

2nd Invitation to Manufacturers of Zinc Products to Submit an Expression of Interest (EOI) for Product Evaluation to the WHO Prequalification Team: medicines

To support national and global efforts to increase access to and the affordability of acute diarrhoea in children, WHO, together with UNICEF, invite manufacturers of 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 ([Prequalification Procedures and Fees: FPPs, APIs & QCLs | WHO - Prequalification of Medical Products \(IVDs, Medicines, Vaccines and Immunization Devices, Vector Control\)](#))
- manufacturing sites, which must adhere to [WHO TRS 957](#) and [WHO TRS 986](#) (GMP)
- clinical sites (if applicable), which must adhere to [WHO TRS 850](#) (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 acute diarrhoea.

In supplement to oral rehydration salts zinc sulfate has been identified by the WHO Department of Maternal, Newborn, Child and Adolescent Health and Ageing as essential to the management of acute diarrhoea in children. Zinc sulfate is included in the [WHO Model List of Essential Medicines](#) and in [The Treatment of Diarrhoea: A Manual for Physicians and other Senior Health Workers](#).

This revision of the EOI is based on a large randomized clinical trial in 4500 children in India and Tanzania age 6 to 59 months with acute diarrhoea. The study compared oral doses of 5 mg, 10 mg, and 20 mg of zinc sulfate for 14 days. Results showed no difference in efficacy and improved tolerability using a 5 mg dose.¹ Healthcare workers should consult the WHO Guideline on management of pneumonia and diarrhoea in children up to 10 years of age, 31 December 2024.²

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.

Products included in WHO treatment guidelines 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 recommended dosage forms and strengths, as specified below:

1. **Zinc (as sulfate or gluconate salt)**

dispersible tablets	5 mg
oral liquid	5 mg per unit dose (e.g., 5 mg/2.5 ml or 5 mg/5 ml)

Because the burden of diarrhoea is in early childhood, especially among children less than 2 years of age, dispersible tablets are the preferred formulation for the ease of administration and logistics.

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 Team: medicines 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.

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

1. Dhingra U et al. Lower-Dose Zinc for Childhood Diarrhea - A Randomized, Multicenter Trial. N Engl J Med 2020; 383 (13):1231-1241; available at <https://www.nejm.org/doi/full/10.1056/NEJMoa1915905>
2. WHO Guideline on management of pneumonia and diarrhoea in children up to 10 years of age, 31 December 2024; available at <https://www.who.int/publications/i/item/9789240103412>