Date: 10-FEB-2023

Urgent Field Safety Notice
ProtoFluor-Z Reagent Kit

For Attention of*: Identify either by name or role who needs to be aware of the hazard and/or take action. If this is multiple recipients then include full list.

Contact details of local representative (name, e-mail, telephone, address etc.)*

Helena Biosciences
Queensway South
Team Valley Trading Estate
Gateshead
Tyne and Wear
NE11 0SD

Email: techsupport-hs@helena-biosciences.com

Company Name/Logo

Rev 1: September 2018
FSN Ref: NC643 FSCA Ref: NC643

Urgent Field Safety Notice (FSN)
ProtoFluor-Z Reagent Kit
Risk addressed by FSN

	1. Information on Affected Devices*
1.	1. Device Type(s)*
	The ProtoFluor-Z Reagent Kit is a component intended for the detection of zinc protoporphyrin. The measurement of zinc protoporphyrin (ZPP) in the red blood cells is used as a diagnostic test for the microcytic hypochromic anaemia of iron deficiency[1-4]. Heme is formed in the developing red cell by insertion of iron into a formed porphyrin ring. In the event of insufficient iron supply (iron deficiency) or impaired iron utilization (extreme lead intoxication), zinc is substituted for iron into protoporphyrin IX. The ZPP formed in the chelation process is stable and remains in the red cell for its 120 day life span. The level of ZPP in the red cell, then, is a functional indicator of the available iron supply at the time of cell maturation. The presence of elevated blood lead levels also results in increased ZPP. The CDC has lowered the recommended lead screening level in children from 25 µg/dL to 10 µg/dL. Lead levels below 25 µg/dL do not significantly affect ZPP formation, and therefore the use of this test as a lead screen is no longer recommended. Lamola and Yamane showed that the fluorescent erythrocyte porphyrin associated with extreme lead intoxication is zinc protoporphyrin (ZPP) and determined its absorption and fluorescence properties within the red blood cell[5]. ZPP can be detected easily in whole blood by use of a front face fluorometer[6-7]. The absorption (424 nm Soret band) and fluorescent maxima (595 nm) of ZPP in blood differ from those metal-free porphyrins associated with various porphyrias. The fluorescent porphyrin associated with iron deficiency anaemia is ZPP which is identical to that produced by lead intoxication. During the hematofluorometer measurement of ZPP, incomplete oxygenation of the blood causes a spectral shift in the haemaglobin that leads to lower results, i.e. false negatives or low sensitivity. With the use of ProtoFluor-Z Reagent, a stable haemoglobin spectrum is produced, avoiding the deoxygenation shift, with results comparable to full oxygenation of the haemoglobin. Without the use of ProtoFluor-Z Reagent a gentle stream of air must be blown over the drop of blood on the test slide just prior to making the measurement. Standardisation of this method is extremely difficult, and significant variations in test results are seen. ProtoFluor-Z Reagent Kit calibrators are reproducible, assayed solutions designed to provide instrument calibration at high and low levels of the ProtoFluor-Z system. They may also be used for day-to-day calibration, reproducibility and linearity for other hematofluorometer systems according to the manufacturer's specifications. Blood porphyrin assays other than hematofluorometry involve extraction of the porphyrin(s) followed by some type of purification step[8]. Hematofluorometry using the ProtoFluor-Z Reagent and ProtoFluor-Z Reagent Kit calibrators provides a very simple, easy, accurate and inexpensive method for determining erythrocyte ZPP levels in the diagnosis of iron deficiency. The method requires only one drop of whole blood and no sample measurements are necessary. In addition to general laboratory diagnosis and nutritional monitoring, the test can be beneficial in specialities such as blood banking, sports medicine and paediatrics where iron status is a particular concern. The principle of hematofluorometry for measuring zinc protoporphyrin requires that the haemoglobin be fully oxygenated. By adding ProtoFluor-Z Reagent to whole blood, the haemoglobin is derivitised to a product having the spectral characteristics of oxyhaemoglobin in the region where the hematofluorometer operates. Thus, the need for oxygenation is circumvented which allows the determination of zinc protoporphyrin with greater accuracy and precision, even in moderately aged and deoxygenated blood.
1.	2. Commercial name(s)
	ProtoFluor-Z Reagent Kit
1.	3. Unique Device Identifier(s) (UDI-DI)
	Complete when this becomes available.
1.	4. Primary clinical purpose of device(s)*
	A component intended for the detection of zinc protoporphyrin. The measurement of zinc protoporphyrin (ZPP) in the red blood cells is used as a diagnostic test for the microcytic hypochromicanaemia of iron deficiency.
1.	5. Device Model/Catalogue/part number(s)*
	2000/2
1.	6. Software version
	Not Applicable
1.	7. Affected serial or lot number range
	11862667 2023-08-31
	8. Associated devices

1.	ProtoFluor-Z Reagent Kit REF: 2000/1, ProtoFluor-Z REF:2006 .

2 Reason for Field Safety Corrective Action (FSCA)*	
2.	1. Description of the product problem*
	Mislabeled bottles of the PFZ reagent kit, which prevents calibration of the PFZ instrument. The calibrators of this lot will not meet the defined reference ranges provided. Therefore, the calibration should be rejected, preventing use of the instrument.
2.	2. Hazard giving rise to the FSCA*
	The risk highlighted by this FSN is limited to a delay on reporting patient results as the calibration will fail if an affected lot is used. Using an alternative lot will mitigate this risk.
2.	3. Probability of problem arising
	Currently, all reconciled kits of this lot have been affected therefore, it is highly likely that all kits of this lot are affected.
2.	4. Predicted risk to patient/users
	The risk to the patient is negligible. The only possible risk is the delay in patient result. This assay is a non critical test with a long turn around time and therefore, a slight delay in reporting will not affect the clinical outcome for the patient .
2.	5. Further information to help characterise the problem
	N/A
2.	6. Background on Issue
	A customer complaint highlighted the inability to calibrate the instrument. Investigations revealed that the calibrators were inverted due to a mislabelling issue.
2.	7. Other information relevant to FSCA
	N/A

	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?	Specify where critical to patient/end user safety Identify and quarantine immediately. Return Device ASAP through MRA.

3.	3. Particular considerations for: IVD Is follow-up of patients or review of patients' previous results recommended? No Provide further details of patient-level follow-up if required or a justification why none is required	
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 Provide further details of the action(s) identified.	
3	6. By when should the action be completed?	Non-critical, 2 months to allow for return of product from field and reconciliation.
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?	
	Choose an item. Choose an item.	

	4. General Information*	
4.	1. FSN Type*	New
4.	2. For updated FSN, reference number and date of previous FSN	N/A
4.	**3.** For Updated FSN, key new information as follows:	
	N/A	
4.	4. Further advice or information already expected in follow-up FSN? *	No
4	5. If follow-up FSN expected, what is the further advice expected to relate to:	
	N/A	
4	6. Anticipated timescale for follow-up FSN	N/A
4.	7. Manufacturer information (For contact details of local representative refer to page 1 of this FSN)	
	a. Company Name	Only necessary if not evident on letter-head.
	b. Address	Only necessary if not evident on letter-head.
	c. Website address	Only necessary if not evident on letter-head.
4.	8. The Competent (Regulatory) Authority of your country has been informed about this communication to customers. *	
4.	9. List of attachments/appendices:	If extensive consider providing web-link instead.
4.	10. Name/Signature	Insert Name and Title here and signature below

	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.