Managing biopharmaceutical products through their lifecycle from discovery to development and launch to obsolescence is complex. The difficulty of the task is compounded by constantly evolving scientific, medical and regulatory environments, and frequent changes to the product during its lifecycle. If you are using informal, non-standard processes to manage change, you have a sure recipe for non-compliance.

A robust and standardized change control process, supported by a centralized master product dataset (also known as the product record), enables Technical Operations and Regulatory Affairs groups to confidently evolve and optimize products while maintaining global regulatory compliance and reducing the cost of product changes.

To do this right, companies need to understand three key elements; why change control is necessary, how to draw the line between change and churn, and when to apply change control during the product lifecycle.

**Why is Change Control Necessary?**

Changes to biopharmaceutical products are made for a variety of reasons, including supply chain changes, expansion to new markets, product transfers from one manufacturing location to another, evolving or new regulations, production changes, and Corrective and Preventative Actions (CAPAs). How companies manage and control changes that result from these events is vital to their compliance with Quality Management Systems regulations.

Regulators require any change that affects the identity, strength, quality, potency or purity of a pharmaceutical product be introduced in a controlled manner. Changes to product materials, procedures or equipment must go through a formal process that ensures comprehensive assessment, documentation, validation and auditability.

A rigorous and formal change control process prevents unintended consequences for customers and patients when introducing product changes, and will help maintain market access by ensuring continued regulatory compliance for the manufacturer.

**Drawing the Line between Change and Churn**

The product development process for biopharmaceuticals is long and often iterative. New experiments and alternative manufacturing and treatment methods are continually explored during the R&D process. Managing each and every design and development decision made during this process through formal change control is cost prohibitive and unnecessary. Here are some guidelines for when a formal change control process is (and is not) needed.

Change control IS needed when the changes:

- Affect product design, features, safety, quality, compliance, manufacturability or cost
- Affect project schedule or cost
- Affect suppliers or functions other than the one initiating the change or require other suppliers or functions to be notified
- Require agreement between multiple functions or with suppliers
- Require customer approval or approval from regulatory authorities
- Require (executive) management approval
Change control is NOT needed in “churn” scenarios including:

- Performing iterations or simulations to optimize product design, features, safety, quality, compliance, manufacturability or costs
- Running scenarios to establish a direction for an item or product
- Evaluating cost impacts of packaging or artwork design options

**When to Start Change Control in the Lifecycle**

Managing the lifecycle of a product from drug discovery to end-of-life involves various stages and handoffs between internal and external parties. Each step along the process can result in product changes that must be controlled and properly documented in order to ensure safety and improve likelihood of future commercial success.

In an earlier whitepaper we advocated the use of one central, compliant product record to store and manage all the key data and supporting information associated with a biopharmaceutical product. To keep the product record accurate and compliant, every product change requires a modification of one or more elements. Change control is active management of the product record.

There are many drivers throughout the lifecycle that require changes to the product record.

<table>
<thead>
<tr>
<th>Pre-Launch</th>
<th>During / Post Launch</th>
<th>Ongoing Lifecycle Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Documenting iterative development/design decisions</td>
<td>• Ensuring compliance</td>
<td>• Ensuring ongoing Compliance</td>
</tr>
<tr>
<td>• Ensuring cross-functional alignment between stakeholders and informing on development progress (e.g., product development, regulatory, quality, supply chain)</td>
<td>• Optimizing manufacturing process</td>
<td>• Implementing CAPAs</td>
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<tr>
<td>• Controlling individual product/process change privileges</td>
<td>• Assessing cost effect (inventory, etc.)</td>
<td>• Managing changes to process and facilities</td>
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<tr>
<td>• Documenting approval from executive management</td>
<td>• Keeping key stakeholders informed on launch progress</td>
<td>• Managing label and packaging changes</td>
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<td></td>
<td>• Ensuring quality documentation alignment</td>
<td>• Managing line extensions, additional indications</td>
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To guarantee that the dossier submitted to the health authorities is equivalent to the product that is delivered to the patient, it is critical to ensure consistency between the different elements of the product record during the change process. To keep up, change control should start well before product launch and continue throughout the lifecycle to end of life.

**Chain Reaction of Changes**

Making changes to a product, particularly post launch, can cause a complex chain reaction of additional changes to data elements that describe that product or other similar products. A robust change control mechanism will keep data synchronized.
The graphic below illustrates a simple case of that chain reaction: a safety profile change generates subsequent changes to other elements of the product including artwork, packaging and labeling. Maintaining product data as a single structured product record helps identify the relationships between the various elements affected by a change and enables efficient and compliant change execution.

Compliance in the pharmaceutical industry is not to be taken lightly. Companies that do not manage product changes with adequate controls can face launch delays for new drug candidates, or significant regulatory and financial consequences for marketing products that fall out of compliance.

Those accountable for ensuring compliance – like Technical Operations and Regulatory Affairs – should wrap a robust, consistent change control process around a single, centralized, compliant set of product data. This will allow product changes to be introduced while maintaining global regulatory compliance and ultimately delivering innovative new products that address significant unmet medical needs.