Update of Q12 Implementation in Japan

Satomi Yagi

Reviewer, Office of New drug IV

Topic lead of ICH Q12 IWG

Pharmaceuticals and Medical Devices Agency (PMDA)

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

Please keep in mind

- Detailed regulations for implementation of ICH Q12 are still under discussion.
- Today I will introduce the DRAFT version of PACMP in Japan and this is subject to change.

Agenda

- Toward implementation of ICH Q12
- PACMP pilot program in Japan
- PACMP based on updated act

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Toward implementation of ICH Q12

- PMDA ICH Q12 WG
  - Members: Associate Center Director, Office Director, Reviewers (chemical, biologic, generic), Inspectors
  - Discuss regulatory, technical and practical issues to implement Q12 within PMDA

- AMED Research Group
  - Members: NIHS, Industries, PMDA
  - Discuss technical and practical issues
  - Report the outcome and proposal to MHLW

- MHLW/PMDA-FPMAJ Task Force
  - Members: MHLW, PMDA, FPMAJ
  - Driven by *"domestic problems"* (not by ICH Q12)
  - rationalize the regulatory procedures for post-approval CMC changes

NIHS: The National Institute of Health Sciences
MHLW: Minister of Health Labor and Welfare
FPMAJ: The Federation of Pharmaceutical Manufacturers' Associations of JAPAN

Toward implementation of ICH Q12

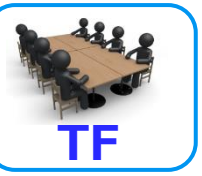
- To Understand Q12 guideline in Japan
  - Will hold briefing session

Q12 J-IWG (JAPAN sub-team)

- Established Conditions （ECs）
  - What is EC/not EC?
  - what is categorized as Partial Change Application/Minor Change Notification?
  - How to describe ECs and their reporting categories (Table/ Flow chart/ Description)

AMED TF

- PACMP
  - Discuss about detailed regulations of PACMP
  - Update our software for new PACMP application
  - Create PACMP mock-up



AMED

AMED(Japan Agency for Medical Research and Development) Research Group; consist of NIH, PMDA, academia and industry

TF(Task force); consist of MHLW, PMDA and industry

Q12 J-IWG(JAPAN sub-team); JPMA and PMDA member of ICH Q12 IWG

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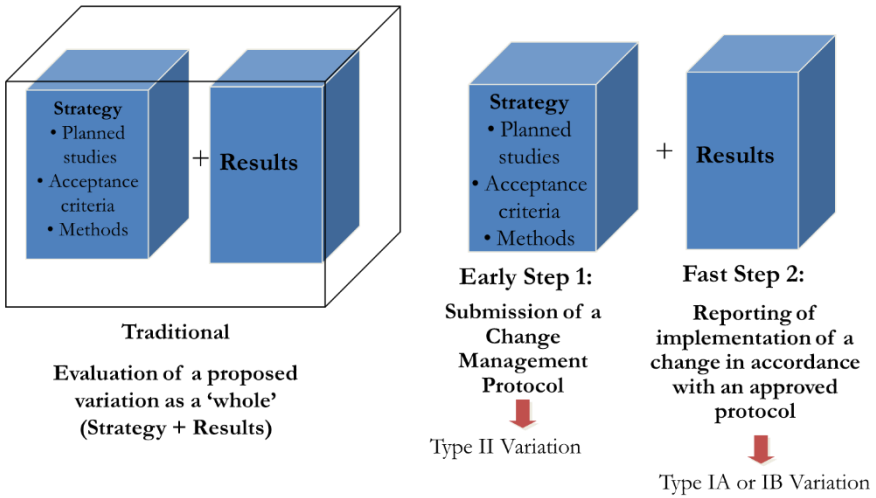
Post-Approval Change Management Protocol (PACMP)

- Regulatory tool that provides predictability and transparency in terms of the requirements and studies needed to implement a CMC change as the approved protocol provides an agreement between the MAH and the regulatory authority
- Already implemented in US (2003-) and EU (2010-)
- PMDA started PACMP pilot program* since April 2018

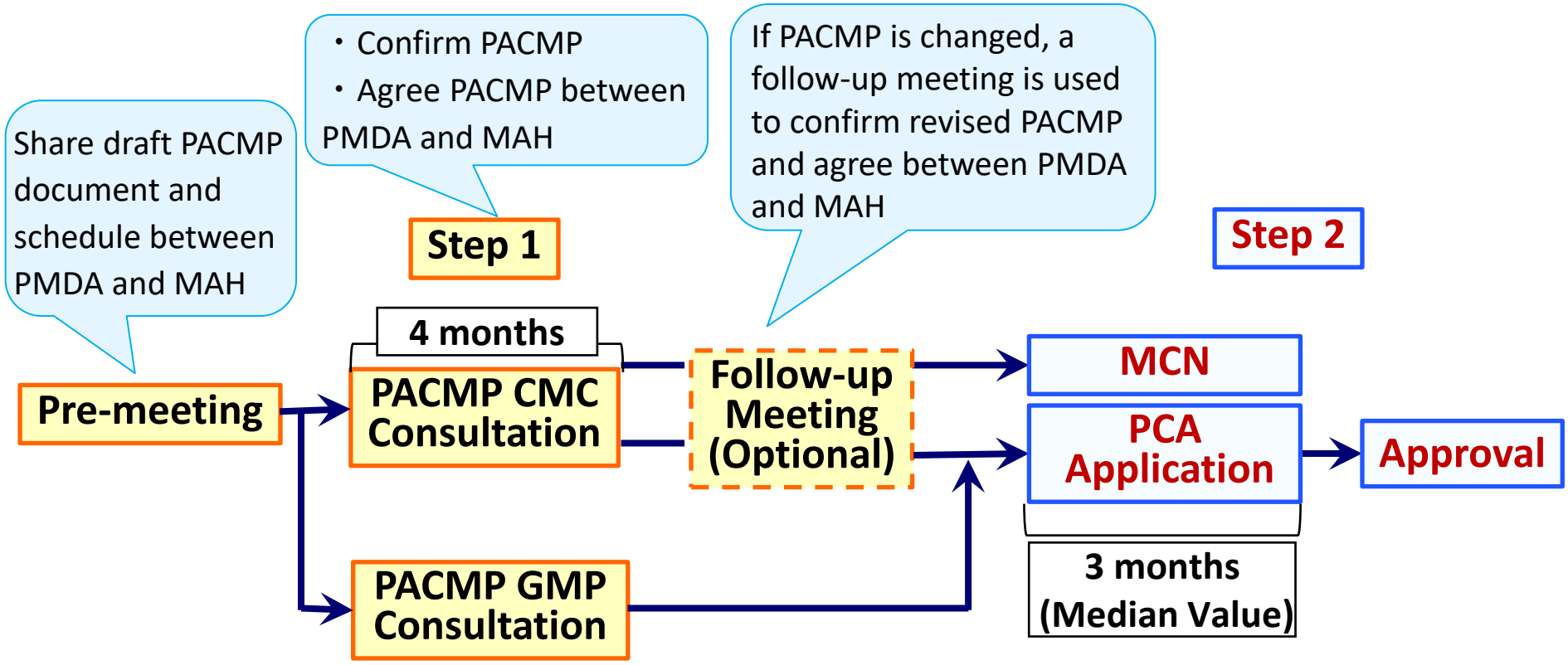
(EU) Principle of PACMP



Questions and answers on post approval change management protocols (EMA/CHMP/CVMP/QWP/586330/2010)

* "Handling of Changes to Approved Product Information Pertaining to the Quality of Drugs" (PSEHB/PED Notification No. 0309-1 and PSEHB/CND Notification No. 0309-1 dated March 9, 2018, jointly issued by the Director of the Pharmaceutical Evaluation Division and the Director of the Compliance and Narcotics Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

Overview of PACMP pilot program in Japan



PCA: Partial Change Approval
MCN: Minor Change Notification

Experiences in PACMP Pilot Program

- From April 2018 to Nov 2020…
  - Number of consultations?
    - more than 10
  - Biotechnological/Biological or small molecule?
    - Biotechnological/Biological: approx. 80%
    - Small molecule: approx. 20%
  - Details of the change?
    - The most common cases are as follows;
      - Addition of new manufacturing site
      - Extension of shelf life

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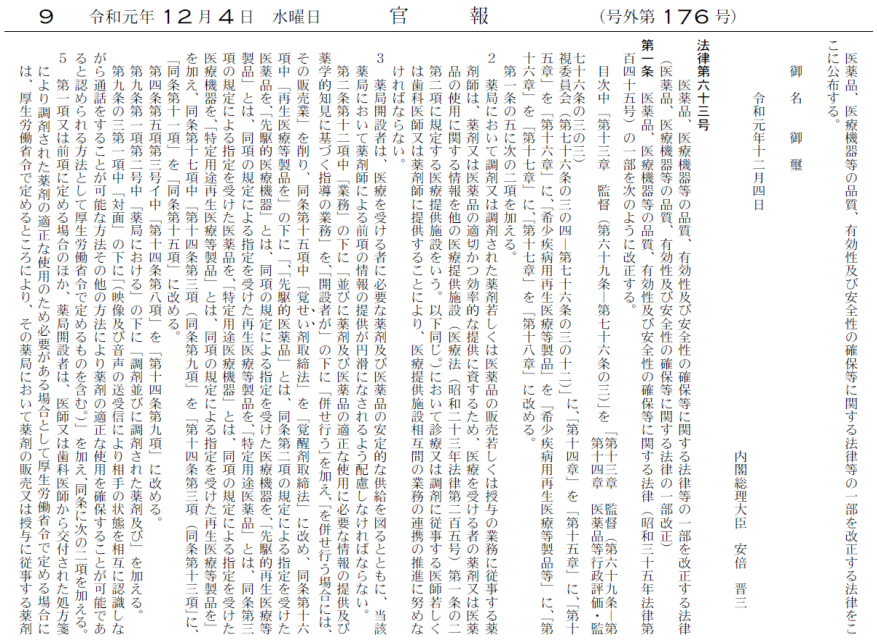
Updated act will come !

- We have introduced the PAMCP into our regulation, ‘Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices’.
- The updated act will come into effect next year.
- Now, PMDA/MHLW are working on detailed regulations of PACMP for the implementation of the updated Act.



９　令和元年１２月４日　水曜日　官　報　（号外第１７６号）

医薬品、医療機器等の品質、有効性及び安全性の確保等に関する法律等の一部を改正する法律をここに公布する。

御名御璽

令和元年十二月四日

内閣総理大臣　安倍　晋三

法律第六十三号

医薬品、医療機器等の品質、有効性及び安全性の確保等に関する法律等の一部を改正する法律

（医薬品、医療機器等の品質、有効性及び安全性の確保等に関する法律の一部改正）

第一条　医薬品、医療機器等の品質、有効性及び安全性の確保等に関する法律（昭和三十五年法律第百四十五号）の一部を次のように改正する。

目次中「第十三章　監督（第六十九条―第七十六条の三）」を「第十三章　監督（第六十九条―第七十六条の三の三）」に、「第十四章　医薬品等行政評価・監視委員会（第七十六条の四―第七十六条の十二）」を「第十四章　医薬品等行政評価・監視委員会（第七十六条の四―第七十六条の十二）」に、「第十五章」を「第十六章」に、「第十六章」を「第十七章」に、「第十七章」を「第十八章」に改める。

第一条の五に次の二項を加える。

2　薬局において調剤又は調剤された薬剤若しくは医薬品の販売若しくは授与の業務に従事する薬剤師は、薬剤又は医薬品の適切かつ効率的な提供に資するため、医療を受ける者の薬剤又は医薬品の使用に関する情報を他の医療提供施設（医療法（昭和二十三年法律第二百五号）第一条の二第二項に規定する医療提供施設をいう。以下同じ。）において診療又は調剤に従事する医師若しくは歯科医師又は薬剤師に提供することにより、医療提供施設相互間の業務の連携の推進に努めなければならない。

3　薬局開設者は、医療を受ける者に必要な薬剤及び医薬品の安定的な供給を図るとともに、当該薬学的知見に基づく指導の業務」を「開設者が」の下に「併せ行う」を加え、「を併せ行う場合には、その販売業」を削り、同条第十五項中「覚せい剤取締法」を「覚醒剤取締法」に改め、同条第十六項中「再生医療等製品を」の下に「、先駆的医薬品」とは、同条第二項の規定による指定を受けた医薬品を、先駆的医療機器」とは、同項の規定による指定を受けた医療機器を、先駆的再生医療等製品」とは、同項の規定による指定を受けた再生医療等製品を、特定用途医薬品」とは、同条第三項の規定による指定を受けた医薬品を、特定用途医療機器」とは、同項の規定による指定を受けた医療機器を、特定用途再生医療等製品」とは、同項の規定による指定を受けた再生医療等製品を」を加え、同条第十七項中「第十四条第三項（同条第九項」を「第十四条第三項（同条第十一項」に、「同条第十一項」を「同条第十五項」に改める。

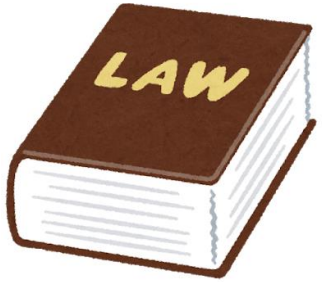
第四条第五項第三号イ中「第十四条第八項」を「第十四条第九項」に改める。

第九条第一項第二号中「薬局における」の下に「調剤並びに調剤された薬剤及び」を加える。

第九条の三第一項中「対面」の下に「（映像及び音声の送受信により相手の状態を相互に認識しながら通話をすることが可能な方法その他の方法により薬剤の適正な使用を確保することが可能であると認められる方法として厚生労働省令で定めるものを含む。）」を加え、同条に次の二項を加える。

5　第一項又は前項に定める場合のほか、薬局開設者は、医師又は歯科医師から交付された処方箋により調剤された薬剤の適正な使用のため必要がある場合として厚生労働省令で定める場合には、厚生労働省令で定めるところにより、その薬局において薬剤の販売又は授与に従事する薬剤

Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices



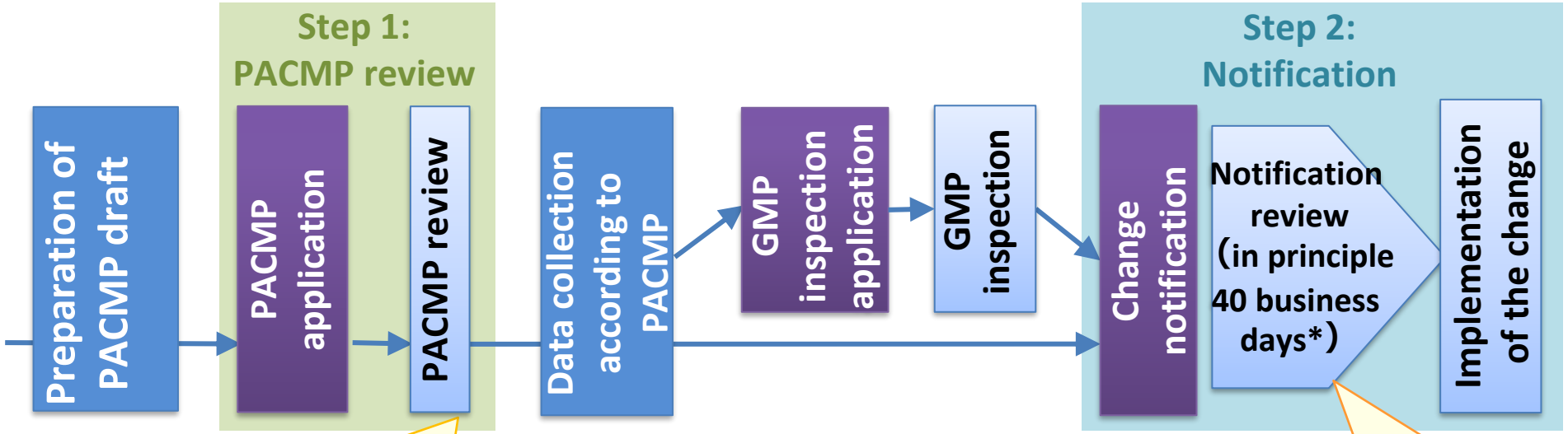
PACMP based on updated act

- Step1
- For changes to approval items related to quality of pharmaceuticals, MAH submit PACMP to MHLW.
- The protocol is reviewed and approved by PMDA/MHLW.

- Step2
- The tests and studies outlined in the protocol are performed.
- If the results/data generated meet the acceptance criteria in the protocol and any other conditions are met, the MAH submits "Notification based on the approved PACMP" to MHLW.
- The change based on PACMP may be implemented if no inquiries are received within 40 or 20 business* days after submitting "Notification based on the approved PACMP" .

*: still under discussion

Outline of PACMP based on updated act



At **PACMP review** process, if a proposed change may significantly affect the quality, it will not be endorsed. In addition, if it is found that a proposed change was out of scope of the system after PACMP review, retraction may occur.

In case a change does not follow PACMP, suspension of a change may be ordered.

Use of PMDA consultation (Optional)

Preliminary consultation | F2F consultation | Post-meeting consultation

e.g.
- Company activities
- Action from company to Agency
- Agency's activity

*: still under discussion

Major Differences

PACMP Pilot Program vs PACMP based on updated act

	PACMP Pilot Program	PACMP based on updated act
Review of PACMP	As PMDA consultation	As application to MHLW
Scope	Prescription drugs (New drugs and marketed products, Biological and chemicals)	Prescription drugs, Cellular and tissue-based products, OTC drugs, Quasi-drugs, and Cosmetics that require approval by MHLW (Pharmaceuticals approved by the governor are excluded)
GMP inspection	By PMDA	By PMDA and prefectural governments
PACMP in original submission	Not available	Will be available
Step2 period	About 3 months	In principle 40 business days (a special case: 20 business days)*
Reporting category(step2)	PCA(prior approval) or MCN(notification)	Notification (Prior notification before implementation of the change)

This is a current plan and subject to change

*: still under discussion

Summary

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  - Will hold briefing session
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Thank you for your attention!

Acknowledgements

- ICH Q12 EWG/IWG
- PMDA Q12 EWG/IWG(Shinichi Okudaira, Yasuhiro Kishioka, Kentaro Hara)
- AMED Research group
- MHLW/PMDA-FPMAJ Task Force
- PMDA Q12 Working Group