Managing Post Approval Changes: yesterday, today and tomorrow

2015 PDA Manufacturing Science Workshop

Pierre-Alain Ruffieux, PhD
Head of Novartis Pharma Quality
This presentation is based on publicly available information.

These slides are intended for educational purposes only and for the personal use of the audience. These slides are not intended for wider distribution outside the intended purpose without presenter approval.

The content of this slide deck is accurate to the best of the presenter’s knowledge at the time of production.

The views and opinions expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of Novartis or any of its officers.
The journey starts with a need for change ...

Trigger

Alternate testing site for the release & stability of a finished product
7th May 2014

Initiation

Change Request Initiated

Setting of:

- Current testing site
- Proposed testing site for release & stability
- Justification
- Record in internal systems
10th July 2014

GMP status: Site not FDA Approved that requires successful FDA inspection therefore classified as Post Approval Supplement (PAS)

- CTD Module ‘Manufacturers’ to be updated
- Highlight need to complete method transfer prior to submission
5th December 2014

Initiation

Evaluation/Planning

Execution

- Method Transfer executed & approved
- Preparation of documentation for dossier update
15th December 2014

- Trigger
- Initiation
- Evaluation/Planning
- Submission
- Execution

After 11 months the journey ends ...

After a successful FDA inspection in 1st week of April, approval was received.
...with the change implemented.

Starting from 15-Apr-2015: new set up in use

☑ Implementation of the change
LOOKS EASY AS PIE DOESN’T IT?
This is not as simple as it looks because....

Highly regulated industry
This is not as simple as it looks because....

1 Highly Regulated Industry

2 The requirements are different from country to country
This is not as simple as it looks because....

1. Highly Regulated Industry

2. The requirements are different from country to country

3. Approval & implementation timelines are different from country to country
130+ marketed brands

700+ submissions packages dispatched per year to countries

14,000+ submissions per year to country Health Authorities

10,000+ stock keeping units

140+ countries supplied
LEARN FROM YESTERDAY
LIVE FOR TODAY
HOPE FOR TOMORROW
What we’ve learned...

1 Yesterday

Data was maintained across multiple systems which required very high level of knowledge to either use or maintain the data

Change control process was fragmented

Focus of the workflows was more on correct handoffs between line functions & information

2 Today

3 Tomorrow
What we’ve seen...

1 Yesterday’s Challenge

2 Today

3 Tomorrow

As a consequence there was:

- risk of non-compliance
- low incentive to make more changes
Based on yesterday’s learnings ...

1 Yesterday

2 Today’s fit for purpose

- A robust system that enables Pharma companies to manage all changes during the life cycle of a product

3 Tomorrow
Every project has its challenges ... 

1 Yesterday

2 Today’s Challenge

3 Tomorrow

- Need to build a new system to unify complex information systems & fragmented processes
- Data migration could disturb ongoing changes
- Requires investment (people & money)
- Requires broad retraining & refining
What we’re implementing

1. Yesterday

2. Today

3. Tomorrow

- Robust & exact process
- Accuracy & completeness of data
- Easy tracking
- Clear roles & proper involvement
- Clear timelines
We want to....

- Quickly adapt to new demand & business
- Have the regulatory relevant product data managed in a single information system.
- Have an easy overview on all product lifecycle events in a single information system.
- Correctness & Usability/Learnability
- Ensure Integrity & Reliability
- Enhance Efficiency & Security
Let’s have a closer look...

...and this is multiplied by number of countries...

The $n$ regulatory relevant information for one product is stored as follows....

This is replicated for each product....
we’ve implemented a fixed workflow process...

Change request
- e.g. Specifications, Production process, Artwork, Master Data

Initiation

Change Notifications

Closed loop change implementation with notification back to requesting initiator

The authorization process captures submission strategies

System-driven with single source of data truth

Products

Countries

Changes in parallel or consolidated based on required implementation schedules

Phase-Gate Based Execution

Evaluation

Implementation

Approval

Submission

Change Notifications

Change request
- e.g. Specifications, Production process, Artwork, Master Data

Products

Countries

Changes in parallel or consolidated based on required implementation schedules

Phase-Gate Based Execution
Clear benefits on the execution...

Increase **ACCURACY** of data & **EFFICIENCY** of data maintenance

Increase **PREDICTABILITY & SPEED** in implementation of Product Lifecycle events

Increase **CAPABILITY** of the organization & **FLEXIBILITY** to handle new demand and business growth
What the future could hold...

1. Yesterday

2. Today's fit for purpose

3. Tomorrow
Our hope for a bright future...

- One common standard facilitating submission of a single harmonized package globally
- Enabling the move from control based bureaucracy to knowledge-based management of the changes
- Risk-based approach and the possibility to manage minor changes through company’s Quality Management System
What would be our hope for tomorrow...

1 Yesterday

2 Today’s fit for purpose

3 Tomorrow’s Challenge

We still need to ensure collaboration between industry, regulators & patient associations
ICH Q12 should facilitate predictability & efficiency of post-approval change management, thus supporting innovation and ensuring sustained product supply.
In conclusion

Post Approval Change is a relatively simple process on the surface...

... but requirements vary significantly from country to country in terms of reporting levels, amount of documentation and approval timelines.

This represents a significant barrier to continuous improvement & a challenge in maintaining compliance...

....ultimately potentially impacting the capacity of the industry to deliver products to patients.

IT systems can facilitate the variability of the process but don’t remove the regulatory complexity....
In conclusion

We aspire to move away from pre-approval “control-based” system to “science-based” knowledge where changes are implemented on a “tell & do” basis and reviewed during routine inspection.
ACKNOWLEDGEMENTS

Ursula BUSSE
Raylene DYSON
Ronan FARRELL
Fedra LIMONCINI
Maria SOLER-NUÑEZ
Klyde TAKALINE