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The Global Fund
To Fight AIDS, Tuberculosis and Malaria

11 February 2008
EECA/MK/028 - 11/02/2008

Dr. Victor Volovei
Executive Director
Project Coordination, Implementation
and Monitoring Unit of the Ministry of Health
of the Republic of Moldova
101, Sciusev Street
Chisinau 2012
Republic of Moldova

Subject: **Program Grant Agreement Number MOL-607-G02-T**
Implementation Letter 2

Dear Dr. Volovei,

Interim Amendment to Quality Assurance Policy for Pharmaceutical Products

We are writing to inform you that the Global Fund Board has decided to make a temporary amendment to the Global Fund Quality Assurance Policy for Pharmaceutical Products (the "QA Policy").

As you are aware, the Global Fund currently classifies pharmaceutical products under its QA Policy into two categories:

(1) Single and Limited-Source Pharmaceutical Products – these are pharmaceutical products for which there are no publicly available quality assurance standards, analytic methods, and reference standards; and

(2) Multi-Source Pharmaceutical Products – these are pharmaceutical products for which the monographs of the finished dosage forms are publicly available in one or more pharmacopoeias (i.e. technical reference standards).

To address concerns raised about the risk of quality assurance problems with products that have recently been classified as Multi-Source Products, the Global Fund Board decided on 12 November 2007 that any drugs for the treatment of HIV/AIDS, tuberculosis and malaria for which the monograph of the finished dosage has been published in International, US or UK Pharmacopeia (i.e. technical reference standards) after 10 October 2002, shall be subject to the QA Policy for Single and Limited-Source Pharmaceutical Products.

This change to the QA Policy will take effect immediately and will apply until the Board considers the issue again in November 2008 following a full review of the Global Fund's QA Policy.

This means that the QA Policy for Single and Limited-Source Pharmaceutical Products (as set out in Attachment 1 to this letter) now applies also to all future procurement of products that are listed in the table set out in Attachment 2 to this letter.

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This also means that any product that is currently classified as a Single or Limited - Source Product, but for which the monograph of the finished dosage is published in International, US or UK Pharmacopeia after the date of this letter will remain subject to the QA Policy for Single and Limited-Source Pharmaceutical Products.

Further information about the QA Policy for Single and Limited-Source Pharmaceutical Products is posted on the Global Fund website: http://www.theglobalfund.org/en/about/procurement/quality/.

Next Steps

You are requested to take the following steps:

1. Please confirm your agreement with the foregoing and the proposed amendments to the Grant Agreement between you and the Global Fund (as set out below) by signing the enclosed copies of this letter, returning one copy to us and retaining one copy for your records.

2. Please check whether any of the products that you are currently procuring or that you intend to procure are on the list set out in Attachment 2 to this letter. If they are, please check that the products comply with the QA Policy for Single and Limited Source Products according to the following:

   a. If you are procuring or plan to procure any products listed in Attachment 2 to this letter that are not prequalified by WHO or approved by a stringent regulatory authority, you should promptly complete the notification form contained in Attachment 3 to this letter and submit it to your Fund Portfolio Manager.

   b. If you are currently procuring any product listed in the Attachment 2 to this letter that does not comply with the QA Policy for Single and Limited Source Pharmaceutical Products, please inform your Fund Portfolio Manager immediately by email and copy all correspondence on the matter to Joelle Daviaud at Joelle.daviaud@theglobalfund.org.

   If you have entered into contracts **before** receiving this letter to procure products listed in Attachment 2 that do not comply with the QA Policy for Single and Limited Source Pharmaceutical Products, the Global Fund will endeavor to find a solution that ensures that patients continue to receive treatment with drugs of acceptable quality.

   However, please be advised that if you do enter into a contract **after** receiving this letter to procure products that do not comply with the QA Policy for Single and Limited Source Pharmaceutical Products, the Global Fund will apply the enforcement measures specified in Attachment 4 to this letter.

Amendments to the Grant Agreement

As a consequence of this Board decision, the Standard Terms and Conditions of the Grant Agreement between you and the Global Fund for the above program effective 18 April 2007 and amended by letters dated 1 November 2007, needs to be amended (the "Grant Agreement").

By signing this implementation letter, the Global Fund and the Principal Recipient agree to amend the Grant Agreement as follows:

(1) by replacing Article 19(i) of the Standard Terms and Conditions with the following provision:

"For any pharmaceutical product for which the monograph of the finished dosage form was published in the international, U.S. or U.K pharmacopoeias before 10 October 2002, the Principal Recipient may verify compliance with applicable quality standards in accordance with existing national procedures of the Host Country."

(2) by replacing the first paragraph in Article 19(j) of the Standard Terms and Conditions with the following paragraph:

"(j) Single or Limited Source Pharmaceutical Products and Other Pharmaceutical Products: Grant funds may be used to procure a single- or limited-source pharmaceutical product (that is, a pharmaceutical product for which there are no publicly available quality assurance standards, analytic methods, and reference standards) or a pharmaceutical product for which the monograph of the finished dosage form was published in the international, U.S. or U.K. pharmacopoeias on or after 10 October 2002, provided that such product meets one of the following standards:.."

(3) by amending Block 4A of the face sheet of the Grant Agreement as follows:

Block 4A: Modification Number: 2 (Implementation Letter 2 dated 11 February 2008).

The face sheet of the Grant Agreement, as amended, is attached. Except as modified herein, the Grant Agreement remains in full force and effect.

Please do not hesitate to contact your Fund Portfolio Manager if you have any queries or need any further clarifications in relation to the above.

As stated above, the Global Fund's primary concern in handling matters related to this Board decision is to ensure that patients continue to receive treatment with drugs of acceptable quality.

Yours sincerely,

Dr Debrework Zewdie
Director of Operations *a.i.*

Agreed and Signed:

For: THE PROJECT COORDINATION, IMPLEMENTATION AND MONITORING UNIT OF THE MINISTRY OF HEALTH OF THE REPUBLIC OF MOLDOVA

By: _____
Authorized Representative: Dr Victor Volovei, Executive Director

Date: _____

cc: Acad. Ion Ababii, Minister of Health and Social Protection, Chair of the Country Coordinating Mechanism, Moldova
Mr. Dan Popov, Manager, PricewaterhouseCoopers, Local Fund Agent, Moldova

Attachment: Face sheet of the Grant Agreement, as amended
Attachment 1 - Quality Assurance Policy for Single and Limited-Source Pharmaceutical Products
Attachment 2 - Table of products affected by the Interim Amendment to the QA Policy
Attachment 3 - Notification Form
Attachment 4 - Enforcement of Quality Assurance Policy for Single and Limited-Source Pharmaceutical Products

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PROGRAM GRANT AGREEMENT

1. Country: Republic of Moldova		
2. Principal Recipient Name and address: Project Coordination, Implementation, and Monitoring Unit, Ministry of Health of the Republic of Moldova, 101 Sciusev Street, MD 2012, Chisinau, Republic of Moldova		
3. Program Title: Strengthening Tuberculosis Control in the Republic of Moldova		
4. Grant Number: MOL-607-G02-T		4A. Modification Number: 2 (Implementation Letter 2 dated 11 February 2008)
5. Phase 1 Starting Date: 1 October 2007	6. Phase 1 Ending Date: 30 September 2009	7. Phase 2 Ending Date: 30 September 2012
7A. Condition Precedent Terminal Date: 1 December 2007	7B. Condition Precedent Terminal Date: 30 June 2008	7C. Condition Precedent Terminal Date: 1 December 2007
7D. Condition Precedent Terminal Date: 30 June 2008	7E. Condition Precedent Terminal Date:	7F. Condition Precedent Terminal Date:
8. Grant Funds: US$ 5,675,507 (Five Million, Six Hundred Seventy-Five Thousand, Five Hundred and Seven United States Dollars)		
9. Program Coverage: Tuberculosis		

10. Information for Principal Recipient Bank Account into Which Grant Funds Will Be Disbursed:

Owner of Bank Account:	The Project Coordination, Implementation and Monitoring Unit of the Ministry of Health of the Republic of Moldova
Account Title:	Special Account (USD)
Account number:	2271880125
Bank name:	BC Moldova-Agroindbank SA Chisinau-Centru Branch
Bank address:	182 Stefan cel Mare str., MD 2004, Chisinau, Moldova
Bank SWIFT Code:	AGRN MD2X
Bank Code: IBAN:	AGRNMD2X723

Routing instructions for disbursements: Citibank, N.A., New York, NY, acc.No.36126158, swift code: CITIUS 33

11. The fiscal year of the Principal Recipient is from 1 January to 31 December.

12. Local Fund Agent ("LFA")
Name: PricewaterhouseCoopers Audit SRL
Address: 37 Maria Cibotari Street, Chisinau 2012, Republic of Moldova
Tel: +373 22 238122 Fax: +373 22 238120
Attention: Mr. Dan Popov
E-mail: dan.popov@ro.pwcglobal.com

13. Name/Address for Notices to Principal Recipient	14. Name/Address for Notices to Global Fund:
Dr. Victor Burinschi TB/AIDS/STI Program Coordinator Project Coordination, Implementation and Monitoring Unit, Ministry of Health of the Republic of Moldova 101 Sciusev Street MD 2012, Chisinau, Republic of Moldova Tel.: +373 22 238751 Fax: +373 22 202437 E-mail: vburinschi@ucimp.md	Urban Weber Ph.D. Team Leader Eastern Europe and Central Asia Cluster Chemin de Blandonnet 6-8 1214 Vernier-Geneva, Switzerland Tel.: +44 22 791 1700 Fax: +41 22 791 1701

This Agreement consists of the two pages of this face sheet and the following:
Standard Terms and Conditions **Annex A – Program Implementation Description**

Attachment 1

Quality Assurance Policy for Single and Limited-Source Pharmaceutical Products.

Grant funds may be used to procure a single- or limited-source pharmaceutical products (that is, a pharmaceutical product for which there are no publicly available quality assurance standards, analytic methods, and reference standards) provided that such product meets one of the following standards:

(1) such product is acceptable under the WHO Prequalification Program; or

(2) such product has been authorized for use by a stringent regulatory authority.

If the Principal Recipient determines that there is only one or no equivalent pharmaceutical product that meets the standards of either (1) or (2), or if the Principal Recipient determines that the products that meet these standards are unavailable[*] and represents the same to the Global Fund, and the Global Fund does not object, then Grant funds may be used to procure another equivalent pharmaceutical product, provided that such product is selected in accordance with the following, in order of priority:

i. *the manufacturer has submitted an application for approval of such product to the WHO Prequalification Program or a stringent regulatory authority and such product is manufactured at a site that is compliant with the standards of GMP, as certified (after inspection) by the WHO or a stringent regulatory authority; or*

ii. *if the manufacturer of such product has not submitted an application for approval of such product to the WHO Prequalification Program or a stringent regulatory authority, such product is manufactured at a GMP-compliant manufacturing site, as certified (after inspection) by the WHO or a stringent regulatory authority.*

The Principal Recipient shall promptly notify the Global Fund in writing if it procures any products pursuant to the criteria in clause i or ii above.

[*] 'Unavailable' is defined as the inability of the manufacturer to supply a sufficient quantity a of finished product within 90 days from the date of the order (12th Board Meeting).

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Attachment 2

List of Multi-Source Products that are now subject to the Global Fund's Quality Assurance Policy for Single and Limited-Sourced Pharmaceutical Products as of 12 November 2007

Antiretrovirals (ARVs)

Non proprietary name (INN)	Dosage Form
Nelfinavir	*Powder for oral solution*
Nelfinavir	*Tablet*
Stavudine	*Powder for oral solution*
Stavudine	*Capsule*
Abacavir	*Tablet*
Didanosine	*Powder for solution*
Lamivudine / Zidovudine	*Tablet*
Lamivudine / Zidovudine / Abacavir	*Tablet*

Anti Malaria pharmaceuticals products

Non proprietary name (INN)	*Dosage form*
Artesunate + Amodiaquine Co-Blistered	*Tablet*
Artesunate +(Sulfadoxine + Pyrimethamine)	*Tablet*
Artemether	*Solution for Injection*
Artemotil	*Solution for Injection*

Anti-TB pharmaceuticals products

Non proprietary name (INN)	*Dosage form*
Capreomycin*	*Powder for injection*
Ethambutol/ Isoniazid	*Tablet*

* The Global Fund requirement for 2nd line TB drugs procurement is that the procurement , using Global Fund grants, must be conducted through the Green Light Committee (GLC) of the Stop TB initiative.

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Attachment 3

To: ..... (*Name of the Fund Portfolio Manager*)
Cc: GF Procurement and Supply Management Team

PR's Notification to the Global Fund of intent to procure Single- and Limited-Source Pharmaceutical product(s) or Other Pharmaceutical Products pursuant to Article 19 (j) i. or ii. of the Grant Agreement

Please find below the required information regarding the following single- and limited-source pharmaceutical product(s) classified according to criteria Ci and/or Cii that we,..... [*Name of the PR*], intend to procure:

Date of notification:	
Country:	
Grant Number:	

(If there is more than one pharmaceutical product to be notified, please provide information for each product in separate table, as follows)

INN†/ Generic product name	**Strength**	**Dosage form**	**Manufacturer/Supplier** (Please indicate manufacturing site)
Main Reason for selecting this Manufacturer/supplier			

INN*/ Generic product name	**Strength**	**Dosage form**	**Manufacturer/Supplier** (Please indicate manufacturing site)
Main Reason for selecting this Manufacturer/supplier			

† INN : International Nonproprietary Name

We look forward to receiving the Global Fund response, in order for us to finalize the selection process of the above listed products.

Sincerely,

Name of the PR
Designation
Address
Email
Phone

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Attachment 4

Enforcement of Quality Assurance Policy for Single and Limited-Source Pharmaceutical Products

Quality Assurance Policy

The Global Fund Board approved the Quality Assurance Policy for the procurement of Single- and Limited-Source Pharmaceutical Products in April 2005 in order to ensure that Global Fund resources are used to procure quality-assured pharmaceutical products.

According to the Quality Assurance policy, Single- and Limited-Source Pharmaceutical Products have been classified into three categories: A, B and C.

Category A products are products that have been found to be acceptable by the WHO UN Pilot Procurement Quality and Sourcing Project.

Category B products have been authorized for consumption in their country by a stringent regulatory authority.[‡]

Category C products are sub-divided into two sub-categories, Ci and Cii. A Ci pharmaceutical product is (1) produced by a manufacturer that has submitted an application for product pre-qualification to the WHO Prequalification Program and/or for product approval by a stringent regulatory authority and (2) the manufacturing site for this product is compliant with Good Manufacturing Practice (GMP) standards as certified by WHO or by one of the stringent regulatory authorities. A Cii pharmaceutical product is manufactured according to GMP standards as certified by WHO or by one of the stringent regulatory authorities. The manufacturer of a Cii pharmaceutical product has not submitted an application for product prequalification to the WHO Prequalification Program and/or for product approval by a stringent regulatory authority.

Pursuant to the Quality Assurance Policy, Category C products may only be purchased if the Principle Recipient determines that there is only one or no equivalent pharmaceutical product that meets Category A or B or if the Principal Recipient determines that such products are unavailable within 90 days. In addition, Cii products can only be purchased if Ci products are unavailable.

Procuring inappropriately under Category C could result in the distribution of products that are not safe for consumption. In particular, failure by PRs to notify the Global Fund that they are purchasing under this category makes it impossible for the Global Fund to conduct random testing of the quality of the products, thereby increasing the risk that patients will be put at risk. To prevent that from occurring, the Global Fund will enforce the corrective measures that are outlined in this document.

Levels of Non-Compliance

The Global Fund has defined two levels of non-compliance as described below.

Level 1 – "No-notification but compliant procurement": A Principal Recipient did not inform the Global Fund of its intent to procure a "C" product before it procured such product(s) and the quality control testing has not been conducted by the Global Fund.

[‡] For the purposes of this policy, a "stringent drug regulatory authority" is defined as a regulatory authority participating in the Pharmaceutical Inspection Cooperation Scheme (PIC/S) and/or the International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use.

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However, the selection of the product(s) procured is compliant with the Quality Assurance policy.

Level 2 – "No-notification and non-compliant procurement": A Principal Recipient did not inform the Global Fund of its intent to procure a "C" product before it procured such product(s), the quality control testing has not been conducted by the Global Fund and the selection of the product(s) is not in compliance with the Quality Assurance policy.

Enforcement of Non-Compliance

In the event of non-compliance with the Quality Assurance Policy, the Global Fund will enforce the following corrective measures, depending on the level of non-compliance.

Level 1 – "No-notification but compliant procurement":

First Instance of no-notification but compliant procurement – The Global Fund will inform the Principal Recipient that it has received information that the Principal Recipient has procured "C" products using grant funds without notifying the Fund Portfolio Manager of its intent to procure such "C" product(s) and will request the Principal Recipient to urgently send written notification to the GF. (To facilitate this notification, a template letter of notification for use by Principle Recipients is contained in Attachment 3 and available on the Global Fund website.)

Once the Principal Recipient sends written notification to the Global Fund, compliance of the procurement with the Quality Assurance policy will be verified before the Global Fund releases any further disbursements related to procurement of pharmaceutical products.

Additionally, the Global Fund will send a warning letter to the Principal Recipient stating that should the Principle Recipient fail to comply a second time, the Global Fund will only disburse funds for procurement of pharmaceutical products directly to a procurement agent or to the supplier.

Second Instance of no-notification but compliant procurement – The Global Fund will inform the Principal Recipient that it has received information that the Principal Recipient has procured "C" products for a second time without notifying the Fund Portfolio Manager of its intent to procure such "C" product(s). The Global Fund will request the Principal Recipient to urgently send written notification (template letter of notification contained in Attachment 3) and will advise the Principal Recipient that all further disbursement of funds for procurement will be made directly to a procurement agent or to the supplier.

Once the Global Fund receives written notification from the Principal Recipient, compliance of the procurement with the Quality Assurance policy will be verified. The Global Fund will only disburse funds for pharmaceutical products directly to a procurement agent or the supplier for the remaining period of the Grant Agreement.

Level 2 – "No-notification and Non-compliant Procurement":

First Instance of no-notification and non-compliant procurement – The Global Fund will inform the Principal Recipient that it has received information that the Principal Recipient has used grant funds to procure "C" products without notifying the Fund Portfolio Manager of its intent to procure such "C" product(s) and that these products are not compliant with the Quality Assurance policy as per the Grant Agreement.

To verify the compliance of this procurement, the Global Fund will request the Principal Recipient to urgently send written notification with all documentation justifying the choice of the product(s).

When the non-compliant procurement is confirmed, the amount paid by the Principal Recipient for the non-compliant products will be deducted from future disbursements and the Global Fund will only disburse funds for pharmaceutical products directly to a procurement agent or a supplier for the remaining period of the Grant Agreement.

Further, non-compliance with this policy may have repercussions on the Country Coordinating Mechanism's (CCM) Request for Continued Funding (also known as the "Phase 2 Request"). For example, if the Global Fund confirms the non-compliant procurement after submission of the Request for Continued Funding, the amount paid by the Principal Recipient for the non-compliant pharmaceutical products will be deducted from the recommended Phase 2 amount, with notification to the Global Fund Board. In addition, the Phase 2 Panel may recommend a "Conditional Go" with conditions attached to compliance with the Quality Assurance Policy. In cases of repeated non-compliance, the Phase 2 Panel may consider recommending no further funding for Phase 2 on that basis.

In cases of repeated non-compliant procurement by Principal Recipients the Global Fund may suspend or terminate a grant and/or replace the Principal Recipient.

Communication about Compliance

As is existing practice, Principal Recipients are reminded that all formal communications with the Global Fund must be sent directly to the Fund Portfolio Manager responsible for the portfolio of grants. The Fund Portfolio Manager will answer any queries or direct the Principal Recipient to in-house technical expertise as needed.

Principal Recipients should be aware that the CCM and the Local Fund Agent (LFA) will be copied on all correspondence in relation to the Quality Assurance Policy and the compliance measures as described in this letter.

The Global Fund is ready to assist with any queries or clarifications regarding the Quality Assurance Policy, its implementation and the enforcement of the policy. I encourage you to be in touch with your Fund Portfolio Manager who can provide guidance and further information.