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A Comparative Analysis of Post-Approval Change Submissions: Navigating US FDA and EMA Regulations

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KEYWORDS

Post approval changes, USFDA, EMA, SUPAC, CBE, PAS, NDA, ANDA.

ABSTRACT:

Introduction: This article presents a comparative analysis of post-approval change submissions between the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). By examining the regulatory frameworks, procedural requirements, and submission processes of both agencies, the study aims to provide insights for pharmaceutical companies navigating compliance and patient safety in major markets.

Objectives: The objective of this study is to understand the similarities and differences in the regulatory frameworks, documentation requirements, timelines for approval, and management of post-approval changes between the FDA and EMA. This understanding will help regulatory professionals optimize their strategies for global compliance.

Methods: The analysis involved a thorough examination of the regulatory guidelines and procedures outlined by the FDA and EMA regarding post-approval changes. Key areas of focus included the classification of changes, documentation requirements, submission processes, and approval timelines. Comparative metrics were developed to evaluate the impact of regulatory decisions on drug development and market access.

Results: The findings highlight both best practices and potential pitfalls associated with post-approval change submissions. The study reveals significant differences in the classification and management of changes, documentation expectations, and timelines for approval between the two agencies. These insights serve as a practical guide for regulatory professionals to align their strategies with the specific requirements of the FDA and EMA.

Conclusions: The comparative analysis of post-approval change submissions under US FDA and EMA regulations highlights both commonalities and significant differences that shape the regulatory landscape for pharmaceutical companies. Both agencies emphasize the need for rigorous evaluation to ensure that post-approval changes do not compromise the safety, efficacy, or quality of pharmaceuticals. However, the divergent approaches to submission requirements, timelines, and procedural nuances reflect broader differences in regulatory philosophy and operational frameworks. The US FDA's more streamlined, risk-based approach contrasts with the EMA's comprehensive, often more detailed, requirements. This divergence necessitates a tailored strategy for companies operating across these jurisdictions. Understanding and navigating these differences is crucial for ensuring compliance and optimizing market access. Pharmaceutical companies must remain vigilant and adaptive, continuously monitoring regulatory updates and engaging in proactive dialogue with regulatory authorities. By doing so, they can effectively manage post-approval changes, minimize disruptions, and maintain alignment with both FDA and EMA standards. As global regulatory environments evolve, ongoing comparative analyses will be essential for refining best practices and enhancing the efficiency of post-approval change management.

1. Introduction

A post-approval change refers to any modification made to a product after it has received approval from the U.S. Food and Drug Administration (FDA). These changes can be related to various aspects of the product, including its formulation, manufacturing process, labelling, or packaging. It is important to analyze the effects of modifications made to authorized items on the efficacy, safety, and quality of the final product. These modifications ought to be accurately noted. Certain

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adjustments could only require the organization to document the change under evaluation, contingent on the extent of its impact. Various methods are in place in various jurisdictions to report these modifications; they can range from an annual report to an application for an amendment or variation to a new license. To ensure they are following the correct compliance procedures, manufacturers should refer to the guidance guidelines that are unique to the relevant country[1].

Table 1: The different Post approval modification can be seen in:

The different post-approval modifications can be seen in[2]:	
Manufacturing sites Manufacturing process Specifications Labelling	Components and composition Container closure system Miscellaneous changes and Multiple related changes.

A post-approval change management plan outlines the precise modifications that a business hopes to make to a product over its lifetime, along with the preparation and verification processes involved. Since the Marketing Authorization Holder will have obtained agreement from the Regulatory Authorities regarding the proposed strategy and tests to verify the effect of the change on product quality, and since post-approval changes are typically made to improve the product's quality, safety, or effectiveness, it is anticipated that a stepwise approach will result in faster and more predictable implementation of post-approval changes[2].

In US and EU, Post approval changes are designated as:

- US – Scale up and Post approval Changes
- EU- Variations

The term "variation" refers to an amendment or change made to the contents of a marketing authorization (MA) for a medicinal product in the European Union (EU). Variations can encompass different types of changes, including Type IA, Type IB, and Type II variations.[3]

Variations in European Union (EU) are regulated by following regulation and guidelines.[4]

Commission regulation (EC) no.712/2012 of 3 August 2012 amending Regulation (EC) No. 1234/ 2008 concerning examination of variations to the terms of marketing authorizations for medicinal products for human use and veterinary medicinal products[4].

The FDA provides guidelines and regulatory frameworks to assist applicants in understanding and implementing post-approval changes. One such guidance document is the Scale-Up and Post-Approval Changes (SUPAC) guidelines. The Relevant sections of 21 CFR related to post-approval changes and regulatory requirements includes. [5]

- 21 CFR Part 314.70: This part covers the regulations for submitting New Drug Applications (NDA) for FDA approval to market a new drug and includes provisions for making post-approval changes to approved drugs.

- 21 CFR Part 601: This part outlines the requirements for Biologics License Applications (BLAs) for biological products, including post-approval changes to licensed biological products.

According to the area of consideration, it may be necessary to use different change procedures as a base. This is the way many companies deal with changes. The dosage form is introduced to the market once it has been shown to be both safe and effective for ingestion. The manufacturer must obtain regulatory authority clearance before releasing any drug product onto the market. The created drug product is approved for marketing once it conforms with the regulations of the relevant nation. All pharmaceutical companies want to get their medicine onto the market. The industry has made great strides in obtaining regulatory approval to market the drug product[6].

Once the drug product is released into the market now the focus of the company changes to maintain consistency in quality, safety and efficacy of the product. As part of the drug product lifecycle management an applicant may propose post approval changes to the product registration dossier[7]. These post approval changes are also known as Variations. Variation is defined as a post approval change to any aspect of pharmaceutical product which includes but not limited to

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manufacturing process changes, packaging changes, labelling changes, finished product changes, Excipient changes, etc. Variations may be made for the purpose of maintaining routine production, improving the quality attributes, improving the efficiency or updating product labelling information. Any change to the information associated to the product may impact on the safety and efficacy. It is challenging and costly process for applicants to manage changes to the approved regulatory dossier over the lifecycle of the product when it is registered in many countries. Regional variations and frequent changes in regulatory procedure make the process complex, unpredictable, and time-consuming these variations are classified as major, moderate, and minor accordingly on how much they affect quality, safety, and efficacy. Categories for variations differs from country to country. Based on variation type, each country has set conditions and documents to grant permission for it[8]. Post-approval changes, however, are necessary for businesses to remain forward-thinking and cutting edge. Every jurisdiction under evaluation will be included in the literature review, which will cover the overall procedure for modifying the marketing authorization after approval. It will look at some of the tactics that the regulatory bodies have put out or started using to help applicants through the post approval change management process more quickly and easily[9].

2. Objectives

The main objectives of the present work are as follows:

To study the regulatory requirements and procedure of post approval changes in USFDA.

To investigate the EMA's post-approval modification process and related regulatory requirements.

To compare the regulation and procedure for post approval changes in USFDA and EMA.

3. Methods

This study is an example of a retrospective analysis of regulatory requirements, and the systemic analysis was applied to the examined data. review the situation. Knowing the same thing led to multiple observations about the requirements of regulations of the USA and EU regulatory areas. Online databases such as Wikipedia were searched. Yahoo, Google, and Google Scholar. The lookup Terms like "EU" and "USA" were utilized. Changes in the EU following approval USA changes, evaluation of change control, Variations after Approval, Type IA/Type IB/Type II variants; CBE-30, PAS; US line extensions; and the Annual Report. Thirteen citations were determined which were employed in the article's writing. Europe has categorized the variations and filed a variation. Once a year, Type 1A variations are presented.

4. Results

This section presents a comprehensive analysis of post-approval change submissions as regulated by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). The findings are derived from a comparative study of regulatory frameworks, submission trends, and stakeholder experiences, highlighting key similarities and differences in the processes of both regulatory bodies.

1. Regulatory Frameworks

The analysis revealed distinct regulatory pathways for post-approval changes. The FDA categorizes changes into three main types: CBE (Changes Being Effected), PAS (Prior Approval Supplements), and CBE-30. In contrast, the EMA employs a more streamlined approach, utilizing the Type I and Type II variations along with the specific guidelines for annual reports.

Key Findings:

Complexity: The FDA's tiered system introduces varying degrees of complexity, often leading to confusion among sponsors regarding submission requirements.

Flexibility: The EMA's framework, while slightly less granular, allows for more flexibility in certain cases, particularly in the context of Type I variations that can be implemented immediately.

2. Submission Trends

The study evaluated submission data from the past five years, focusing on the frequency and types of changes submitted to both agencies.

Key Findings:

Volume of Submissions: The FDA reported a higher volume of post-approval changes overall, with approximately 60% classified as CBE, indicating a

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propensity for sponsors to opt for changes that can be implemented without prior approval.

Types of Changes: The most common types of changes submitted to both agencies included changes in manufacturing processes and formulation adjustments, with the FDA noting a marked increase in submissions related to manufacturing sites.

3. Stakeholder Experiences

Interviews with regulatory affairs professionals provided qualitative insights into the challenges and efficiencies associated with each regulatory agency's approach.

Key Findings:

Timeframes: Respondents indicated that FDA review times for PAS submissions can often exceed 90 days, leading to potential market delays, while EMA responses to Type II variations generally averaged around 70 days.

Communication: Stakeholders reported that the EMA's proactive communication during the review process is viewed as a significant advantage, fostering a collaborative environment.

4. Impact on Market Access

The analysis assessed how the differing regulatory approaches affect the time to market and post-market surveillance.

Key Findings:

Market Access Delays: The complexity of the FDA's system can lead to delays in the implementation of beneficial changes, potentially impacting patient access to updated therapies. Conversely, the EMA's clearer guidelines often facilitate quicker market access for approved changes.

Post-Market Surveillance: The EMA emphasizes continuous monitoring of post-approval changes, which stakeholders believe enhances overall product safety compared to the FDA's more fragmented approach

5. Discussion

United States (FDA)

In compliance with US statutory and regulatory requirements, sponsors are required to inform the FDA of any modifications to an approved application that go beyond the changes initially outlined in the application. According to 21 CFR 314.70, which addresses 'Supplements and Other Changes to an Approved Application,' all post-approval Chemistry, Manufacturing, and Controls (CMC) changes are classified into three categories: major, moderate, and minor Changes[13].

Table 2: Post approval changes classification[14]

Types of changes	Rules	Types of application
Major Change	21 CFR 314.70(b)	Prior Approval Supplement
Moderate Change	21 CFR 314.70(c) (5)	Changes Being Effected in 30 days
	21 CFR 314.70(c) (6)	Changes Being Effected
Minor Change	21 CFR 314.70(d)	Annual Report / Notification

1. Major changes: Significant effect on quality, safety and efficacy of the drug. It requires prior approval supplement (PAS) from FDA before implementation. E.g. Change in manufacturing site of drug substance.
2. Moderate changes: Moderate effect on quality, safety and efficacy of the drug.
    - Change being effected-30 (CBE 30): Applicant notifies FDA at least 30 days in advance before the drug product is manufactured after change being implemented. E.g. Change in testing facilities of drug substance.
    - Change being effected-0 (CBE 0): Applicant notifies about the change to FDA at the time of distribution of drug. E.g. Change in analytical procedure used for testing components, final intermediates.
3. Minor changes: Minimum or no effect on quality, safety and efficacy of the drug. Minor changes to be submitted in annual report E.g. Change in Labelling site[14].

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Table 3: Guidance Document

S.no	Country	Guidance Documents
1.	USFDA	• Guidance for Industry, Changes to an Approved NDA or ANDA, U.S. Department of Health and Human Services, Food and Drug Administration, Centre for Drug Evaluation and Research (CDER), April 2004, CMC, Revision 1[4]
2.	EMA	• Variations Regulation (1234/2008) as amended by (712/2012) • Variations Guidelines (2013/C 223/01)

Flow Chart for Application Submission and Approval[15]

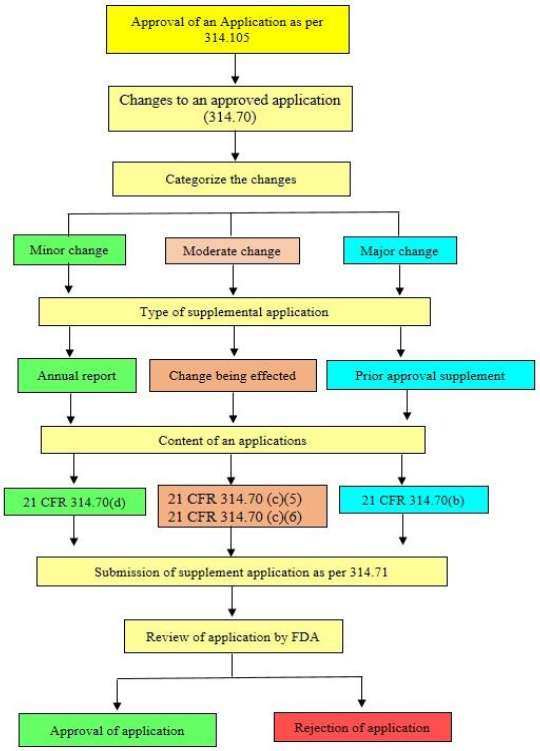

Figure 1: Flow Chart for Application Submission and Approval in US

European Union:

Amendment in variation regulation is governed under "Commission Regulation (EC) No 1234/2008." Guidance document provide details on classification of variation, submission process and approval of variation[16].

Categories of variation:

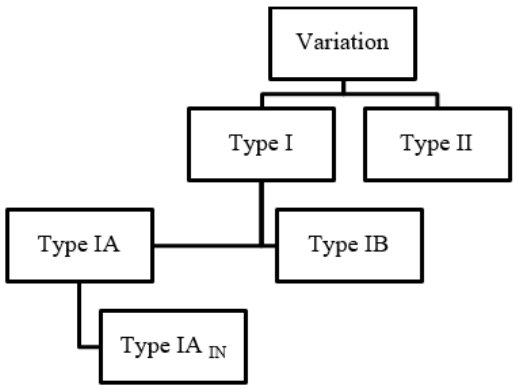

Figure 2: Classification of variation in EU

1) Minor variations (Type IA):
   - No prior approval
   - 'Do & Tell'
   - Notification within 12 months from amendment of variation
2) Minor variations (Type IB):
   - Notified before implementation of change.
   - 'Tell, wait & Do'
   - Waiting period: 30 days
3) Major variations (Type II):
   - Substantial effect on the Quality, Safety or Efficacy of drug product.
   - Variation is implemented after approval[16]

Approval process:

Approval procedure of Type IA: [15]

- Type IA variation excludes prior inspection by the regulatory agency. However, the notification of relevant variation is sent within 12 months from date of execution to the agency. Agency reviews Type IA

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notification and informs applicant about outcome by day 30. Immediate rejection is applied in case applicant fails to provide supporting documents.

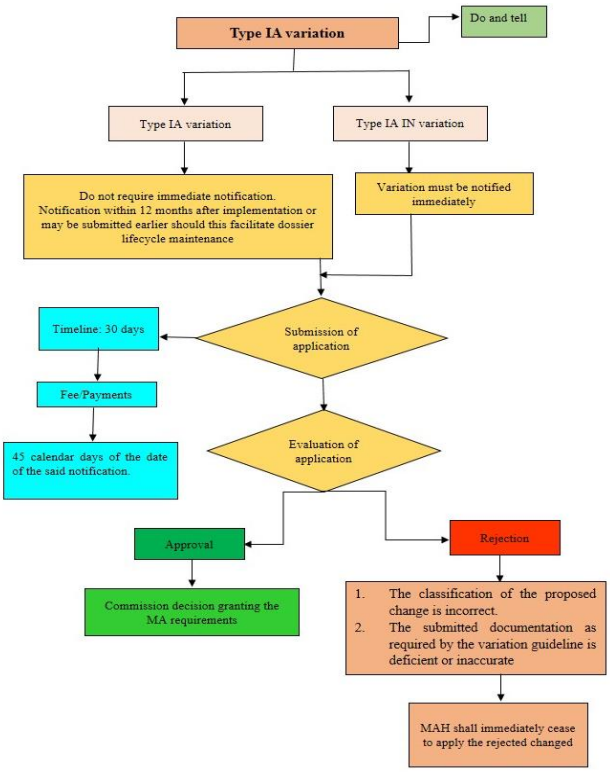


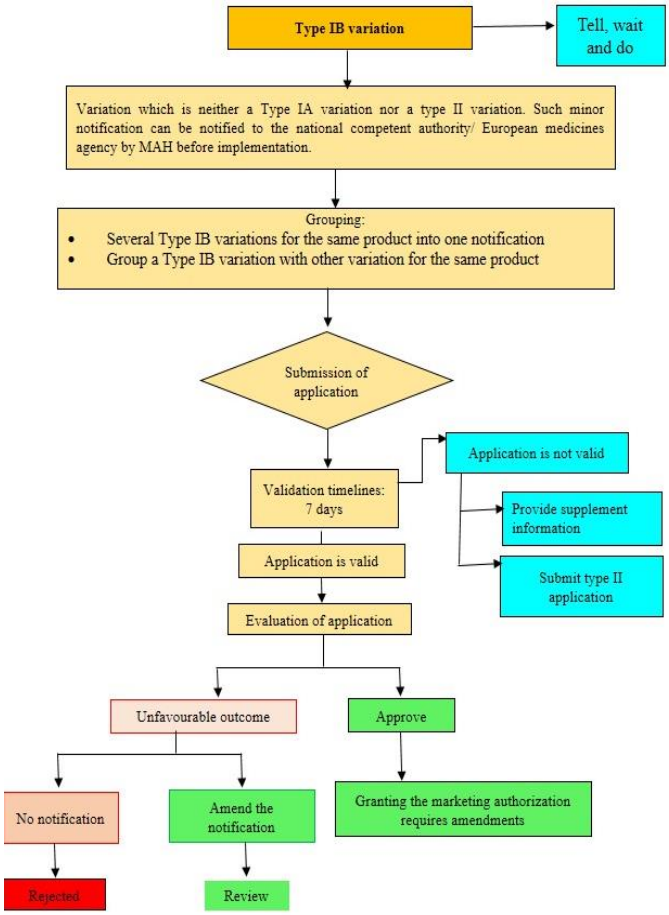
Figure 3: Approval procedure for Type IA variation in EU

Approval procedure of Type IB: [15]

Type IB notification is notified before implementation. 30 days wait period is applied to confirm that the notification is considered to be acceptable by the relevant regulatory agencies before executing variation. After receiving notification, it is handled as follows:

Within 7 calendar days agency evaluates application whether change is considered as Type IB variation or not. If not, application is rejected. If yes, applicant will be informed and procedure starts. After receiving acknowledgment of receipt, applicant should provide opinion on the notification by regulatory authority within 30 days. If applicant fails to get opinion from regulatory authority, then the notification is considered to be acceptable. For

Figure 4: Approval procedure for Type IB variation in EU



Approval procedure of Type II: [15]

Notification for major changes is submitted to concerned member states, to national competent authority. The authority will accept receipt of valid application and evaluation process will start. 60 days evaluation period will apply that can be decreased in case of emergency. If agency request for supplementary information, then 1-month suspension period is applied to justify the request. In case of mutual recognition procedure, reference member state prepares a draft evaluation result of variation and circulate them to the concerned member state to comment on variation within specified timeline. The final decision is provided by the reference member state by considering concerned member state's opinion.

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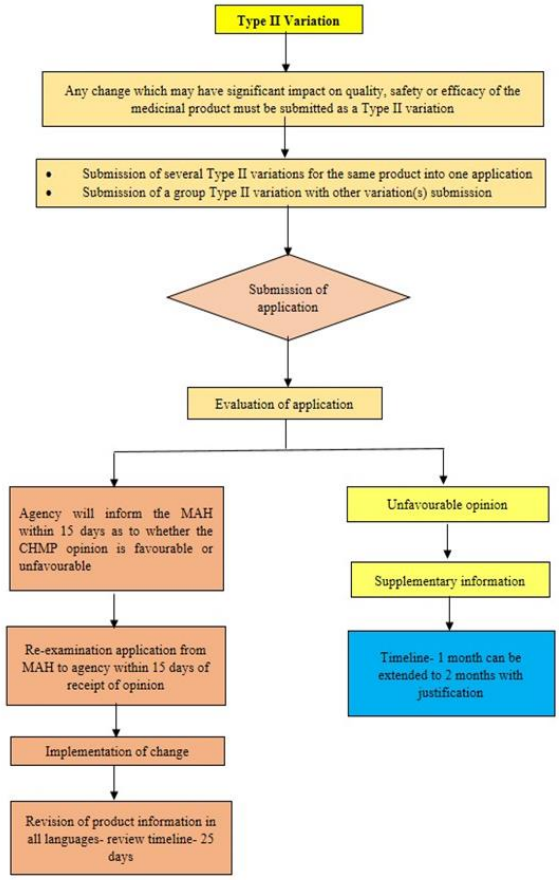

Figure 5: Approval procedure for Type II variation in EU

- Evaluation period of type II variation: 60 Days
  In the event of a safety emergency, this time frame may be shortened to 30 days, or it can extend to 90 days in order to group variations.

Comparison table of regulatory requirements on post-approval changes in USFDA, EMA.

TABLE 4: TYPES OF POST APPROVAL CHANGES

USFDA[14]	EMA[4,15]
Major Change • Change that has a Substantial Potential to have an adverse effect on the identity, strength, quality, purity, or potency of a drug product. • Prior Approval Supplement (PAS). • PDUFA V goal date – 4 months	**Type II Variation** • A significant impact on the Quality, Safety or Efficacy of a medicinal product. • Prior Approval Procedure. • Validation + (30, 60, 90) CHMP + 15 days to review and approve.
Moderate Change • It is a change that has a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product. • CBE 30 – Submission at least 30 days before distribution of the post change product. • CBE 0 – Distribution can occur when FDA receives the supplement.	**Type IB Variation** • Minor variation which is neither a Type IA variation nor a Type II variation nor an Extension. • Notification Procedure. • Validation + 30 days.
Minor Change • Minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product. • Annual Reportable.	**Type IA/IA IN Variation** • A minimal impact or no impact at all, on the quality, safety or efficacy of the medicinal product concerned. • Notification Procedure. • 30 days.

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Table 5: COMPARISON OF USFDA and EMA.

USFDA[14]	EMA[4,15]
1. Composition Changes:	
Major Changes	**Type II Variation**
Changes are those that are likely to have a significant impact on formulation quality and performance. Tests and filing documentation vary depending on the following three factors: therapeutic range, solubility, and permeability.	Qualitative or quantitative changes in one or more excipients that may have a significant impact on the safety, quality or efficacy of the medicinal product.
Moderate Changes Changes are those that could have a significant impact on formulation quality and performance.	**Type IB variation** Replacement of a single excipient with a comparable excipient with the same functional characteristics and at a similar level.
Minor Changes Changes are those that are unlikely to have any detectable impact on formulation quality and performance.	**Type IA variation** Any minor adjustment of the quantitative composition of the finished product with respect to excipients.
2. Manufacturing Site Changes:	
Major Changes	**Type II Variation**
A move to a different manufacturing site	Site which requires an initial or product specific inspection.
Moderate Changes	**Type IB**
A move to a different manufacturing site for the manufacture or processing of any drug product, in-process material, or drug substance that is not otherwise provided for in this guidance.	Site where any manufacturing operation(s) take place, except batch release, batch control, primary and secondary packaging, for non-sterile medicinal products.
Minor Changes	**Type IA**
A move to a different manufacturing site for secondary packaging	site for secondary packaging Deletion of manufacturing sites for an active substance, intermediate or finished product, packaging site.
3. Batch Size Changes:	
Major Changes	**Type II Variation**
Changes in batch size beyond a factor of ten times the size of the pilot/biobatch.	The change requires assessment of the comparability of a biological/immunological active substance.
Moderate Changes	**Type IB**
Change in batch size, up to and including a factor of 10 times the size of the pilot/bio-batch.	More than 10-fold increase compared to the originally approved batch size.
Minor Changes	**Type IA**
Not Mention	Up to 10-fold compared to the originally approved batch size.
4. Manufacturing Process Changes:	
Major Changes	**Type II Variation**
Change in the type of process used in the manufacture of the product, such as a change from wet granulation to direct compression of dry powder.	Substantial change to the manufacturing process of the active substance which may have a significant impact on the quality, safety or efficacy of the medicinal product.
Moderate Changes	**Type IB**
Any change in the process, process parameters, and/or equipment except as otherwise provided for in this guidance.	Minor change in the manufacturing process of an aqueous oral suspension.
Minor Changes	**Type IA**
Changes to equipment of the same design and operating principle.	Minor change in the manufacturing process.

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5. Container Closure System Changes:

Major Changes	Type II Variation
For liquid and semisolid dosage forms a change to or in polymeric materials of primary packaging components	The change relates to a less protective pack where there are associated changes in storage conditions and/or reduction in shelf life.
Moderate Changes	**Type IB**
A change in the size and/or shape of a container for a nonsterile drug product, except for solid dosage forms without a change from one container closure system to another.	Change in immediate packaging of semi-solid and non-sterile liquid pharmaceuticals.
Minor Changes	**Type IA**
A change in the number of unit or labelled amount of nonsterile solid dosage form in a multiple-unit container.	Change in shape or dimensions of the container or closure for non-sterile medicinal products.

6. Specifications changes:

Major Changes	Type II Variation
Relaxing an acceptance criterion except as otherwise provided for in this guidance.	Deletion of a specification parameter which may have a significant effect on the overall quality of the active substance and/or the finished product.
Moderate Changes	**Type IB**
Any change in a regulatory analytical procedure other than those identified as major changes or editorial changes.	Addition or replacement of a specification parameter with its corresponding test method as a result of a safety or quality issue.
Minor Changes	**Type IA**
Tightening of acceptance criteria.	Deletion of a non-significant specification parameter.

7. Stability changes:

Major Changes	Type II Variation
Change in a approved stability protocol.	Change in storage conditions of biological/ immunological active substances.
Moderate Changes	**Type IB**
Reduction of an expiration dating period to provide increased assurance of the identity, strength, quality, purity, or potency of the drug product.	Extension of the shelf life of the finished product.
Minor Changes	**Type IA**
Addition of time points to the stability protocol or deletion of time points beyond the approved expiration dating period.	Reduction of the shelf life of the finished product.

8. Labelling Changes:

Major Changes	Type II Variation
Changes based on post marketing study results, including, but not limited to, labelling changes associated with new indications and usage.	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data.
Moderate Changes	**Type IB**
Addition of an adverse event due to information reported to the applicant or Agency.	Implementation of change(s) for which no new additional data is required to be submitted by the MAH.
Minor Changes	**Type IA**
Changes in the layout of the package or container label.	Implementation of wording agreed by the competent authority.

9.Administrative Changes:

Not Mentioned	Type II Variation
	Not Mentioned.
Not Mentioned	**Type IB**

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	Change in the (invented) name of the medicinal product.
Not Mentioned	**Type IA**
	Change in the name and/or address of: a manufacturer.

References

1. U.S. Food and Drug Administration [Internet]. Availablefrom:https://www.fda.gov/regulatory-information/search-fda-guidance-documents/supac-mr-modified-release-solid-oral-dosage-forms-scale-and-postapproval-changes-chemistry [Accessed on 03 August 2023].
2. Lokesh MS, Gupta NV, Belagoankar BD. Comparative study of process of post approval change application submission and approval for marketing authorization variations in EU, US, India, Saudi Arabia and Singapore. Int J Drug Dev Res. 2015 7(1):0975-9344.
3. European Medicines Agency. Type-IA variations: questions and answers - European Medicines Agency [Internet]. European Medicines Agency. 2018. Available from: https://www.ema.europa.eu/en/human-regulatory/post-authorisation/variations/type-ia-variations-questions-answers [Accessed on 03 August 2023]
4. Commission regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorizations for medicinal products for human use and veterinary medicinal products (Text with EEA relevance) [Internet].Availablefrom:https://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:334:0007:0024:en:PDF [Accessed on 04 August 2023]
5. Guidance for Industry Changes to an Approved NDA or ANDA [Internet]. 2004. Available from: https://www.fda.gov/files/drugs/published/Changes-to-an-Approved-NDA-or-ANDA.pdf [Accessed on 04 August 2023]
6. Ahmed SS, Shailesh T, Kumar HS, Gangadharappa HV, Gowrav MP. An overview on post approval changes to an approved ANDA in US-FDA. Res J Pharma Tech. 2021;14(1):506-12. [Accessed on 05 August 2023] Available from: https://www.indianjournals.com/ijor.aspx?target=ijor:rjpt&volume=14&issue=1&article=092
7. Ankit T, Shrikalp D, Maitreyi Z, Praveenkumar J, Kiran K. Regulatory procedure of post approval changes and comparative requirements of EU and USA regulatory regions. Journal of Pharmaceutical Research International. 2021 Oct 21;33(46B):304-17.[Accessed on 07 August 2023]Available from: https://doi.org/10.9734/jpri/2021/v33i46B32944
8. Kumar P, Yadav V, Kaushik D. Post-Approval Changes in Pharmaceuticals: Regulatory Perspectives in Europe. Applied Clinical Research, Clinical Trials and Regulatory Affairs. 2015 1;2(2):60-8. [Accessed on 10 August 2023] Available from: https://www.eurekaselect.com/article/71057
9. Chakraborty K, Yadav K. Drug approval process in US, Europe and India and its regulatory requirements: A Review. International Journal of Drug Regulatory Affairs (IJDRA).2018;6(3):31-9. https://www.indianjournals.com/ijor.aspx?target=ijor:ijdra&volume=6&issue=3&article=005
10. Kamnoore K, Venkatesh MP, Kumar TM. Study on post approval source change of active pharmaceutical ingredient in the finished product and its regulatory requirements in EU and US. 2022;46(1):11-9. [Accessed on 14 August 2023] Available from: https://digital.car.chula.ac.th/tjps/vol46/iss1/2/
11. Goswami M, Maheshwari. Comparative Study of Regulatory Requirements for Post- Approval Changes in Us, Europe & South Africa. J Pharma BR [Internet].2014 [Accessed on 19 August 2023] Available from: https://www.sierrajournals.com/index.php/IJAPSR/article/view/981
12. Van Buskirk GA, Asotra S, Balducci C, Basu P, DiDonato G, Dorantes A, Eickhoff WM, Ghosh T, González MA, Henry T, Howard M. Best practices for the development, scale-up, and post-approval change control of IR and MR dosage forms in the current quality-by-design paradigm. AAPS PharmSciTech. 2014 Jun;15:665-93. [Accessed on 24 August 2023] Available from:

Journal of Chemical Health Risks

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JCHR (2024) 14(5), 1728-1738 | ISSN:2251-6727

https://link.springer.com/article/10.1208/s12249-014-0087-x

13. Guidance for Industry NDA or ANDA https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=314.70
14. Changes to an Approved NDA or ANDA [Internet]. [cited 21 june 2024]. Available from: https://www.fda.gov/media/71846/download
15. M L, Gupta V, Belagoankar B. Comparative Study of Process of Post Approval Change Application Submission and Approval for Marketing Authorization Variations in EU, US, India, Saudi Arabia and Singapore [Internet]. 2015 [cited 9 June 2024]. Available from: http://www.ijddr.in/drug-development/comparative-study-of-process-of-post-approval-change-applicationsubmission-and-approval-for-marketing-authorization-variations-in-euus-india-saudi-arabia-and-singapore.php?aid=5470