ANNEX 1

SECOND ROUND OF WHO MALARIA RDT PRODUCT TESTING PROGRAMME

This document includes details of the Second Round of WHO Malaria RDT Product Testing Programme and criteria for inclusion of products.

The only action necessary at present for a manufacturer interested in participating in this Programme, is to send the details of the products considered for submission to the WHO Second Round Product Testing Programme, in accordance with the instructions described below. Such an Expression of Interest will not be binding on either party, but must be received by WHO by 14 November 2008 to allow participation in the Second Round of testing (which is scheduled to commence at the end of March of 2009).

A. Introduction

WHO is proposing to undertake this evaluation to assess the performance of antigen-detecting malaria rapid diagnostic tests (RDT). All product testing will be conducted at the Malaria Branch, Division of Parasitic Diseases, and Centers for Disease Control and Prevention, Atlanta, U.S.A. with an additional stability assessment performed at the site of manufacturer. The Programme will be coordinated jointly by the WHO-Regional Office for the Western Pacific (WHO/WPRO) and the UNICEF-UNDP-World Bank-WHO Special Programme for Research and Training in Tropical Diseases (WHO/TDR), under a joint work plan with the Foundation for Innovative New Diagnostics (FIND) and funded predominantly by AusAID and the Bill and Melinda Gates Foundation.

Testing will be conducted in two phases. A total of 2200 Malaria RDTs, consisting of 1100 tests from each of the two separate lots for each product, will be required to be submitted for the programme. Phase I of the testing process will be performed against a panel of cryo-preserved preparations of cultured parasites and recombinant antigens. Phase II will be performed against a panel containing diluted cryo-preserved preparations of wild parasites, and parasite-negative samples. Manufacturers cover the courier cost and associated costs of transport of RDTs to US CDC and the cost of transport of proficiency panels from CDC to the site of manufacturer.

A subset of the product test panel prepared from cultured P. falciparum malaria parasites will be made available to manufacturers for their own quality control testing prior to submission of products to the Product testing Programme (optional), and for a stability test at the manufacturing site required later (mandatory) as part of the product-testing programme.

Submission of a request for inclusion of products (Expression of Interest) in the initial round of testing will close by 14 November 2008. Only these products listed on the Appendix A will be eligible for the Second Round of Product Testing Programme. WHO reserves the right to limit the number of products per manufacturer if the total number of products in the EOI is beyond the capacity for testing by the programme in a single round of Product Testing.

As with the First Round of Product testing, the Second Round of WHO Malaria RDT Product Testing Programme will provide the performance data for WHO prequalification of Malaria RDTs, currently under development. Results of the product testing will form the basis of procurement recommendations of WHO and the WHO tendering programme until the full prequalification programme is in place. RDTs must be submitted to Round 1 or Round 2 of Product Testing Programme to be eligible for future WHO prequalification programme in 2009. Products accepted for the product testing programme will be listed on the WHO web site.

Data on product performance during testing will be published by WHO as an addition to the published results of the First Round of Product Testing in 2008 and will guide future procurement of RDTs by WHO, other UN Agencies and national health authorities, and subsequently WHO prequalification. Manufacturers will be informed of the performance results, in accordance with the terms of the attached sample confidentiality
agreement. (The confidentiality agreement in APPENDIX B should not be signed at this stage, but will be required at the time of final product submission for the WHO Product Testing Programme – see diagram on page 6).

If products were submitted to First Round of Product Testing (May 2008) then this is sufficient for currently being listed for the WHO procurement and for applying for Prequalification. It is not necessary to resubmit these products for the Second Round of testing. However, products submitted to First Round maybe re-submitted to Second Round, on which the results of First Round will be replaced by results of Second Round.

WHO will list all products evaluated as part of the WHO Malaria RDT Product Testing Programme together with their performance data on a dedicated page of the WHO website and in a hard copy publication. WHO may remove a product from the website list or require re-submission of a product for performance testing if changes in product specifications listed in ANNEX 2 indicate that the RDT should be considered a new product, or performance data obtained from lot testing in the field are considered to be consistently outside those of the product testing programme published by WHO. The manufacturer of a listed product of which the product specifications have been changed, is required to inform WHO of such changes prior to the commercial release of the changed product.

Publication of data on product performance and/or inclusion in the above mentioned website list does not guarantee that the RDTs in question will actually be procured by WHO or any other party.

Participation in the Product Testing Programme, publication by WHO of the testing results and/or inclusion in the website list may not be used by the manufacturers and suppliers concerned for commercial or promotional purposes. Under no circumstances is a manufacturer or supplier authorized to refer to WHO, the manufacturers' or suppliers' participation in the Product Testing Programme, the publication of the testing results by WHO and/or inclusion in the website list, in any statement or material of an advertising or promotional nature, press release and/or similar public statement and/or other material aimed at promoting the manufacturer or supplier and/or its products.

Publication of the testing results and/or inclusion in the website list does not furthermore in any way imply an endorsement, certification, warranty of fitness or recommendation by WHO of any company or product for any purpose, and does not imply preference over products of a similar nature that are not mentioned. WHO will not accept any liability or responsibility whatsoever for any injury, death, loss, damage, or other prejudice of any kind that may arise as a result of, or in connection with the procurement, distribution and use of any product, as to which WHO has published the testing results and/or which is included on the list.

B. Relationship of WHO Malaria RDT Product Testing to WHO prequalification of Malaria RDTs

The product testing data obtained through the Product Testing will form part of the WHO Prequalification programme currently under development for Malaria RDTs. The Prequalification programme is coordinated by WHO/DLT (Diagnostics and Laboratory Technologies) and includes a dossier review and inspection of manufacturing site. For further information and enquiries on prequalification please visit http://www.who.int/diagnostics_laboratory/evaluations/en/.

C. Criteria for entry to the Product Testing Programme

Conditions of entry are derived from the recommendations of WHO expert consultations at Geneva, Kisumu and Atlanta in 2006.
WHO-Malaria Product Testing Programme – Round 2

Conditions for testing of products as part of the WHO Malaria Diagnostics Product Testing Programme¹ (see Diagram on page 7)

1. By 14th November 2008: Submission of an Expression of Interest to the WHO (as in the attached Appendix A).

Documents to be submitted by E-mail and hard copy to WHO:

Dr. David Bell
Scientist (Malaria Diagnostics)
Malaria, Vector borne, and Other Parasitic Diseases
World Health Organization
Regional Office for the Western Pacific
UN Avenue, Ermita
1000 Manila
Philippines

Tel.: +63 2 528 9756
Fax: +63 2 521 1036
Email: mal-rdt@wpro.who.int

2. By 12th December 2008 (if EOI is accepted): Fulfillments of the requirements for taking part in the Second Round of Product Testing Programme including:

a) Current ISO 13485:2003 (By E-mail)

b) Provision of an acceptable heat stability protocol of internal quality assurance (ANNEX 3). (By E-mail)

(Manufacturers who already fulfills these criteria and participated in the First Round of WHO RDT Product Testing and are included in the WHO RDT website (http://www.wpro.who.int/sites/rdt) under list of commercially available malaria RDTs, are not required to submit further evidence concerning this).

c) Submission of 2 original copies of the Confidentiality agreement (APPENDIX B) and acceptance of conditions for product testing and publication of results, including the undertaking to perform a stability test of submitted product lots according to a protocol specified by WHO and to submit the results thereof to WHO for publication² (By hard copy and E-mail)

c) Final Product List (APPENDIX C) and product leaflets (By hard copy and E-mail)

3. By End of March 2009: Free supply and delivery of Malaria RDTs to US CDC, Atlanta. (see point E below)

4. Re-labelled products that are manufactured at the same site and under the same conditions as a tested product, and fulfills the criteria in APPENDIX D may be jointly listed with the tested product under the criteria and conditions listed in APPENDIX D.

5. The above actions should be undertaken if and when WHO so notifies the manufacturer. No product testing will take place unless the manufacturer has fulfilled the above conditions by the dates set by WHO and in accordance with WHO’s instructions.

D. Supply of products for testing

¹ It is planned to include a product specific audit as a criteria in the future, through a mechanism to be determined by WHO
A total of 2200 tests consisting of 1100 tests from each of the two separate lots must be submitted for the Programme.

All RDTs must be received at US CDC by a given deadline (not before middle of March 2009) in order to be accepted for product testing. (Temperature monitors for the duration of the transportation can be obtained from WHO free of charge at request)

All products will be stored at 4°C from time of receipt until actual testing occurs (the product testing site will determine the order in which testing will be conducted)

Sufficient product of each lot should be provided (as mentioned) to conduct both phases of testing against the challenge panel (Towards quality testing of malaria rapid diagnostic tests: Evidence and methods. Manila, World Health Organization, 2006). If a product does not display sufficient performance against the Phase 1 panel, the lot will not be tested against the Phase 2 panel.

Important note on RDT format

Manufacturers may submit products in any format and for any target antigen. RDTs with the same product name but different format (e.g. cassette and dipstick) are considered separate products and will require separate submission and testing. On publication of the testing results by WHO, the introductory text accompanying the table of product performance characteristics will emphasize the current WHO recommendation that cassettes are preferred to dipsticks for field use in endemic countries. Manufacturers are therefore advised to consider submitting only tests in cassette format.

It is noted that few products together P. falciparum pLDH were submitted to Round 1 of Product Testing (2008). Manufacturers are suggested to consider inclusion of such products.

E. Oversight: Specimen Bank Review Committee

The Malaria Specimen Bank (currently at US CDC), is the repository of characterized samples against which product testing will occur, and includes recombinant antigen, culture-derived and wild-type malaria parasites, and negative samples. The wild-type parasites are collected from a geographically-diverse network of collection sites in Asia, Africa and South America, and prepared according to standard protocols.

A Specimen Bank Review Committee will oversee the technical and logistical aspects of the testing and evaluation process, including the development of Standard Operating Procedures (SOPs), oversight of ethical approval for the collection sites contributing to the Specimen Bank (including submission to the WHO Ethics Committee, and local ethical review board) and oversight of the product testing and reporting of results.

Terms of reference of the Specimen Bank Review Committee:

The Malaria RDT Specimen Bank Review Committee will provide recommendations to WHO on:

- Development and modifications of SOPs for specimen collection and use
- Accumulation and content of the Specimen Bank, and characterization and maintenance
- Policy on access to the Specimen Bank
- Protocols for laboratory-based testing of the accuracy and stability of malaria RDTs, including product testing and lot testing
- Interpretation of the results of product testing, prior to publication.
WHO-Malaria Product Testing Programme – Round 2

Composition

Core:
WHO/TDR [2],
WHO/WPRO [1],
Foundation for Innovative New Diagnostics (FIND), [2]
US Centers for Disease Control and Prevention (CDC), [2]
Kenya Medical Research Institute (KEMRI) [1]
Médecins sans Frontières, [1]

Collection sites: 1 African, [1]
1 non-African, [1]

Specimen characterization centers:
Hospital for Tropical Disease, UK [1]
Army Malaria Institute, AU, [1]

\(^2\) Figure in brackets indicates the number of representatives.
WHO Malaria RDT Product Testing Programme

Step 1: Submission of Expression of Interest (Appendix A)
Deadline for Receipt 14 NOV 2008

Step 2: WHO sends EOI Acceptance letter to manufacturers, final number of tests per manufacturers that can be submitted to Round 2 and details for obtaining the optional culture panel from CDC for manufacturer quality control testing.
Deadline for Receipt 20TH NOV 2008

Step 3: Submission of ISO 13485:2003 and Provision of heat stability protocol of internal quality assurance (if not already submitted previously), TWO signed ORIGINAL copies of Confidentiality Agreements (APPENDIX B), Final list of products (APPENDIX C), and Product inserts/leaflets for each product submitted.
Request for Temperature monitor for duration of RDT transportation (Optional)
Deadline for Receipt 12 DEC 2008

Step 4: Review of the submissions by Steering committee
DEC 2008

Step 5: WHO sends Confirmation of acceptance of Final list of products for the Product Testing Programme
Early JAN 2009

Step 6: Applicant submits a total of 2200 tests consisting of 1100 tests from each of two separate lots to US CDC
Deadline for Receipt END of MAR 2009

Step 7: Applicant obtaining parasite specimen samples from US CDC for the stability testing at manufacturer site
MAR/APR 2009

Step 8: Applicant submits results of the stability test performed at the manufacturer site every 3 monthly until the end of the specified shelf life

Step 9: Results of the Product Testing Programme at US CDC will be available
LATE 2009
F.  Further Information

This document and its Appendices and an outline of the methods for product testing can be found at the WHO malaria RDT website at:  http://www.wpro.who.int/sites/rdt/who_rdt_evaluation/call_for_testing.htm

Further information on the Product Testing Programme can be found in:


All the above documents can also be found at: www.wpro.who.int/sites/rdt (http://www.wpro.who.int/sites/rdt/who_rdt_evaluation/call_for_testing_round2.htm)

Or can be obtained by sending an email to: mal-rdt@wpro.who.int