MOLECULAR HEALTH GUIDE

Patient ID —
Case ID —
Date of birth —

Diagnosis Lung adenocarcinoma
ICD-10-CM code —
MeSH ID/term —
Additional MeSH IDs —

Sex	Male	Primary tumor site	—	Collected	—	Ordering physician	—
Ethnicity	—	Surgical pathology	—	Tumor cellularity	—	Facility	—
Country	US	Tissue type	—	Barcode	—	Email	—
Trial ZIP code	—	Metastatic	—	Sample type	—	Phone	—
		General dataset ID	—	Labtest	—	Fax	—
		CVI dataset ID	—			Product	MH Guide
		Organizational unit	—	Software version	—	Report	—

Mutational status of commonly mutated genes in the patient disease

ABCB1	ALK	BRAF	EGFR	ERBB2	KRAS	MET	NF1	NRAS	PIK3CA	RET
not identified	1 fusion, 1 SNV	not identified	not identified	not identified	not identified	not identified	not identified	not identified	not identified	not identified

ROS1	STK11	TP53
1 del	not identified	not identified

SUMMARY

Overview of potential treatment impacts

3 Effective | 2 Ineffective | 1 Safety

Overview of prognostic and diagnostic findings

0 Prognostic | 0 Diagnostic

Clinical trials found

8 Trials

Potential impact	Treatment	Drug approval*	Biomarker	VAF	Biomarker score		Trials
Effective	Lorlatinib	Approved	ALK/EML4 (fusion)	—	AMP Tier I A	7 Clinically Approved	2
Effective	Ceritinib	Approved	ALK/EML4 (fusion)	—	AMP Tier I A	7 Clinically Approved	3
Effective	Brigatinib	Approved	ALK/EML4 (fusion)	—	AMP Tier I A	7 Clinically Approved	5
Safety	Dabrafenib	Approved	G6PD p.R285H (SNV)	99.56%	AMP Tier I A	7 Clinically Approved	—
Ineffective	Crizotinib	Approved	ALK p.L1196M (SNV)	23.80%	AMP Tier I B	6 Clinical	—
Ineffective	Alectinib	Approved	ALK p.L1196M (SNV)	23.80%	AMP Tier II D	3 Preclinical	—

* in the patient's disease; VAF = Variant allele frequency

Biomarker score: AMP score and CVI score. **Clinically approved:** Approved biomarker (by the FDA, EMA, or NCCN) to predict a specific effect in the patient's disease. **Clinical:** Not yet approved biomarker for the patient's disease. Observed in clinical studies as a potential biomarker to predict a specific effect of the drug. **Preclinical:** This biomarker has not yet been observed/tested in patients to predict a specific effect of the drug. It is supported by preclinical evidence or translational data.

You can find more details on the biomarker score (AMP and CVI score) in the glossary.

MEDICAL GUIDELINES

Relevant treatment information from medical guidelines and potential impact based on detected biomarkers

Potential impact	Treatment	Disease	Disease details	Guideline	Evidence Level
Effective	Brigatinib	Non-Small Cell Lung Cancer	Squamous cell carcinoma, Adenocarcinoma (with mixed subtypes), Large cell carcinoma	NCCN	1 for first-line therapy as a single agent if ALK rearrangement discovered prior to first-line systemic therapy 2A for all others 2B for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of disseminated disease

Recommended use:
Single-agent therapy for ALK rearrangement-positive recurrent, advanced or metastatic disease

- as first-line therapy
- for patients who are intolerant to crizotinib
- as subsequent therapy following disease progression on first-line therapy with crizotinib, except in cases of symptomatic systemic disease with an isolated lesion
- as continuation of therapy if used first line, except in cases of symptomatic systemic disease with multiple lesions

Potential impact	Treatment	Disease	Disease details	Guideline	Evidence Level
Effective	Ceritinib	Non-Small Cell Lung Cancer	Squamous cell carcinoma, Adenocarcinoma (with mixed subtypes), Large cell carcinoma	NCCN	1 for first-line therapy as a single agent if ALK rearrangement discovered prior to first-line systemic therapy 2A for all others 2B for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of disseminated disease

Recommended use:
Single-agent therapy for ALK rearrangement-positive recurrent, advanced or metastatic disease

- as first-line therapy
- for patients who are intolerant to crizotinib
- as subsequent therapy following disease progression on first-line therapy with crizotinib except in cases of symptomatic systemic disease with an isolated lesion
- as continuation of therapy if used first line, except in cases of symptomatic systemic disease with multiple lesions

Potential impact	Treatment	Disease	Disease details	Guideline	Evidence Level
Effective	Lorlatinib	Non-Small Cell Lung Cancer	Squamous cell carcinoma, Adenocarcinoma (with mixed subtypes), Large cell carcinoma	NCCN	2A for all others 2B for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of

Potential impact	Treatment	Disease	Disease details	Guideline	Evidence Level
					disseminated disease

Recommended use:
Single-agent therapy for ALK rearrangement-positive recurrent, advanced or metastatic disease

- following disease progression on first-line therapy with crizotinib and subsequent therapy with alectinib, brigatinib, or ceritinib except in cases of isolated lesions
- following disease progression on first-line therapy with crizotinib and subsequent therapy with crizotinib for asymptomatic disease or isolated lesions
- following disease progression on first-line therapy with alectinib, brigatinib or ceritinib and subsequent therapy with alectinib, brigatinib or ceritinib except in cases of multiple lesions
- as subsequent therapy following disease progression on first-line therapy with alectinib, brigatinib, or ceritinib for multiple lesions

BIOMARKER DETAILS

ALK/EML4 (fusion)

The ALK tyrosine kinase receptor activates RAS/MAPK and PI3K/AKT signaling pathways to promote cell proliferation and survival. Gene fusions involving ALK occur in approximately 5% of non-small cell lung cancers (NSCLC), with EML4 as the most common fusion partner. ALK fusions have been shown in preclinical studies to activate the PI3K and RAS/MAPK pathways. The ALK tyrosine kinase inhibitors crizotinib, ceritinib, and alectinib are indicated for primary treatment of patients with metastatic NSCLC harboring ALK fusions. Alectinib demonstrated improved efficacy, also in patients with brain metastases, and a more favorable side effect profile compared to crizotinib. Brigatinib is approved for treatment of NSCLC patients intolerant of or with progression on crizotinib. Lorlatinib is indicated for second- or third-line treatment of ALK-positive metastatic NSCLC.

PubMed ID
29074098, 28475456, 25754348, 25170012, 28501139

Potential impact	Treatment	Drug approval*	Biomarker score	
Effective	Lorlatinib	Approved	AMP Tier I A	7 Clinically Approved
Effective	Ceritinib	Approved	AMP Tier I A	7 Clinically Approved
Effective	Brigatinib	Approved	AMP Tier I A	7 Clinically Approved

* in the patient's disease

G6PD p.R285H (SNV)

Glucose-6-phosphate dehydrogenase (G6PD) is an essential enzyme that is involved in the metabolism and the defense against oxidizing agents. G6PD is highly polymorphic. Many variants of G6PD have reduced enzymatic activity and can be associated with clinical symptoms. G6PD variants are classified into I to V according to their enzymatic activity (from low to high) compared to wild type. A mutation designated as a class II/III variant leads to strongly reduced enzymatic activity (<10–60% of normal enzyme activity), conferring a G6PD deficient phenotype in men. Women must be homozygous (with two deficient alleles) to have this effect. It is well established that patients with class II/III variants are at increased risk of acute hemolytic anemia, favism, and neonatal jaundice that is associated with certain treatments that cause oxidative stress in red blood cells, such as rasburicase and dabrafenib. Cell lines also suggested similar effects for doxorubicin and carmustine. Daunorubicin may show increased sensitivity because the active drug is not metabolized as rapidly, however, this also leads to toxicity concerns.

PubMed ID
870569, 539595, 26417175, 24787449, 20196170

Potential impact	Treatment	Drug approval*	Biomarker score	
Safety	Dabrafenib	Approved	AMP Tier I A	7 Clinically Approved

* in the patient's disease

ALK p.L1196M (SNV)

The ALK tyrosine kinase receptor activates RAS/MAPK and PI3K/AKT signaling pathways to promote cell proliferation and survival. In preclinical studies, this variant showed increased receptor signal transduction. Clinical studies of patients with non-small-cell lung cancer (NSCLC) revealed that this variant confers resistance to crizotinib but some tumors responded to ceritinib and lorlatinib treatment. Preclinical models showed in addition that this mutation is associated with resistance to alectinib but retains sensitivity to brigatinib.

PubMed ID
27780853, 30892989, 24670165, 29074098, 30662002

Potential impact	Treatment	Drug approval*	Biomarker score
Ineffective	Crizotinib	Approved	AMP Tier I B; 6 Clinical
Ineffective	Alectinib	Approved	AMP Tier II D; 3 Preclinical

* in the patient's disease

Biomarker score: AMP score and CVI score. **Clinically approved:** Approved biomarker (by the FDA, EMA, or NCCN) to predict a specific effect in the patient's disease. **Clinical:** Not yet approved biomarker for the patient's disease. Observed in clinical studies as a potential biomarker to predict a specific effect of the drug. **Preclinical:** This biomarker has not yet been observed/tested in patients to predict a specific effect of the drug. It is supported by preclinical evidence or translational data.
You can find more details on the biomarker score (AMP and CVI score) in the glossary.

CLINICAL TRIALS

The following trials are potentially best suited for your patient's indication, considering all reported treatment recommendations. See https://clinicaltrials.gov (clinical trials from NCT) or https://apps.who.int/trialsearch (clinical trials from other registries) for more information.

Title	Distance (km)	Trial phase and ID	Intervention	Disease	Location	Age and sex
A Study of Lorlatinib in Advanced ALK and ROS1 Rearranged Lung Cancer With CNS Metastasis in the Absence of Measurable Extracranial Lesions	1	Phase 2; NCT02927340	Lorlatinib	Carcinoma, Non-Small-Cell Lung; Lung Neoplasms	Boston, Massachusetts	Age: 18, Gender: Both
Biomarker/ALK Inhibitor Combinations in Treating Patients With Stage IV ALK Positive Non-squamous Non-small Cell Lung Cancer (The NCI-NRG ALK Protocol)	129	Phase 2; NCT03737994	Brigatinib; Ceritinib; Lorlatinib	Lung Neoplasms	Springfield, Massachusetts	Age: 18, Gender: Both
An Efficacy Study Comparing Brigatinib Versus Alectinib in Advanced Anaplastic Lymphoma Kinase-Positive (ALK+) Non-Small-Cell Lung Cancer (NSCLC) Participants Who Have Progressed on Crizotinib	650	Phase 3; NCT03596866	Brigatinib	Carcinoma, Non-Small-Cell Lung	Fairfax, Virginia	Age: 18, Gender: Both
A Study of Brigatinib in Participants With Anaplastic Lymphoma Kinase-Positive (ALK+), Advanced Non-Small-Cell Lung Cancer (NSCLC) Progressed on Alectinib or Ceritinib	650	Phase 2; NCT03535740	Brigatinib	Carcinoma, Non-Small-Cell Lung	Fairfax, Virginia	Age: 18, Gender: Both
Trial of Brigatinib After Treatment With Next-Generation ALK Inhibitors	979	Phase 2; NCT02706626	Brigatinib	Carcinoma, Non-Small-Cell Lung; Lung Neoplasms	Durham, North Carolina	Age: 18, Gender: Both
Ceritinib and Everolimus in Treating Patients With Locally Advanced or Metastatic Solid Tumors or Stage IIIB-IV Non-small Cell Lung Cancer	2588	Phase 1; NCT02321501	Ceritinib	Carcinoma, Non-Small-Cell Lung; Lung Neoplasms; Neoplasms; Solid tumor	Houston, Texas	Age: 18, Gender: Both
Local Consolidative Therapy and Brigatinib in Treating Patients With Stage IV or Recurrent Non-small Cell Lung Cancer	2588	Early Phase 1; NCT03707938	Brigatinib	Lung Neoplasms	Houston, Texas	Age: 18, Gender: Both
Ceritinib + Trametinib in Patients With Advanced ALK-Positive Non-Small Cell Lung Cancer (NSCLC)	4337	Phase 1/ Phase 2; NCT03087448	Ceritinib	Carcinoma, Non-Small-Cell Lung; Lung Neoplasms	San Francisco, California	Age: 18, Gender: Both

DESCRIPTION KEY

- Potentially effective treatments. These treatment recommendations are based solely on tumor biology and do not override your oncologist's clinical treatment plan.
- Potentially ineffective treatments. These treatments, in combination with the biomarkers identified in the patient tumor, have been reported to predict lack of effectiveness. Treatment of a patient with any of these reported drugs may lead to disease progression.
- Treatments with potential to cause an adverse reaction. These treatments, in combination with the biomarkers identified in the patient tumor, have been reported to predict safety issues. Treatment of a patient with any of these reported drugs may lead to serious drug-related toxicities.
- Biomarkers identified in the patient tumor that have been reported to have a prognostic relevance.
- Biomarkers identified in the patient tumor that have been reported to have a diagnostic relevance.
- The report contains conflicting evidence about the potential effect of the treatment.

MOLECULAR HEALTH GLOSSARY

AMP score:
Displays the classification of a biomarker according to the recommendations of the Association for Molecular Pathology (AMP). Source: Marilyn M. Li, Michael Datto, Eric J. Duncavage, Shashikant Kulkarni, Neal I. Lindeman, Somak Roy, Apostolia M. Tsimberidou, Cindy L. Vnencak-Jones, Daynna J. Wolff, Anas Younes, and Marina N. Nikiforova "Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer," Journal of Molecular Diagnostics, vol. 19, no. 1, pp. 4-23 ,2017, doi: 10.1016/j.jmoldx.2016.10.002.

- Tier IA: Variants of strong clinical significance. FDA-approved therapy or biomarkers included in professional guidelines.
- Tier IB: Variants of strong clinical significance. Well-powered studies with consensus from experts in the field.
- Tier IIC: Variants of potential clinical significance. FDA-approved therapies for different cancer types or investigational therapies. Multiple small published studies with some consensus.
- Tier IID: Variants of potential clinical significance. Preclinical trials or a few case reports without consensus.
- Tier III: Variants of unknown clinical significance.
- Tier IV: Benign or likely benign variants.

Note that in the evidence-based variant categorization context, therapy refers to the combination of variant, drug, and disease.

Biomarker:
In general, a biomarker is any characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathological processes, or pharmacological response to a therapeutic intervention. In the context of MH Guide, reported biomarkers predict a patient's response to therapy and are based on the characterization of the patient/tumor genomic DNA. Depending on the analysis type, such genomic characteristics can include single nucleotide variants (SNVs), insertions and deletions (indels), fusion genes, and copy number alterations (CNAs).

Biomarker score:
Displays the AMP score and the CVI score of the biomarker.

CVI score:
The clinical variant interpretation (CVI) scores 7-1 indicate the reliability of a biomarker to predict a specific patient outcome. This can include predictive treatment effects; in this case, the scores 7-1 apply for biomarkers associated with a single drug or drug combination.
The CVI scores are defined as follows:
7, Clinically approved: The biomarker has been approved by a regulatory agency such as the FDA to predict a specific effect (i.e., response, resistance, or toxicity) in the patient's disease or cancer type.
6, Clinical: Patient's disease: The biomarker has not yet been approved by a regulatory agency for the patient's disease. However, the biomarker has been observed in at least one large cohort study to predict a specific effect of the drug (i.e., to be effective, resistance) in the patient's disease. Other diseases: The biomarker has been approved by a regulatory agency to predict a specific effect of the drug (response, resistance) with other diseases or conditions. This CVI will be available for matching with the less-specific disease Neoplasms in CVIs. Biomarkers predicting toxicity: For all disease matches, this score indicates that there is evidence from a randomized controlled trial or its meta-analysis for biomarkers predicting a drug to be toxic.
5, Clinical: The biomarker has not yet been approved by a regulatory agency for the patient's disease. However, this biomarker has been observed to predict a specific effect of the drug (i.e., response, resistance) on patients with other diseases or conditions. For biomarkers predicting a drug to be effective or resistant, there is evidence from some patients in several cohort studies and additional preclinical evidence. For biomarkers predicting a drug to be toxic, there is evidence from >1 prospective studies or meta-analyses from prospective and/or retrospective studies.
4, Clinical: The biomarker has not yet been approved by a regulatory agency for the patient's disease. However, this biomarker has been observed to predict a specific effect of the drug (i.e., response, resistance) on patients with other diseases or conditions. For biomarkers predicting a drug to be effective or resistant, there is evidence from a few clinical case reports and additional preclinical evidence. For biomarkers predicting a drug to be toxic, there is evidence from a prospective study, >1 retrospective studies, or >1 cohort studies.
3, Preclinical: The biomarker has not yet been observed/tested in patients to predict a specific effect. The biomarker has been observed in preclinical experiments. There is experimental evidence from cell lines or mouse models, for example.
2, Preclinical: The biomarker has not yet been observed/tested in patients or preclinical models to predict a specific effect. However, this effect can be inferred when drug-sensitivity data are available for another variant. This applies only if the two variants have the identical functional impact on the same downstream pathway.
1, Preclinical: The biomarker has not yet been observed/tested in patients or preclinical models to predict a specific effect. However, this effect can be inferred when drug-sensitivity data are available for another variant. This applies only if both variants have the identical functional impact on the protein.

Drug approval:
The development stage of the treatment for the patient's indication in the patient's country.

- **Approved** - This drug is launched for the primary or a secondary patient disease.
- **Off-label** - This drug is launched for a disease other than the primary or secondary patient diseases.
- **Investigational** - This drug is currently under clinical development in the patient disease.
- **Other** - None of the other stages are applicable. The drug is, for example, suspended, discontinued, or withdrawn. Other is also used for the drug approval stage of drug classes.

Drug-drug interactions:
A drug-drug interaction is a situation in which a substance (usually another drug) affects the activity of one or both drugs when both are administered together. In the MH Guide report, drug-drug interactions are reported where a drug is predicted to affect the activity of the agent(s) in the treatment option.

Medications with potential for adverse reaction or ineffectiveness.:
Medications with potential for adverse reaction or ineffectiveness refers to Molecular Health's ability to identify treatments that are predicted to be associated with negative physiological responses to a drug therapy (i.e., drug resistance and toxicity).

Open trials:
Clinical trials that are currently recruiting patients with specific disease indication(s) to assess the clinical efficacy and safety of the listed treatment.

Potential impact:
The specific drug effect predicted by the identified mutation (i.e. response, resistance, or toxicity).

PubMed ID:
A PubMed identifier is a unique number assigned to each PubMed record - also termed PMID. A PMID can be used to retrieve a specific publication from the PubMed database by entering the PMID in the search box on the PubMed site at http://www.ncbi.nlm.nih.gov/pubmed.

Treatment:
The generic name of the therapeutic agent listed on the report.

MOLECULAR HEALTH DISCLAIMER

Molecular Health GmbH (MH) develops and operates software systems for the integrated analysis of clinical and genomic patient data to support physicians in choosing the optimal treatment for individual patients with respect to effectiveness and safety.

Molecular Health Guide (MH Guide) is a bioinformatics software tool to aid clinical decision making by processing genetic variant data from a patient's tumor through a variant detection pipeline. This enables generation of a customizable clinical report with a summary of potentially effective medications, potentially ineffective medications, and medications that may pose a higher risk of adverse reactions.
The MH Guide variant detection pipeline covers:

1. Primary identification of genetic alterations from next-generation sequencing (NGS) data by the variant detection pipeline, either from the patient's tumor (targeted panel analysis) or from both the patient's tumor and the control sample (whole exome analysis) (optional).
2. Aggregation, integration, collation, and maintenance of up-to-date biomedical reference information relevant for clinical decision support in clinical oncology.
3. Mapping of the patient's genetic alterations to the biomedical reference information.
4. Integration of the patient's genetic alterations based on the mapping to biomedical reference information.
5. Computational integration of the above information into a summary of potentially effective, ineffective, and toxic medications, for the individual patient. Also, prognostic and diagnostic biomarkers may be detected and shown for the given disease context.
6. Generation of a customizable clinical report by a trained user (MH-certified physician), providing links to the sources of evidence of the information displayed for full traceability.

The information consolidated in the clinical report provided to the patient's treating physician is the result of a comprehensive filter setting based on values defined by the MH-certified physician. The MH-certified physician is neither a contractor nor an employee of MH. The information provided in the report must be evaluated by the treating physician in conjunction with all other relevant clinical information of the patient before the appropriate course of medication is selected by the treating physician. The selection of any, all, or none of the medications identified in the report is at the sole discretion of the treating physician and not of MH or the MH medical staff.

The information provided in this disclaimer may not be applicable when the product is used in other configurations than the MH standard configuration.

MH Guide is designed for processing the molecular data from patients diagnosed with cancer. Diseases beyond this are out of the scope of the application. In particular, the following data cannot be determined using MH Guide: blood groups; infections and infectious diseases; irregular anti-erythrocytic antibodies; the hereditary disease phenylketonuria; the HLA tissue groups DR, A, and B; the tumoral marker PSA, and the risk of trisomy 21.

The patient disease must be provided in MeSH ontology format for correct interpretation of patient data. Other disease ontologies such as ICD must be converted to the correct MeSH term by the certified physician.
Any genetic findings outside of the intended use of treatment decision support in cancer care, e.g., risk factors for potential future diseases of a patient or variants that indicate that the patient is a genetic carrier for hereditary diseases are not annotated and reported, even though corresponding variants or risk factors may be identified as a result of an MH Guide analysis.

The identification of a genomic biomarker does not necessarily imply pharmacological effectiveness or ineffectiveness. The medications identified by the treating physician may or may not be suitable for use on a particular patient. Thus, the clinical report does not guarantee that any particular agent will be effective in the treatment of any particular condition. Also, the absence of a recommendation for a medication by MH Guide does not determine the effectiveness or predict an ineffective or safety-relevant effect of a medication selected by the treating physician.

The contents of the clinical report, a result of mapping patient data against the MH Guide database, and selection of treatment-relevant information by the MH-certified physician are to be used only as an additional aid to the clinical decision by the treating physician. Interpretation of the report contents must occur in consultation with a medical expert. Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all applicable information concerning the patient's condition, such as patient and family history, physical examinations, information from other diagnostic tests, and patient preferences, in accordance with the applicable standard of care. Decisions regarding care and treatment should not be based solely on the information contained in this report.

MH Guide can detect single nucleotide variants (SNVs), insertions and deletions (indels), fusion genes (from DNA or RNA data in unpaired analyses or from RNA data in paired analyses), copy number alterations (paired analyses only), microsatellite instability (MSI-H, paired analyses only) and tumor mutational burden (TMB) from NGS data.
The clinical validity of TMB defined by the underlying lab test has not been established.

The detection methods for indels, fusion genes and copy number alterations from FASTQ and BAM were validated using synthetic data only. Therefore, indel, fusion gene, and CNA detection in MH Guide must be validated with an orthogonal method (e.g., Sanger sequencing) before a treatment is recommended. MSI status of unclassified cases or MSS cases should be assessed with orthogonal methods before a treatment decision is made based on the MSI status.

It is the responsibility of the MH-certified physician to assess the pre- and post-alignment QC results within MH Guide and to communicate with the treating physician any data which are of suboptimal quality.

If genetic aberration signals are submitted in the format of a VCF file for processing in MH Guide, the quality of the results from MH Guide depends on the quality of the input data submitted by a lab on behalf of the MH-certified physician. The accuracy, analytic sensitivity and specificity of the variant lists is the sole responsibility of the MH-certified physician.

For ethnicity Japanese (JPT) a population-specific reference genome based on ToMMo 3.5KJPNv2 (MAF>=1%) is used for sequencing alignment. Additionally, population frequencies from ToMMo 3.5KJPNv2 (MAF>=1%) are available in the application for display and filtering.

MH Guide uses and contains data and information obtained from third-party sources. MH uses reasonable efforts to ensure that this information is as accurate as possible in a tightly controlled curation process. However, MH cannot guarantee that data from any third party are accurate, comprehensive, and complete. Thus, MH Guide may not contain all relevant or all up-to-date information. Third-party databases or other sources in MH Guide may only be updated from time to time with new or revised information.

MH Guide has not been cleared or approved by the U.S. Food and Drug Administration (FDA). However, MH Guide using VCF as input is offered as a bioinformatics service under CLIA.
In the European Union, MH Guide is registered as an in vitro diagnostic medical device (IVD). The products MH Guide IVD and IVD premium are covered by the IVD registration. MH Guide Onco report and Onco report+ are for research use only.

MH is the legal manufacturer of MH Guide as a stand-alone software, and the statutory provisions of the German Medical Devices Act (MPG) and the European Directive 98/79/EC apply to MH. We therefore maintain a quality management system according to EN ISO 13485 for the scope of “Design, Development and Manufacture of software systems for the integrated analysis of clinical and genomic patient data to support treatment decisions and provision of related services”. MH has also received CLIA certification and CAP accreditation for the provision of MH Guide as a dry lab service to clinical laboratories in the US.