

⁷ Trade-facilitating measures taken by some members is available on the WTO TFA Database: see <https://tfdatabase.org/trade-facilitation-committee/experience-sharing>.

- A rolling review of vaccine and therapeutics dossiers can shorten approval time.
- Agile inspections could be conducted or alternatives found (e.g. through remote means).
- Building transparency by design – for all parties, including regulators and manufacturers – could enable agile and informed regulatory decision-making during a pandemic and strengthen collaboration for more efficient vaccine development.
- NRAs can enhance transparency and openness (e.g. sharing data nationally with experts and explaining the process and findings at public briefings) and gather independent expert advice in real time to mitigate any potential risks of expedited processes.
- The pharmaceutical industry could improve transparency and data integrity by providing better access to clinical data for all new medicines and vaccines (including to the approximately 50% of clinical trials that go unreported because the results are negative⁸).
- Sharing data between regulators in real time can facilitate multi-country approvals.
- Regulatory systems in developing countries can be strengthened for scaling up the local manufacture of vaccines.
- Greater use of reliance and work sharing for safety and vigilance could be encouraged (e.g. *WHO COVID-19 Vaccines: Safety Surveillance Manual* recommends, among other things, regulatory reliance).

3.4. Therapeutics and pharmaceuticals

- Global harmonization with guidelines set by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) (e.g. guidelines on pharmaceutical development (Q8), on specifications (Q6), on impurities (Q3) and on stability (Q1)) would allow pharmaceuticals to be developed faster and to move more quickly between countries by overcoming conflicting or varying pharmacopeia requirements.

3.5. Diagnostics and medical devices

- The Medical Device Single Audit Program of the International Medical Device Regulators Forum (IMDRF) could be used to overcome barriers to on-site inspection during a pandemic.
- The IMDRF could establish guidance for the regulatory flexibility needed during a pandemic.
- The WHO provides recommendations in *Global Model Regulatory Frameworks and Regulatory Reliance for Medical Devices*.
- NRAs could implement a good regulatory practice (GRP) policy and related standard operating procedures.
- WHO guidance on recognition and reliance for pre- and post-market activities could be implemented.
- National standards and conformity assessment procedures (based on international standards) could be developed for local manufacturing of PPE.
- A common international regulatory framework that better defines criteria for effectiveness, quality and use cases for diagnostics should be developed. SRAs could work together to develop international assessment protocols and guiding principles in addition to more effective quality assurance processes.
- The streamlining of existing EUA pathways in the context of pandemics could result in diagnostics being registered and made accessible with less delay.
- Sharing best practices and data could mitigate delays and reduce uncertainty.
- Multiple-source supply chains can ensure that trade flows as freely as possible and with the minimal of export restrictions. A delay in the shipment of a single component, which might not be classified as a medical product in itself, could halt the entire production in a factory. Multiple-source supply chains allow manufacturers to respond to unanticipated spikes in demand. The reliance on multiple-source supply chains underscores the need for policy-makers to commit to reducing trade restrictions.

3.6. General regulatory aspects

- Mutual recognition agreements could be promoted, as well as the recognition of marketing authorization procedures and the unilateral recognition of marketing authorizations. Recognition of good manufacturing practice (GMP) inspections (e.g. Pharmaceutical

⁸ See [https://www.who.int/news/item/07-05-2021-joint-statement-on-transparency-and-data-integrityinternational-coalition-of-medicines-regulatory-authorities-\(icmra\)-and-who](https://www.who.int/news/item/07-05-2021-joint-statement-on-transparency-and-data-integrityinternational-coalition-of-medicines-regulatory-authorities-(icmra)-and-who).

Inspection Co-operation Scheme (PIC/S)) could help to avoid duplication, and inspections could be further harmonized through enhanced cooperation between regulators (building on PIC/S) to address country-specific requirements, reducing burdens.

- Encouraging the sharing of regulatory workflows, data and review information could accelerate access to essential medical goods.
- The use of existing cooperation arrangements and guidelines (e.g. ICH, IMDRF, PIC/S, International Coalition of Medicines Regulatory Authorities (ICMRA)) could be strengthened to improve preparedness for future pandemics.
- Global alignment of clinical trial requirements (e.g. patient vs. healthy volunteer studies, crossover study vs. parallel study, different end points) can increase the pace at which vaccines, therapeutics and diagnostics can be developed.
- Timelines for the evaluation and approval of medical products and clinical trials could be shortened if approval has already been granted by trusted regulatory authorities.
- Transparency could be enhanced by providing regularly updated information online for the public on regulatory decisions and processes.