Requirements for Review of Medical Products for Emergency Use Authorization against COVID-19

This document describes the eligibility criteria and technical requirements for CRS' verification review of medical products for emergency use. These requirements are aligned with the recommendations of the Pan American Health Organization (PAHO) to national regulatory authorities for the use of reliance to facilitate emergency use authorization (EUA) for medical products during pandemics.

Scope
This document describes the procedure used for verification review of medical products developed for the prevention, diagnosis, treatment (including investigational use) of the novel coronavirus 2019 (COVID-19). Medical products referred to in this document are: medicines, vaccines, and in vitro diagnostics (IVDs). Antibody tests will only be accepted based on the recommendations of the World Health Organization.

Applications may be submitted by authorized importers / distributors, manufacturers or market authorization holders.

Eligibility
The medical product must meet one of the following criteria:

(I) Be granted Emergency Use Authorization (EUA) for prevention, treatment or in vitro diagnosis of COVID-19, by the WHO Emergency Use Listing for SARS-CoV-2; or

(II) Be granted authorization for emergency use for prevention, treatment or diagnosis of COVID-19 by one of the national regulatory authorities of reference based on type of product shown in Table 1.

Table 1: Regulatory Authorities of Reference (Reference Authorities) by Product Type

<table>
<thead>
<tr>
<th>Countries / Agencies with Recognized RAs</th>
<th>Pharmaceuticals</th>
<th>Vaccines</th>
<th>In Vitro Diagnostics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina, Australia, Brazil, Canada, Chile, Colombia, Cuba, European Union, Mexico, United States of America, United Kingdom</td>
<td>Australia, Canada, European Union, Iceland, Japan, Liechtenstein, Norway, Switzerland, United Kingdom, United States of America</td>
<td>Australia, Canada, Japan, Singapore, United States of America</td>
<td></td>
</tr>
</tbody>
</table>
Technical Requirements

The CRS will apply an approach that uses recognition of the product EUA from the reference authorities, and reliance on supporting documentation in English that describe key aspects of product information, manufacturing, and labelling. Underlying safety, effectiveness and quality information may be required in a summative format.

Applicants should provide the following documentation:

1. Assurance of sameness
   - A formal declaration (cover letter (see Appendix 1)) confirming the product / presentations offered to the NRA correspond in all respects (e.g. qualitative/quantitative formula, manufacturing facilities, stability, summary product characteristics and labelling, etc.) to the product approved by the reference authority or WHO Prequalification program;
   - The product EUA or marketing authorization certificate issued by the reference authority; and
   - The corresponding web-link to the registration database.

2. Product Description and Information
   - Product description and product information including the Summary of Product Characteristics (SMPC) approved by the reference authority, if a medicine, or variants (configurations) and accessories /instruments, if the product is an IVD.
     - Note: the information must include the approved product name, overview, intended use, the shelf life and storage conditions. If an IVD, a general description of the principle of the assay method, and principles of operation should be provided.

3. Manufacturing information
   - List of all sites involved and accepted by the reference authority in the manufacturing process, including name, current address and manufacturing responsibilities and/or activities of each site; and
   - Certificate of GMP compliance of the finished product manufacturer or equivalent accepted by the reference authority (ISO 13485 certificate, if IVD).

4. Product labelling
   - The supplier must provide a complete set of PDF artworks in English, including labelling associated with the product offered. If an IVD, this should include instructions for use as well as an instrument manual and any other instructional materials provided to the user.
     - Note: Labels must include the product name, manufacturer contact information, reagent/ingredient name, expiry date, any special storage and/or handling conditions, warning and precautions, lot/batch/serial
number, particular product conditions (e.g. sterility), names of all included reagents in each box on the outer package label, as applicable.

- For IVDs: The instruction for use should, where possible, comply with the principles of labelling for medical devices and in vitro diagnostics (IVDs) of IMDRF/GRRP WG/N52 FINAL: 2019.
- If the product requires associated instrumentation, an electronic version of the instrument manual and/or associated operator manuals must be available in case countries request it.

5. Post Market Surveillance

- For products that are designated as ‘high risk’, the supplier must commit to provide a copy of the Risk Management Plan/Vigilance Report when it becomes available (e.g. Periodic Safety Update Report/Periodic Benefit Risk Evaluation Report). For in vitro diagnostics, the plan must be in alignment with the “WHO guidance on post-market surveillance of in vitro diagnostics”.
- If there have been safety issues reported for the product, a copy of the safety report submitted to the regulatory authority’s vigilance and/or post-market surveillance system is required.

Note: A product is considered ‘high risk’ if there is insufficient information on its safety in populations, or it is known to cause severe adverse reactions when used in humans.

The CRS reserves the right to request additional information to guide decision-making.

CRS Letter of Recommendation

Upon successful review, the CRS will recommend the product for emergency use authorization by NRAs in CARICOM. A certificate / letter of recommendation will be issued by the CRS to the applicant, which will include the following:

- The product name
- The product strength, formulation (for medicines and vaccines)
- Diagnostic method (for IVDs)
- CRS Reference number
- Market authorization holder
- Manufacturer of finished product
- Emergency Use Indication(s)
- Period of validity
- CRS Contact information for questions / concerns / reports.

Additional statements of conditions:

The recommendation for EUA is based upon minimal and incomplete documentation due to pandemic urgency.

The recommendation is granted under the following conditions:
For Use Only during the Pandemic Period
For Use Only by authorized agencies and personnel
For Use Only in the listed groups at high risk
The market authorization holder is responsible for adherence to any additional post-market safety reporting requirements of the NRA
The market authorization holder or applicant is required to provide the CRS with any information related to any approved post-authorization changes or modifications to the EUA granted by the reference authority, including withdrawal or suspension of the EUA.

Suspected adverse reactions, substandard / falsified / unregistered products may be reported to the CRS through its VigiCarib network via email (vigicarib@carpha.org) or via online reporting form at: https://form.jotform.co/72934157245864.

The products recommended for emergency use will be published on the CRS website along with the period of validity and the reference authority.

Limitations
Submission of a product for review by the CRS is voluntary, and recognition of the recommendation by NRAs in CARICOM is also voluntary. The recommendation is not a guarantee of market authorization or procurement. The recommendation will be valid for a period not exceeding the duration of the EUA granted by the reference authority, unless new safety information emerges or the information submitted for review is found to be false. For instance, where the reference authority has granted EUA for 1 year, the CRS will provide a recommendation for no more than 1 year.

The issuance of a recommendation by the CRS does not constitute endorsement of any given market authorization holder or product. It provides verification that the EUA granted by the regulatory authority of reference for the product is valid and that the same product is on the market in the relevant country or region. Any market approvals, authorization or import approvals by national regulatory authorities that are based on the CRS’ recommendation are subject to the respective laws, regulations and policies of the national regulatory authority. This includes the scope of approved use for products granted emergency use authorization.

The CRS may retract this recommendation at any time, based on emerging evidence, such as changes in validation data or emerging safety issues.
APPENDIX I: Cover Letter Template

[COMPANY LETTERHEAD – Name, address, phone number, email]

<Insert Date>

TO: Technical Coordinator
    Caribbean Regulatory Authority
    Caribbean Public Health Agency
    16-18 Jamaica Boulevard, Federation Park
    Port of Spain, Trinidad and Tobago

Dear Sir/Madam,

SUBJECT: Application for Recommendation for Emergency Use Authorization (EUA): <Insert Trade Name>
(<<Insert International Nonproprietary Name of product>>)

<Insert NAME OF APPLICANT> of <Insert ADDRESS OF APPLICANT> has submitted this application for EUA of the aforementioned product. The details of the product are included in the submitted application.

<Insert TRADE NAME> has an EUA or marketing authorization in <Insert REFERENCE AUTHORITY (RA) COUNTRY NAME>. The current EUA/marketing authorization was issued by <Insert RA NAME> on <Insert DATE OF ISSUANCE> and will expire on <Insert DATE OF EXPIRY, if applicable>.

We confirm that the product, including but not limited to composition/formulation, strength, manufacturing, specifications, packaging, and product information, will, at the time of submission and after EUA, be the same in all respects as the product given EUA or marketing authorization with <Insert RA NAME>. Note, there is an exception for different languages on labelling and packaging, if applicable.

We confirm that all the information in the accompanying documentation concerning this application is true and correct.

We confirm that we have read and understood the CARPHA Caribbean Regulatory System’s guidance document on applications for EUA.

We therefore kindly request that the CARPHA Caribbean Regulatory System considers the submitted application for this product in order to grant a recommendation for emergency use authorization.

Yours faithfully,

[Insert signature]_________________
[Insert Full Name of Signee]
[Insert Company Position]
[Insert Signee’s Email and Phone number (if different from that stated otherwise)]
# APPENDIX 2: Summary of Requirements for Various Product Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Pharmaceuticals</th>
<th>Vaccines</th>
<th>In vitro Diagnostics</th>
</tr>
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<tbody>
<tr>
<td><strong>Assurance of Sameness</strong></td>
<td>*Cover letter; *EUA or marketing authorization certificate</td>
<td>*Cover letter; *EUA or marketing authorization certificate</td>
<td>*Cover letter; *EUA or marketing authorization certificate</td>
</tr>
<tr>
<td><strong>Product Description</strong></td>
<td>* Summary of Product Characteristics (SPC/SMPC), Product monograph, or equivalent, and Package insert/prescribing information approved by reference authority * Finished product release specifications</td>
<td>* Summary of Product Characteristics (SPC/SMPC), Product monograph, or equivalent, and Package insert/prescribing information approved by reference authority * Finished product release specifications</td>
<td>*Technological summary *Variants and configurations *Instructions for use</td>
</tr>
<tr>
<td><strong>Manufacturing Information</strong></td>
<td>*List of all sites involved in manufacturing process; *GMP Certification of FPP manufacturing site accepted by reference authority</td>
<td>*List of all sites involved in manufacturing process; *GMP Certification of FPP manufacturing site accepted by reference authority</td>
<td>*List of all sites involved in manufacturing process; *ISO 13485 certificate</td>
</tr>
<tr>
<td><strong>Product Labeling</strong></td>
<td>*PDF of artworks including labelling, primary/secondary packaging, and product leaflet</td>
<td>*PDF of artworks including labelling, primary/secondary packaging, and any product leaflet</td>
<td>*PDF of artworks including labelling, primary/secondary packaging, and any informational inserts</td>
</tr>
<tr>
<td><strong>Post Market Surveillance</strong></td>
<td>*A copy of the Risk Management Plan and Vigilance Report approved by the reference authority (e.g. Periodic Safety Update Report/Periodic Benefit Risk Evaluation Report) when they become available * Report submitted to the regulatory authority’s PV/PMS system, if problems</td>
<td>*A copy of the Risk Management Plan and Vigilance Report approved by the reference authority (e.g. Periodic Safety Update Report/Periodic Benefit Risk Evaluation Report) when they become available * Report submitted to the regulatory authority’s PV/PMS surveillance system, if problems</td>
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**Key:** EUA – emergency use authorization; FPP - finished pharmaceutical product; GMP – good manufacturing practices; PV/PMS – pharmacovigilance (technovigilance) and/or post-market surveillance
KEY REFERENCES


