1st Invitation to manufacturers of medicinal products for treatment of Apnoea in Preterm infants 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 affordability of medicinal products for care and treatment of apnoea in preterm infants and extubation of preterm infants born before 34 weeks' gestation, WHO invites manufacturers of selected 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 prequalified medicinal products that are considered to be acceptable for procurement by UN organizations and others.

Article 2. Medicinal products included on the 1st Invitation

The aim of this, the 1st EOI, is to ensure the availability of quality assured caffeine citrate. The recommended active ingredient, dosage forms, and strengths listed in this document have been identified by WHO's Department of Maternal, Newborn, Child and Adolescent Health and Ageing for effective treatment of apnoea in preterm infants and extubation of preterm infants born before 34 weeks' gestation. This formulation is included in the WHO Model List of Essential Medicines (EML) 23rd list, 2023 and in the WHO Preterm guidelines.

Products included in the WHO Model List of Essential Medicines or WHO technical report series are selected on the basis of an assessment of the quality of evidence for benefits, harms, costs, and appropriateness for use in a variety of situations, taking into account needs of special populations, and the values and preferences of the groups (professional and patient) using them.

Interested manufacturers are encouraged to submit documentation for the medicinal product as specified below:

Single ingredient medicine to prevent and treat Apnoea of prematurity and support extubation of preterm infants born before 34 weeks' gestation

- Caffeine Citrate Injection: 20 mg/mL (equivalent to 10 mg caffeine base/mL).
- Caffeine Citrate Oral liquid: 20 mg/mL (equivalent to 10 mg caffeine base/mL).
- Caffeine Citrate Injection: 10 mg/mL (equivalent to 5 mg caffeine base/mL).
- Caffeine Citrate Oral liquid: 10 mg/mL (equivalent to 5 mg caffeine base/mL).

Article 3. How to submit an EOI

In order to submit an expression of interest for product evaluation, the manufacturer must send the required documentation, arranged according to the information provided on the WHO Prequalification Unit – Medicines Assessment Team (PQT/MED) website at https://extranet.who.int/prequal.

Article 4. Quality assessment procedure following submission of an EOI by a manufacturer

The quality assessment is undertaken to assess 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.

Previous evaluation conducted by the relevant National Drug Regulatory Authority (NDRA) may be taken into account during the evaluation conducted by WHO, provided that the NDRA has expertise in the product area. If appropriate, the relevant NDRA may be invited to collaborate with WHO on the quality assessment. Any manufacturer who submits a product for evaluation is therefore encouraged to authorize its NDRA to discuss relevant product files with WHO representatives, during assessments and inspections, if required (subject to appropriate confidentiality provisions, if necessary).

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 Medicines.

Article 5. References and further information

1. World Health Organization. Recommendations For Care of the Preterm or Low Birth Weight Infant 15 November 2022. (available at WHO recommendations for care of the preterm or low-birth-weight infant/).

For further information on the WHO Prequalification Unit (PQT), please visit PQT's website at: https//extranet.who.int/prequal. Should you have any questions relating to the procedure for responding to an EOI, please write to the WHO Prequalification Unit at: prequal@who.int. Your question(s) will be directed to the prequalification team member who can best advise you.