M-Clarity™ Program

Explanation of Notifiable Changes

According to our M-Clarity™ Program products with different Quality Segments get a different extent of Change Notification. This table provides a detailed description of each Notifiable Change type of the M-Clarity™ Change Type Matrix of Notifiable Changes.

This table is not intended to be exclusive. A change team can determine whether a change is notifiable outside of the tables as determined by a risk assessment.

All change types relate exclusively to the finished product.

Notifiable Changes for Chemicals and Consumables

Change	Extended Description
Discontinuation of ISO certifications (e. g. ISO 9001, ISO 14001, ISO 13485 where applicable)	Our company will notify on discontinuation of certifications relevant for the contracted items.
Change to published/analytical release specification acceptance criteria (excluding compendial specifications)	Changes visible in the list of specified tests. Limits or test definitions incl. adding or discontinuing a test. In accordance with IPEC guide changes based on revisions of pharmacopeial monographs are not notifiable. **Definition "Compendial Change":** A change is only a "Compendial Change" when the change is explicitly following the change of compendial requirements (e. g. USP, Ph. Eur., ACS, E-Norm, FCC). **Examples:** Typically, compendial changes are changes to the specification when the substance monograph of the referenced compendium is broadened, tightened, introduced, or deleted. An analytical method is revised, and we are implementing the required analytical method.
Obsolescence – catalog number is discontinued	Our Company only notifies if an item number is not offered any more. Discontinuation of individual pack sizes are very frequent and are not notifiable.
Releasing QC testing site	Change to the site that is responsible for the release of a product. Individual tests may be performed in other locations.
Downgrade of Quality Segment or change of Quality Segment category	Quality Segment downgrade means a reduction of service and Quality Attributes. Therefore, it is considered notifiable. A Quality Segment upgrade, by contrast, is not notifiable. Change of Quality Segment category of a product indicates a different set of service and Quality Attributes, it is considered notifiable.
Revision of Discriminating Quality Attribute/ Matrix of Notifiable Changes	We notify our customers of changes of our M-Clarity™ Attributes table and Matrix of Notifiable Changes.
Shelf life (expiration date or recommended retest date)	Changes in shelf life or recommended retest date are considered notifiable.
Change of our immediate supplier – no disclosure of the source	Our Company will notify on the change of our supplier independent of the Original Manufacturer. The supplier may be identical to the manufacturer, or it may be a distributor. The original manufacturer will not be disclosed at this Quality Segment. This change is often quoted as "vendor change".
Change to the primary manufacturing and/ or repackaging/down-filling site	For some products more than one manufacturing/ repackaging/ down-filling site may exist. For technical reasons, ERP systems hold one of the sites as the leading site. It is regarded notifiable if the leading site is changing. The process type "repackaging" includes handling of third party manufactured goods.
Change in test method (non-compendial and those affecting quality documents (CoA/CoQ) or label)	Our Company considers a change of test method as a change in the underlying technique (wet chemistry to chromatography, TLC to HPLC, etc.). Adaptations within the methodology (amount of solvents etc.) are not notifiable. Compendial changes (see above) are not notifiable.
Changes in the manufacturing process impacting specification, where process uses a substantially different route of synthesis or manufacture (chemicals)	Notifiable if the change is to the limits of the required release tests, or of the chemical reaction. Also, notifiable if change from batch to continuous processes or vice versa.

Notifiable Changes for Chemicals and Consumables

Change	Extended Description
Primary packaging materials and/ or container closure / change in materials of construction (not including customized packaging)	Change to the chemical nature of the material in contact with the product or a change to the nature of the tamper evident seal.
Change to raw materials affecting the CoA or CoQ or specification	We are only notifying our customers if changes to the raw material affect the CoA or CoQ of the end product (chemicals, consumables, cell culture media, clean meat media). For chemicals this change type only includes changes to materials used in the synthesis of a substance if a part of the molecular structure of the starting material is directly transferred into the structure of the synthesis product. For custom Cell Culture Media (CCM) this change type refers to changes in raw material manufacturing platform (e. g. synthetic, plant, animal, etc.) as well as original manufacturer changes of the raw material – no disclosure of source. In rare cases (MQ400) if original manufacture of the raw material is unknown, changes to the immediate supplier will be notified. For single use and filters a raw material is defined as a material or resin which is in the final product (device/ assembly…). Additionally, a third party finished good (e. g. sampling port, O-ring) may be part of the final product. If raw materials are changed in either instance a notification will be determined by the appropriate risk assessment.
Labeling – change to item name or number / changes in the labeling regarding product name, specification, shelf life or storage	A notifiable change of labeling is a change in the layout of the label, or if information is removed or added to the label. A name change includes all details that are part of the given product name including declarations of compendia or product brand name.
Change in the nature of the raw materials with TSE/BSE relevance resulting in an increased risk for the finished product with respect to EMA/410	EMA/410 is the globally accepted guideline on the risk assessment, also outside of EU. Increase in risk is considered to be notifiable.
Changes in the manufacturing process impacting specification, or intended use, form/fit/function (disposable/devices/ single use items only)	Form, fit or function are key attributes of single use and filter products. Any change that affects these attributes requires customer notification.
Change of Original Manufacturer (OM) – disclosure of OM not guaranteed (Confidentiality Commitment required in case of disclosure)	The original manufacturer must be known by our Company. With this notification type our Company will inform that the manufacturer is changing. Neither the former nor the new manufacturer is identified on the change notification. Customers may be informed of the manufacturer name and address on request through the Quality Services process.
Changes to the equipment – impacting the manufacturing process, specifications or intended use	A change in manufacturing/testing/production equipment that may cause changes to the product impacting product specifications or intended use is considered notifiable.
Change in GMP status	We will notify on up – as well as on downgrades on GMP compliance.
Change of Original Manufacturer (OM) – disclosure with Confidentiality Commitment	The original manufacturer must be known by our Company. With this notification type our Company will inform that the manufacturer is changing. Neither the former nor the new manufacturer is identified on the Change Notification. Customers will be informed of the manufacturer name and address on request through the Quality Services process.
Changes to Instructions for Use and change in risk level	Change Notification as defined in Medical Devices Regulations. Other customer-facing documentation changes are not considered notifiable (e. g. data packages, user guides...)
Change of Original Manufacturer (OM) – disclosure w/o Confidentiality Commitment	The original manufacturer must be known by our Company. With this notification type our Company will inform that the manufacturer is changing. The former and the new manufacturer is identified on the Change Notification.
Change of CEP revision	Customers are informed about changes as obligatory in the scope of regulatory guidance. Applies to CEPs, DMFs, Technical Files for Diagnostics products etc.

Notifiable Changes for Equipment and Spare Parts

Change	Extended Description
Obsolescence of product	We notify of part numbers which are not going to be available to customers when current stock is depleted.
Downgrade of Quality Segment or change of Quality Segment category	Quality Segment downgrade means a reduction of service and Quality Attributes. Therefore, it is considered notifiable. A Quality Segment upgrade, by contrast, is not notifiable. Change of Quality Segment category of a product indicates a different set of service and Quality Attributes, it is considered notifiable.
Revision of Discriminating Quality Attribute/ Matrix of Notifiable Changes	We notify our customers of changes of our M-Clarity™ Attributes table and Matrix of Notifiable Changes.
Change requiring retrofit	A requirement to modify existing equipment to fit to parts or services not available at the time of manufacture is called a retrofit. Retrofits are often due to the upgrade of consumables and are considered to be notifiable events.
Major software change	Our Company notifies of any software change evaluated as major during a risk assessment.
Change affecting form, fit or function	Changes to form, fit, function impact the way spare parts look, fit or work with associated item numbers. Any change that affects these attributes requires customer notification.
Change to raw material in contact with the fluid path	We notify of changes to those raw materials which are in contact with the processed products.

Merck KGaA
Frankfurter Strasse 250
64293 Darmstadt, Germany

MK_FL11727EN Ver. 1.0
53692
01/2024