Rev 1: September 2018
FSN Ref: FSN2024-001 FSCA Ref: FSCA2024-001
Date: 08.01.2024

Urgent Field Safety Notice
Device Commercial Name

For Attention of*: Distributors and end users of AsperGenius® Resistance Multiplex real-time PCR kit, PN-002, LPN2023063

Contact details of local representative (name, e-mail, telephone, address etc.)*
If you have any questions, contact your local our QA/RA Manager Leah Evers (e-mail: leah.evers@pathofinder.com/contact number: +31 (0)43 3030400

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Urgent Field Safety Notice (FSN)
Device Commercial Name
Risk addressed by FSN

1. Information on Affected Devices*	
1.	1. Device Type(s)*
	The AsperGenius® real-time PCR assay aids in the diagnosis of invasive pulmonary aspergillosis (IPA) in 'at risk' patients, such as patients with hematological malignancies , Solid Organ Transplant (SOT) and allogenic transplant patients and patients with chronical lung diseases (eg. CF, COPD), when used in combination with other clinical and laboratory findings. Negative results do not necessarily indicate absence of an (fungal) infection. Negative results should not be used as the sole basis for diagnosis, therapy, or other treatment decisions. Positive results do not exclude co-infection with other pathogens. The pathogen(s) detected may not be the definite cause of disease. Other laboratory testing and assessment of clinical presentation must be included in the final diagnosis. The product is for use by laboratory professionals only.
1.	2. Commercial name(s)
	AsperGenius® Resistance Multiplex real-time PCR kit
1.	3. Unique Device Identifier(s) (UDI-DI)
	8719326750996
1.	4. Primary clinical purpose of device(s)*
	AsperGenius® multiplex assays are designed for the detection of Aspergillus DNA. The assays are composed of ready to use optimized mixtures of target specific primers and probes for the detection of Aspergillus species and identification of the most prevalent mutations conferring resistance against multi-azole drugs. The AsperGenius® assays are based on real-time polymerase chain reaction (PCR) technology for the detection of A. fumigatus DNA and the identification of resistance/susceptibility patterns. For this technology PathoNostics is using fluorescent probes enabling detection and identification of single nucleotide polymorphisms (SNP´s) using melting curve analysis. SNP´s and a tandem repeat (TR) which are related to resistance can be identified with this technology resulting in discrimination between the wildtype and the mutant (resistant) strain. SNP´s are targeted by the specific probes and differentiation of approximately 2 °C (TR34) or 4-5 °C (L98H, T289A, Y121F) in melting temperature can be accomplished.
1.	5. Device Model/Catalogue/part number(s)*
	Catalogue number PN-002
1.	6. Software version
	NA
1.	7. Affected serial or lot number range
	LPN2023063
1.	8. Associated devices
	LightCycler® 480 II (Roche), Rotor-Gene® Q (QIAGEN), CFX96TM (Bio-rad), QuantStudio 5, ABI7500 (Thermo Fisher Scientific) or Mic qPCR (Bio Molecular Systems) instruments.

2	**Reason for Field Safety Corrective Action (FSCA)***
2.	1. Description of the product problem*
	Reported by MolPLUZ -LAG that the results do not show melting curves for TR34 (533-580 channel) in the resistance PCR, whereas the melting curves in the other 3 channels and also the amplification plots in the species PCR are completely normal. When they performed the 2nd derivative analysis on the 533-580 channel of the resistance PCR, they saw the amplification plots. Without color compensation, they didn't observe melting curves for TR34 (533-580 channel), but this was due to spectral overlap with the 533-610 channel.
2.	2. Hazard giving rise to the FSCA*
	Invasive pulmonary aspergillosis (IPA) is the most frequent invasive mold infection in immunocompromised patients and is mainly caused by Aspergillus fumigatus (A. fumigatus). Spores of the Aspergillus species can be inhaled and can cause an infection in the lower lungs during immune suppression. A false interpretation can lead to the wrong treatment but the chance is very low due to the multiplex mix that can detect different mutations. However, the kit needs to be discarded because it doesn't work fully complaint to our specifications.
2.	3. Probability of problem arising
	The problem was initially identified by the end-user by testing of patient extracts, which contain genomic DNA. After performing a comparison run in-house with a previously released lot of Resistance mastermix and A. fumigatus culture extracts, the problem could be confirmed.
2.	4. Predicted risk to patient/users
	Not likely since the affected target (TR34) is joined with another resistance marker in the same multiplex mix (L98H FAM) that can still confirm whether a patient sample would contain azole resistance or not. Therefore, the kit doesn't work properly but contains an internal system to prevent misinterpretation.
2.	5. Further information to help characterise the problem
	NA
2.	6. Background on Issue
	After internal investigation by comparing this lot with a previous one, it was noticed that melting peaks were present in the previous lot but were weak in the current lot. The detection for the rest of the targets was fine. The reason is most likely that the ratio of primers for this target has not been pipetted correctly. A specific ratio of forward versus reverse is necessary to obtain a melting peak.
2.	7. Other information relevant to FSCA
	NA

	3. Type of Action to mitigate the risk*
3.	**1. Action To Be Taken by the User***
	☒ Identify Device ☐ Quarantine Device ☐ Return Device ☒ Destroy Device ☐ On-site device modification/inspection ☐ Follow patient management recommendations ☐ Take note of amendment/reinforcement of Instructions For Use (IFU) ☐ Other ☐ None Provide further details of the action(s) identified.

3.	2. By when should the action be completed?	As soon as possible, immediately!
3.	3. Particular considerations for: IVD Is follow-up of patients or review of patients' previous results recommended? NO Not likely since the affected target (TR34) is joined with another resistance marker in the same multiplex mix (L98H FAM) that can still confirm whether a patient sample would contain azole resistance or not. Therefore, the patient will still get the correct treatment which excludes the risk to death.	
3.	4. Is customer Reply Required? * (If yes, form attached specifying deadline for return)	Yes
3.	**5. Action Being Taken by the Manufacturer** ☒ Product Removal ☐ On-site device modification/inspection ☐ Software upgrade ☐ IFU or labelling change ☐ Other ☐ None Lot LPN2023063 is discarded from ODOO and cannot be sold anymore.	
3	6. By when should the action be completed?	Performed last Friday 05/01/2024.
3.	7. Is the FSN required to be communicated to the patient /lay user?	No
3	8. If yes, has manufacturer provided additional information suitable for the patient/lay user in a patient/lay or non-professional user information letter/sheet?	
	NA NA	

	4. General Information*	
4.	1. FSN Type*	New
4.	2. For updated FSN, reference number and date of previous FSN	NA
4.	**3.** For Updated FSN, key new information as follows:	
	NA	
4.	4. Further advice or information already expected in follow-up FSN? *	Choose an item. Yes
4	5. If follow-up FSN expected, what is the further advice expected to relate to:	
	The Removal of the resistance mastermix will be sufficient. The customer needs to discard the whole kit. The customers will be provided with a replacement of the PN-002 kit. The customer needs to confirm that the kit is removed and replacement is well received.	
4	6. Anticipated timescale for follow-up FSN	End of January if Final QC is passed
4.	7. Manufacturer information (For contact details of local representative refer to page 1 of this FSN)	
	a. Company Name	**PathoNostics BV.**
	b. Address	**Randwycksingel 45, 6229EG, Maastricht, The Netherlands, Phone: +31 43 3030400**
	c. Website address	**www.pathonostics.com**
4.	8. The Competent (Regulatory) Authority of your country has been informed about this communication to customers. * IGJ is informed.	
4.	9. List of attachments/appendices:	**NA**
4.	10. Name/Signature	**Leah Evers, QA/RA manager PathoFinder/ PathoNostics** 

	Transmission of this Field Safety Notice
	This notice needs to be passed on all those who need to be aware within your organisation or to any organisation where the potentially affected devices have been transferred. (As appropriate) Please transfer this notice to other organisations on which this action has an impact. (As appropriate) Please maintain awareness on this notice and resulting action for an appropriate period to ensure effectiveness of the corrective action. Please report all device-related incidents to the manufacturer, distributor or local representative, and the national Competent Authority if appropriate, as this provides important feedback..*

Note: Fields indicated by * are considered necessary for all FSNs. Others are optional.