Webinar

Unlocking efficiency through reliance: Navigating the EMA post-authorization framework

3 April 2025

13:30-15:00 Central European Time

Translations will be provided in French, Portuguese, and Spanish

Agenda

1) EMA's current post-authorization framework (variations) with related tools for reliance *(15 min)*

- Elsie Merken *(Scientific Officer Procedures Office, EMA)*

2) Reliance for PACs in practice *(10 min)*

- Asmaa Fouad *(Head of Central Administration of Biological & Innovative Products & Clinical Trials at EDA, Egypt, and representative of EDA in ICH. Advisory member of ECBS-WHO)*

3) Q&A Session *(15 min)*

Moderator: Andrew Deavin *(Senior Director Vaccines Global Regulatory Affairs Asia Pacific & China, Vaccines Europe)*

Participants:

- Elsie Merken *(Scientific Officer Procedures Office, EMA)*
- Victoria Palmi Reig *(Senior International Affairs officer, EMA)*
- Alberto Gañán Jiménez *(Head of Committees and Quality Assurance Department, EMA)*
- Isabelle Colmagne-Poulard *(Head of International Global Regulatory & Scientific Policy, Merck)*
- Susanne Ausborn *(Global Head International Regulatory Policy, Roche, EFPIA)*
- Asmaa Fouad *(Head of Central Administration of Biological & Innovative Products & Clinical Trials at EDA, Egypt, and representative of EDA in ICH. Advisory member of ECBS-WHO)*
- Marie Valentin *(Team Lead, Facilitated Product Introduction, Regulation and Prequalification Department, World Health Organisation)*

4) EMA's future post-authorization framework (variations) *(15 min)*

- Virginia Rojo Guerra *(Head of Procedures Office, EMA)*

Agenda

5) EMA's renewal framework *(10 min)*

- Rachel Turner *(Scientific Officer Therapies for Endocrine and Cardiovascular Diseases Office, EMA)*

6) Q&A Session *(15 min)*

Moderator: Isabelle Colmagne-Poulard *(Head of International Global Regulatory & Scientific Policy, Merck, EFPIA)*

Participants:

- Elsie Merken *(Scientific Officer Procedures Office, EMA)*
- Virginia Rojo Guerra *(Head of Procedures Office, EMA)*
- Rachel Turner *(Scientific Officer Therapies for endocrine and cardiovascular diseases Office, EMA)*
- Victoria Palmi Reig *(Senior International Affairs officer, EMA)*
- Martin Harvey Allchurch *(Head of International Affairs, EMA)*
- Alberto Gañán Jiménez *(Head of Committees and Quality Assurance Department, EMA)*
- Asmaa Fouad *(Head of Central Administration of Biological & Innovative Products & Clinical Trials at EDA, Egypt, and representative of EDA in ICH. Advisory member of ECBS-WHO)*
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- Andrew Deavin *(Senior Director Vaccines Global Regulatory Affairs Asia Pacific & China, Vaccines Europe)*
- Susanne Ausborn *(Global Head International Regulatory Policy, Roche, EFPIA)*

7) Final remarks *(5 min)*

- Martin Harvey Allchurch *(Head of International Affairs, EMA)*
- Susanne Ausborn *(Global Head International Regulatory Policy, Roche, EFPIA)*

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EMA post-authorisation framework

Tool to support reliance for variations

Overview

- EU Variations Regulatory Framework
- Transparency: information published by EMA
- EMA procedures and reliance documents generated alongside variations
- Take home messages

EU Variations Regulatory Framework

European Union

EUR-Lex

Variation Regulation (EC) No 1234/2008, as amended

B.I.b) *Control of active substance*

B.I.b.1 Change in the specification parameters and/or limits of an active substance, starting material/intermediate/reagent used in the manufacturing process of the active substance	Conditions to be fulfilled	Documentation to be supplied	Procedure type
a) Tightening of specification limits for medicinal products subject to Official Control Authority Batch Release	1, 2, 3, 4	1, 2	IA_{IN}
b) Tightening of specification limits	1, 2, 3, 4	1, 2	IA
c) Addition of a new specification parameter to the specification with its corresponding test method	1, 2, 5, 6, 7	1, 2, 3, 4, 5, 7	IA
d) Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	1, 2, 8	1, 2, 6	IA
e) Deletion of a specification parameter which may have a significant effect on the overall quality of the active substance and/or the finished product			II
f) Change outside the approved specifications limits range for the active substance			II

Variations Classification Guideline

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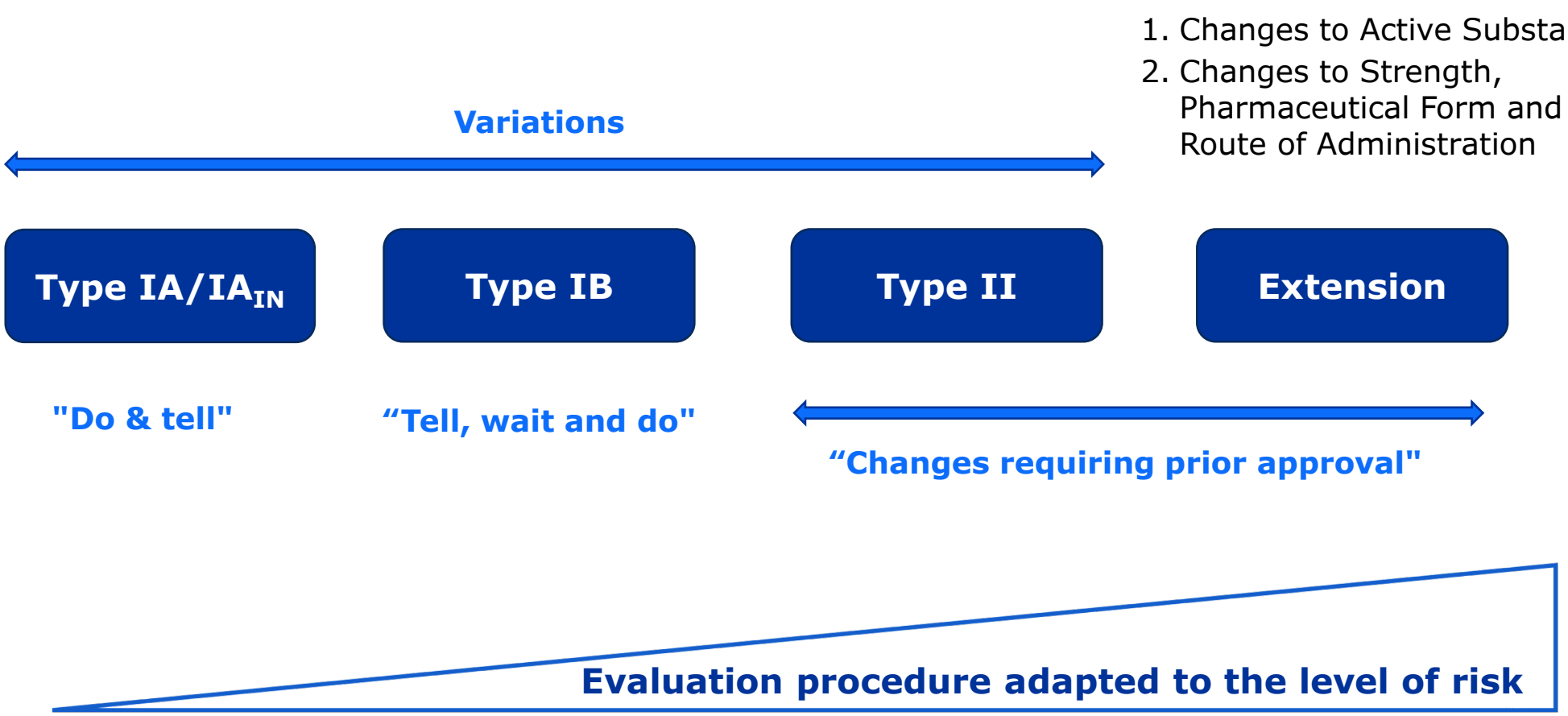
HMA
Heads of Medicines Agencies

Procedural and Scientific Guidance

EMA

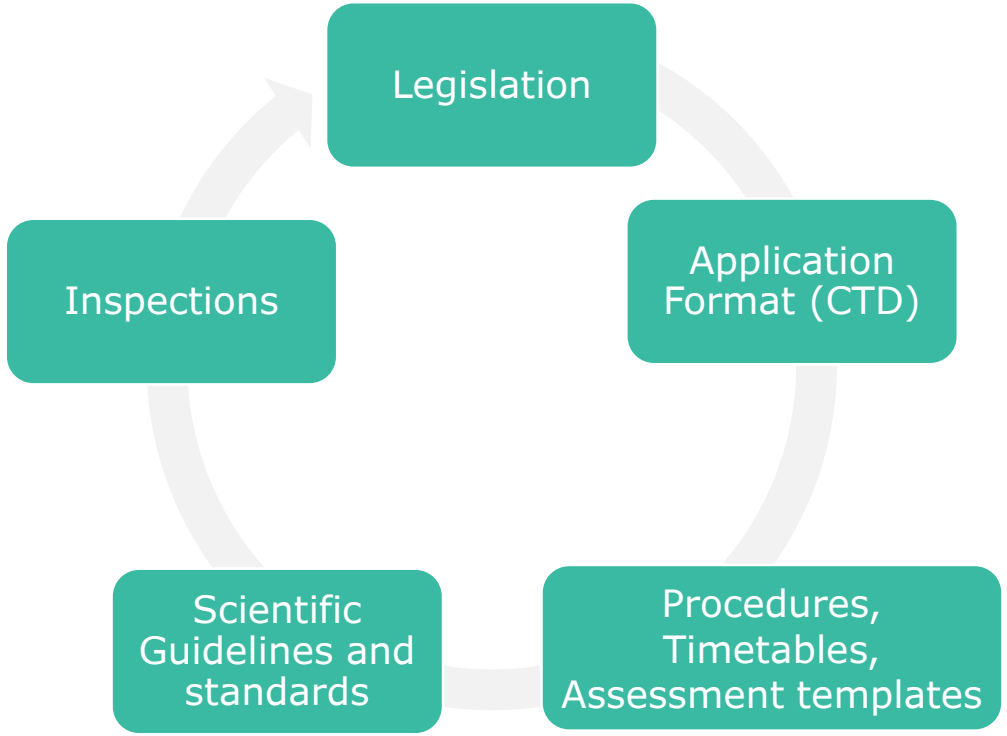
EU Risk based categorisation of variations

1. Changes to Active Substances
2. Changes to Strength, Pharmaceutical Form and Route of Administration



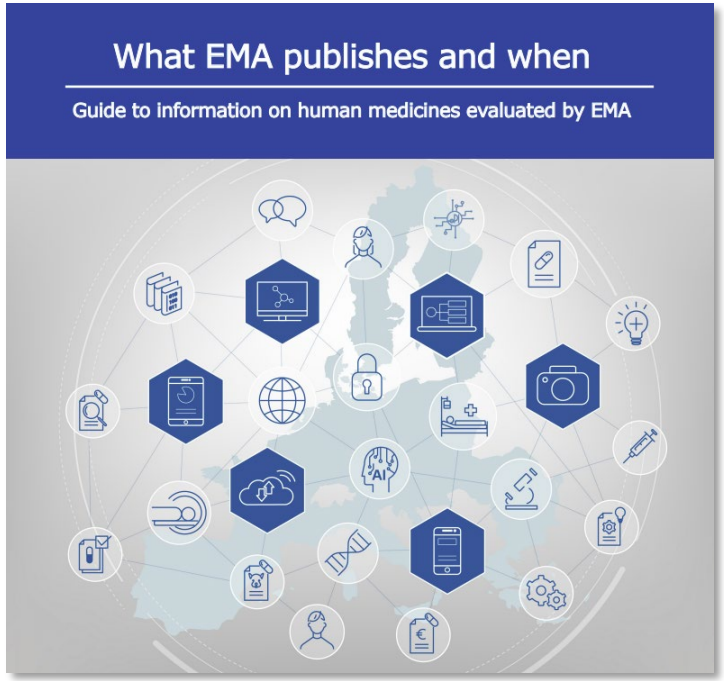
Reliance in the EU network required standardisation

A common and single system based on full transparency enabling worksharing and reliance



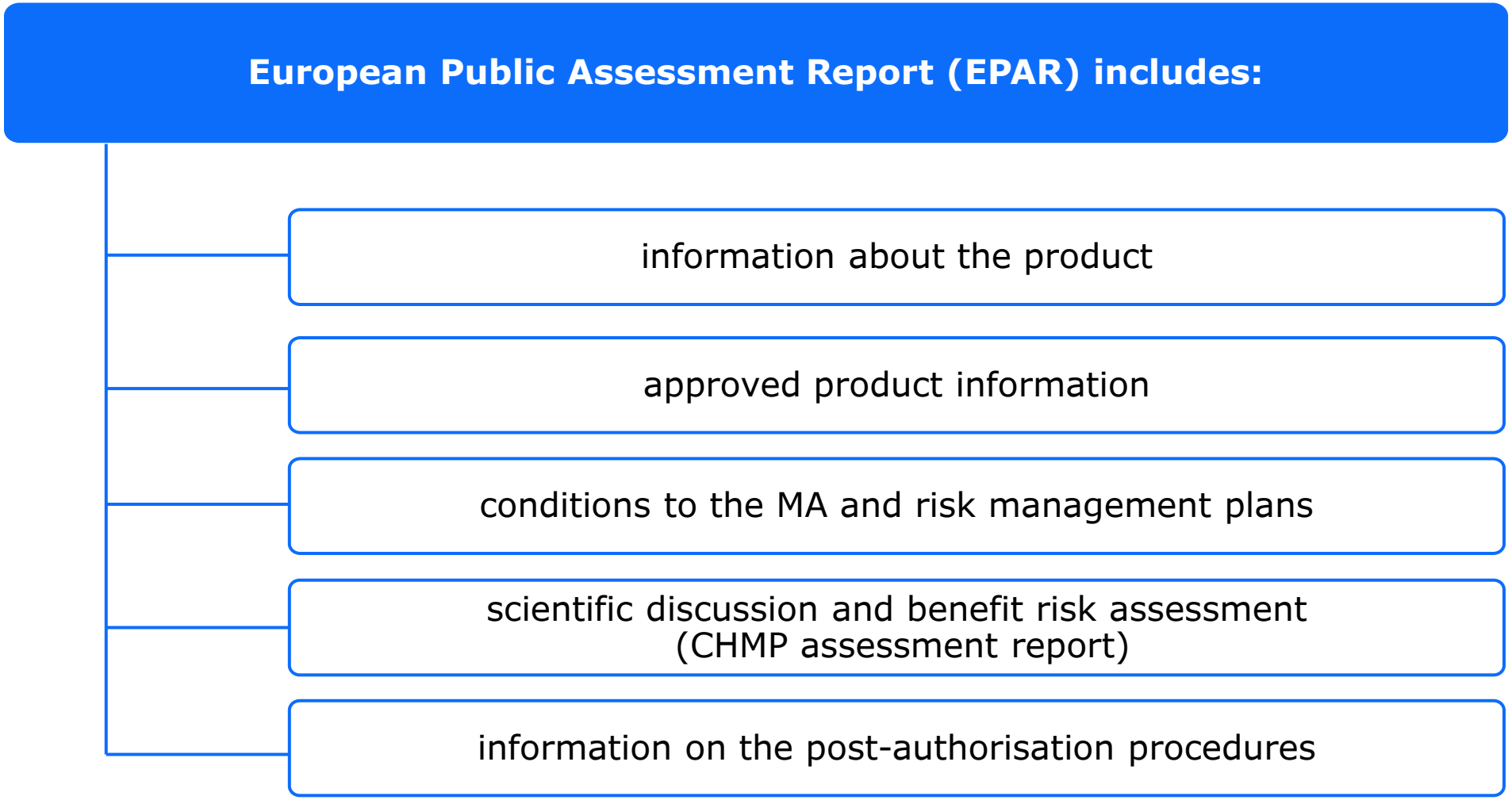
Transparency: what EMA publishes and when

- Framework for transparency is embedded in EU legislation.
- EMA publishes information on human medicinal products at various stages of their life cycle, from the early developmental stages through our evaluation of authorisation applications, RMPs, post-authorisation changes, safety reviews and withdrawals.
- This guidance helps stakeholders know what kind of publications to expect on medicines undergoing evaluations and many other regulatory procedures.
- This transparency enables many regulatory authorities to rely on EMA's assessment of medicines.
- A comprehensive set of documents, including **European Public Assessment Report (EPAR),** is published on the medicine's page.

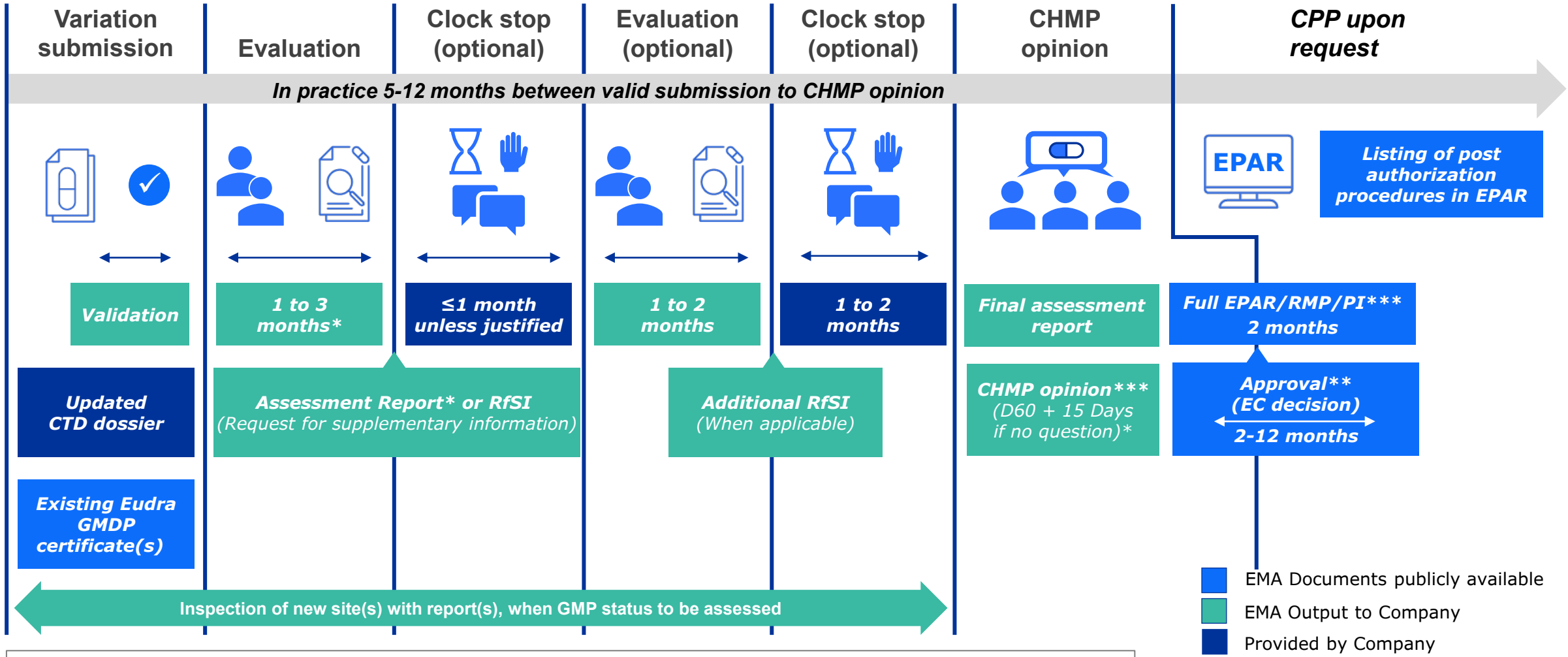


Guide to information on human medicines by EMA

Information published by the EMA

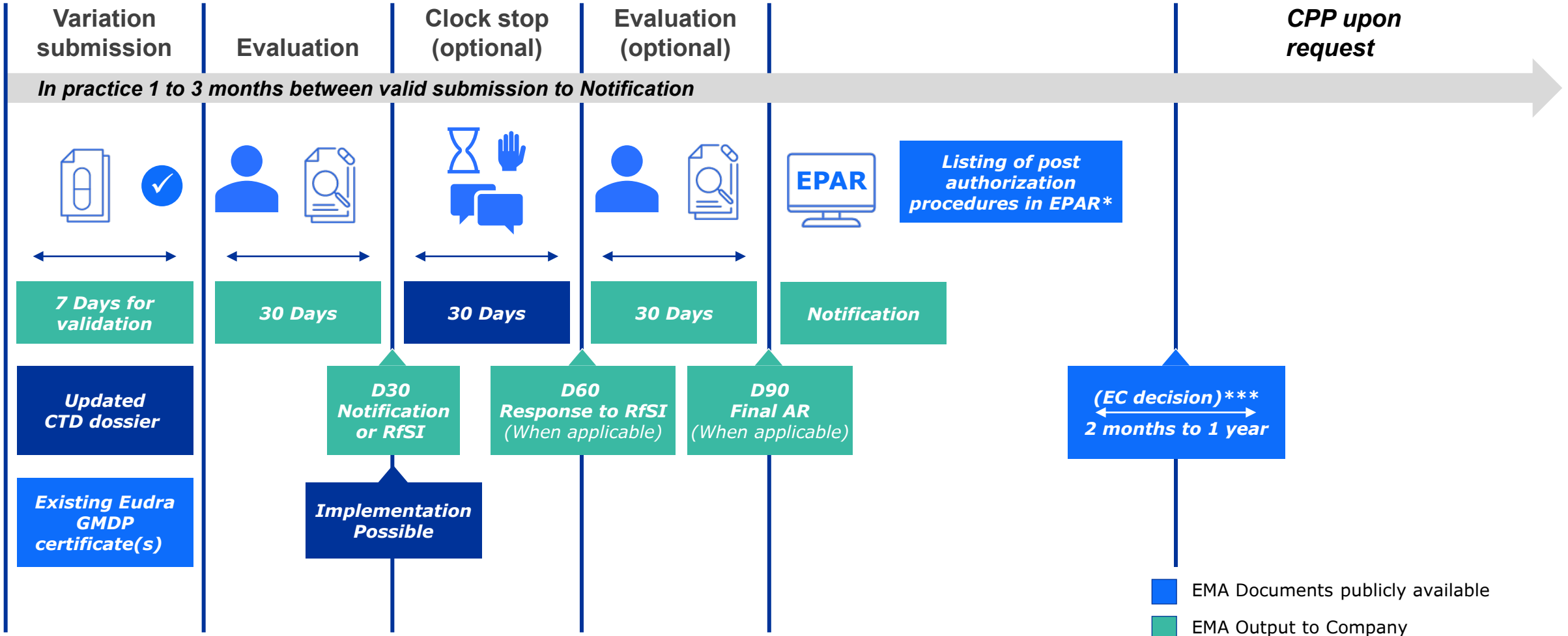


Reliance documents generated alongside a type II variation



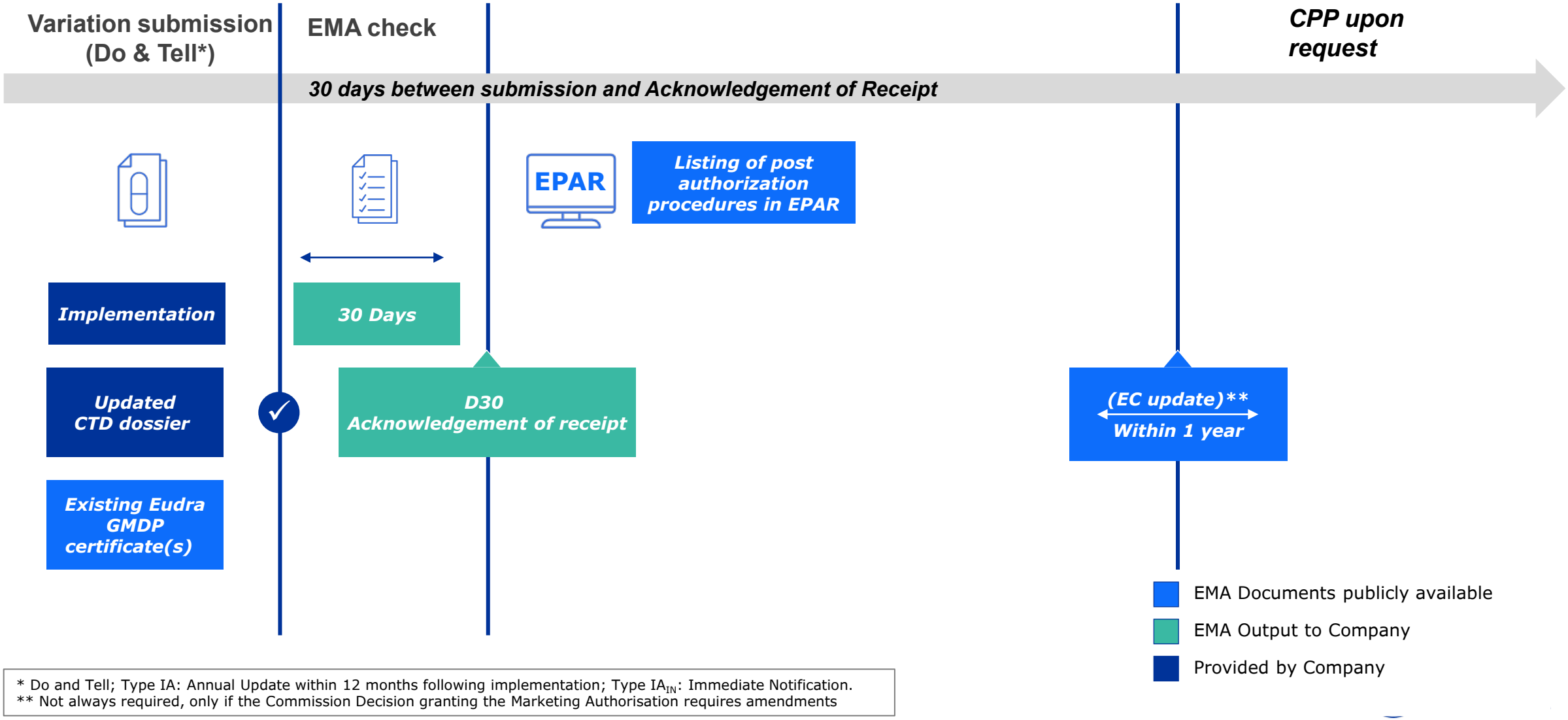
*Most cases are 60 days ; May be reduced to 30 days for urgent safety issues, or extended to 90 days for changes to therapeutic indication(s) or grouping
** Not always issued (only if EC Annexes affected): within 2 months (Art. 23.1a(a)) to 1 year after CHMP opinion (regulation 712/2012)
*** Not always publicly issued (only if changes/new or changes to indications or contra-indications or posology): 2 months after approval

Reliance documents generated alongside a type IB variation



* Procedures requiring immediate Commission Decision: EPAR publication following adoption of the EC decision
** Not always required (only if the Commission Decision granting the Marketing Authorisation requires amendments)
i.e EC Annexes affected: within 2 months (for changes to indications, contra-indications, posology) to 1 year after Valid notification
AR = Assessment Report ; RfSI = Request for supplementary information

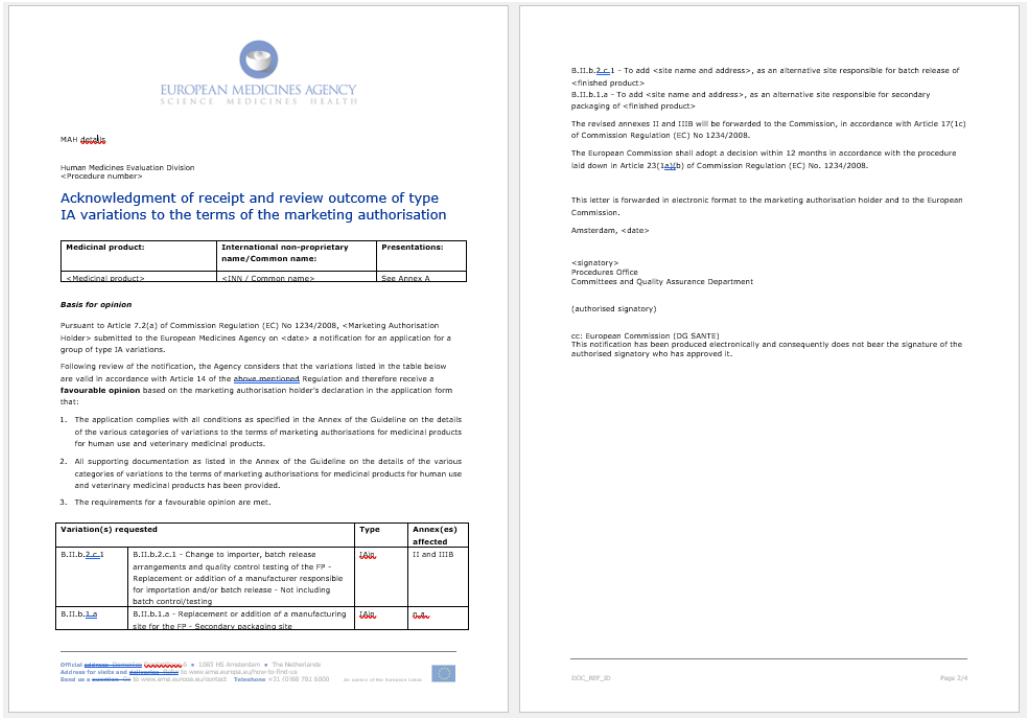
Reliance documents generated alongside a type IA/IA$_{IN}$ variation



* Do and Tell; Type IA: Annual Update within 12 months following implementation; Type IA$_{IN}$: Immediate Notification.
** Not always required, only if the Commission Decision granting the Marketing Authorisation requires amendments

Type IA/IA$_{IN}$ Acknowledgment of Receipt

Agency reviews the notification:
- Correct classification
- All conditions are met
- Supportive documentation



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MAH details

Human Medicines Evaluation Division
<Procedure number>

Acknowledgment of receipt and review outcome of type IA variations to the terms of the marketing authorisation

Medicinal product:	International non-proprietary name/Common name:	Presentations:
<Medicinal product>	<INN / Common name>	See Annex A

Basis for opinion

Pursuant to Article 7.2(a) of Commission Regulation (EC) No 1234/2008, <Marketing Authorisation Holder> submitted to the European Medicines Agency on <date> a notification for an application for a group of type IA variations.

Following review of the notification, the Agency considers that the variations listed in the table below are valid in accordance with Article 14 of the above mentioned Regulation and therefore receive a **favourable opinion** based on the marketing authorisation holder's declaration in the application form that:

1. The application complies with all conditions as specified in the Annex of the Guideline on the details of the various categories of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products.
2. All supporting documentation as listed in the Annex of the Guideline on the details of the various categories of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products has been provided.
3. The requirements for a favourable opinion are met.

Variation(s) requested		Type	Annex(es) affected
B.II.b.2.c.1	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	IAIN	II and IIIB
B.II.b.1.a	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	IAIN	II-A,

B.II.b.2.c.1 - To add <site name and address>, as an alternative site responsible for batch release of <finished product>
B.II.b.1.a - To add <site name and address>, as an alternative site responsible for secondary packaging of <finished product>

The revised annexes II and IIIB will be forwarded to the Commission, in accordance with Article 17(1c) of Commission Regulation (EC) No 1234/2008.

The European Commission shall adopt a decision within 12 months in accordance with the procedure laid down in Article 23(1a)(b) of Commission Regulation (EC) No. 1234/2008.

This letter is forwarded in electronic format to the marketing authorisation holder and to the European Commission.

Amsterdam, <date>

<signatory>
Procedures Office
Committees and Quality Assurance Department

(authorised signatory)

cc: European Commission (DG SANTE)
This notification has been produced electronically and consequently does not bear the signature of the authorised signatory who has approved it.

DOC_REF_ID

Page 2/4

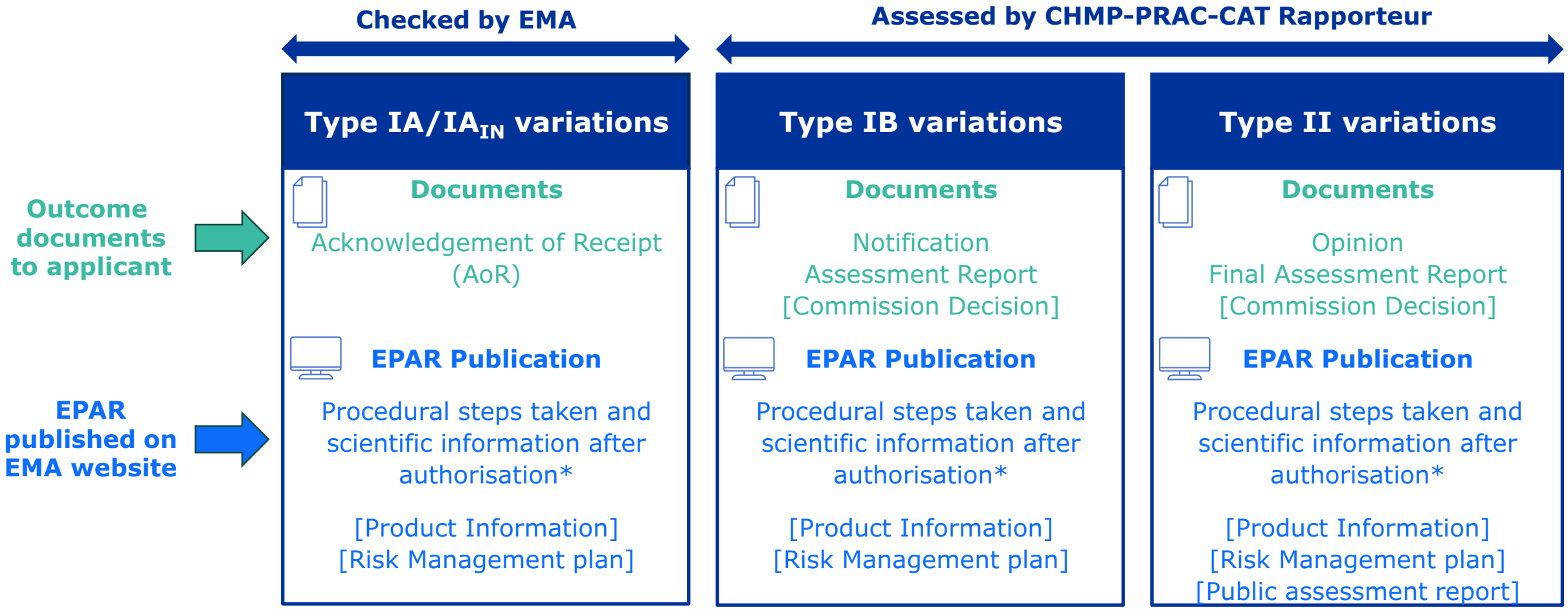
B.I.b.2	Change in test procedure for active substance or starting material/ reagent/intermediate used in the manufacturing process of the active substance	Cond. to be fulfilled	Docum. to be supplied	Proced. type
a)	**Minor changes to an approved test procedure**	**1, 2, 3, 4**	**1, 2**	**IA**

	Conditions
1	Appropriate validation studies have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the former test procedure.
2	There have been no changes of the total impurity limits; no new unqualified impurities are detected.
3	The method of analysis should remain the same (e.g. a change in column length or temperature, but not a different type of column or method).
4	The test method is not a biological/immunological/immunochemical method, or a method using a biological reagent for a biological active substance. (does not include standard pharmacopoeial microbiological methods).

	Documentation
1	Amendment of the relevant section(s) of the dossier (presented in the EU-CTD format or NTA volume 6B format for veterinary products, as appropriate), , including a description of the analytical methodology, a summary of validation data, revised specifications for impurities (if applicable).
2	Comparative validation results, or if justified comparative analysis results showing that the current test and the proposed one are equivalent. This requirement is not applicable in case of an addition of a new test procedure.

An aligned variations classification system facilitates reliance

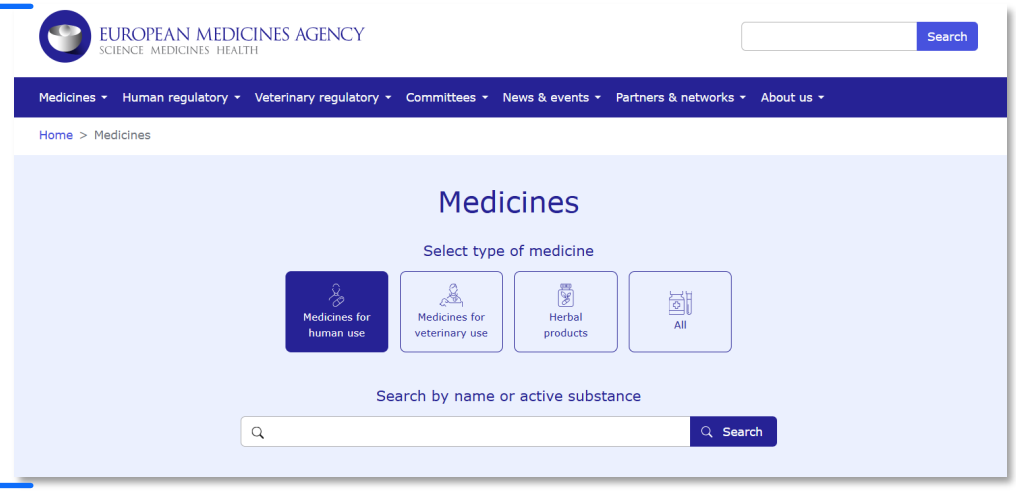
EMA output documents for variations



* EPAR, including listing of post authorization procedures, is published following finalization of procedures affecting PI or RMP
[…] published when relevant

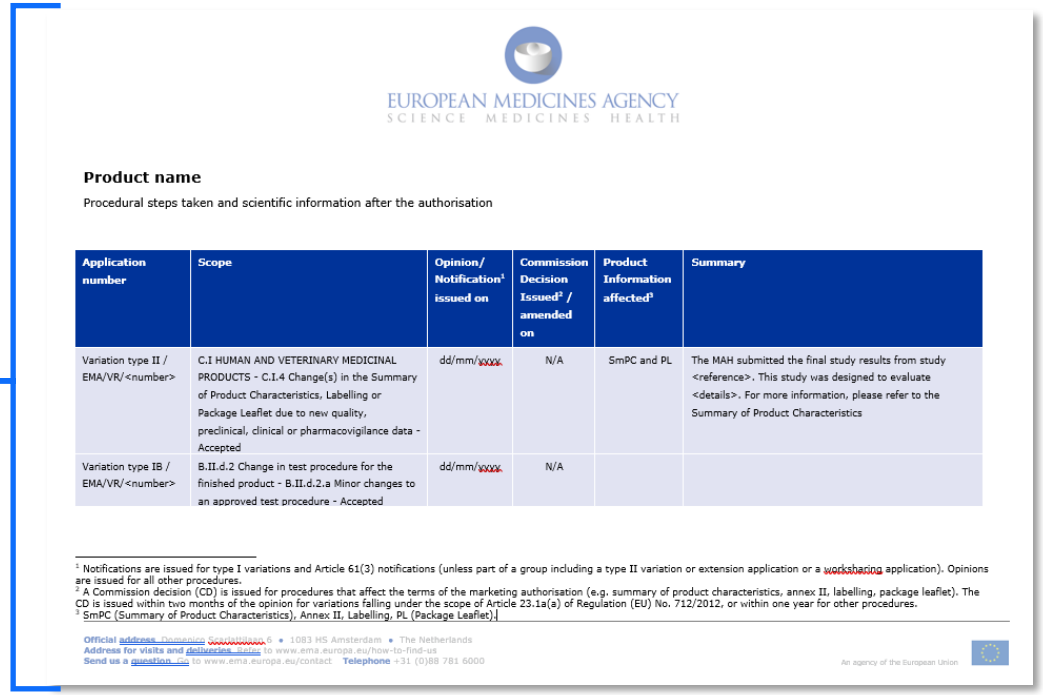
EPAR

[Medicines | European Medicines Agency (EMA)]



Page contents

- Overview → Risk Management Plan
- Product information → Authorised product information All EU languages
- Product details → Authorised presentations
- Authorisation details → Changes since initial authorisation of medicine Procedural steps taken and scientific information after authorisation
- Assessment history → Assessment report post-authorisation procedures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Product name

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
Variation type II / EMA/VR/<number>	C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted	dd/mm/yyyy	N/A	SmPC and PL	The MAH submitted the final study results from study <reference>. This study was designed to evaluate <details>. For more information, please refer to the Summary of Product Characteristics
Variation type IB / EMA/VR/<number>	B.II.d.2 Change in test procedure for the finished product - B.II.d.2.a Minor changes to an approved test procedure - Accepted	dd/mm/yyyy	N/A		

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact Telephone +31 (0)88 781 6000
An agency of the European Union

The EPAR is updated when variations affect the product information or the risk management plan.

Take home messages

- The **outcome generated** following a variation procedure provides a **good basis for informed reliance** on the work done by the Agency.
- This includes:
  - **Output documents generated by the Agency** and shared with the applicant
  - **Information published on the Agency's website** as part of the EPAR
- **Only the EPAR or Final assessment report represents the final scientific discussion and conclusions**. Other EMA assessment reports only represent the status of the evaluation at different timepoints.
- An aligned variations classification system facilitates reliance.

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Thank you

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هيئة الدواء المصرية

Reliance Practices in the Egyptian Drug Authority
A story of Trust & Transparency

Asmaa Fouad.

Head of Central Administration of Biological, Innovative products and Clinical Trials, EDA. Member of Supreme Council for Clinical Research Ethics oversight.

EDA, Egypt representative in ICH and vice-chair of IPRP management committee.

Advisory member in ECBS, WHO- TAG member in LPTT,WHO.

INDEX

Introduction

About EDA

August 2019

- President issue Law No. 151 of 2019 to establish **the Egyptian Drug Authority (EDA)"The official drug regulatory body in Egypt"**

January 2020

- President Issue Decree number 18 of 2020 for Formulation of board of directors

March 2020

- Prime minister decree 777 of 2020
- The executive regulations of Law No. 151 of 2019.

EDA movements internationally empowering Reliance

2022:

EDA reached Maturity Level 3 (ML3) for Vaccines & became a Transitional WHO Listed Authorities (tWLA)

2024

The Egyptian Drug Authority (EDA) attained ML3 for medicines

World Health Organization

List of National Regulatory Authorities (NRAs) operating at maturity level 3 (ML3)[1] and maturity level 4 (ML4)[2] (as benchmarked against WHO Global Benchmarking Tool (GBT)

(in alphabetical order) - As of December 2024

Country	Regulatory authority	Maturity Level (ML)	Scope of products	Year of announcement
China	National Medical Products Administration (NMPA)	ML3	1. Vaccines (producing)	2022
Egypt	Egyptian Drug Authority (EDA)	ML3	1. Medicines 2. Vaccines (producing)	2022 (vaccines) 2024 (medicines)
Ghana	Food and Drugs Authority (FDA)	ML3	1. Medicines 2. Vaccines (non producing)	2020
India	Central Drugs Standard Control Organisation (CDSCO)	ML3	1. Vaccines (producing)	2017 2024
Indonesia	National Agency of Drug and Food Control (BADAN POM)	ML3	1. Vaccines (producing)	2019

https://cdn.who.int/media/docs/default-source/medicines/regulatory-systems/wla/list-of-nras-operating-at-ml3-and-ml4.pdf?sfvrsn=ee93064f_23&download=true

EDA movements internationally empowering Reliance

2021:

EDA Joined ICH as Observer

EDA became member in IPRP

IPRP
International Pharmaceutical Regulators Programme

eda

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IPRP – 9th Meeting – Public Statement

13 Jun 2022

The ninth meeting of the Management Committee (MC) of the International Pharmaceutical Regulators Programme (IPRP) was held on the 25th and 26th of May 2022 in Athens, Greece. 23 IPRP Members and Observers were represented at the meeting, which was organised in a hybrid format with both in-person and virtual participation. The MC welcomed the Egyptian Drug Authority – EDA, Egypt as a new IPRP Member. Dr. Peter Bachmann from EC, Europe and Mr. Diogo Penha Soares from ANVISA, Brazil were re-elected as IPRP MC Chair and Vice-Chair respectively, to serve for another 1-year term from the end of the meeting.

File(s)

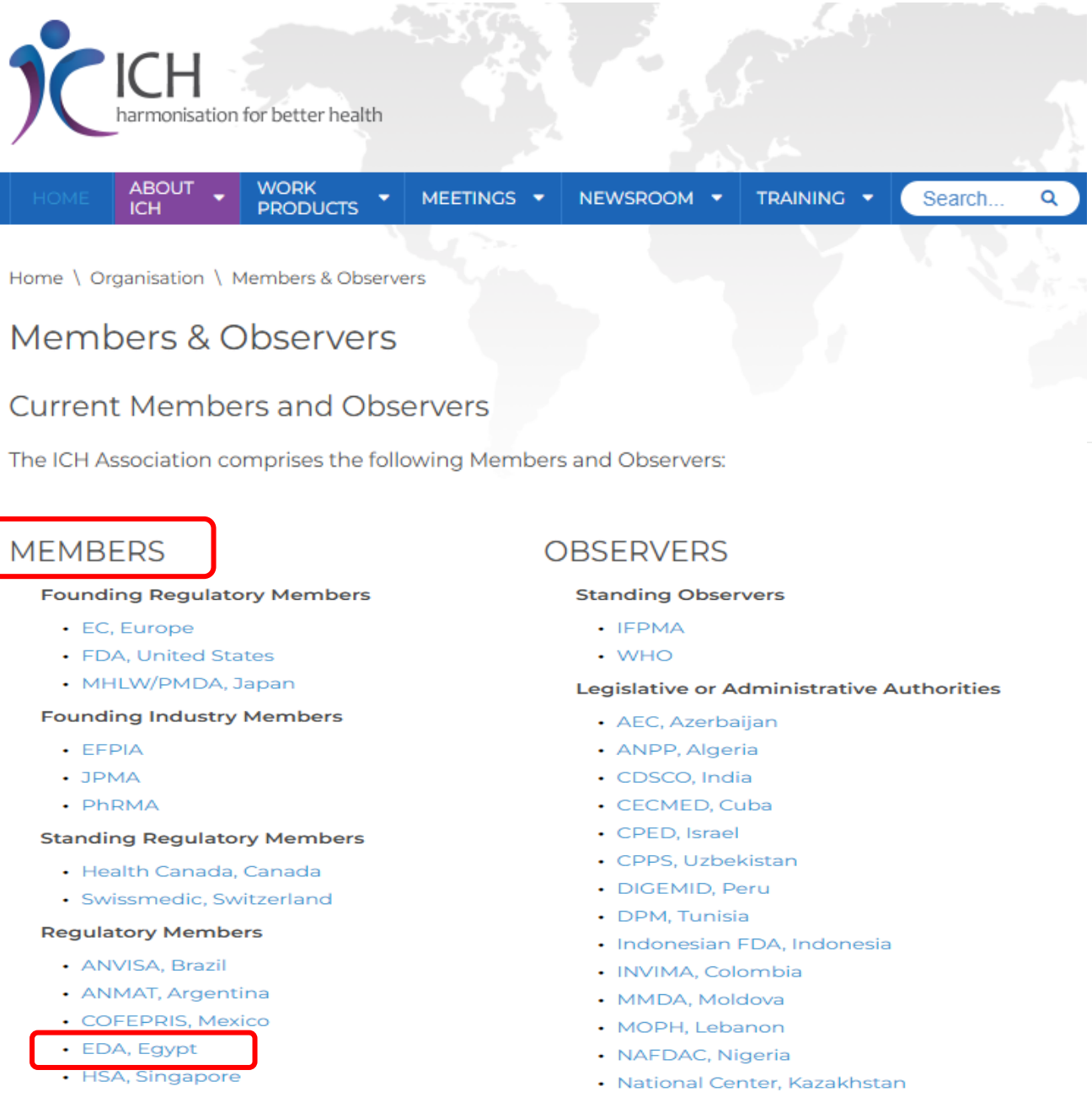
IPRP9_PublicStatement_Final_2022_0613_0.pdf

EDA movements internationally empowering Reliance

2023:

EDA become an ICH member

as 1st African and 2nd Arabic member



OPPORTUNITIES & CHALLENGES EDA FACED

CHALLENGES EDA FACED

- Need for regulations update to include reliance in the legal framework.....Issued

- Need for clear vision, regulatory supportive tools (Reference agency assessment reports, CPPs, inspection reports.....etc.)& procedures for implementation.....Done

- Regulators mind shift towards proper & good reliance practices (Change management).....Improved

- Elevated backlogs & regulatory resources constraints specially during pandemic.....Controlled

OPPORTUNITIES EDA CAPTURED

EDA still sees more opportunities for more Reliance through:

-More harmonization of technical requirements that makes harmonization of regulatory requirements easier.

-Continuous update of the dynamic list of reference authorities based on justified selection criteria.

-More investment in Regulatory System Strengthening to move from relying agency to WLA as per WHO evaluation.

-Technology as an enabler through more engagement in Pilots with EMA

-Use of CRP/WHO soon.

Reliance Practices over the time & Over the functions.

Reliance Practices over the time & over the functions

2015

- Reliance on the GMP inspection

2016

- Reliance on the MA approval from EMA and/or FDA

2022

- Reliance on the assessment of EMA and/or FDA for MA

2023

- Reliance on the assessment of PAC

2024

- Reliance in Lot Release for Biologicals
- Reliance in CT protocol

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Post-approval Changes & Reliance through Product life cycle

POST-APPROVAL CHANGES

A post-approval change to a Marketing Authorisation refers to:

Any change to the dossier status that is present in its latest version at the Authority

Any change in the **quality**, **safety**, **efficacy** or in the **administrative information** of a product is considered a

Post-Approval Change (PAC)

IMPORTANT

Certain major changes, such as introduction of different strength, changes in dosage form, route of administration, and/or presentation may necessitate the filing of a new application for marketing authorization and cannot be evaluated as post-approval changes

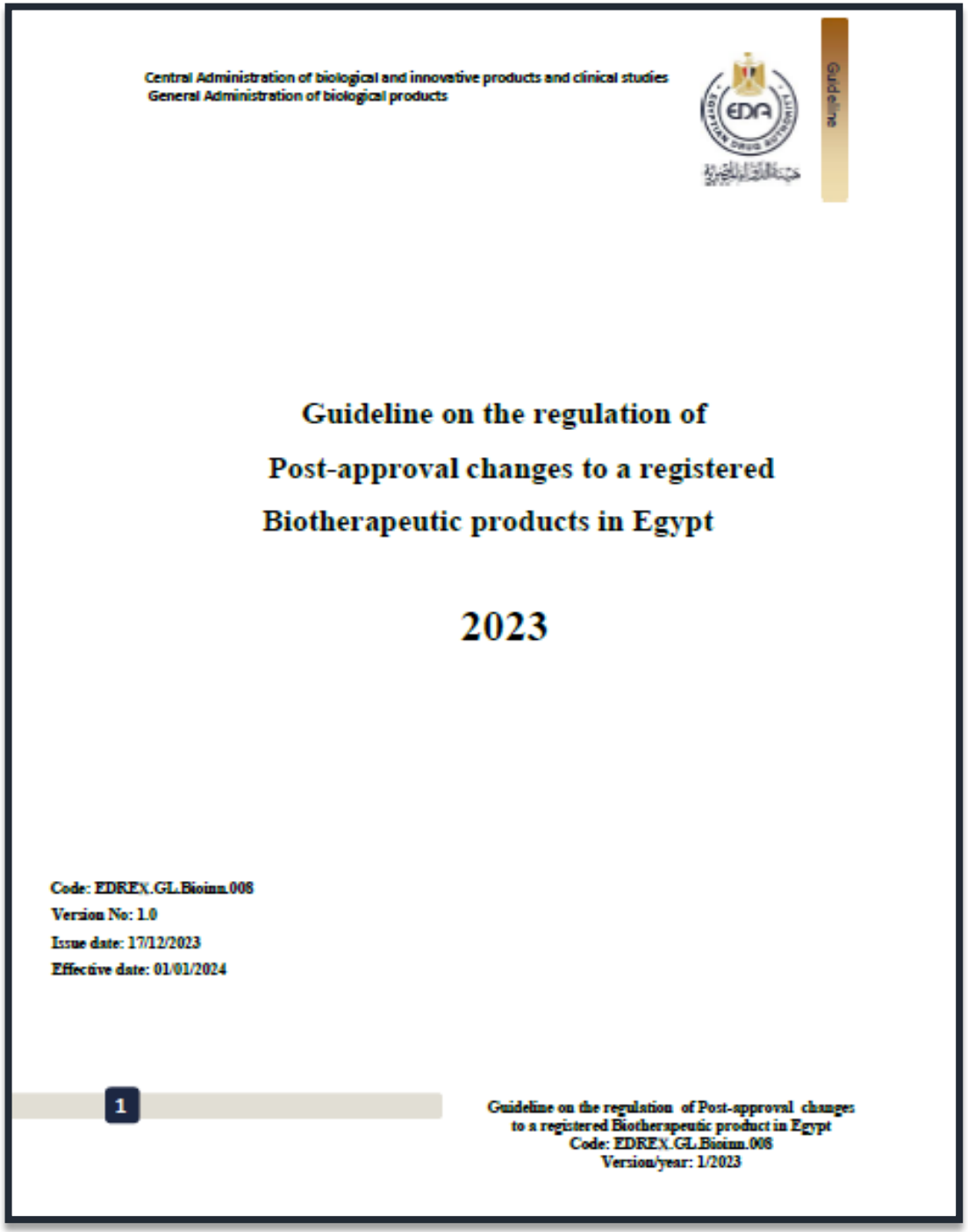
Since the regulation of changes to an approved products is the **key** to ensure that the **post change products** are of consistent quality, safety and efficacy

On 17-12-2023

EDA published

“Guideline on the regulation of Post-approval changes to a registered Biotherapeutic products in Egypt”

After displaying the draft guidance for public consultation and considering the comments of different stakeholders



Reporting categories of Post-Approval Changes

i. Quality changes

- Major quality change
- Moderate quality change
- Minor quality change
- Quality change with no impact

ii. Labelling changes

- Safety and efficacy change **(i.e Scientific data update)**
- Product labelling information change **(i.e Safety data update)**
- Administrative product labelling information change

iii. Administrative

Changes related to the administrative as well as the legal information of the biotherapeutic product.

(i.e. **MAH change, name and address of manufacturing facility, etc**.).

PAC SUBMISSION PATHWAYS

Normal pathway

- **Normal track**
- **Parallel submission** NEW

The simultaneous submission of the same change to multiple regulatory authorities

Reliance pathway NEW

Notification NEW

Applicant submits required documents as described in *"Guideline on the regulation of Post-approval changes to a registered Biotherapeutic products in Egypt"* **and receives acknowledgment of Submission after 20 WDs**

RELIANCE FOR PAC

EDA extended Reliance practice to Post approval changes by applying a verification route with shortened times for approving post-approval changes to quality and product labels changes.

Procedures for handling are expected to be more expedite

Time line will be shorter than in the normal track

RELIANCE FOR PAC..LIST OF REFERENCE COUNTRIES.

Pathway	
Applicable on	
Eligible products	
Timelines	
Prior appointment required	

No.	Country	No.	Country
1	U.S. A	13	Belgium
2	Australia	14	Austria
3	UK	15	Iceland
4	Canada	16	Denmark
5	Japan	17	Netherlands
6	Ireland	18	New Zealand
7	Norway	19	Luxembourg
8	Germany	20	Spain
9	France	21	Italy
10	Switzerland	22	Portugal
11	Finland	23	South Korea
12	Sweden	24	Singapore

https://www.edaegypt.gov.eg/media/d30jby1q/note-to-applicant-eda-list-of-reference-countries_.pdf

Normal track

Submission Phase

Validation Phase

Quick review of the proposed scope of variation and documentation and provides the applicant with a validation Report

within 5 WDs

Scientific review phase

Detailed review of the proposed scope of variation

Complementary documents (if any) are fulfilled and rest of the documents are verified

Final Decision

Reliance track

Submission Phase

Verification Phase

Submitted documentation is checked versus the reliance checklist to verify that the mandatory documents are fulfilled

within 5 WDs

The MAH shall receive an e-mail showing the submission status (Received/Not received)

within specified timelines

Complementary documents (if any) are fulfilled and rest of the documents are verified

Final Decision

Normal and Reliance pathways Timelines

Normal track

Reporting category	Review timeline
Administrative changes	10 WDs
Quality changes	
Major quality changes	60 WDs
Moderate quality changes	40 WDs
Minor/Annual report	NA
Labelling changes	
Safety and efficacy changes	40 WDs
Product labelling information changes	30 WDs
Administrative product labelling changes	10 WDs
Pack update	10 WDs

Reliance track

Reporting category	Review timeline
Quality changes	
Major quality changes	15 WDs
Moderate quality changes	10 WDs
Labelling changes	
Product labelling information changes	10 WDs

RELIANCE FOR PAC

Assuring "**sameness of product**" is essential for the use of reliance 

Number of PAC decisions issued through Reliance pathway since Jan 2024

PAC category	Number
Quality Changes	138

RELIANCE FOR PAC

Significant increase in number of PAC decisions monitored

Number of PACs decisions after new guideline/since Jan. 2024	Number of PACs decisions begore new guideline (from August 2022-December 2023)
951	676
For 5 quarters, an increase by 140% of work output was observed	

LESSONS LEARNT FROM EDA JOURNEY .

LESSONS LEARNT FROM EDA JOURNEY

- **Informed Reliance** is a key to set the system & change the culture.
- **Harmonization** is an enabler to good reliance practices.
- **International cooperation** & sharing best regulatory practices are mandatory for Reliance.
- Agile & **fit-for-purpose regulations** are all-time enablers to good regulatory practices.
- Always be **patient-centric** regulator…don't keep them waiting!
- It is all about **Trust & Transparency**.


EGYPTIAN DRUG AUTHORITY
EDA


THANK YOU
GRACIAS
ARIGATO
SHUKURIA
DANKSCHEEN
BÏYAN
SHUKRIA
TINGKI
TASHAKKUR ATU
YAQHANYELAY
SUKSAMA
EKHMET
MEHRBANI
GRAZIE
MAAKE
KOMAPSUMNIDA
JUSPAXAR
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Changes to the EU variations framework

WEBINAR ON RELIANCE FOR POST-AUTHORIZATION

3rd April 2025

Presented by: Virginia Rojo

Head of Procedures Office - EMA

Changes to the Variation Regulation

- **Last revision of the Variation Regulation was in 2012.** Mounting pressure from the network and stakeholders to review the variations framework (Regulation and Guidelines).

- Aim to **improve the existing system** by incorporating experience gained and **make the lifecycle management** of medicines more:
  - **Efficient** for regulators and MAHs
  - **Future proof** with scientific and technological progress

- **Simplify** and enable an **agile review** of classification guideline and operational procedures

Relevant changes of the amended Variation Regulation

Efficiency gains

- **Super-grouping of Type IAs** when the same change(s) impacts more than one MA
- **Annual update of type IA variations**: previously optional, now **mandatory** with exceptions to keep some flexibility (including flexibility for reliance).
- **Worksharing procedure** (same variation applicable to different MA with no product specific assessment):
  - **Mandatory WS** (same MAH): previously optional. Significant gains in terms of resources and harmonisation are expected.
  - **Voluntary WS** (different MAHs): legal recognition, pending agreement from Competent Authorities
  - WS procedure timelines no longer aligned with type II variations, but according to highest type of variation included

Relevant changes of the amended Variation Regulation

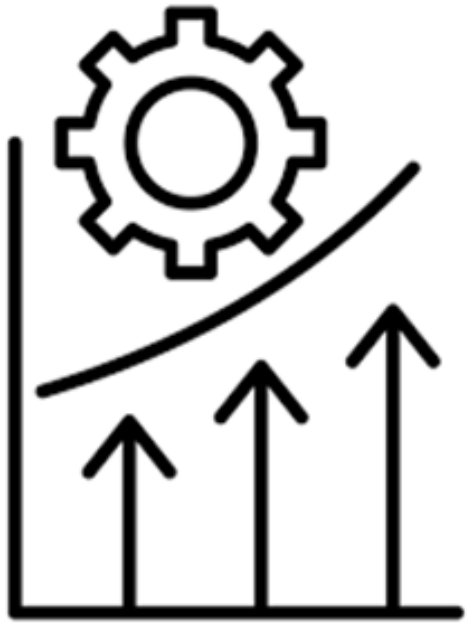
Future proofing

- **End of automatic Type II for biological products** based on experience acquired in the last decade*.
- **Additional regulatory tools:** legislative recognition/update of design space and post approval change management protocol (PACMP) to build on product-specific approach*.
- **Medical devices:** legislative recognition of life-cycle for medicinal products combined with a medical device*.
- **Health threats: lessons learnt from pandemic**
  - Possibility of a fast-track procedure for annual (seasonal) update of covid strains, if needed.
  - Extension of flexibility to update vaccines to address a declared public health emergency beyond influenza or covid.

** Provisions to be materialised with the revision of the EC Variations Guidelines*

Relevant changes of the amended Variation Regulation

Agile update of the variation classification:



- **Ongoing revision of the EC Variations guidelines aligned with the amended Variation Regulation.**
- Article 5 recommendation: **optimisation of the process** (recommendation delivered within 60 days) and introduction of a mandatory consultation between EMA/CMDh**.**
- Possibility of **regular (annual) update** of the guideline with publication of an **electronic** version in the Commission website.

Type IA variations

Previous Regulation

IA variations can be submitted at any time within 12 months after implementation

New Regulation (IAs implemented from Jan 2025)

IA variations should be collected and submitted as '**IA annual update**' between 9-12 months from the first implementation date included in the submission.

Exceptions: grouping, supergrouping, re-submission and exceptions listed in guidance (shortages, public health emergencies, prior to an inspection or MA transfer, **when third countries require a CPP or EU authorization**)

There should be no impact on reliance

IG: one or more IAs impacting several MAs from the same MAH

Supergrouping: one or more IAs impacting several MAs from the same MAH. Mix of CAPs and NAPs may be possible in the future

Revision of Variations Classification guideline

Principles for the revision of the Variations guidelines

- All categories of variations were reviewed based on the **experience** acquired and the **scientific and technical progress**.
- Aim to **improve efficiencies** ensuring the protection of public health.
- When appropriate, **streamline the variation framework** (e.g. *decreasing, downgrading and simplifying the various categories of variations*).
- When possible, **future proof** the variations framework for the upcoming changes (e.g. adapt/prepare for innovation).
- The changes proposed should be **compatible** with the options put forward by the Commission with the targeted revision of the Variations Regulation.

Main proposals

Procedural part

- **Operational details shifted** to EMA/CMDh guidance for **easiest updates** in the future.
- **Change the current code system (numbering)** to facilitate the implementation and the transitional period
- **Implementation of new/updated procedural tools** from the amended Variation Regulation

A. Administrative variations

- Reduction/simplification list from 8 to 5 scopes.

B. Quality variations

Review of all categories:

- **Downgrade** certain scopes when scientifically justified (risk/based approach).
- **Removed conditions for biological** medicinal products, in certain circumstances allowing Type IA variations.
- **Implementation of PACMP** as Type IB or Type IA also for BIO.
- New section on **In-house reference materials.**
- New scopes for **Medical devices** (co-packed, integral, referenced) in line with MDR. Wording has been kept general, focusing on impact and risk. To be complemented with EMA/CMDh Q&A.

C. Safety, Efficacy, PhV variations

- **Deletion** of scopes (C.I.9, C.I.10, as now done via Art. 57 database).
- C.I.3 **expanded to include** implementation of **PRAC signals** and **joint recommendations of EU authorities.**
- New scope for submission of **results** of assessments carried out on **target patient groups**.

D. PMF

- Reduction/simplification list from 23 to 16 scopes.

Implementation

- **Revision of the EC Variations Guidelines ongoing.** Publication by the Commission is **expected in Q2 2025.**

- **A transitional period** will be foreseen between the publication and the entry into force to allow companies and regulators enough time to prepare. **Until the updated version becomes applicable the current classification applies.**

- **Implementation work** will be needed: **EMA will publish specific implementation guidance** and will update references to new Variations guideline of existing regulatory and scientific guidance. There will be changes in systems due to new scopes, different numbering.

- **Public webinar information** session **on the amended Variations Guidelines** will be organized in due time.

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EMA post-authorisation framework

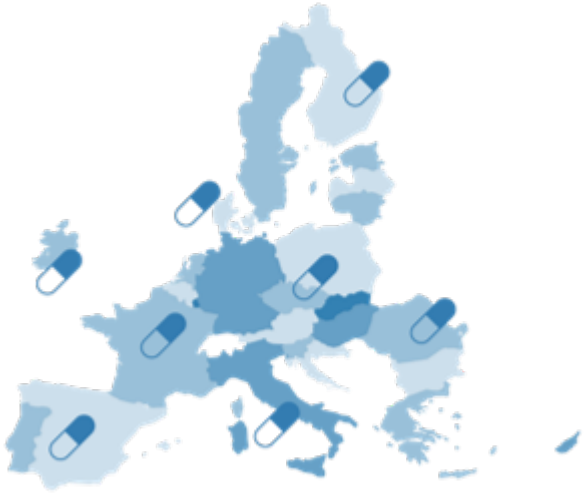
5- year renewal

Overview

1. Legal Framework
2. Key principles of the renewal procedure
3. Renewal submission content
4. Addendum to the quality overall summary
5. Addendum to clinical Overview
6. Reliance documents generated
7. Take home messages

1. Legal Framework – 5-yr renewal

- In accordance with Article 14(1) of Regulation (EC) No. 726/2004, a marketing authorisation (MA) is valid for **five years**
- In accordance with Article 14(3) of Regulation (EC) No. 726/2004, **once renewed,** an MA **shall be valid for an unlimited period**, unless there are PhV grounds justifying one additional renewal.
- Typically, a product will be renewed **once** in the product life cycle for an indefinite period



5-year renewal

2. Key principles of the renewal procedure

- The renewal assessment is based on a **general re-evaluation of the benefit/risk (B/R) balance** of the product
- MAH have an obligation to update the MA throughout the life-cycle of the product as data emerge
- Renewals are not a substitute for submission of safety or efficacy data as they become available (type I/II variations, PSUR* or other relevant procedures must be submitted as applicable)
- Renewal applications are not an opportunity to update Module 3; Quality changes must be submitted by the appropriate variation as they occur

*Periodic safety update reports (PSURs) | European Medicines Agency (EMA)

3. Renewal submission content

5- year renewal*	
Module 1	• Application form • PI • RMP (as applicable) • A statement, or certificate of GMP compliance
Module 2	• Addendum to quality overall summary (expert declaration) • Addendum to non-clinical overview (expert declaration) • Addendum to Clinical Overview (PSUR structure + expert declaration)
Module 3-5	• Not applicable

*Full submission requirements:
Renewal and annual re-assessment of marketing authorisation | European Medicines Agency (EMA)

4. Addendum to the quality overall summary

- No updating of Module 3 quality data at renewal. The MAH has an obligation to keep it updated on an on-going basis throughout the lifecycle of the product
- Declaration of compliance with Article 16(1) of Regulation (EC) No 726/2004 (the MAH has considered technical and scientific progress on the manufacturing and control methods)
- Confirmation that all changes relating to the quality of the product have been made following applications for variations and that the product conforms to current CHMP Quality guidelines
- Currently authorised specifications for the active substance and the finished product (with date of latest approval and procedure number)
- Qualitative and quantitative composition in terms of the active substance(s) and the excipient(s)(with date of latest approval and procedure number)

5. Addendum to clinical Overview

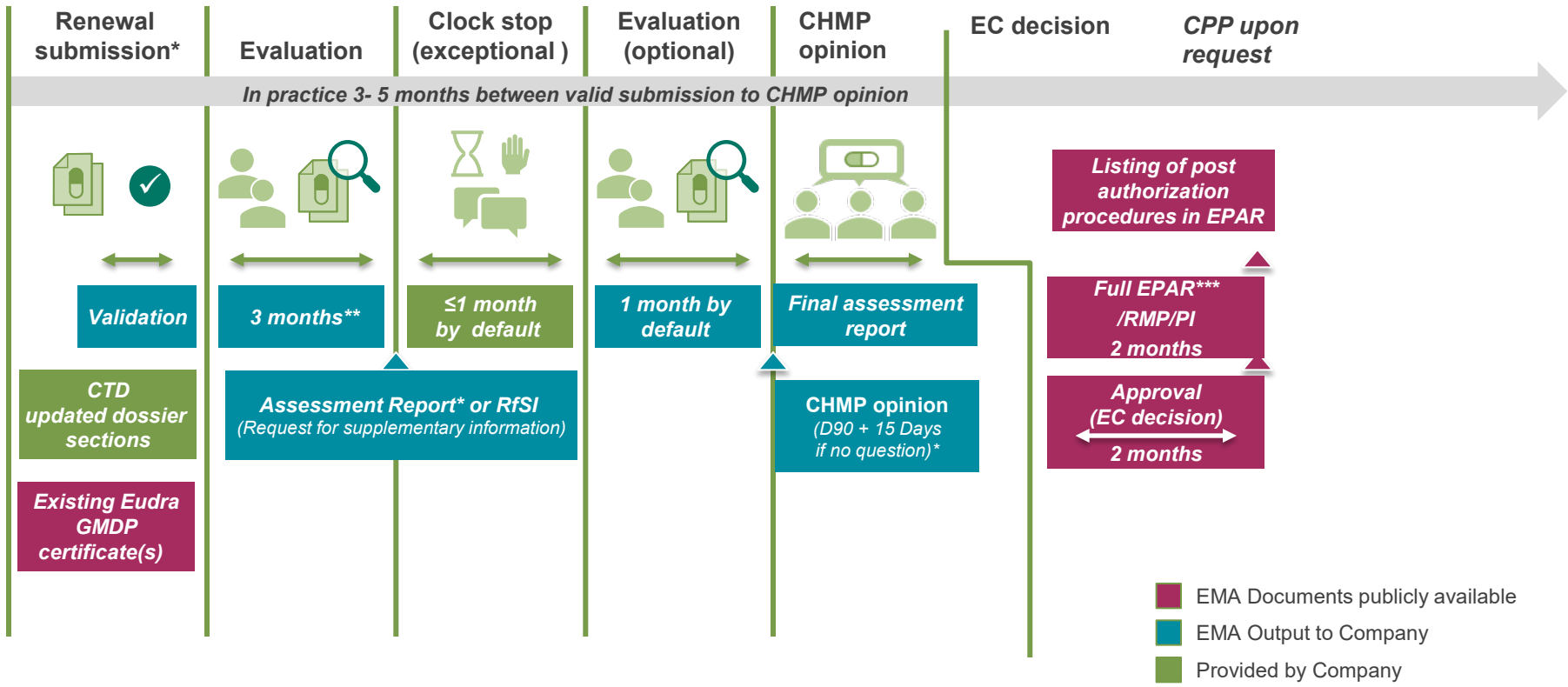
- A discussion on the current benefit-risk balance for the product

- Based on data previously included in the PSUR and safety/efficacy data accumulated since the granting of the MA or the last renewal, making reference to relevant new information in the public domain

- Clinical statements* confirm that the product information is up to date, and authorities have been kept informed of any additional data that could impact on the B/R and the product can be renewed

*Clinical Expert Statement (confirmatory statements – as reflected in Annex II of the Guideline on the processing of renewals in the centralised procedure)

6. Reliance documents generated alongside a 5-year renewal



* At least 9 months prior to expiry **90 days as standard ; *** Full EPAR not routinely published (only if major public health interest) Annexes and RMP published if affected : 2 months after approval
RfSI = Request for Supplementary Information (Q&As)

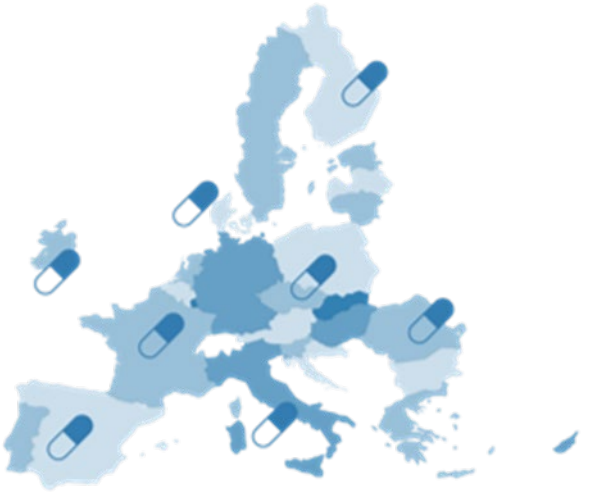
Take home messages

The 5-year renewal typically takes place **once** during the lifecycle of a product

The scope is a B/R assessment; in practice the renewal is an **administrative exercise** as the MAH has the obligation to update the MA as data emerge

Published draft new pharmaceutical legislation mentions the removal of the renewal concept

Thank you for your attention



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Guidance documents

- Guideline on the processing of renewals in the centralised procedure

Q&A at the EMA website :

- Renewals of marketing authorisations

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