**Overview of World Health Organization Prequalification of Diagnostics**
**Impacts on Diagnostics and Medical Technology to Patients**

## AdvaMed

AdvaMed member companies produce the medical devices, diagnostic products and health information systems that are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. Our members produce nearly 90 percent of the health care technology purchased annually in the United States and more than 50 percent purchased globally annually. AdvaMed's 1,600 members range from the largest to the smallest medical technology innovators and companies. They bring medical technology to patients around the world in every setting.

## EDMA

EDMA, the European Diagnostic Manufacturers Association is the trade association that represents the In Vitro Diagnostic (IVD) industry active in Europe. EDMA membership brings together 23 National Associations in European countries and 41 major companies engaged in the research, development, manufacture or distribution of IVD products. Through its affiliated National Associations, EDMA represents in total more than 500 companies (or over 700 legal entities) across Europe. Since its establishment in 1979, EDMA acts in co-operation with other European and international trade associations representing medical devices, pharmaceuticals and biotechnology in general, as well as with scientific societies and patients organisations to make a real difference in health and life quality.

## Background

In June of 2008 the World Health Organization (WHO) launched a prequalification program applicable to all diagnostics proposed for procurement by UN agencies, and began accepting applications for designated high priority categories limited to HIV, malaria, and hepatitis diagnostics[1]. CD4 enumeration technologies have recently been added to the list. Prequalification is a multi-step process that involves 1) submission of a product summary application for initial consideration, 2) with acceptance of application form, manufacturer signs letter of agreement and pays program fee, 3) manufacturer submits detailed product dossier for review, 3) upon approval of dossier, WHO conducts manufacturing site inspection, 4) laboratory evaluation of diagnostic is performed by WHO Collaborating Center, 5) if manufacturer satisfies WHO requirements then product is eligible for inclusion in UN procurement tenders, 6) when product is purchased, manufacturer agrees to participation in WHO post market surveillance program.

Communications from WHO indicate that the organization recognizes global differences in national and regional regulatory processes but makes no distinction between products that have undergone rigorous review procedures by a mature regulatory authority and those with less or no regulatory review. Examples of rigorous regulatory processes would include those of the US, EU, and Japan. WHO indicates that diagnostic "certification from a stringent regulatory authority" may speed up the process but does not replace it, because "conditions in countries with stringent regulations are different from resource-limited settings". The rationale for laboratory evaluation of diagnostics is so that WHO laboratories and WHO Collaborating Centers assess technical performance based on the "suitability of the product for testing services in resource-limited settings." WHO inspection of manufacturing sites is explained as necessary to "assess the adequacy and effectiveness of manufacturer's quality management system and the correct implementation of documented procedures", with the inspection "based on internationally recognized standards".

The WHO website shows over 100 applications received to date.[2] Based on the website information, none of these products have progressed beyond the initial dossier review stage and no products have been prequalified. Several applications have been rejected because the products do not fit current high priority targets as defined by WHO.

**Key Principles**

AdvaMed and EDMA strongly support WHO's mission to increase access to affordable diagnostics of assured quality in underserved regions of the world. We share WHO's concern for the quality and suitability of diagnostic products intended for use in those regions of the world, and we recognize the need for a product and quality system review of manufacturers not already subject to appropriate regulation. For manufacturers and products already subject to review and acceptance by mature regulatory systems and authorities, however, much of the WHO pre-qualification process is duplicative and may add significant delays to the procurement of these diagnostics. This duplication and delay undermines WHO's important mission to increase timely access to much needed quality diagnostics in underserved regions of the world.

A two tiered approach to diagnostics prequalification that would streamline access to these types of diagnostic medical devices, while ensuring that products not already subject to stringent regulation undergo the full WHO prequalification process, represents the best approach to fully address the needs of underserved regions. This approach would provide a platform for manufacturers to work with WHO to assure product quality and strengthen regional regulatory processes while maximizing availability of quality diagnostics in a timely and cost effective manner. This approach would also allow WHO to better allocate the organization's resources by focusing more effectively on those manufacturers and products that would most benefit from interaction with WHO under the full prequalification program. Undertaken in collaboration with the Medical Technology industry, this approach would address the critical points identified by WHO:

- ***Promote and facilitate access to safe and appropriate diagnostic technologies of good quality.*** This goal, perhaps the most important single objective of the WHO program, is also shared by reputable diagnostic manufacturers. There are a number of steps that WHO and the Medical Technology industry can take to address the quality of diagnostic products while utilizing stringent regulatory systems that are already in place. Based on regulatory guidance developed through the Global Harmonization Task Force (GHTF)[i] process, WHO could establish a list of existing regulatory systems that have been found to have all the necessary elements to ensure the performance and safety of diagnostic medical devices.

  - Tier 1 products that have undergone review and registration in one of these stringent regulatory systems could automatically be registered by the manufacturer with WHO as available for consideration for procurement in the UN tender process.

  - Tier 2 products would include all products not already subject to stringent regulatory procedures or for which manufacturers are unable to provide all Tier 1 documentation. Tier 2 products would undergo review by WHO through the existing diagnostics prequalification program.

  This approach would ensure a consistent and rigorous regulatory standard for manufacturers while allowing WHO resources to focus on review of products not already covered by stringent regulatory review.

- ***Increase access to affordable diagnostic technologies of assured quality that are appropriate for use in resource limited settings.*** This important objective would also be better

supported by a two-tiered prequalification approach, which would establish a comparable regulatory baseline for Tier 1 and Tier 2 products. With critical regulatory and quality issues already assessed, questions around suitability of individual products for use in unique settings could then be addressed in dialogue between diagnostics manufacturers and WHO, focused specifically on this question. In some cases, it might be necessary for manufacturers to provide additional information to address the use of a particular diagnostic in a specific setting. This approach would allow both manufacturers and WHO to better apply their limited resources to address product usage in resource limited settings and other critical aspects of diagnostics intended for underserved regions.

- ***The program provides Member States, UN agencies and other partners with technical information and advice***. Reputable diagnostics manufacturers routinely provide detailed information, training and product support tailored to individual customer needs. This objective represents an important opportunity for collaboration between diagnostics manufacturers and WHO focused on the specific requirements of affordable diagnostics intended for use in resource limited settings.

- ***Assess the manufacturer's quality management system based on internationally recognized standards*.** For manufacturers not already subject to inspection under one or more stringent regulatory systems, a WHO inspection program would be appropriate. In other instances, documented evidence of ISO 13485 certification and/or current good standing in FDA or Japanese MHLW inspection programs could be provided to WHO in lieu of inspection.

- ***Laboratory Assessment of performance characteristics.*** Diagnostic products approved by recognized authorities and for which performance data on sensitivity, specificity, ease of operation and shelf life/storage conditions have been generated in actual user settings and reviewed as part of a stringent regulatory process should not require additional generation of data or review of those product registration data by WHO.

- ***The assessment of the quality and the performance of commercially available test kits and technologies is a global requirement; however, regulatory capability and capacity is limited in many countries.*** WHO recognition of the stringent regulatory requirements embodied by the US, EU, and Japan regulatory systems, coupled with adoption of the most important aspects of GHTF guidance, would strengthen development of global regulatory standards and provide a consistent standard in resource limited countries. Again, this approach would allow WHO and its member states to focus limited resources on critical needs with regard to regional or local regulatory support, and other aspects of diagnostics for use in resource limited settings.

- ***The recent increase in diagnostic products manufactured and/or sold in markets without effective and recognized regulatory procedures is a cause of concern and warrants attention.*** This concern underlines the need for a two-tiered approach that would speed access to diagnostics that have already undergone rigorous review, while allowing WHO to focus its finite resources on manufacturers and products in those markets that lack stringent regulatory procedures. Recognition of Tier 1 product standards would also provide a model of stringent regulatory requirements for application in regions that lack effective regulatory procedures.

- ***To increase country capacity to effectively regulate diagnostics and diagnostics manufacturers and to monitor the quality of diagnostics on their market.***
Post market surveillance requirements for diagnostics registered under stringent regulatory systems include detailed adverse event reporting to one or more appropriate agencies, including a reputable European Notified Body, US FDA or Japan's MHLW. Adverse event reporting for

product marketed in new regions would also be required, and periodic summaries could be submitted by manufacturers to WHO.

## Conclusion

AdvaMed and EDMA strongly support WHO's mission to increase access to affordable diagnostics of assured quality in underserved regions of the world.

The current WHO diagnostic prequalification program, however, creates unnecessary additional regulatory hurdles for manufacturers who already comply with product registration and Quality System requirements under stringent regulatory authorities such as those in the US, EU, or Japan. For companies that routinely and reliably manufacture diagnostics already meeting stringent regulatory requirements, the program adds significant delay and potentially undermines WHO's important mission to increase access to much needed diagnostics in underserved regions of the world.

We echo WHO's longstanding concern for the quality and suitability of diagnostic products intended for use in critical regions of the world, and we recognize the potential need for a product and quality system review of manufacturers not already subject to appropriate regulation. We urge WHO to adopt a two-tiered approach similar to that outlined in this paper as the best means of addressing the organization's concerns over regulatory, quality, and manufacturing standards to be met by diagnostic products procured through its programs. This important step provides a means for WHO to improve regulatory requirements for all products while opening the way for timely access to high quality diagnostics. This also allows better utilization of both industry and WHO resources to specifically address the unique requirements of products for use in underserved regions of the world.

*1st September 2010*

## References


1. http://www.who.int/diagnostics_laboratory/evaluations/en/
2. http://www.who.int/diagnostics_laboratory/pq_status/en/index.html
3. http://www.ghtf.org