

Implementation of changes aligned to regulatory framework

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Type II variations require prior approval before implementation – known as the "Prior authorisation" procedure.

Type II variations are normally processed according to a 60 day timescale; however, the Regulation additionally specifies a reduced (30 day) or extended (90 day) timescale.

Classification guidance on minor variations of type IA, minor variations of type IB and major variations of type II

Changes are from different areas:
A) Administrative changes; B) Quality changes; C) Safety, Efficacy and Pharmacovigilance changes and D) Specific changes to Plasma Master Files and Vaccine Antigen Master Files.

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- Above are some familiar terms from regulatory activities.

- However, the issue is:

  Why change?

  How it could be handled?

  Man hour or money involved?

  Does Change mandatory?

- Let’s see the story in the next slides!

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- Changes might be frequent
- Some changes possess true weight, some do not have.
- Some changes are skeptic to assess their true individual weight, should they really need to implement?
- Formulators (DP manufacturers) do not have control on all the changes always. Sometimes they have to swallow changes implemented by others e.g. API or excipients suppliers/ manufacturers
- This is something like that, Pain originated in a tissue eventually spread over the whole system even in the whole body!
- In maximum cases, changes are not as important as they are considered, yet changes are inspired to implement.
- Sky might have the limit, interestingly, expectation do not have. A process or a product could be improved up to beyond the imagination; however, every change for that way creates a set of new regulatory requirement and that has to be justified with respect to customer need i.e. in time product availability in the market.

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- Some regulatory authorities are flexible to accept changes; some are too conservative to accept even changes are minor.
- Marketers have to obey regulatory guidelines of specific market and they cannot change it.
- Same change accepted and granted to a specific regulatory body in a defined region might be considered as 'critical' and could take longer time to get approval to another body at another region.
- Batch size increase or change of any process equipment for better market supply sometimes lead an urgent drug 'market out' situation just because of lengthy regulatory procedures. Patient sufferings might be serious for such cases.
- Changes to renovation of API synthetic process/ route or remedial steps of weak point product (WPP) has to be assess at the very beginning phase of change plan including regulatory impact supposed to the existing or prospecting market so as to get necessary preparation and management of tight regulatory timelines mandatorily to be followed during variation submission.

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- DP manufacturers might be frequently inspired to change even an established, reliable & qualified DS suppliers/ manufacturers for better price negotiation to keep medicine price affordable as advised by their ComOps colleagues and makes change to an alternate source development, even interestingly, sometimes two or more sources.
- Ethically, every change should be aligned to product's quality & efficacy and finally to patient's safety.
- Every change either formulation, analytical specification, process or equipment related, API or excipient change, batch size and so on, there involved a lot of variations which means a set of new requirements on regulatory aspect. Head counts in every function along with non-human resources are ideally proportional to the assigned jobs. Thus frequent decision of any change apparently seems to be beneficial, however, finally could be disfavor able.

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'Change' is assumed as the seed of progress to the next step, thus change is required of course. However, any proposed change needs 360° view before planning to implement.

'No change' means 'everything is going 100% percent okay' sometimes create question about the true functionality of the system in place. Moreover, 'no change' means 'no ambition' or 'no initiative/ attempt' to 'the new progress' which leads even good intention to stalemate.

Therefore, frequent change??

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- 'Frequent change' would create another doubt seems to be more critical to handle even than to 'no change' and is about the robustness of the system in place. This might be harmful even to the integrity of the whole operation.

- There need to ensure a 'check & balance', in another term, 'proper justification, assessment & impact' for every change.

A false example here!

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- People might be inspired to implement change just because of simplify the process e.g. change of API synthetic route. Interestingly, this simplification
- Might be e.g. due to avoid/ hide any impurity appeared beyond the accepted limit and no reasonable clue would get during laboratory investigation! If happen so, such type of incident would harm operational competencies and integrity.
- Do you have some connections to work with regulatory team?
- Now it's your turn to handle all the frequent/ infrequent changes made so far to different countries/ regions being aligned to regulatory framework.

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- The process is rather easy to follow guidelines mentioned in the EU, LATAM, MEA, APAC or US market. Everything is clearly defined, which thing you need to provide to which regulatory authority for which type of changes and within how many days. Probably, it would be challenging for you to keep every change within the track so as to get timely approval from different regulatory authorities.

  Best of luck!

Thanks for your patience hearing!

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