M-Clarity™ Program

Matrix of Notifiable Changes

Change	Change Notification Commitments Supported per Quality Level					
	MQ 100	MQ 200	MQ 300	MQ 400	MQ 500	MQ 600
Discontinuation of ISO certifications (e.g. ISO 9001, ISO 14001, ISO 13485 where applicable)		✓	✓	✓	✓	✓
Change to published/Analytical Release Specification Acceptance Criteria (excluding compendial specifications)		✓	✓	✓	✓	✓
Obsolescence - catalog number is discontinued		✓	✓	✓	✓	✓
Releasing QC testing Site		✓	✓	✓	✓	✓
MQ Level Downgrade		✓	✓	✓	✓	✓
Shelf Life (expiration date or recommended retest date)			✓	✓	✓	✓
Change of our Immediate Supplier - no disclosure of source			✓			
Change to primary manufacturing and/or Repackaging/Downfilling site			✓	✓	✓	✓
Change in test method (non-compendial and those affecting quality document (CofA/CofQ) or label)			✓	✓	✓	✓
Changes in the Manufacturing Process impacting specification, where process uses a substantially different route of Synthesis or manufacture (Chemicals)			✓	✓	✓	✓
Primary Packaging Materials and/or Container Closure Change in Materials of Construction (not including customized packaging)			✓	✓	✓	✓
Change to Raw Materials affecting the CoA or CoQ or Specification				✓	✓	✓
Labeling - Change to item name or number / Changes in the labeling regarding product name, specification, shelf-life or storage				✓	✓	✓
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				✓	✓	✓
Changes in the Manufacturing Process impacting specification, or intended use, form/fit/function (Disposable/Devices/Single Use items only)				✓	✓	✓
Change of Original Manufacturer (OM) - disclosure of OM not guaranteed (Confidentiality Commitment required in case of disclosure)				✓		
Changes to the Equipment - impacting the manufacturing process, specifications or intended use				✓	✓	✓
Change in GMP Status					✓	✓
Change of Original Manufacturer (OM) - disclosure with Confidentiality Commitment					✓	
Changes to Instructions for use and change in Risk level						✓
Change of Original Manufacturer (OM) - disclosure w/o Confidentiality Commitment						✓
Change of CEP Revision						✓

The life science business of Merck KGaA, Darmstadt, Germany
operates as MilliporeSigma in the U.S. and Canada.

M-Clarity™ Program

Notifiable Change Table

According to our M-Clarity program products with different MQ levels 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.

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.

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 pharmacopoeial 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.
MQ Level Downgrade	MQ-Level downgrade means a reduction of service and Quality Attributes. Therefore, it is considered notifiable.
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 MQ level. 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 or the required release tests, or of the chemical reaction is changed. Also, notifiable if change from batch to continuous processes or vice versa.
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	Extended Description
Change to Raw Materials affecting the CoA or CoQ or Specification	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 source change (e. g. synthetic, plant, animal etc.) that may impact specifications. 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.
Labelling - 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 brand names (PharmaGrade, CertiPur, EMPROVE, Histopaque, Selectophore…).
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 theQuality Services process.
Changes to Instructions for use and change in Risk level	Customer 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.

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