1st Invitation to manufacturers of medicinal products for treatment of bacterial infections in children 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 care and treatment of infections in children, 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 in the Invitation

This 1st EOI is intended to encourage the availability of quality-assured products specifically designed for use in children. The recommended active ingredients, dosage forms, and strengths appearing in this document have been identified by WHO's Department of Maternal, Newborn, Child and Adolescent Health and Ageing, and the Research for Health Department. The medicines are targeted for treatment of a) possible serious bacterial infection (PSBI) in newborn and young infants and pneumonia in children (amoxicillin), b) lower urinary tract infections (nitrofurantoin), and c) cholera, enteric fever, trachoma, yaws; and a second choice for acute invasive bacterial diarrhoea (azithromycin). These formulations are included in the WHO Model List of Essential Medicines (EML) 23rd list, 2023.

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

- **Single ingredient medicine to treat possible serious bacterial infection (PSBI) in newborn and young infants and pneumonia in children**

Amoxicillin dispersible tablet 125 mg (scored), 250 mg (scored)

Medicine for treating lower urinary tract infections in children

- Nitrofurantoin orodispersible multiparticulates (minitablets or sprinkles) 5mg per unit dose, preferred; dispersible tablets 5mg,10mg (scored) as alternative.

Medicine for treating children with cholera, enteric fever, trachoma and yaws; also as a second choice for acute invasive bacterial diarrhoea, and potentially other infections.

- Azithromycin orodispersible multiparticulates (minitablets or sprinkles) 50mg per unit dose or scored dispersible tablet 100mg, as preferred; dispersible tablets 50 mg as alternative.

Manufacturers interested in developing multiparticulate products (e.g. orodispersible minitablets or sprinkles) should contact PQT/MED indicating the intended dosage form, presentation, and dose for administration.

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).

Article 5. References and further information

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.

1. Paediatric drug optimization standard procedure. Geneva: World Health Organization; 2021 (https://apps.who.int/iris/handle/10665/349315). Licence: CC BY-NC-SA 3.0 IGO.

2. Paediatric drug optimization for antibiotics: meeting report, 30 November, 5–7 December 2022. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/366533). Licence: CC BY-NC-SA 3.0 IGO.

3. Accelerating the development of priority formulations for antibiotic use in children. Target product profiles for paediatric formulations of priority antibiotics azithromycin and nitrofurantoin. 7–9 May 2024, Geneva, Switzerland: World Health Organization; 2023 (https://iris.who.int/handle/10665/366533). Licence: CC BY-NC-SA 3.0 IGO.

4. World Health Organization. Integrated Management of Childhood Illness: management of the sick young infant aged up to 2 months. IMCI chart booklet. Geneva, Switzerland: WHO, 2019 (available at https://www.who.int/maternal_child_adolescent/documents/en/).

5. World Health Organization. Guideline: Managing possible serious bacterial infection in young infants when referral is not feasible. Switzerland: WHO, 2015 (available at https://apps.who.int/iris/bitstream/handle/10665/181426/9789241509268_eng.pdf?sequence=1).

6. World Health Organization. Revised WHO classification and treatment of childhood pneumonia at health facilities: Evidence summaries. Switzerland: WHO, 2014. (available at https://apps.who.int/iris/bitstream/handle/10665/137319/9789241507813_eng.pdf?sequence=1)

7. World Health Organization. Integrated Management of Childhood Illness (IMCI): Chart Booklet. Geneva, Switzerland: WHO, 2014. (available at https://www.who.int/maternal_child_adolescent/documents/IMCI_chartbooklet/en/

8. World Health Organization. Guideline on management of pneumonia and diarrhoea in children up to 10 years of age. Geneva, Switzerland: WHO, 2024. (available at https://www.who.int/publications/i/item/9789240103412)

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.