Contact person: [redacted]
Department: Quality Management

Molecular Health GmbH Kurfürsten-Anlage 21 69115 Heidelberg Germany

Phone: [redacted]
Fax: [redacted]
E-mail [redacted]

Date: 03-April-2023

Recipient's name

Recipient's address

Street

City, etc. + code

Country

Urgent Field Safety Notice

MH Guide

False positive reporting of Clinical Variant Interpretations (CVIs)

FSCA_2023-01_159188

Dear MH Guide User,

We hereby inform you about a safety-related quality problem which may occur when using *MH Guide* within your organization. With this Field Safety Notice we would like to draw your attention to this voluntary Field Safety Corrective Action:

Several patient cases require your re-assessment of MH Guide results and clinical reports to mitigate any potential patient hazard.

Important! Please read the attached Field Safety Notice carefully.

Molecular Health became aware of a data anomaly related to Clinical Variant Interpretations (CVIs). The dataset installed on 27-March-2023 (ID 155294623798) annotates the variant BRCA2 c.7806-14T>C with a CVI indicating an approved biomarker status (CVI score 7/IA) and an effective treatment option with Parp-inhibitors, although the variant represents a benign variation based on its population frequency, and therefore does not represent a biomarker for the annotated treatment option.

The cause of the data anomaly was identified as a curation error in a data source used for CVI creation. The data anomaly existed in the period from 27-March-2023 to 29-March-2023 and was resolved with a configuration change on 29-March-2023.

Thus, there is a possibility that MH Guide results calculated with the affected dataset and the clinical reports generated from them in the period from 27-March-2023 to 29-March-2023 may display the approved effective treatment option for this variant. The incorrect display of the CVI could lead to false positive results of the associated biomarker and misinterpretation of patient cases.

Molecular Health GmbH
Kurfürstenanlage 21
69115 Heidelberg
Germany

Geschäftsführer: Dr. Friedrich v. Bohlen und Halbach (Sprecher), Dr. Stephan Brock
Handelsregister: Amtsgericht Mannheim - HRB 338037
Steuernummer: DE242954829

Bankverbindung: Commerzbank
Kontonummer: 0194111100
Bankleitzahl: 67240039
Swift/BIC-Code: COBADEFFXXX
IBAN-Nummer: DE36672400390194111100

We can assure you our full commitment to market only the products with highest quality to assist you with the best clinical data analysis and treatment decision support. Our goal is to empower physicians with the evidence base to make better treatment decisions for their cancer patients.

We apologize for the inconvenience caused and thank you for your understanding and support for the implementation of the corrective action.

Yours sincerely,

[redacted]
SVP Quality Management
Person Responsible for Regulatory Compliance according to (EU)2017/746

Attachments:

Urgent Field Safety Notice

Customer Reply Form

Molecular Health GmbH
Kurfürstenanlage 21
69115 Heidelberg
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Please read the Field Safety Notice carefully. Several *MH Guide* Reports are affected which were generated with *MH Guide* software release 6.0.2.

1- Reason for Field Safety Corrective Action (FSCA)	*MH Guide* is a bioinformatics software application that supports the intended users in the creation of clinical reports by annotating and reporting genetic alterations in the human genome. Clinical Variant Interpretations (CVIs) describe the interplay between treatments (drugs), diseases, genetic variants or variant combinations, and variant lineage and zygosity. The CVIs can have the impact Effective, Ineffective, Safety, Prognostic, or Diagnostic. Due to a data anomaly in the affected dataset (ID 155294623798), *MH Guide* annotated the variant BRCA2 c.7806-14T>C with a Clinical Variant Interpretation (CVI), which indicates an approved biomarker status (CVI score 7/IA) and an effective treatment option with Parp-inhibitors although the variant represents a benign variation based on its population frequency, and therefore does not represent a biomarker for the annotated treatment option. Thus, there is a possibility that MH Guide results calculated with the affected dataset and the clinical reports generated from them in the period from 27-March-2023 to 29-March-2023 may incorrectly display the effective treatment option for this variant. The incorrect display of the CVI could lead to false positive results of the associated biomarker and misinterpretation of patient cases. In the following patient cases the variant was identified and eventually annotated with the errornous CVI. A re-evaluation of MH *Guide* results and clinical reports from affected patient cases is needed to minimize the risk of a potentially erroneous decision on treatment options.	
2- Patient Hazard	In individual cases, incorrect decision-making of therapeutic options by the intended user might occur due to the incorrect display of CVIs.	
3- Affected Device	**Affected Device:**	*MH Guide 6.0.2*
	UDI:	*Basic UDI-DI*: 4260563550237VS *UDI-DI:* 04260563550275
	Affected Organizational Unit:	<Name>
	Affected Patient Cases:	<Patient Case ID(s)>

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4- Action To Be Taken by the User	The re-assessment of MH Guide results and clinical reports is required for the following patient cases to mitigate any potential patient hazard: • <Patient Case ID(s)> The affected patient cases <Patient Case ID(s)> were **recalculated by** Molecular Health after correction so that the faulty CVI is no longer displayed. The case <Patient Case ID> was not recalculated as the variant was excluded from reporting by the user already. If a treatment recommendation for Parp-inhibitors due to **the** BRCA2 variant c.7806-14T>C has been made, a corresponding re-evaluation of the respective patient case is necessary. This safety notice needs to be passed on all users of *MH Guide* who need to be aware within your organization. Please sign and return the Customer Reply Form attached to the Field Safety Notice back to Molecular Health via fax or email to Molecular Health by 24-Apr-2023 at the latest.
5- Action Being Taken by Molecular Health	Users have been informed about data anomaly related to Clinical Variant Interpretations (CVIs), which may have caused false positive reporting of a biomarker biomarkers and impaired interpretation of patient cases. Molecular Health eliminated the data anomaly by a configuration change on 29-Mar-2023.
6- Further Information	Please contact Molecular Health's Customer Success Team, if you require further assistance in interpretation of MH Guide results and already created clinical reports.
7- Manufacturer Information	Molecular Health GmbH Kurfuersten-Anlage 21 69115 Heidelberg Germany SRN: DE-MF-000012861 Customer Success Team: CustomerCareAsia@molecularhealth.com www.molecularhealth.com

Customer Reply Form

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I hereby confirm receipt of the Field Safety Notice and that I read and understood its content.

The information of the Field Safety Notice has been brought to the attention of all relevant users and all actions requested to be taken by your organization have been executed.

I will, in any case, contact Molecular Health to clarify any outstanding questions.

Name (plain text) :

Date, Signature : _____

Please return acknowledgement to Molecular Health	
Email	CustomerCareAsia@molecularhealth.com
Fax	+49 6221/43851-100

It is important that your organisation takes the actions detailed in the Field Safety Notice and confirms that you have received the Field Safety Notice.

Your organisation's reply is the evidence we need to monitor the progress of the corrective action.