Dresden, 2023-09-06

URGENT FIELD SAFETY NOTICE (FSN)

for

In-vitro-Diagnostic Medical Device (IVDD) Mentype® DIPquant HLD 84-D CE IVD

Issue: Malperformance for Mentype® DIPquant HLD 84-D CE IVD

Necessary Field Safety Corrective Action (FSCA):

Carefully review this safety notification to users (FSN) with recommendation of measures as part of a Field Safety Corrective Action (FSCA)

Sender:

BIOTYPE GmbH
Moritzburger Weg 67
01109 DRESDEN
GERMANY

Addressee:

To: Distributors, Laboratory Manager and End-users of IVDD Mentype® DIPquant CE-IVD

Dear BIOTYPE GmbH Customer

BIOTYPE GmbH is starting a Field Safety Corrective Action (FSCA) for the above-named product. This document contains important information and requires immediate action from you.

Identification of the affected product:

45-01579-0025, Mentype® DIPquant HLD 84-D

Article number / Name with allele specification (kit size) / Lot number:

45-01579-0025, 25 rxn, kit lot: **DIP01439** and **DIP01557**

Manufacturer and internal transaction number:

BIOTYPE GmbH, C_20230825_DIQ_BT

Description of the issue, its cause and potential risks:

Technical problem:
Internal testing of Mentype® DIPquant HLD 84-D has identified a malfunction in a way that clinical performance claims are not still met. In detail, increased Ct values were observed over a wide DNA input range, inaccurate chimerism analyses for the single marker, as well as high measurement variations.

Previous analyses of the batch did not show any abnormalities; therefore, a stability problem is assumed. The clinical performance of the assay can no longer be guaranteed due to the observed performance fluctuations.

Risk assessment:

No serious incident of a patient, end-user or a third person has been reported to the manufacturer which is related to this issue. The issue is related to an internal notification, but directly related to the claimed clinical performance.

Product claims to be affected are: sensitivity and stability.

The kit is intended for monitoring after allogeneic hematopoietic stem cell transplantation (allo-HSCT). The kit series consists of a set of 56 allele specific monoplex qPCRs. According to IFU at least 2 to 3 different informative markers (to distinguish individual pairs of donors and recipients) and a control monoplex qPCR should be used for relative quantification. Results are always interpreted in comparison to former measurements with the same biomarker sets. Therefore, the data are always relied on earlier measurements (monitoring) and proper controls. Single outlier values are to be observed by the professional user, trained on molecular biological techniques, due to high standard deviations in comparison with other single markers or due to unrealistic Ct values for the DNA input used. Due to the assumed stability problem, the abnormalities could not be observed close after manufacturing.

Finally, a medical decision will not be carried out solely based on this kit. Additional measurements are for example blood count and/or specific genetic or serological markers derived from HLA-typing of donor/recipient pairs, previous cancer diagnosis of the patient and other parameters related to treatment failure (e. g. graft rejection). However, a residual risk for the performance of the kit has been assessed as moderate.

FSCA which should be taken by you:

- Since the clinical performance of the assay can no longer be guaranteed, stored kits are to be destroyed. The end user is requested to dispose of stored kits of the batches DIP01557 and DIP01439 in compliance with local and national legal regulations.
- Carefully review data obtained with the affected kit lots. Please contact our Customer Support (support@biotype.de) if suspicious results occurred.
- Since, according to the current state of knowledge, this is probably a stability problem, close support will be offered for data evaluation.
- Furthermore, please follow the below mentioned instructions regarding the handling of already generated data:

  According to the intended use, analyzing chimerism after allo-HSCT, 3 informative DIPquant assays in duplicates or 2 assays in triplicates are to be used. It is recommended to exclude single, conspicuous outliers of the HLD84-D batches DIP01557 and DIP01439 from the analysis or, if necessary, to remeasure with other informative markers or a new batch of the HLD84-D. Conspicuous abnormalities are defined as Ct-values with a large standard deviation in comparison to other informative markers or unrealistic, absolute Ct values depending on the DNA input used. Please contact BIOTYPE's Customer Support for case-specific analysis (support@biotype.de).

- The manufacturer BIOTYPE GmbH will provide the end user with a new batch of Mentype® DIPquant HLD 84-D as soon as possible (latest by 25.09.23).
- For questions or uncertainties regarding the evaluation, always read the IFU. Please contact us if you have any further questions. You will find the current version of the IFU on our homepage (www.biotype.de).
- Please contact immediately our support (support@biotype.de) in any cases of uncertainness regarding this FSN.
- To ensure that all affected users are notified and according to applicable national statutory provisions, we are obliged to provide the proof of notification in the market to the National Competent Authorities (NCA). Therefore, please complete and sign the included acknowledgment of the receipt form (Appendix A) within the **next 10 days** and either email it to support@biotype.de or fax it to +49 (0)3518838403.

Actions which were performed by the manufacturer:

- The affected lots have been immediately blocked after awareness of the problem.
- A Field Safety Corrective Action has been implemented.

Circulation of the information:

Please make sure that the information of this FSN will be passed to all users within your organization and all other persons who should be informed. Please forward a copy of this information if you have delivered the product to third parties or inform a representative of our company, as named below. Please keep this information until the closure of this FSCA.

A copy of this Urgent FSN was sent to the national competent authorities of the affected countries.

Your Contact Person at BIOTYPE GmbH:

Name: Goss, Jana
Phone number: +493518838448
E-Mail: j.goss@biotype.de

Yours sincerely,

[redacted]

Person Responsible for Regulatory Compliance

Appendix A: Acknowledgment of Receipt

Appendix A: Acknowledgment of Receipt

Please return to:

BIOTYPE GmbH
Moritzburger Weg 67
01109 DRESDEN
GERMANY

Fax: 0351-8838 403

E-Mail: support@biotype.de

C_20230825_DIQ_FSNen_v1

Sender:
Name of the Organization / Company:

_____

Contact Person:

_____

Address:

_____

Customer Number, if available:

_____

Please check

( ) I confirm the receipt of this letter and declare that I have taken the necessary actions:

- Disposal of affected kit lots **DIP01439** and **DIP01557** of Mentype® DIPquant HLD 84-D
- Approval of data already analyzed. Please contact support@biotype.de in any cases of uncertainness.

Title, first name, family name readable: _____

Place, Date, Signature: _____