1st Invitation to Manufacturers of Therapeutics for Sickle Cell Disease to Submit an Expression of Interest (EOI) for Product Evaluation to the WHO Prequalification Unit (PQT)

To support national and global efforts to increase access to and the affordability of care and treatment of Sickle Cell Disease (SCD), WHO, together with UNICEF, UNAIDS and UNITAID, invite manufacturers of selected pharmaceutical products to submit Expressions of Interest (EOIs) for product evaluation.

ARTICLE 1. PROCEDURE FOR THIS INVITATION

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 Procedures & Fees section of the website of the WHO Prequalification Unit – Medicines Team (PQT/MED)
- 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 INCLUDED IN THE 1st INVITATION

The aim of this 1st Invitation is to promote the development of formulations of hydroxyurea, including those appropriate for paediatric use. WHO has made a recommendation for the use of hydroxyurea in children and adolescents from 9 months to 19 years with sickle cell anaemia regardless of clinical severity in the guidelines for the management of sickle cell disease in children and adolescents (https://iris.who.int/items/cf46d05f-26c1-4385-ac39-de0c281ff5b6).

The paediatric formulations of hydroxyurea listed in this 1st Invitation have been identified by a Target Product Profile development group meeting convened by WHO and the Global Accelerator for Paediatric formulations (GAP-f). This process identified clear development needs and provided actionable guidance for formulation design for product development, regulatory strategy and accelerated manufacturing through partnerships. The formulations included in the TPP balance feasibility, acceptability, dose flexibility, and suitability for LMIC programme conditions.

Interested manufacturers are encouraged to submit documentation for recommended dosage forms and strengths, as specified below. The appropriate solid dosage formulations, which are scored for flexible dosing purposes, should be supported by relevant evidence on equal distribution of active ingredients in the scored products (functional scoring). Additional information on optimum and minimum characteristics of the 100 mg and 500 mg single-scored soluble or dispersible tablets can be found in the WHO Target product profile for formulations of hydroxyurea for the management of sickle cell disease in children,

Hydroxyurea

500 mg capsules

100 mg and 500 mg single-scored soluble or dispersible tablets preferred[a]

500 mg single-scored soluble or dispersible tablets as a minimum requirement[a]

ARTICLE 3. HOW TO SUBMIT AN EXPRESSION OF INTEREST (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 in the Procedures & Fees section of PQT's website at https://extranet.who.int/prequal

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.

Previous evaluation conducted by the relevant national medicines regulatory authority (NMRA) may be taken into account during the evaluation conducted by WHO, provided that the NMRA has expertise in the product area. If appropriate, the relevant NMRA 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 NMRA 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 Medicinal Products.

[a] Target product profile for formulations of hydroxyurea for the management of sickle cell disease in children. World Health Organization. Geneva. 2026.

ARTICLE 5. REFERENCES AND FURTHER INFORMATION

For further information on the WHO Prequalification Unit – Medicines Team, please visit the PQT 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 its email address: prequal@who.int. Your question(s) will be directed to the prequalification team member who can best advise you.

For further information on WHO t guidelines for management of SCD in children and adolescents, please consult:

Guidelines for the management of sickle cell disease in children and adolescents. Geneva: World Health Organization; 2026 (https://iris.who.int/handle/10665/385614). Licence: CC BY-NC-SA 3.0 IGO.

Target product profile for formulations of hydroxyurea for the management of sickle cell disease in children. In press

Paediatric Drug Optimization for Sickle Cell Disease. Meeting Report. In press.