1st Invitation
to Manufacturers of therapeutics against COVID-19
to submit an Expression of Interest (EOI) for Product Evaluation
to the WHO Prequalification Unit

To support national and global efforts to increase access to and the affordability of Dexamethasone and Remdesivir products, WHO invites manufacturers of these pharmaceutical products to submit Expressions of Interest (EOI) for product evaluation.

ARTICLE 1. PROCEDURE FOR THIS INVITATION TO EOI

The current Invitation is published in accordance with the Procedure for Prequalification of Pharmaceutical Products, adopted in 2001 by the 37th WHO Expert Committee on Specifications for Pharmaceutical Preparations, and amended subsequently as part of the 45th report of the Committee, published as No. 961 of the WHO Technical Report Series in 2011.

Assessment of product(s) submitted under this Invitation will include evaluation of:
- product dossiers, which must include product data and information as specified in the guidelines for submission (see Procedures & Fees)
- manufacturing sites, which must adhere to good manufacturing practices (GMP)
- clinical sites (if applicable), which must adhere to good clinical practices (GCP).

If evaluation demonstrates that a product and its corresponding manufacturing (and clinical) site(s) meet WHO recommended standards, it will be included in the list of medicinal products that are considered to be acceptable for procurement by UN organizations and others.

ARTICLE 2. MEDICINAL PRODUCTS INVITED

The aim of this Invitation is to increase the range of selected products and sources available in relation to management of the COVID-19 pandemic.

Dexamethasone, a corticosteroid, is included in the WHO Model List of Essential Medicines, with clinical uses in multiple diseases and conditions, mainly as an anti-inflammatory agent. In Covid-19, a randomised controlled clinical trial (“Recovery”) has shown that dexamethasone reduced deaths by one-third in ventilated patients and by one fifth in other patients receiving supplemental oxygen compared to usual care alone. There was no benefit among those patients who did not require respiratory support.

Remdesivir is a nucleotide analogue prodrug that inhibits SARS-CoV-2 viral RNA polymerases. In a randomised controlled clinical study NIAID-ACTT-1, sponsored by the US National Institute of Allergy and Infectious Diseases (NIAID), patients treated with remdesivir recovered after about 11 days, compared with 15 days for patients given placebo. This effect was neither observed in patients with mild to moderate disease nor in patients who started remdesivir when they were already on mechanical ventilation or ECMO (extracorporeal membrane oxygenation). Data on the proportion of patients who died up to 28 days after starting treatment are currently being collected for final analysis. Data from other ongoing trials of remdesivir are also expected in the next few months.
Products included in the WHO Model List of Essential Medicines are those which satisfy the priority health care needs of a population. They are selected on the basis of disease prevalence, evidence on efficacy and safety, and comparative cost-effectiveness.

Interested manufacturers are encouraged to submit documentation for recommended dosage forms as specified below:

**Dexamethasone products**:  
1. Dexamethasone tablet, containing dexamethasone base 1.5mg, 2mg, 6mg  
2. Dexamethasone oral solution, containing dexamethasone base 2mg/5ml or 10mg/5ml, as the base or sodium phosphate  
3. Dexamethasone solution for injection, containing dexamethasone base 3.3mg/ml or 6.6mg/ml*, as the sodium phosphate  
   *equivalent to dexamethasone phosphate 4mg/ml or 8mg/ml, respectively

**Remdesivir products**:  
1. Remdesivir 100mg/20ml (5mg/ml) concentrate for solution for infusion  
2. Remdesivir 100mg powder** for concentrate for solution for infusion (to be constituted to 20ml solution containing 5mg/ml of Remdesivir for further dilution for infusion)  
   **preferred due to stability considerations.

**ARTICLE 3. HOW TO SUBMIT AN EXPRESSION OF INTEREST**

In order to submit an expression of interest for product evaluation, the manufacturer must send the requested documentation, arranged according to the information provided on the WHO Prequalification Unit – Medicines Assessment Team (PQT/MED) website in the Procedures and Fees section.

**ARTICLE 4. QUALITY ASSESSMENT PROCEDURE FOLLOWING SUBMISSION OF AN EXPRESSION OF INTEREST BY A MANUFACTURER**

The quality assessment is undertaken to evaluate whether the pharmaceutical product being evaluated meets the requirements recommended by WHO, and is manufactured in compliance with good manufacturing practices (GMP).

The procedure established by WHO for quality assessment incorporates:

- general understanding of the production and quality control activities of the manufacturer;
- assessment of product data and information on safety, efficacy and quality submitted by the manufacturer, including product formulation, manufacture and test data and results;
- assessment of the manufacturing site’s adherence to GMP, and its consistency in production and quality control of starting materials, with specific emphasis on active pharmaceutical ingredients, and finished product;
- assessment of clinical testing units or organizations (i.e. parties performing one or more clinical trials with the product) for compliance with good clinical practices and good laboratory practices, as appropriate;
- random sampling and testing of medicines supplied.

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1 Other dexamethasone products with similar strengths as the ones listed may be considered. Please contact PQT.
Once WHO is satisfied that quality assessment has been completed for the manufacturer of the relevant starting materials, the finished pharmaceutical product, and the clinical testing units, and that the product meets WHO recommended standards, the product (as produced at the specified manufacturing site) is added to the WHO List of Prequalified Medicinal Products.

ARTICLE 5. REFERENCES AND FURTHER INFORMATION

Dexamethasone
Recovery Trial, preliminary pre-print report
https://www.medrxiv.org/content/10.1101/2020.06.22.20137273v1.full.pdf

Remdesivir
Remdesivir for the Treatment of Covid-19 — Preliminary Report of the ACTT-1 Trial

Remdesivir EMA SmPC

EMA Press release: First COVID-19 treatment recommended for EU authorisation