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## COMMENTARY

# Managing Excipient Supplier Name and Address Changes in the Pharmaceutical Quality System

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**ABSTRACT:** It is important to identify, assess, and address current barriers to implementation of post-approval changes that are intended to ensure continued (uninterrupted) operations and drive innovation and continual improvement in a maximally efficient, agile, and flexible pharmaceutical manufacturing sector. Leveraging the International Conference for Harmonisation Quality Guideline Q10 provides regulatory relief when it comes to addressing changes related to excipients, specifically excipient supplier's name and address changes, which will ensure a sustainable, reliable global supply and the availability of high quality product to patients through the entire commercial lifecycle of a product without extensive regulatory oversight.

**KEYWORDS:** Regulatory, Chemistry, Manufacturing and Controls (CMC), International Conference for Harmonisation (ICH) Q10, Pharmaceutical quality system (PQS), Post-approval change (PAC), Excipient supplier name changes, Risk Implementation, Quality risk management, Regulatory relief.

## Introduction

It is important to identify, assess, and address current barriers to the implementation of post-approval changes (PACs) that are intended to ensure continued (uninterrupted) operations, avoid drug shortages, and drive innovation and continual improvement in a maximally efficient, agile, and flexible pharmaceutical manufacturing sector. An industry One-Voice-of-Quality (1VQ) working group, sponsored by the chief quality officers (heads of quality) of >25 multinational pharmaceutical companies in conjunction with the Parenteral Drug Association (PDA), is extensively working on standard industry solutions to address these barriers by

1. leveraging enhanced science and risk-based assessment of Chemistry, Manufacturing and Controls (CMC)

PACs based on the International Conference of Harmonisation (ICH) Q12 (1) decision tree and expectations from ICH Q10 (2) and ICH Q9 (3), along with

2. effective management of PACs within the pharmaceutical quality system (PQS).

The objective is to utilize the potential opportunity identified in ICH Q10 Annex 1 of "enhanced regulatory approaches" via "optimized science and risk-based PAC processes to maximise benefits from innovation and continual improvement." These approaches will ensure a timely, sustainable, and reliable global supply and the availability of high quality product to patients through the entire commercial lifecycle of a product, without extensive regulatory oversight.

## Problem Statement

How can we leverage ICH Q10 to provide regulatory relief when it comes to addressing administrative changes specifically to the excipient supplier's name and address? Based on evolving regulatory expectations in some markets, within different geographical regions of the world, regulatory notification/approval is still required for these administrative changes even when there is no change to

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<sup>1</sup>It is recognized that the regulatory mechanism is regionally dependent and will vary in terms of regulatory notification vs health authority approval in a given market.

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the excipient manufacturing site, equipment, material, process, or grade/specifications.<sup>1</sup>

### Context

ICH Q10 section 3.2.3 describes specific expectations for change management within the PQS: application of quality risk management principles to the evaluation of changes, review of the changes in relation to the original marketing authorization and current product and process understanding, as well as continuous evaluation to ensure that the changes were effective in the anticipated way without unanticipated negative impacts. Further, as part of the PQS, controls must be in place to ensure that any changes to raw material manufacturing and testing procedures and to production equipment are defined, evaluated, and approved before use in manufacturing. In turn, under ICH Q10, manufacturers with sound product and process knowledge should be able to leverage the application of proper risk assessment and the demonstration of an effective PQS to manage certain changes within the PQS only, without notification or prior approval by the regulators.

Key aspects of changes to the excipient supplier's name or address:

- These changes are administrative.
- The manufacturer/sponsor may not always have immediate visibility to them, so many are made retrospectively or must be implemented within a limited timeframe.
- The degree and type of supplier information within the registration details may vary depending on the age of a product [e.g., legacy product vs recent Biologics License Application (BLA) or New Drug Application (NDA)].
- Regulations and guidance are not always clear about which information in a product registration is legally binding and how to maintain and update the non-binding information over the product's life cycle.

### Industry's Position

In the absence of changes in the manufacturing site, equipment, material, process, or grade/specification, changes to the excipient supplier's name and/or address

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do not affect the manufacturing process or product quality and safety. These changes are entirely administrative. Health authorities should allow drug manufacturers and sponsors to manage these changes internally within the company PQS, without prior approval from or notification to the health authority, provided that the change does not affect product quality and/or safety.

Because changes to the excipient supplier name and address are often retrospective, a regulatory reporting requirement results in unnecessary and unplanned work. It also requires the expenditure of valuable resources by the sponsor and (perhaps more importantly) the regulatory authority even when there is no potential quality impact.

In fact, most health authorities around the world recognize that these supplier changes can be managed within the PQS, with possible exceptions in the cases of release-controlling excipients and excipients that are considered novel. However, a limited number of countries still require notification or prior approval of these types of changes.<sup>2</sup>

As supported by ICH Q10, a risk- and science-based approach should be considered when evaluating these administrative excipient supplier name/address changes. Specifically, these changes should not require reporting to or authorization by the health authority when the following conditions are met:

1. There are no changes to the excipient's manufacturing process, in-process controls, or its specifications (i.e., the control strategy);
2. There are no other changes required to implement the post-change supplier material in the manufacturing process in which the material is used;

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<sup>2</sup>Health authority expectations, in some markets, are rapidly evolving in which the changes described in this position paper trigger a regulatory event, regardless of what is considered registered in the common technical document. Industry benchmarking conceptualizes the concept presented here, as there is a basic set of implementation practices utilized within different companies based on interpretation of the regulations for this change type, ranging from a traditional approach in which all changes are submitted and approved before implementation to a risk-based approach where this change type is implemented without a regulatory submission. The intent of this position paper is to create awareness of the challenges when there is no impact to quality and to seek regulatory relief.

3. There are no changes to the performance, characteristic, or quality of the product manufactured using the post-change material, and the supplier is not required to report the changes to any referenced drug master file, active substance master file, or certificate of suitability;
4. The information is not listed in the common technical document; and
5. The evaluations associated with items 1–4 above are clearly documented within the firm's PQS.

#### **Conflict of Interest Declaration**

There are no conflicts of interest to declare for any of the authors.

#### **References**

1. International Conference for Harmonization, *Quality Guideline Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management*. ICH: Geneva, 2019. <https://www.ich.org/page/quality-guidelines> (accessed Aug 15, 2019).
2. International Conference for Harmonization, *Quality Guideline Q10: Pharmaceutical Quality System*. ICH: Geneva, 2010. <http://www.ich.org/products/guidelines/quality/article/quality-guidelines.html> (accessed Aug 15, 2019).
3. International Conference for Harmonization, *Quality Guideline Q9: Quality Risk Management*. ICH: Geneva, 2006. <http://www.ich.org/products/guidelines> (accessed Aug 15, 2019).

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