



## Post-Approval Regulatory Lifecycle Management Checklist

**Instructions:** The Post-Approval Regulatory Lifecycle Management checklist will guide you through what to expect after your product has received Marketing Authorization Approval, including post-approval changes/variations, renewals, pharmacovigilance, and annual reports.

### POST-APPROVAL CHANGES/VARIATIONS:

If there is a reportable change to your product, the license holder, the manufacturer, the labeling, etc., you may need to file a post-approval variation. Reportability and classification (i.e. minor, major, annual notification, etc.) are frequently established based on the potential for the change to adversely affect product quality, safety, and/or efficacy. Common reportable changes include but are not limited to: Address changes, alternate facilities or suppliers, manufacturing process and/or composition, analytical methods and/or specifications, shelf life, packaging, etc. Here's how to get started with preparing a post-approval change or variation:

Identify the country-specific guidelines for post-approval variations.

Using the guidelines, determine what level of reporting is required based on the change (e.g. notification, variation, etc.).

**NOTE:** *Note: some changes (e.g. manufacturing process changes) will require time-sensitive reporting, while others can wait until the annual report (if applicable).*

Collect the required information for the appropriate reporting category and assemble it into a submission package.

Identify whether product samples or labeling mock-ups are required.

Submit the post-approval variation, making sure to collect a confirmation of receipt from the regulatory authority once you have submitted.

Identify the expected timeline for approval based on the reporting category. Depending on the reportable change, you may or may not receive approval from the regulatory authority.

- Some changes cannot take effect until approved by the National Medicines Regulatory Authority (NMRA). Examples include but are not limited to: product manufacturing changes and/or composition, manufacturing site changes, primary packaging changes, etc.
- Some minor changes may automatically go into effect after a certain period of time if the regulatory authority has not communicated otherwise. Examples include but are not limited to: minor changes to analytical procedures, secondary packaging changes, update specifications to comply with an officially recognized pharmacopoeia monograph, etc.

### RETENTION/RENEWALS:

Registration retention or renewal is typically required to be filed every five (5) years for any registered product. Longer or shorter renewal periods might be established by the National Regulatory Authority (NRA) as indicated in the Marketing Authorization Approval Letter. During the renewal reporting period, you may also be able to submit post-approval changes that are identified as annually reportable in the guidelines.

Identify the country-specific guidelines for registration retention/renewals.

Using the guidelines, determine what documentation is required for a registration retention/renewal.

Identify whether product samples or labeling mock-ups are required.

Identify any required fees for a registration retention/renewal and pay the fees according to the fee schedule. This may be prior to submission (such that a receipt of fee payment is submitted with the application), or at the time of submission.

Submit the retention/renewal application, making sure to collect a confirmation of receipt from the regulatory authority once you have submitted.

### PHARMACOVIGILANCE:

The goal of pharmacovigilance is to detect, assess, and understand adverse events related to a medical product. Pharmacovigilance requirements are put in place by regulatory authorities to ensure patient safety for marketed medical products.

Identify country-specific guidelines for pharmacovigilance.

Determine who will be responsible for pharmacovigilance tracking and reporting, and ensure that their systems are implemented according to country guidelines.

Ensure that product labeling reflects up to date pharmacovigilance information, if required per country guidelines.

Report pharmacovigilance events as required by each country.

### ANNUAL REPORTS:

In some countries, annual reports are required to be submitted to the applicable NRA while the product is on the market. In other countries, annual reports are not a requirement but are expected to be available on request or at the time of inspection. Reporting requirements should be confirmed in the country-specific guidelines. Below you will find a sample list of annual report requirements per the US-FDA.<sup>1</sup>

**Summary:** Summary of significant new information from the previous year that might affect the safety, effectiveness, or labeling of the drug product.

**Distribution data:** Information about the quantity of the drug products distributed and quantities distributed for domestic and foreign use.

**Labeling:** Currently used labeling (labels, inserts, brochures, etc.) and representative sample of the product.

**Chemistry, manufacturing, and controls changes:** Reports of experiences, investigations, studies, or tests involving chemical or physical properties, or any other properties of the drug.

**Nonclinical laboratory studies:** Copies of unpublished reports and summaries of published reports of new toxicological findings in animal studies and in vitro studies.

**Clinical data:** Published clinical trials of the drug (or abstracts of them), including clinical trials on safety and effectiveness; clinical trials on new uses; biopharmaceutic, pharmacokinetic, and clinical pharmacology studies; and reports of clinical experience pertinent to safety.

**Status reports of post-marketing study commitments:** A status report of each post-marketing study of the drug product concerning clinical safety, clinical efficacy, clinical pharmacology, and nonclinical toxicology.

<sup>1</sup> <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=314.81>