

Quality Assurance (QA) for Health Products

QA Information Notice

IN N° 2021-06 Version: 07 June 2022	Precautionary measures for GenoType MTBDRplus Ver 2.0 and MTBDRsl Ver 2.0 supplied by Hain Lifescience GmbH, Germany
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Addressees

- Any person using the products for clinical decision making in the intended use
- Any person having products in stock, in transit or under custom clearance
- Any procurers, buyers with a pending order

Purpose

The Global Fund QA is issuing this QA Information Notice to provide recommendations and advice regarding the urgent Field Safety Corrective Action (FSCA) issued by Hain Lifescience GmbH, Germany regarding certain lots.

This notice is for internal and external dissemination and country teams are expected to communicate this information to their relevant stakeholders.

Identification of the product(s) and manufacturer

Name of Manufacturer	Hain Lifescience GmbH Hardwiesenstraße 1, DE-72147 Nehren, Germany
Product Name / code	GenoType MTBDRplus VER 2.0 (30496A and 304A and 30496AGL) GenoType MTBDRsl VER 2.0 (31796A and 317A)
Product Code	See above
Packaging & Pack size	Multiple
Batch(es)	Multiple
Expiry Date	Multiple

Background

On the 18th of November 2021, GF QA received information from Global Drug Facility (GDF), an urgent Field Safety Corrective Action (FSCA) issued by Hain Lifescience GmbH, concerning quality issues for diagnostic kits (two items). Until further notice, the manufacturer recommended to perform tests with a positive control in each run according to a standard application note already included as an inlay in each kit box.

Nature of defect(s)

Details of defect or problem.	<p>The amplification control in about 12 lots for GenoType MTBDR plus VER 2.0 and 2 lots of GenoType MTBDRsl VER 2.0 may show a weak positive signal in some cases, even if no amplification is performed. This can lead to a false-negative interpretation of the result.</p> <p>The cause of this behavior is a slight activity of the hot-start polymerase at room temperature.</p>
Is there any evidence or suspicion of a risk to public health?	<p>The consequences for false negative (FN) results can be a potential increased risk of patient morbidity and mortality, and continued community transmission of drug-resistant TB. The harm for these patients without XDR-TB detected by SL-LPA may be the initiation of an MDR-TB regimen with doubtful efficacy.</p>
Extent of the problem (eg. how many batches).	<p>12 lots for GenoType MTBDR plus VER 2.0 2 lots of GenoType MTBDRsl VER 2.0</p> <p>Extended to newer batches according to the application note (see annex 2).</p>
Extent of distribution of the product / batch (es).	<p>The following countries procured affected lots with TGF funding:</p> <p><u>For GenoType MTBDR plus VER 2.0:</u></p> <ul style="list-style-type: none"> • Belarus • Burkina Faso • Dominican Republic • Gabon • Gambia • Guatemala • Guinea • Haiti • Jordan • Kazakhstan • Malawi • Mozambique • Nicaragua • Niger • Pakistan • Somalia • Tajikistan • Ukraine

	<ul style="list-style-type: none"> • Uzbekistan • Zimbabwe <p><u>For GenoType MTBDRsl VER 2.0:</u></p> <ul style="list-style-type: none"> • Philippines • Guinea <p>But potentially all countries receiving Hain products are concerned.</p>
Number of patients potentially impacted	No impacted patients are reported to The Global Fund at this moment in time.
<u>Other products potentially impacted</u>	Other GenoType products independent of lot numbers used with hot-start polymerase with the quality issue. Extended to newer batches according to the application note (see annex 2).

Action/Investigations taken

- GDF identified the countries that were impacted by the affected lots of **GenoType** FSCA, provided the list to GF QA and have contacted the PRs of the concerned countries recommending distributing the FSCA and returning the confirmation to the manufacturer.

Next Steps

Based on the information available to date and until further notice, the following actions are recommended by The Global Fund QA:

- Distribute the FSCA, ensure implementation and returning the confirmation to the manufacturer (see FSCA in the annex for more detailed guidance) if not already done
- Check that newer batches are accompanied by the manufacturer's application note (see annex 2) and follow the instructions, ie adding a positive sample as an amplification control (complementing the AC band).
- Do not recall the above referenced products and maintain distribution of the products within the supply chain until the end destination.
- Do not cancel orders in process given the negative consequences that delays would cause to country programs
- To contact and liaise on the same with National Regulatory Authority.

Contacts

This IN requires a specific written response from the PR on **GenoType** FSCA to the manufacturer.

PRs and Procurement Service Agents should copy GF QA Team on any direct or indirect correspondence to the manufacturer regarding the confirmation of the reception.

Please direct the respective answers and any questions about this matter to the technical contacts listed below:

Organisation	Name / Function	E-mail address
Global Fund / Supply Operations	René Becker-Burgos, Specialist, Diagnostic Products Quality Assurance	rene.becker-burgos@theglobalfund.org
Global Drug Facility	Nigorsulton Muzafarova, Lead QA Officer	nigorsultonm@stoptb.org

Annex 1: Manufacturer’s Field Safety Corrective Action



Hain Lifescience GmbH
 Hardwiesenstraße 1
 72147 Nehren
 Germany

To Whom It May Concern

Date: 09/11/2021

Urgent Safety Information
(FSCA 12102021)

Information for the safe use

of the IVD products:

GenoType MTBDRplus Ver 2.0/2,0 // GenoType MTBDRsl 2.0

Addressee

Users and distributors

Identification of concerned IVD products.

Ref#	Product Name	Lot#		
30496A	GenoType MTBDRplus VER 2.0	OV00253	OV00244	OV00245
		OV00246	OV00248	OV00250
		OV00251	OV00252	-
304A	GenoType MTBDRplus VER 2.0	OU00243	OU00247	OU00249
		OU00254	-	-
317A	GenoType MTBDRsl VER 2.0	AAW00111	-	-
31796A	GenoType MTBDRsl VER 2.0	AAX00112	-	-

30496AGL	GenoType MTBDRplus VER 2,0	VR00126	VR00128	VR00129
		VR00130	VR00131	VR00132
		VR00133	VR00134	-

Product Issue Statement and summary of root cause:

According to our records, you have received at least one kit of the above-mentioned kit lots.

We would like to inform you that the amplification control in the above-mentioned lots may show a weak positive signal in some cases, even if no amplification is performed. This can lead to a false-negative interpretation of the result. The cause of this behavior is a slight activity of the hot-start polymerase at room temperature.

The amplification control serves to check the correct execution of the test and the functionality of the kit components, as well as an inhibition control for the amplification.

Results already generated are to be regarded as valid if a positive control was included in the PCR run or a positive result was present in the same run. If all the results are exclusively negative and do not match the overall clinical picture, additional diagnostic methods should be used.

What actions are to be taken by the addressee?

To avoid misinterpretation due to false-negative results, it is necessary to carry out a positive control.

In addition, preparation of the PCR should be carried out quickly without any interruptions. The PCR run should be started within one hour after preparing the PCR master mix.

Disclosure of described information:

Please ensure in your organisation that all users of the above Products and other persons are informed of this Urgent Safety Information.

If you have transferred the products to third parties, please forward a copy of this information or inform us via the contact details provided below.

Please retain this Safety Information Document at least until the measure has been completed.

The German Federal Institute for Drugs and Medical Devices has received a copy of this "Urgent Safety Information".

Contact at Hain Lifescience:

Diagnosics.support@bruker.com

Signature



Kay Scherer

Response to Urgent Safety Information (FSCA 1210202) concerning:

Ref#	Product Name	Lot#		
30496A	GenoType MTBDRplus VER 2.0	OV00253	OV00244	OV00245
		OV00246	OV00248	OV00250
		OV00251	OV00252	-
304A	GenoType MTBDRplus VER 2.0	OU00243	OU00247	OU00249
		OU00254	-	-
317A	GenoType MTBDRsl VER 2.0	AAW00111	-	-
31796A	GenoType MTBDRsl VER 2.0	AAX00112	-	-
30496AGL	GenoType MTBDRplus VER 2,0	VR00126	VR00128	VR00129
		VR00130	VR00131	VR00132
		VR00133	VR00134	-

By E-Mail to Diagnostics.support@bruker.com

[Address Customer/Trading Partner]

Confirmation of acknowledgment of the urgent safety information by Hain Lifescience GmbH

I / we hereby confirm that I / we have received and acknowledged the urgent safety information regarding the above mentioned IVD Kit lots from Hain Lifescience GmbH and ensure the required procedure.

Place, Date, Name

Annex 2: Manufacturer's Application Note dated 24-May-2022

Hain Lifescience GmbH • Hardwiesenstr. 1 • 72147 Nehren

To whom it may concern

Hain Lifescience GmbH
Hardwiesenstraße 1
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Germany

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info.mdx.de@bruker.com
www.bruker.com

GenoType MTBDRplus v2.0 (REF 30496A & 30496AGL)
GenoType MTBDRsl v2.0 (REF 31796A)

Date: 2022/05/24

Dear Valued Customer,

I would like to inform you that with the new batches of GenoType MTBDRplus VER 2.0 (from Batch # OV00270, OV00271 & OU272), GenoType MTBDRplus VER 2.0 (from Batch # VR00136) and GenoType MTBDRsl VER 2.0 (from Batch # AAW00122), we will be providing together with the Kit an application note stating that a positive sample has to be included in each run. This positive sample serves as an amplification control (complementing the AC band) and confirms that the PCR reaction performed as was expected in this run.

The content of this application note will be implemented in the next version of the IFU for both Kits.

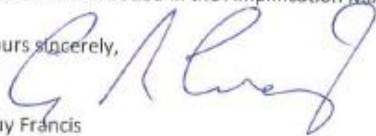
I would like to emphasize that this change will have no impact whatsoever on the Quality of the Kit, nor on the Test Results achieved.

The mechanism of AC band development in the GenoType MTBDRplus VER 2.0, GenoType MTBDRplus VER 2.0 and GenoType MTBDRsl VER 2.0 Test Kits, reacts with high sensitivity to minimal differences in residual Polymerase activity at room temperature prior to heat treatment. This residual enzyme activity at room temperature can lead to an AC band staining, if the time from MasterMix preparation to PCR is too long or if the Thermocycler is not working properly.

The residual enzyme activity at room temperature does not negatively influence the performance data of the Test Kits. The effect is limited to AC band development only.

The minimal differences in residual enzyme activity at room temperature can be decreased but not completely prevented. Therefore, in order to detect failures due to suboptimal conditions the inclusion of a positive sample in each run is a risk mitigation for false negative results and is 100% complementary to the amplification control mechanism included in the Amplification Mix.

Yours sincerely,



Guy Francis
Director of Operations and Managing Director
Hain Lifescience GmbH

Geschäftsführer: Dr. Wolfgang Pusch | Guy Francis | Bernd Merkl

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