

# WHO Prequalification Of In Vitro Diagnostics

## G6PD Prequalification: Public Announcement to Stakeholders

The WHO Prequalification team would like to announce it is expanding the scope of its programme to include G6PD deficiency, a condition that affects 400 million people globally and is most prevalent in Africa. After upcoming consultations with experts in Q3 2016 to determine dossier requirements and evaluation protocols, applications will be considered for the prequalification of assays intended for G6PD starting Q4 2016. In the meantime, manufacturers of relevant in vitro diagnostics may submit an expression of interest under [the ERP mechanism established by the Global Fund to Fight AIDS, Tuberculosis and Malaria \(GFATM\) and UNITAID](#), and coordinated by WHO.

### Background

A major source of *Plasmodium vivax* (*P.vivax*) disease burden is due to relapse which can be prevented by the widespread implementation of safe, radical cure using primaquine, an 8-aminoquinoline. Specifically, a 14-day treatment with high dose primaquine (0.25-0.5mg/kg bw daily) eliminates the liver stage (hypnozoites) parasite. This treatment course is often not administered due to the risk of haemolysis that is associated with this drug class in individuals with glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency.

G6PD deficiency affects 400 million people globally, is prevalent in malaria endemic countries and is associated with variable levels of acute haemolytic anaemia following exposure to primaquine which could be potentially fatal in patients with G6PD deficiency. The lack of access to quality-assured, in vitro diagnostics (IVDs) for use at point-of-care (POC) to determine G6PD deficiency stymies widespread, safe radical cure and progress towards elimination of *P.vivax*. Current WHO guidelines recommend the evaluation of G6PD status prior to primaquine therapy<sup>1</sup>.

Very few commercial assays suitable for use at or near to POC for G6PD testing compatible with tropical settings (high humidity, high temperature conditions) are available to date. In addition, this category of IVDs lacks any stringent regulatory oversight, making it challenging to assure their quality.

Given the high public health impact of potential widespread implementation of G6PD testing, the Global Malaria Programme at WHO in agreement with key partners, has recommended the addition of IVDs for G6PD for use at POC to the scope of the WHO Prequalification of In Vitro Diagnostics. This will ensure that these assays undergo a standardised assessment of safety, quality and performance. The prequalification assessment will be compatible with the risk associated with these IVDs based on their intended use in malaria endemic countries.

### WHO Prequalification of In Vitro Diagnostics

The [WHO prequalification of in vitro diagnostics](#) comprises a comprehensive assessment of individual in vitro diagnostics through a standardized procedure aimed at determining if the product meets WHO prequalification requirements.

The prequalification assessment process includes three components:

- Review of a product dossier;

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<sup>1</sup> Guidelines for the treatment of malaria. Third edition. (WHO, April 2015)

- Independent performance evaluation, including operational characteristics; and
- Manufacturing site(s) inspection.

### **Type of Assessment**

Products intended for G6PD testing in view of treatment with 8-aminoquinoline will be classified as Class C IVDs as per GHTF risk classification which has been adopted by WHO for the purpose of prequalification (more information on risk classification and its implications is available [here](#))<sup>2</sup>. Class C IVDs are defined as IVDs presenting a high risk to the individual patient with a moderate public health risk. Furthermore, G6PD assays are currently regulated as low risk IVDs given that currently available assays are not specifically intended to guide clinical decision making on administration or withholding of anti-malarial treatment for radical cure of *P.vivax*. Consequently, all products submitted for WHO prequalification will undergo a full prequalification assessment.

### **Product Pipeline**

For decades, the Fluorescent Spot Test (FST) has been the only G6PD assay that could be used at or near to POC without the need of general laboratory equipment and infrastructure. However, over the past few years, new technologies more adapted to resource-limited settings and their associated limitations (temperature, humidity, technical skills) have been developed and commercialized.

### **Consultation**

A consultation will be held in Q3 2016 to define technical requirements and acceptance criteria for the documentary evidence required in the product dossier and to agree on the performance evaluation protocols. Starting Q4 2016 following finalization of the outcomes of this consultation, applications for assays intended for G6PD testing in view of treatment with 8-aminoquinoline that can be used at or near to POC, including qualitative rapid diagnostic tests and quantitative biosensor assays that are commercially available, will be considered for prequalification.

### **Expert Review Panel for Diagnostics (ERPD)**

The ERPD mechanism set up by GFATM and UNITAID, coordinated by WHO, aims to assess the potential risks and benefits associated with the procurement of IVDs that may have a high public health impact, but have not yet undergone a stringent regulatory assessment, either by WHO Prequalification or by a stringent regulatory agency (SRA)<sup>3</sup>. Based on the advice of the ERPD, assays are eligible for procurement using grant funds for a time limited period of one year with the understanding that manufacturers will seek approval from an SRA or submit an application to WHO Prequalification during the this time.

In an effort to mitigate risks related to the procurement of G6PD assays that have not undergone stringent regulatory oversight, UNITAID and GFATM launched on 26 February 2016 an [invitation to IVD manufacturers to submit an Expression of Interest \(EOI\) for product evaluation by ERPD](#). This process will allow the identification of assays meeting a minimal set of requirements for temporary eligibility for procurement by GFATM.

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<sup>2</sup> Principles of IVD Medical Devices Classification SG1 Final Document GHTF/SG1/N045:2008

<sup>3</sup> Stringent regulatory authority is defined as a founding member of the Global Harmonization Task Force.