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Urgent Field Safety Notice

MH Guide

False negative reporting of Curated Variant Information (CVIs)

FSCA_2025-01_187104

Dear MH Guide User,

We hereby inform you about a safety-related quality problem that 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 recalculation ("apply changes") and your re-assessment of MH Guide results and clinical reports to mitigate potential patient hazards.

Important! Please read the attached Field Safety Notice carefully.

Molecular Health became aware of two anomalies associated with Curated Variant Information (CVIs):

a) The October dataset (180419234502) did not fully label CVIs that have general validity for solid tumors. Thus, there is a possibility that the clinical reports generated with the October dataset may display CVI information for variants that is less specific to the patient indication.
b) With the MH Guide 7.0 release, an adjustment has been made for the prioritized display of CVIs, to ensure that CVIs with the highest specificity for the patient indication are selected for display. As part of the creation of the CVI datasets, variant definitions that cover multiple possible aberrations at the variant position are expanded into the specific possible aberrations and made available for variant-specific display. In the presence of other CVIs for an expanded variant, this may lead to MH Guide not displaying the CVI information with the highest specificity for the patient indication for these variants. Thus, there is a possibility that clinical reports generated with MH Guide may display CVI information for individual variants that do not have the highest specificity for the patient indication.

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The incorrect display of CVIs could lead to false negative results for associated efficacy biomarkers that are approved in the patient indication or inefficacy biomarkers of clinical relevance and thus to a misinterpretation of patient cases.

The cause of the data anomaly in the October dataset was identified as an incomplete labeling of CVIs for solid tumors. The data anomaly existed in the period from 27-Oct-2025 to 06-Nov-2025 and was eliminated with the hotfix "Hotfix - Guide 8.2 Content Release October 2025 - Solid tumor expansion" on 06-Nov-2025.

A limitation in CVI prioritization was identified as the cause of the anomaly in the prioritization of CVIs for expanded variants. This anomaly existed in the period from 07-Aug-2024 to 13-Nov-2025 and was addressed with the November dataset release "2025-11-04 Guide 8.2 - Core Content Release" for affected CVIs.

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

We apologize for any inconvenience and thank you for your understanding and support in implementing the corrective action.

Yours sincerely,

Dr. Niels Bojunga
SVP Quality Management & Regulatory Affairs
Person Responsible for Regulatory Compliance

Attachments:

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Link to Acknowledgement Form

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Please read the Field Safety Notice carefully. Several *MH Guide* Reports generated with *MH Guide* software releases since release 7.0.

1- Reason for Field Safety Corrective Action (FSCA)	*MH Guide* is a bioinformatics software application that supports intended users in the preparation of clinical reports by reporting and annotating genetic or molecular alterations. Curated Variant Information (CVI) is based on published knowledge about the impact of a genetic variant in the respective disease context. The impact can be either predictive, prognostic, or diagnostic. Due to the following anomalies, there is a possibility that clinical reports generated with MH Guide may display CVI information for individual variants that do not have the highest specificity for the patient indication: a) The October dataset (180419234502) did not fully label CVIs that have general validity for solid tumors. b) With the MH Guide 7.0 release, an adjustment has been made to the prioritized display of CVIs, to ensure that CVIs with the highest specificity for the patient indication are displayed. As part of the creation of the CVI datasets, variant definitions that cover multiple possible aberrations at the variant position are expanded into the specific possible aberrations and made available for variant-specific display. In the presence of other CVIs for an expanded variant, this may lead to MH Guide not displaying the CVI information with the highest specificity for the patient indication as CVI information for these variants. In the following patient cases false negative display of efficacy biomarkers that are approved in the patient indication was detected. Instead, the patient cases displayed CVIs that have a lower specificity and that missed the display of a treatment option that is approved in the patient indication. A recalculation ("Apply changes") and re-evaluation of the MH Guide results and clinical reports of the affected patient cases is necessary to minimize the risk of a possibly erroneous decision for treatment options.	
2- Patient Hazard	In individual cases, incorrect decision-making related to therapeutic options by the intended user may occur due to the incorrect display of CVIs.	
3- Affected Device	**Affected Device:**	*MH Guide*

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	UDI:	*Basic UDI-DI: 4260563550237VS* UDI-DI(s): 04260563550299 04260563550312 04260563550329 04260563550343
	Affected Organizational Unit:	<Name>
	Affected Patient Cases:	<Patient Case ID(s)>
4- Action To Be Taken by the User	The affected patient cases contain an ETV6/NTRK3 gene fusion that does not report the biomarker approved for solid tumors and therefore does not indicate the treatment option 'repotrectinib'. The recalculation ("apply changes") and 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)> This safety notice needs to be passed on all users of *MH Guide* who need to be aware within your organization. Please fill out the Acknowledgement Form that is accessible via the link on the Customer Acknowledgement page below by 04-Dec-2025 at the latest.	
5- Action Being Taken by Molecular Health	Users have been informed about data anomaly related to Curated Variant Information (CVIs), which may have caused false negative reporting of biomarkers and impaired interpretation of patient cases. Molecular Health eliminated the anomalies with the hotfix "Hotfix - Guide 8.2 Content Release October 2025 - Solid tumor expansion" on 06-Nov-2025 and with the November dataset release "2025-11-04 Guide 8.2 - Core Content Release" on 13-Nov-2025.	
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: customerservice@molecularhealth.com www.molecularhealth.com

Acknowledgement Form

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Important

To confirm receipt and understanding of this Field Safety Notice, please fill out this **Acknowledgement Form:** link

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.