Changes to Marketed Product: Keeping Pace With Your Product Lifecycle

Ruth James / Regulatory Affairs / May 02, 2019
Change Cycle

1. Proposed Change
2. Change Approved
3. Change Ready to be released
4. Change Released into Production

- Initial Regulatory Impact Assessment
- Final Regulatory Impact documented
- Release signed off by RA
Biggest Challenges with Product Lifecycle Changes

• Understanding the Change(s)!
• Volume of changes
• Turnover timeline
Change Assessments

US

EU

Global
Change Cycle

Proposed Change → Change Approved → Change Ready to be released → Change Released into Production

Initial Regulatory Impact Assessment

Final Regulatory Impact documented

Release signed off by RA
Initial US Assessment
Quality System regulation requires manufacturers of finished medical devices to review and approve changes to device design and production (21 CFR 820.30 and 820.70) and document changes and approvals in the device master record (21 CFR 820.181).
Deciding When to Submit a 510(k) for a Change to an Existing Device (Oct 25 2017)

This procedure defines the required process for making 510(k) decisions when a modified medical device is proposed for marketing in the United States or entering interstate commerce throughout the United States.
### US Assessment Example

<table>
<thead>
<tr>
<th>SECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exemptions From 510(k) Premarket Notification</td>
</tr>
<tr>
<td>510(k) / No 510(k) Determination</td>
</tr>
<tr>
<td>Labeling Change</td>
</tr>
<tr>
<td>Technology, Engineering or Performance Change</td>
</tr>
<tr>
<td>Materials Change</td>
</tr>
<tr>
<td>Risk-Based Assessment of Modified Product</td>
</tr>
<tr>
<td>Final Regulatory Determination</td>
</tr>
</tbody>
</table>
Initial RA Assessment: Potential Outcomes

The product change under evaluation (choose one):

- Requires 510(k) Premarket Notification

- Does Not Require 510(k) Premarket Notification

- Does Not Require 510(k) Premarket Notification based on current information – to be confirmed by results of testing and risk assessments supporting the change. Complete a Final Determination.

- Requires 510(k) Premarket Notification prior to implementation of this change due to the aggregation of minor changes since the last 510(k).
FDA Says: If the initial decision following the risk-based assessment is that submission of a new 510(k) is not required, this decision should be confirmed by successful, routine verification and validation activities. (Final Determination).
FDA notes that only highlighting the flowcharts in their FDA Guidance, or simply answering “yes” or “no” to each question without further details or justification, is not sufficient documentation. The manufacturer should provide an appropriately robust justification of a decision that submission of a new 510(k) is not required.
Don’t Forget!

Does an FDA device listing need to be created or revised as a result of the product change under evaluation (refer to 21 CFR Part 807.28 and Device Listing Procedure xx)?

• Yes, requires a new device listing or update to current device listing

• No, does not require a new device listing or update to current device listing
Initial EU Assessment
NBOG’s Best Practice Guide 2014-3, Guidance for manufacturers and Notified Bodies on reporting of Design Changes and Changes of the Quality System

• Only those changes need to be notified which “could affect conformity with the essential requirements”.

• The manufacturer must report to the Notified Body any plan of “substantial” changes before implementation.
EU Assessment Example

<table>
<thead>
<tr>
<th>SECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes to Manufacturing Process, Facility, Equipment, and Finished Good Specifications</td>
</tr>
<tr>
<td>Changes to the Product Design</td>
</tr>
<tr>
<td>Changes to Materials</td>
</tr>
<tr>
<td>Changes to Labeling</td>
</tr>
<tr>
<td>Kits/Trays with Class III Products: Changes to Sterilization and Shelf Life</td>
</tr>
<tr>
<td>Changes to Device Software</td>
</tr>
<tr>
<td>Final Regulatory Determination</td>
</tr>
</tbody>
</table>
The product change(s) under evaluation is a (choose one):

- **Non-Substantial Change**. Complete and sign this document.

- **Non-Substantial Change** based on current information – to be confirmed by results of testing and risk analysis supporting the change. Complete a **Final Determination**.

- **Substantial Change**, Notified Body Approval Required.
Don’t Forget!

Although non-reportable the impacts of any changes on the Technical Documentation must be evaluated as well!

- Document that you have carried out this evaluation on the Technical Documentation to close the loop in your EU Assessment.
Initial Global Assessment
Global Assessment

Any High Level Global Triggers?

- Yes → Request for Further Info. (RFI)
- No → No Global impact
Examples of High Level Global Triggers

• Does the change result in a product discontinuation or change to or a new Product Name or Product Code?
• Change to Labeling?
• Patient Contacting Material Change?
• Patient Contacting Component Change
• Is the change to packaging materials?
• Is the change to the shelf life of the product?
• Is there a change to sterilization method/dose/parameters?
• Is the change an update or new revision of the device software?
• Is the change to the name of the manufacturing site (e.g. manufacturing, sterilization or packaging site), material supplier or component supplier?
Initial RA Assessment: Potential Outcomes

The product change(s) under evaluation is a (choose one):

- **Non-Substantial Change**. complete and sign this document.

- **Non-Substantial Change** based on current information – to be confirmed by results of testing and risk analysis supporting the change. Complete a Final Determination.

- **Substantial Change**, send out RFI to Global market.
• There is RA Impact:
  • in US – approval needed prior to change
  • in EU – approval needed prior to change

• There is (potential) RA impact in Global - will need to send out RFI. Details will be documented and given to team in a RA Plan.

• There is no RA Impact in US, EU and/or Global Markets.

• There is no RA impact, however a final determination will need to be made once results of testing and risk analysis supporting the change have been confirmed.
Final Regulatory Impact
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Document Results from Global RFI

<table>
<thead>
<tr>
<th>Country</th>
<th>Impact</th>
<th>Timing</th>
<th>Deliverables</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

Document all your countries!
V&V/Testing/Risk Assessments

The following documents have been reviewed in support of the product change:

<table>
<thead>
<tr>
<th>Reference Document #</th>
<th>Reference Document Name</th>
</tr>
</thead>
</table>

Do the results of the verification, validation activities, testing and/or risk assessment listed above confirm the initial determination?

- **No**; there were unexpected results which require that additional testing be performed or otherwise prove to be inadequate to validate this change(s) and/or there were new issues of safety or effectiveness (new risks or significantly modified risks identified).

  **Reevaluation from Regulatory Affairs is required.**

- **Yes**; the determination has been confirmed and is now final.
Change Release
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Manage Change Release

Release change to those countries that are able to receive it
- they had no impact
- they can receive the change while they are doing their notifications

Do not release the change to countries
- that have RA impact – require preapproval!
Repeat process for each change!
Summary

Benefits of Proceduralizing your Change Assessments

• Consistent approach to assessing changes for each market

• Reduce/Eliminate Margin of Decision Error
  – Different RA personnel should come to the same decisions for the same change!

• Speed up processing time

• Have more confidence in the decisions that have been made
Assess RA Impact via standardized format based on:

- **US** - Deciding When to Submit a 510(k) for a Change to an Existing Device (Oct 25 2017)
  - **AND** 21 CFR Part 807.28 (Device Listing)

- **EU**: NBOG’s Best Practice Guide 2014-3, Guidance for manufacturers and Notified Bodies on reporting of Design Changes and Changes of the Quality System
  - **AND** Assess impact on Technical Documentation

- **Global Markets**: High Level Triggers then RFI for more input.
Final Thought

NO IMPACT – need to verify with V&V results