A Step of Challenge to Post-Approval Change Management Protocol (PACMP)

12th APAC
Manufacturing, Quality Control and Supply-TF
(MQS-TF)

The views and opinions expressed in this presentation are those of the presenter and should not necessarily represent the views and opinions of the regulated laws.

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Expansion of PACMP utilization in Asia

MQS would like to propose to discuss the benefit of PACMP to both industry and regulatory authority at 12th APAC meeting. MQS TF would like your support and cooperation for the success of next year's session

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A. Change Controls

A2. What post approval changes categories are applicable in your economy?

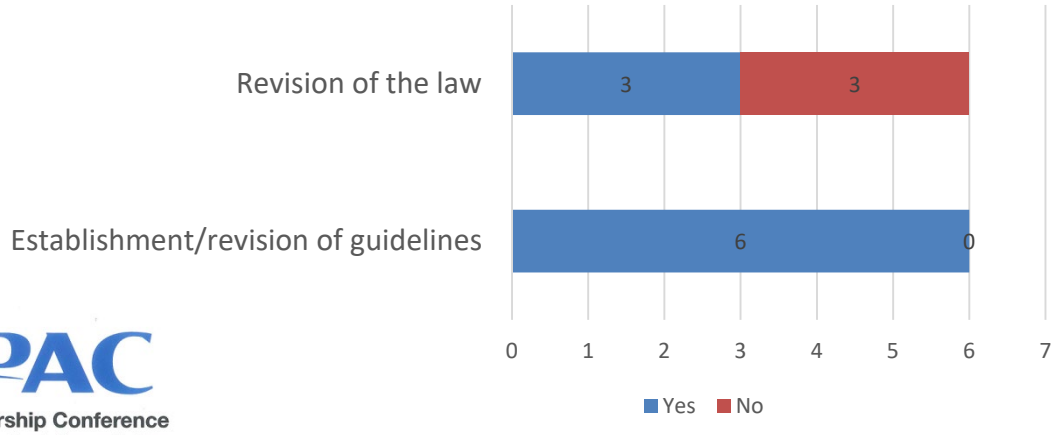
Category	US	EU	Japan	Economy A	Economy B	Economy C	Economy D	Economy E	Economy F
Major	PAS	Type II	Supplement	MaV	Major	MIV-1	Major	Major	PAC-1 (Major)
Moderate	CBE-30	Type IB	Notification	MiV-PA	Minor	MIV-2	Minor	Minor-PA	PAC-2 (Minor)
Moderate/Minor	CBE-0	Type IA_{IN}		-	IR		-	-	
Minor	AR	Type IA		MiV—N	AR		Notification	Notification -Minor	

Tell & Do

Do & Tell

B. PACMP

B3. Please check the actions required when introducing PACMP in your economy?



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B. PACMP

B3. What do you think are the benefits of PACMP introduction?

Benefit	Economy A	Economy B	Economy C	Economy D	Economy E	Economy F
Implementing change in a predicable	YES	YES	YES	YES	YES	
Faster implementation of the change	YES		YES		YES	YES
A potential down grade of change category	YES		YES			
Ensuring supply continuity of medicines	YES				YES	
Improvement of quality management system in line with the global harmonization		YES				
Minimizing administrative work			YES			

All economy think that PACMP is useful, and many economies expect implementing change in a predicable and faster implementation of the change.

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B. PACMP

B4. If you think there is any concern that may occur in future, if the introduction of PACMP system is delayed in your economy whereas the approvals based on PACMP in other economies have become a common practice, please describe it.

Any concerns	Economy A	Economy B	Economy C	Economy D	Economy E	Economy F
Affecting approval timeline (Longer, being delayed)	YES		YES		TBD	
Country specific behaviors (More data, following specific guideline)	YES			YES		YES
Left behind from other countries (Recall risk, not being prioritized)	YES	YES	YES			
Supply impact (unstable)	YES		YES			

A half of economies have any concerns for their economy specific matters, and for affected to being left behind from other economies.

TECHNICAL AND REGULATORY CONSIDERATINS FOR PHARMACEUTICAL PRODUCT LIFECYCLE MANAGEMENT

ICH Q12

A new ICH guideline topic since 2014 to discuss the pharmaceutical product lifecycle.

The guideline discuss on the introduction to change categories and tools that are useful to manage the product throughout the lifecycle based on the contents in ICH Q8-Q11, for the effective and efficient review of the proposed changes to sustain the stable supply of product and introduce innovations.

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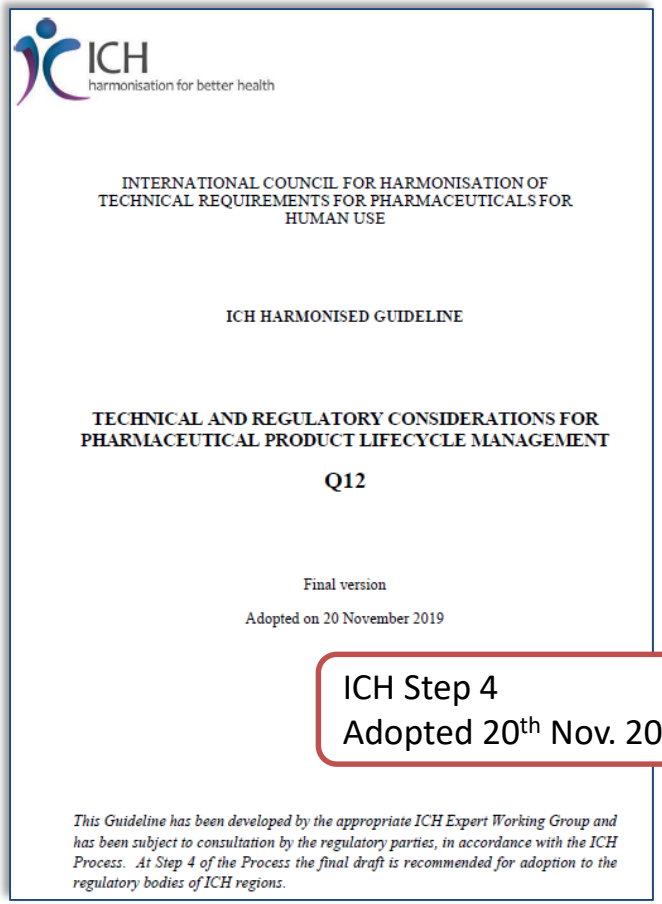
TECHNICAL AND REGULATORY CONSIDERATINS FOR PHARMACEUTICAL PRODUCT LIFECYCLE MANAGEMENT
ICH Q12



ICH harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

TECHNICAL AND REGULATORY CONSIDERATIONS FOR PHARMACEUTICAL PRODUCT LIFECYCLE MANAGEMENT

Q12

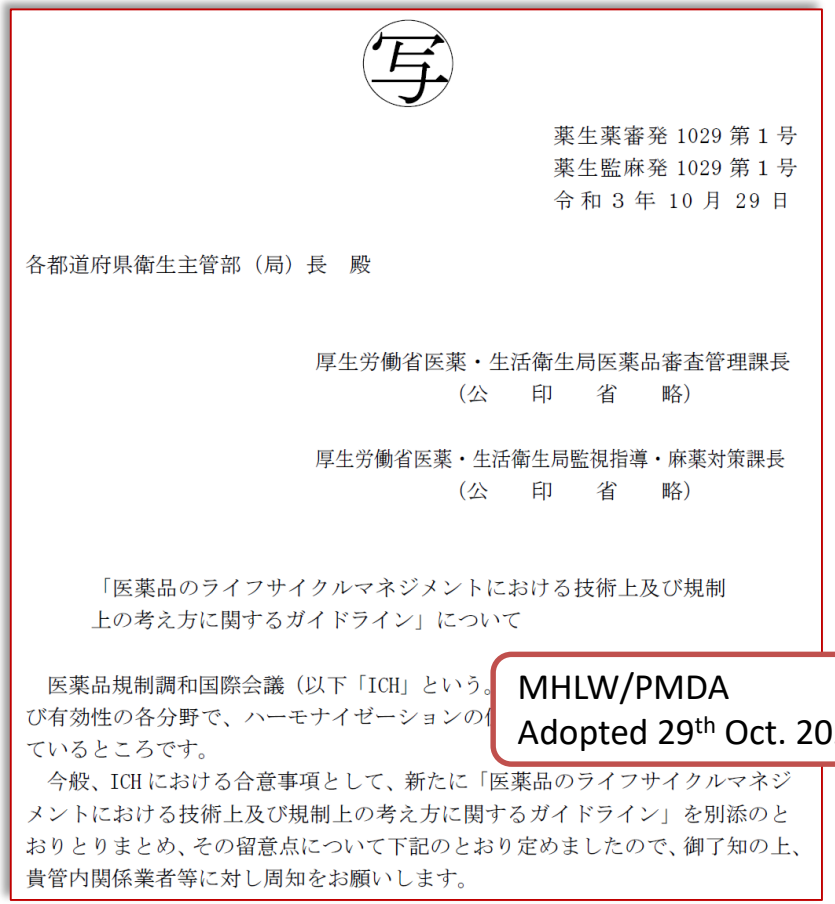
Final version

Adopted on 20 November 2019

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of ICH regions.

ICH Step 4
Adopted 20th Nov. 2019

1yr



写

薬生薬審発 1029 第 1 号
薬生監麻発 1029 第 1 号
令 和 3 年 10 月 29 日

各都道府県衛生主管部（局）長　殿

厚生労働省医薬・生活衛生局医薬品審査管理課長
（公　　印　　省　　略）

厚生労働省医薬・生活衛生局監視指導・麻薬対策課長
（公　　印　　省　　略）

「医薬品のライフサイクルマネジメントにおける技術上及び規制上の考え方に関するガイドライン」について

医薬品規制調和国際会議（以下「ICH」という。び有効性の各分野で、ハーモナイゼーションの…ているところです。

今般、ICH における合意事項として、新たに「医薬品のライフサイクルマネジメントにおける技術上及び規制上の考え方に関するガイドライン」を別添のとおりとりまとめ、その留意点について下記のとおり定めましたので、御了知の上、貴管内関係業者等に対し周知をお願いします。

MHLW/PMDA
Adopted 29th Oct. 2021

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ICH Q12 Chapter 4

POST-APPROVAL CHANGE MANAGEMENT PROTOCOL (PACMP)

- A PACMP is a **regulatory tool that provides predictability and transparency in terms of the requirements and studies needed to implement a change** as the approved protocol provides an agreement between the MAH and the regulatory authority
- A means of method to **make changes to the Established Condition (EC) under efficient and predicable approach** under the protocol and execution
- A PACMP can address one or more changes for a single product, or may address one or more changes to be applied to multiple products
- The PACMP may be submitted with the original MAA or subsequently as a stand-alone submission
- **The PLCM document can be located in CTD Module 3.2.R. (In some regions, the PLCM may be included in Module 1)**

POST-APPROVAL CHANGE MANAGEMENT PROTOCOL (PACMP)

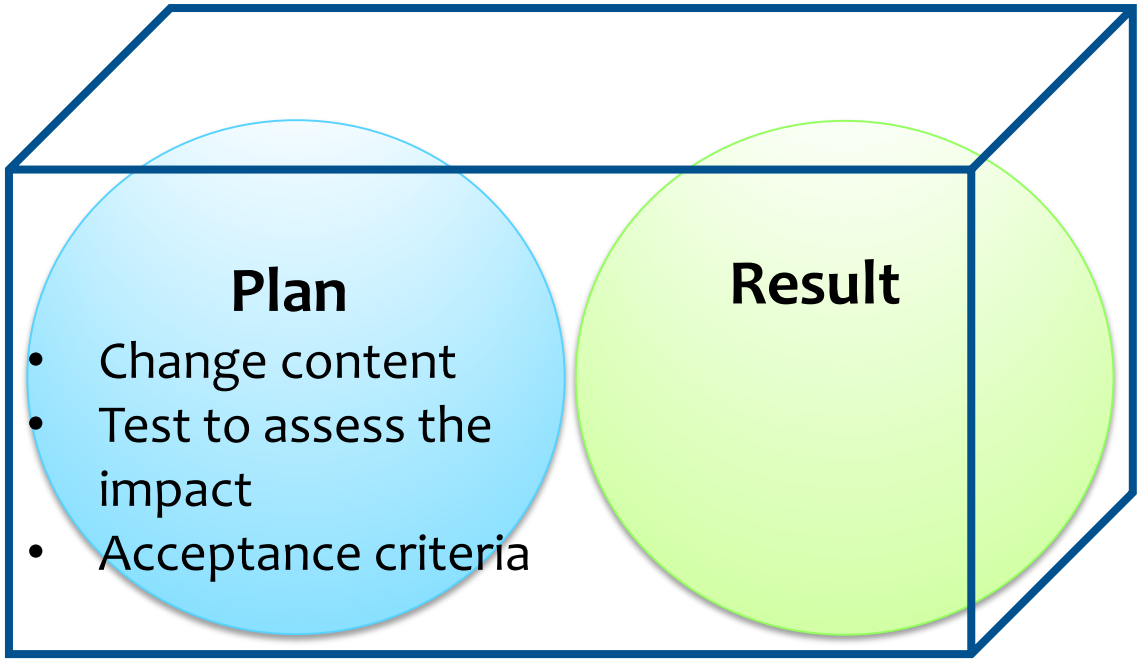
Step 1

- Submit Protocol
  - Change proposal based on scientific sound logic
  - Risk management activities
  - Proposed approach (study) and acceptance criteria to assess the change impact
  - Any other fulfilling condition (is available)
  - Proposed change category
  - Any other justification to support the change
- Need to be approved by regulatory agency

Step 2

- Execute the experiment and work as in the protocol
- Confirm that the result have fulfil the acceptance criteria and any other condition in the protocol and submit such results to the regulatory agency according to the protocol
- In some cases, some change category may not be necessary to obtain an approval from the regulatory agency

Ordinary Partial Change



Submit test plan and result as a package for the review

May be asked for additional test

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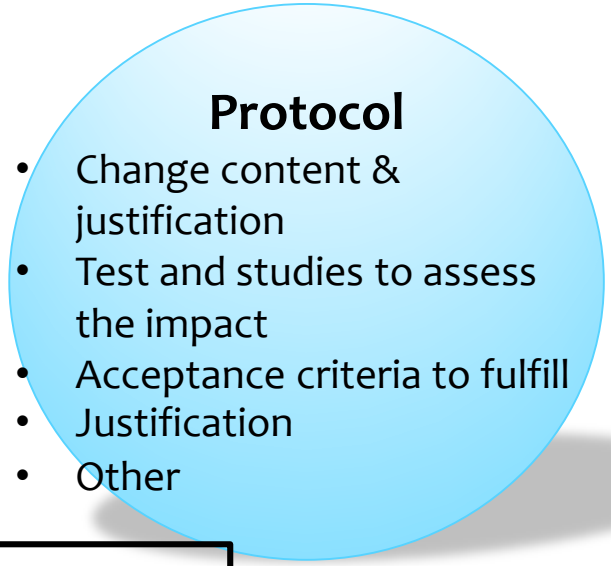
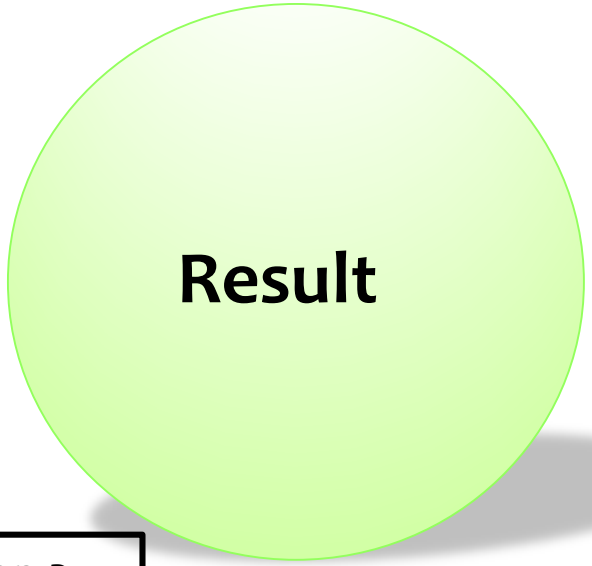
When Using PACMP





Step 1

Submit PACMP→content is assess and approved by regulatory agency

In Japan, as a step 1, "**Application for Change Protocol Review**" is created

Step 2

- Execute test and studies as in PACMP
- In case obtain results/data satisfied the acceptance criteria and other conditions in the protocol, MAH will submit such information to the regulatory agency and assess (depending on the change category, there may be a case additional approval is not necessary)

In Japan, step 2 process is "**Submission of implementing changes in accordance with change protocol**"

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PACMP in Global

"Comparability protocols" have been in US regulations for decades

- US comparability protocol draft guidance in 2003 and 2016 and final guideline published in Oct. 2022

"PACMPs" have been part of EU regulations since 2010

- EMA Q&A published in 2012

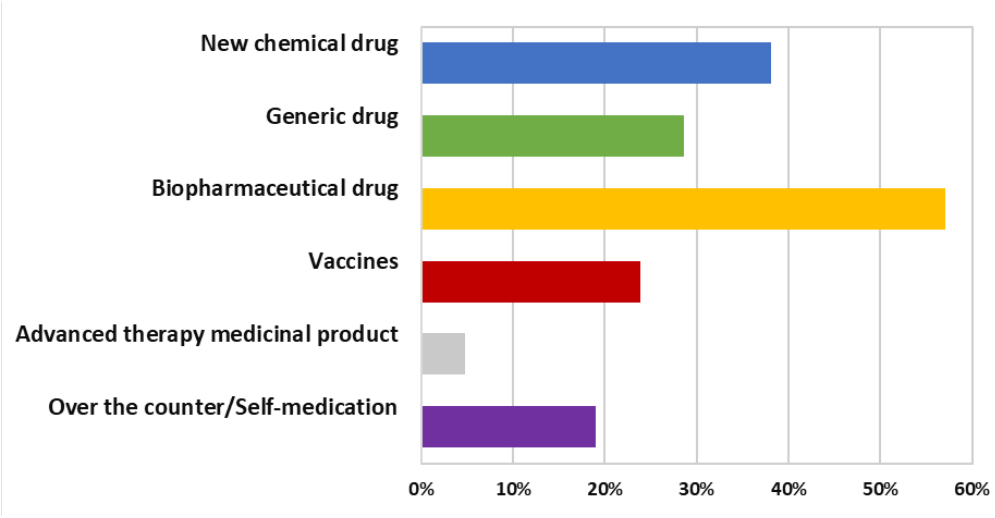
Japan performed a pilot program for PACMPs in 2018 and included in the regulation from 2021

- Step 1 is through a meeting rather than a variation

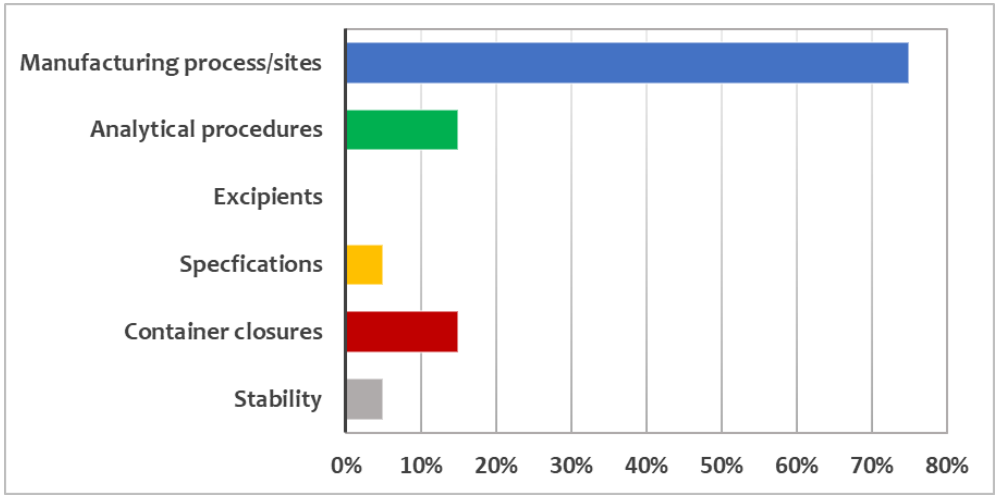
A few countries will accept PACMPs even though not specifically in regulations (e.g., Switzerland, South Africa)

Example of PACMP in EU

What kind of product was applied to PACMP?



What kind of change was applied to PACMP?



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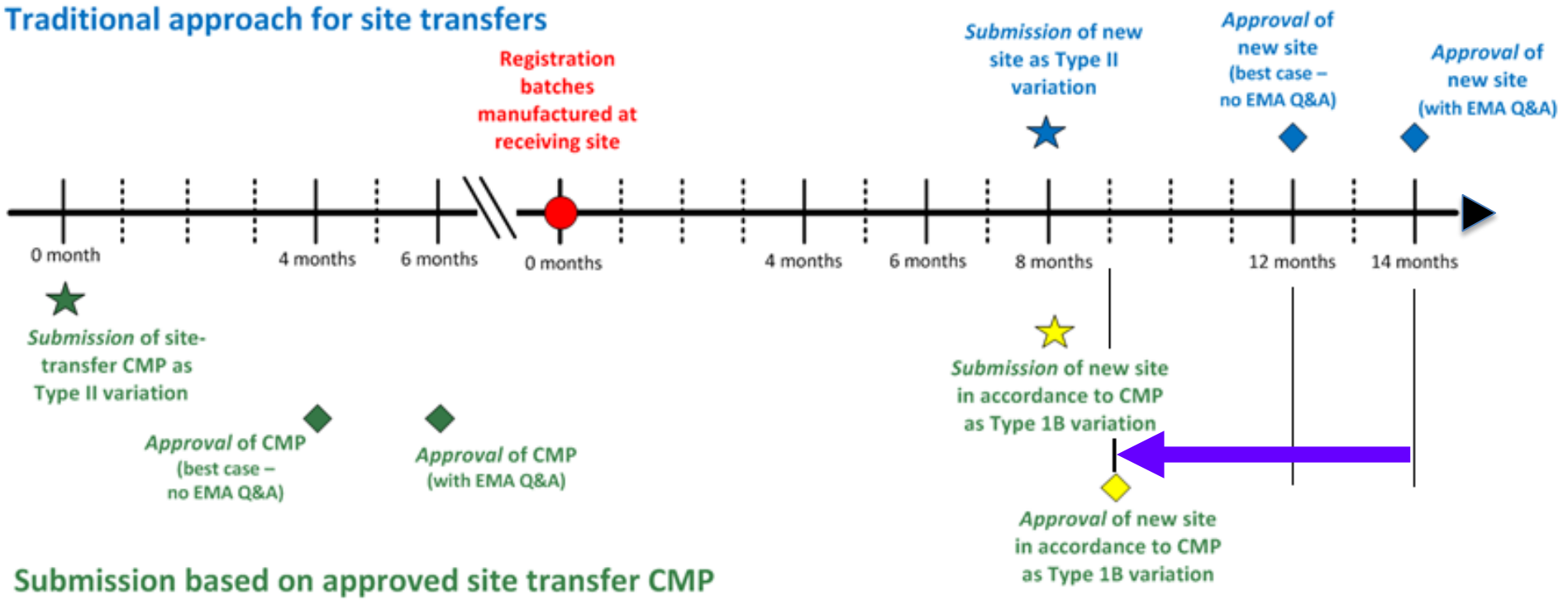
Example (EU): Biologics DS manufacturing site transfer - Benefit of PACMP Approach vs. „Traditional“ Approach*



➢ **3-5 months faster approval of the site change using a PACMP**

**Note: approval timelines for type II variation in this scheme include positive CHMP opinion and Commission Decision*

Revising Change Control Process Management to PACMP

Benefit of Introduction

* For the submission that may take a time to review, there is **a potential to shorten the review period**

* Since the change process starts with initial submission, there will be a flexibility to set the timing to implement the process change and replacement of the product with changed process, that **effectively contributes the supply chain management**

* When a company create a change protocol, it is necessary to collect enough information on the new method or new technology. Therefore, **a potential enhancement in the capability of using innovative technology and/or quality control**

※ May not applicable to all pharmaceutical products

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Benefit of PACMP

- **Realization of review of change and GMP inspection** in 2 steps of PACMP
- **A potential down grade of change category** in a predicable manner (exclude some products)
- **Clarify the conditions to implement change in a predicable and under transparency** (change implemented in accordance with agreed protocol)
- **Faster implementation of the change** by satisfying the PACMP condition for the faster release of pharmaceutical products to the patient
- **A potential tool to introduce break through technology** and early phase application, if there is an agreement

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