FSN Ref: QA2023-05_2

Date: DD: MM: YYYY

Updated information regarding Field Safety Notice

For Attention to customers using EliA GBM Well

Contact details of local representative	
Name	
Address	
Email address	
Telephone number	

Approved by Fredrik Mirenborn, 2024-Jun-03 10:39 CET
Doc.no. 810004 Ver. 1.0 Page 1(8)

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Updated information regarding Field Safety Notice (FSN)

Risk addressed by FSN

1. Information of affected device(s)	
1.1	Device Types(s) EliA GBM Well
1.2	Commercial name(s) EliA™ GBM Well
1.3	Unique Device Identifier(s) (UDI-DI) 14-5514-01: 07333066010670 14-5514-10: N/A 14-5514-41: 07333066018553
1.4	Primary clinical purpose of device(s) Intended use: The EliA GBM Wells are part of the EliA IgG System. They are intended for the in vitro quantitative measurement of IgG antibodies to α3 chain of collagen IV in human serum and plasma as an aid in the clinical diagnosis of Goodpasture syndrome and anti-GBM disease. EliA GBM uses the EliA IgG method on Phadia instruments.
1.5	Device Model/Catalogue/ part number(s) 14-5514-01 14-5514-10 14-5514-41
1.6	Affected serial or lot number range All lots available on the market

Approved by Fredrik Mirenborn, 2024-Jun-03 10:39 CET
Doc.no. 810004 Ver. 1.0 Page 2(8)

Approved by Fredrik Mirenborn, 2024-Jun-03 10:39 CET
Doc.no. 810004 Ver. 1.0 Page 3(8)

2. Reason for Field Safety Corrective Action (FSCA)

2.1 Description of the problem

Phadia AB distributed a Field Safety Notice (QA2023-05) informing users that specific samples may produce false positive EliA GBM results due to an unspecific reaction towards a BSA component in the coating solution used in the EliA GBM Well.

This updated FSN (QA2023-05_2) is to inform you about the CAPA conclusions and recommended actions for future use of the EliA GBM Well.

Risk mitigation options were assessed firstly by design of the product and secondly by the introduction of additional controls. However, any risk mitigation measures in these areas cannot be performed without negatively impacting the performance of the test. Further, the recommended retesting of positive samples by applying an alternative method (according to QA2023-05) has raised concerns about potential BSA reactivity, different sensitivities, and delays to obtain results.

The incidence of false positive results is within the range seen in our clinical performance data and therefore the performance claims of diagnostic sensitivity (93,5%) and specificity (100% (95% CI: 95.4% - 100%)) of EliA GBM are met.

The Clinical Risk Assessment for the EliA GBM has been updated during the CAPA investigation. A new Health Hazard Evaluation (HHE) has been performed as the risk of potentially false positive test results due to specific patient samples reacting to the BSA component in the EliA GBM Well remains.

The most recent international kidney guideline (KDIGO guideline) indicates that a kidney biopsy remains the gold standard test for diagnosing Anti-GBM. Therefore, patients presenting with suspected Anti-GBM would be given a kidney biopsy to confirm the diagnosis or potentially provide alternative therapeutic/ management guidance.

The use of the EliA anti-GBM test provides additional information which, when used with other clinical information, allows the attending physician to determine that patients testing negative may not require a biopsy. Therefore, preventing a significant number of patients from having to undergo a kidney biopsy. This would allow such patients to be transferred to more appropriate care pathways earlier than would otherwise be the case.

The small number of patients who test positive for anti-GBM using the EliA test would still require a kidney biopsy to confirm the positive result, as per the KDIGO Guidance. A kidney biopsy inevitably carries some risks, however numerous studies have demonstrated the low risk associated with renal biopsy even in patients over the age of 80. These risks are considered acceptable when compared to the risk of leaving a patient undiagnosed with life-threatening RPGN. No IVD test is 100% accurate and therefore a small number of false positives results will occur. This is indicated in our claimed performance characteristics, sensitivity (93,5%) and specificity (100% (95% CI: 95.4% - 100%)).

	When taken in full context therefore, overall benefits outweigh the overall risks of the test, including preventing a large proportion of patients from having to undergo a biopsy and enabling other clinical pathway options to be explored more rapidly for these patients.
2.2	Probability of problem arising Based on data and information provided by customer and internal investigations, the probability of a sample to be BSA-reactive and therefore lead to a false-positive test result is estimated to be 0,2%. Goodpasture's syndrome, also known as anti-Glomerular Basement Membrane (anti-GBM) disease) is defined as a rare disease, with a global incidence rate reported from 0,5 to 1 case per million each year.
2.3	Predicted risk to patient/ users. The probability of medically reversible or transient adverse health consequences is estimated to be remote.
2.4	Hazards giving rise to the FSCA Falsely elevated levels of anti-GBM antibodies may be caused by pre-analytical error, improper use of the analyzer and device, improper calibration of the instrument/assay, by rare assay interference or by post-analytical error, which has no association with the status or health risk of the patient. When anti-GBM antibodies are falsely elevated and conflicts with other assessments, a delay in the diagnosis and treatment may occur. In acute situations, treatment may be initiated based on this result and the clinical presentation prior to results of confirmatory tests, which may potentially lead to unnecessary treatment such as plasmapheresis and immunosuppressive therapy, which carry limited risks but would likely be reevaluated upon repeat testing or confirmation. The confirmatory tests for the diagnosis of anti-GBM (Goodpasture) disease would include a kidney biopsy and would likely occur in conjunction with antibody testing.

Approved by Fredrik Mirenborn, 2024-Jun-03 10:39 CET
Doc.no. 810004 Ver. 1.0 Page 4(8)

Approved by Fredrik Mirenborn, 2024-Jun-03 10:39 CET
Doc.no. 810004 Ver. 1.0 Page 5(8)

3. Type of Action to mitigate the risk	
3.1	Action(s) to be taken by the user ☐ Identify Device ☐ Quarantine Device ☐ Return Device ☐ Destroy Device ☐ On-site device modification/inspection ☐ Follow patient management recommendations. ☐ None ☒ Take note of amendment/reinforcement of instructions for use (DFU) See information under 3.3. ☒ Other 1. We no longer recommend the need for retesting of samples with a positive test result for EliA GBM Well (>10 EliA U/ml) as previously suggested in QA2023-05. 2. Use of the EliA GBM Well can continue as detailed in the user manual and the DfU.
3.2	Is customer reply required? Yes
3.3	Action(s) to be taken by the manufacturer ☐ Product removal ☐ On-site device modification/ inspection ☐ Software upgrade ☐ Other ☐ None ☒ IFU or labeling change 1. Corrective and preventive actions (CAPA) investigation have been finalized and corrective actions in the DfU will be implemented. 2. The EliA GBM DfU will be updated. The following information will be added to the "Limitations" chapter within the EliA GBM DfU: “When assessing the clinical significance of a positive test result, it should be considered that anti-GBM disease is a very rare condition, which impacts the positive predictive value of the test. Falsely elevated test results can occur due to specific binding of serum antibodies to blocking reagents, such as BSA.”

Approved by Fredrik Mirenborn, 2024-Jun-03 10:39 CET
Doc.no. 810004 Ver. 1.0 Page 6(8)

4. General information		
4.1	FSN type	Update
4.2	For updated FSN, reference number and date of previous FSN: Field Safety Notice (FSN)/Recall Letter QA2023-05, May 3rd 2023	
4.3	For updated FSN, key new information as follows: Section 2, 3.1 and 3.3	
4.4	Further advice or information already expected in follow- up FSN?	No
4.5	Manufacturer information	
	Company name	Phadia AB
	Address	Rapsgatan 7P, P.O Box 6460 75137 Uppsala, Sweden
	SRN	SE-MF-000014170
4.6	The Competent (Regulatory) Authority of your country has been informed about this communication to customers	
4.5	List of attachments/ appendices: Customer reply form FSN2023-05_2	
4.6	Name:	
	Title:	
	Signature:	

Transmission of this Field Safety Notice
This notice needs to be passed on all those who need to be aware within your organization or to any organization where the potentially affected devices have been transferred. (As appropriate) Please transfer this notice to other organizations 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.

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Doc.no. 810004 Ver. 1.0 Page 7(8)

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