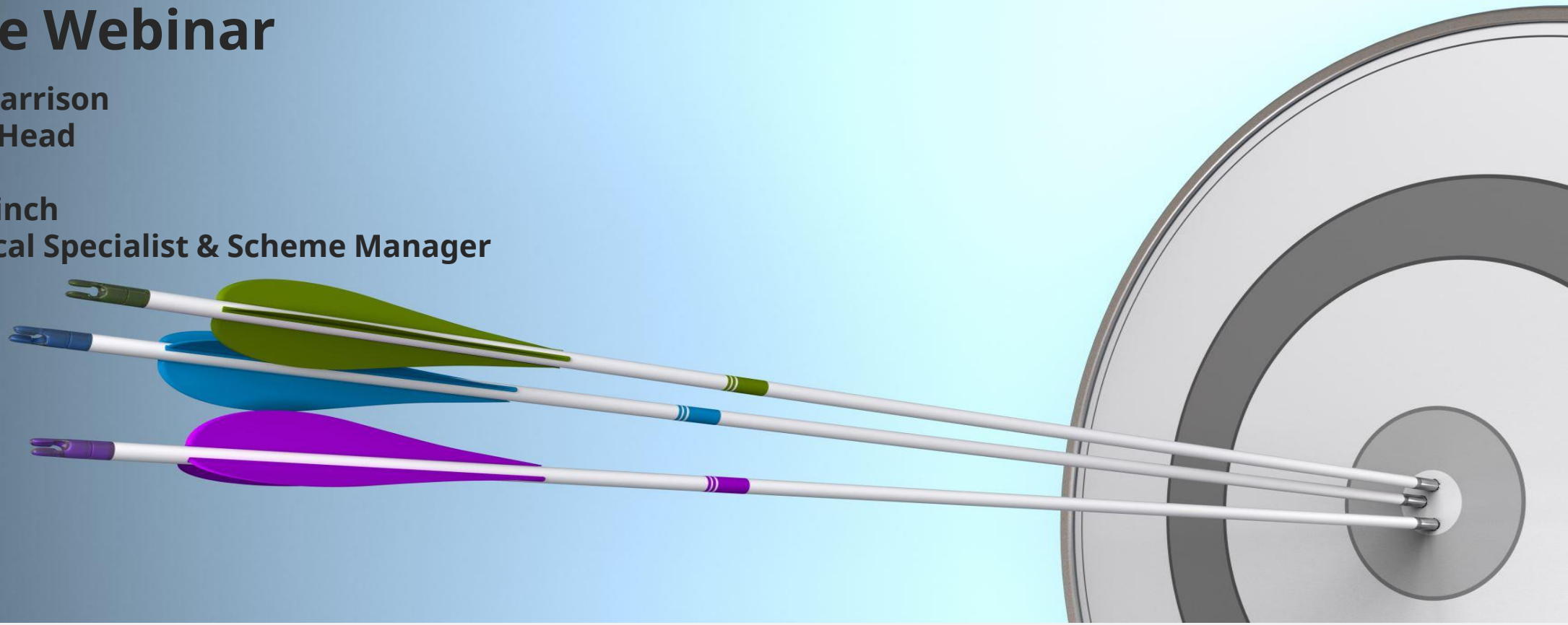
IVDR Companion Diagnostics (CDx) Update Webinar

Elizabeth Harrison
IVD Global Head

Elizabeth Linch
IVD Technical Specialist & Scheme Manager



BSI IVDR Companion Diagnostic Status

Elizabeth Harrison

BSI IVDR Companion Diagnostic Status

Three companion diagnostic IVDR certificates issued

Four EMA consultations completed with positive opinions

- PCR based oncology device
- Immunohistochemistry oncology device
- Immunoassay device for markers of prior infection
- FISH based oncology device

- Combination of pivotal clinical trial devices and follow-on devices

Other IVDR companion diagnostic applications in progress

- NGS, PCR, IHC, FISH, ISH
- Predominantly oncology devices with a transition deadline of May 2026

Agenda

IVDR Requirements for CDx Devices

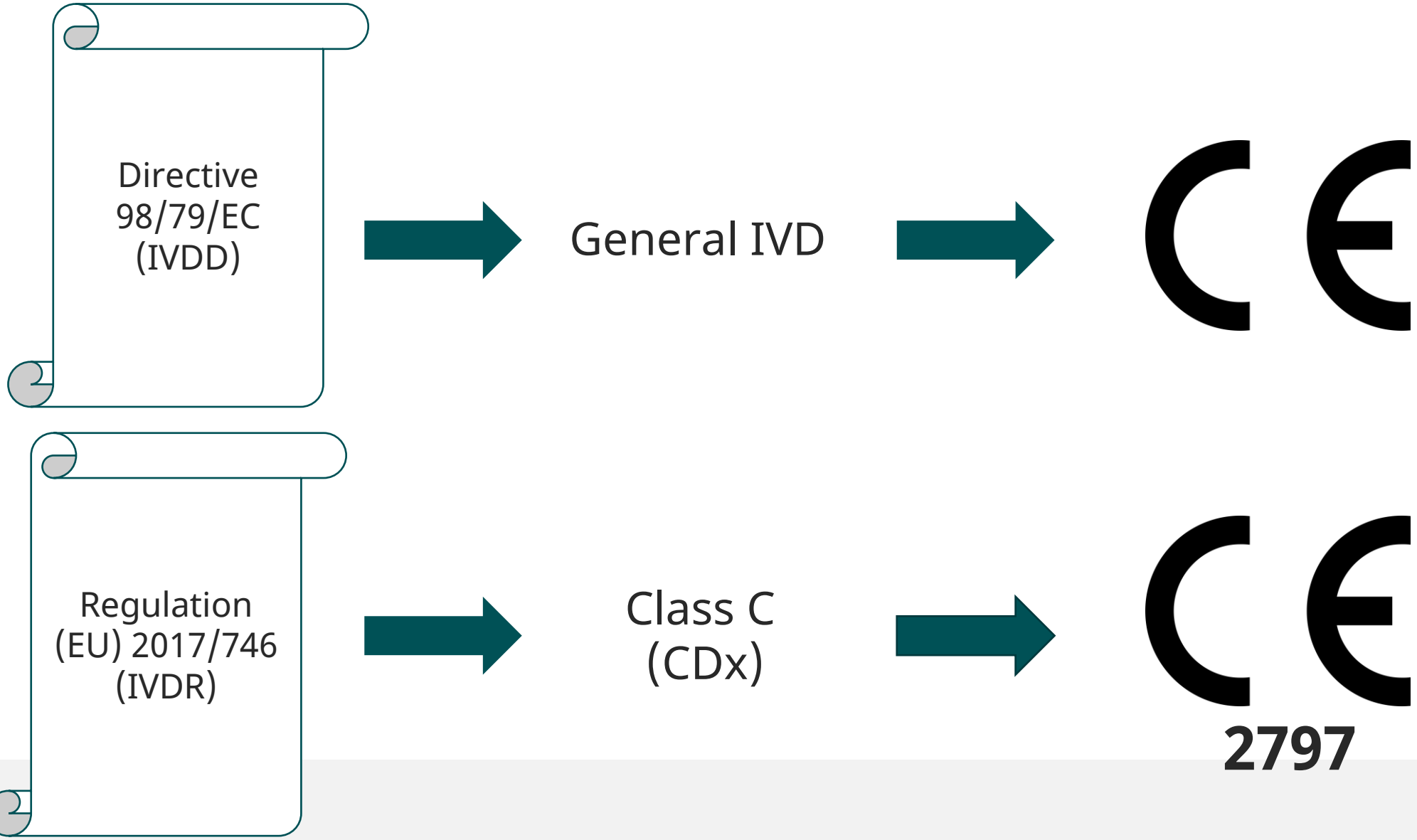
Conformity Assessment Process for CDx Devices

Technical Documentation Best Practices

IVDR Requirements for CDx Devices

Elizabeth Linch

CDx Regulatory Framework in Europe



Definition of a CDx under the IVDR

REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

Article 2 - Definitions

(7)
'companion diagnostic' means a device which is **essential** for the safe and effective use of a corresponding **medicinal product** to:

a)identify, before and/or during treatment, patients who are most likely to **benefit from the corresponding medicinal product**; or

b)identify, before and/or during treatment, patients likely to be at **increased risk of serious adverse reactions as a result of treatment with the corresponding** medicinal product;

Definition of a CDx under the IVDR

REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

Whereas:

(11)
Companion diagnostics are **essential** for defining patients' **eligibility** for specific treatment with a **medicinal product** through the **quantitative** or **qualitative** determination of specific markers

Such biomarker or biomarkers can be present in **healthy subjects** and/or in **patients**

Classification of a CDx under the IVDR

REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

ANNEX VIII – Classification Rules

2.2. Rule 3

Devices are classified as **C** if they are intended:

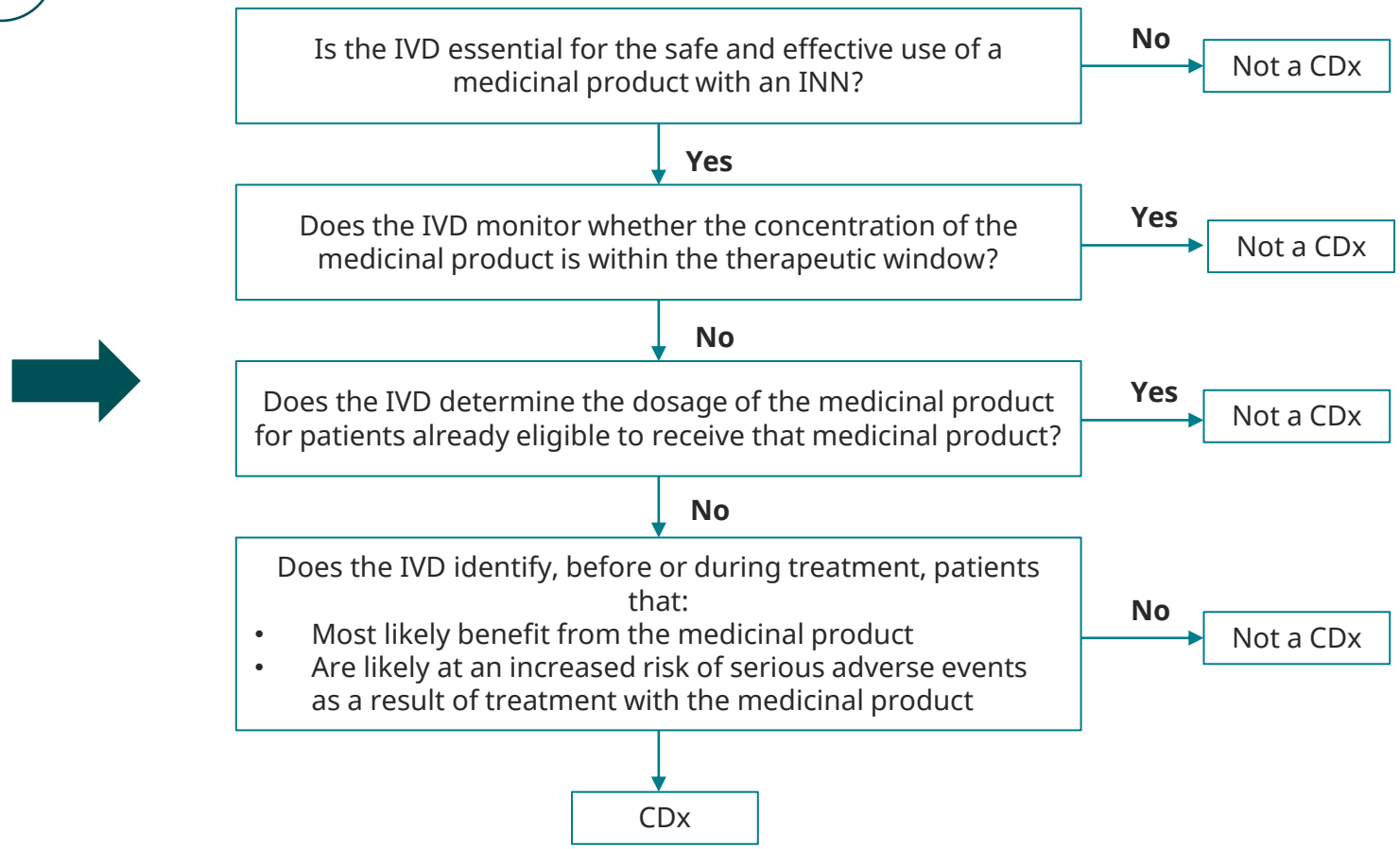
(f) to be used as companion diagnostics

Definition of CDx device – MDCG Guidance

MDCG 2020-16 (rev.2)

Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746

Annex II: Flowchart to held determine whether an IVD is a CDx



Definition of CDx device – MDCG Guidance

MDCG 2020-16 (rev.2)

Guidance on

Classification Rules for in vitro Diagnostic Medical Devices under

Regulation (EU) 2017/746

Section 4 – Explanation of the IVDR Classification Rules

Devices are not considered to be CDxs:

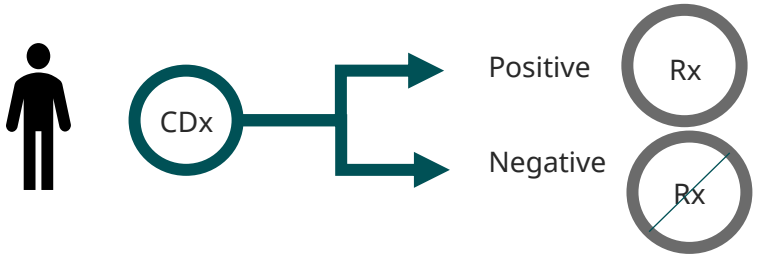
Device that are intended to be used for **monitoring treatment with a medicinal product** to ensure that the concentration of relevant substances in the human body is within the therapeutic window.

Devices intended to determine quantitative or qualitative specific marker(s) to **establish the dosage of a particular medicinal product**, for patients that are **already eligible** to receive that medicinal product.

Comparison of FDA vs. IVDR Definition of a CDx

FDA Definition

Device which provides information that is essential for the safe and effective use of a corresponding drug or biological product to:



Identify patients who are most likely to **benefit** from a particular therapeutic product

Identify patently likely to be at **increased risk** for serious side effects as a result of treatment with a particular therapeutic product

Monitor response to treatment with a particular therapeutic product for the purpose of **adjusting treatment** to achieve improved safety or effectiveness.

IVDR Definition

Device which is essential for the safe and effective of a corresponding medicinal product to:

Identify, before and/or during treatment, patients who are most likely to **benefit** from the corresponding medicinal product

Identify, before and/or during treatment, patients likely to be at **increased risk** of a serious adverse reaction as a result of treatment with a corresponding medicinal product

CDx Development – 3 Scenarios

Co-developed CDx
(aka Original CDx)

Device that is developed in a clinical development program together with the medicinal product.

- Typically, the CDx used in the pivotal clinical trial for the medicinal product.
- Co-development can be in the context of initial marketing authorization or a change in the indication of the medicinal product.

Follow-on CDx

Device that seeks the same indication in its intended use as the original CDx but was not developed in the clinical development program with the medicinal product.

- Can use a different assay technology than the original CDx.

Legacy CDx

CDx placed on the market under IVDD.

- Can be a co-developed or follow-on CDx.

Conformity Assessment Process for CDx Devices


Technical Documentation Review
Annex IX
Chapter II
Sections 4 & 5.2
Competent Authority or EMA Consultation
Annex IX
Chapter II
Section 5.2
QMS Audit
Annex IX,
Chapters I & III

EU Quality Management System Certificate

Regulation (EU) 2017/746,

Annex IX Chapter I and III

EU Technical Documentation Assessment Certificate

Regulation (EU) 2017/746,

Annex IX Chapter II

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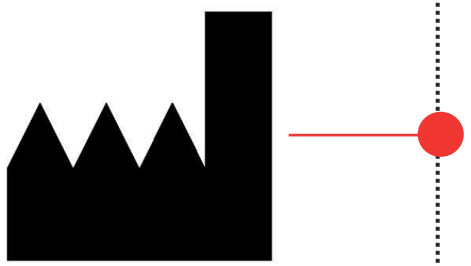
Technical Documentation Review Process & Best Practices for CDx Devices

BSI Roles & Responsibilities for Delivering Technical Documentation Reviews

Per IVDR Annex VII & NBOG BPG 2017-2



BSI Scheme Manager

Project Leader
Final Reviewer

BSI Technical Specialist(s)

Product Reviewer(s)

BSI IVD Project Management

BSI Internal Clinician

BSI Decision Maker

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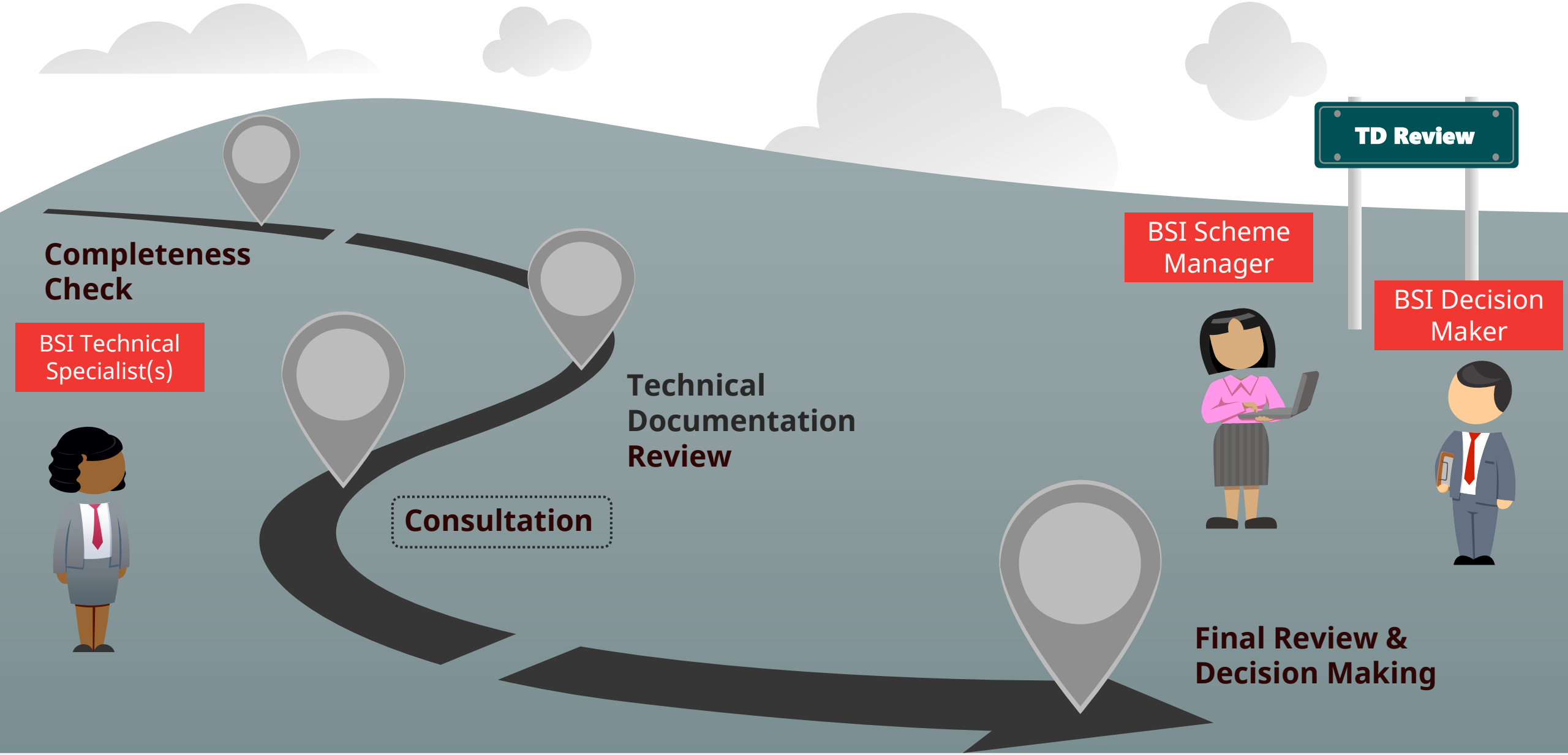
TD Review
Completeness Check
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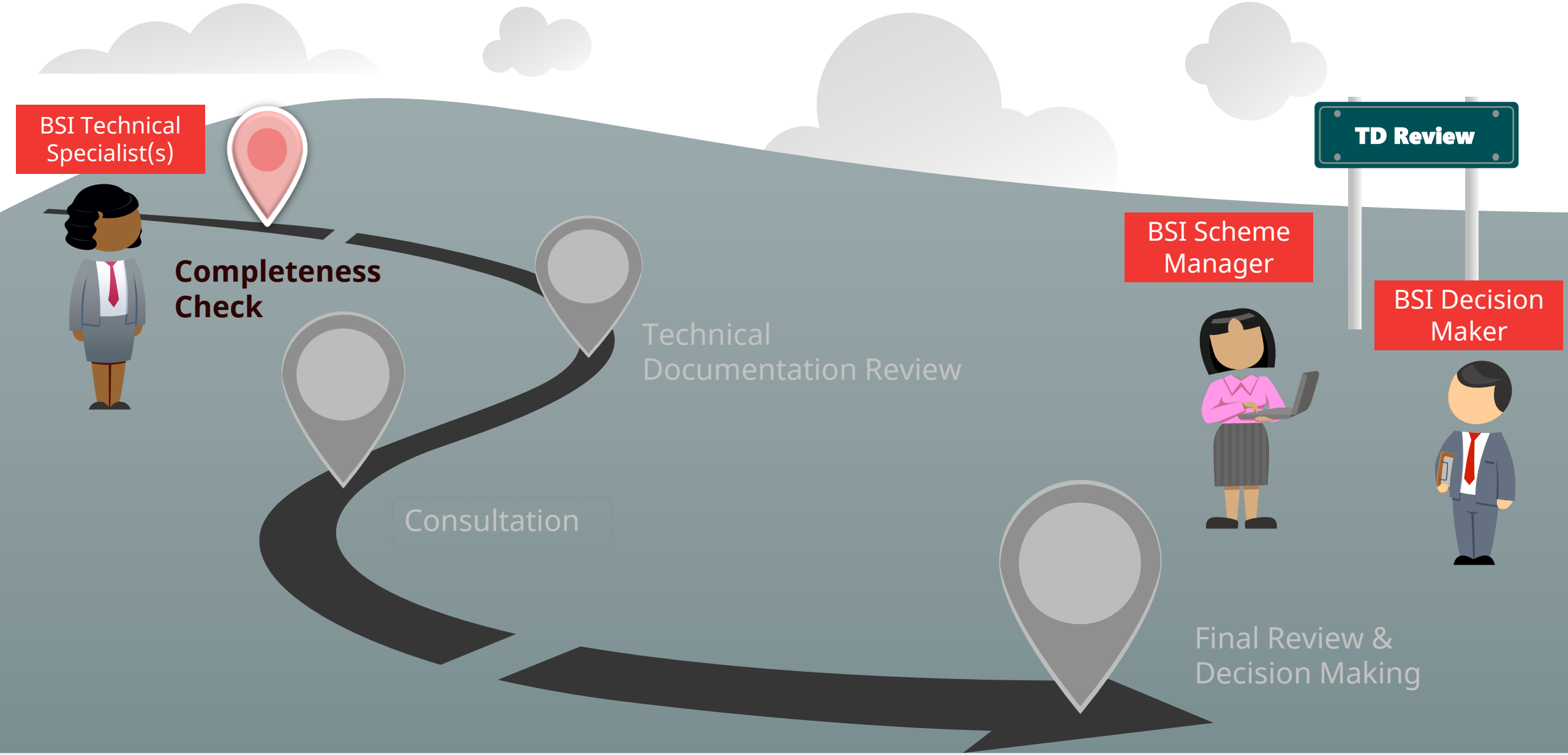
Final Review & Decision Making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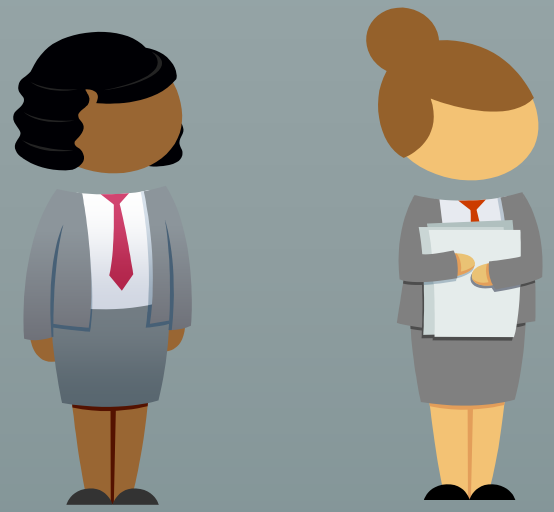
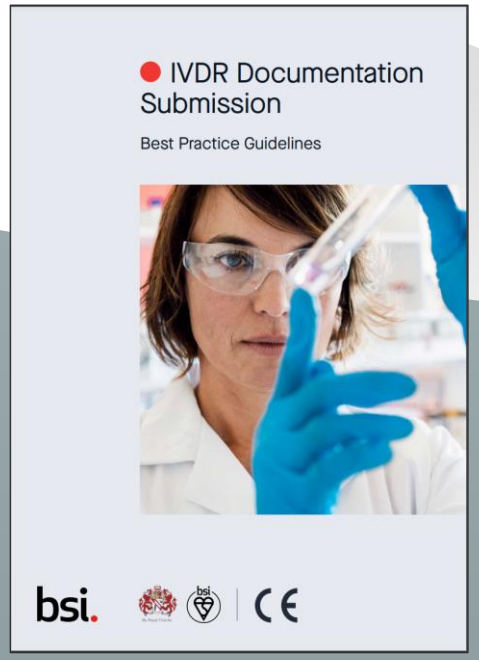
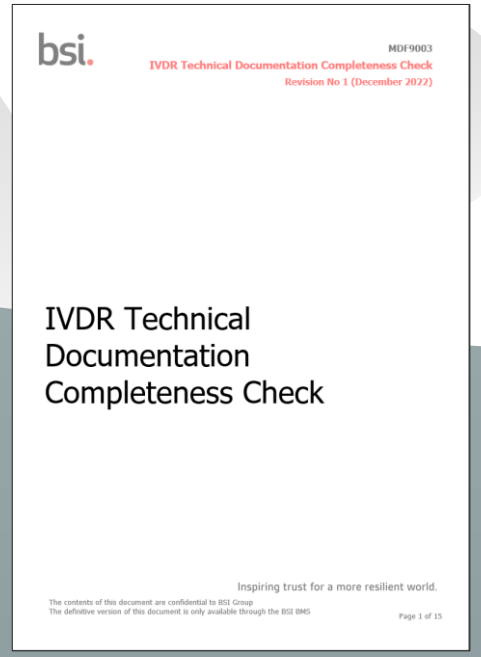
BSI Technical Specialist

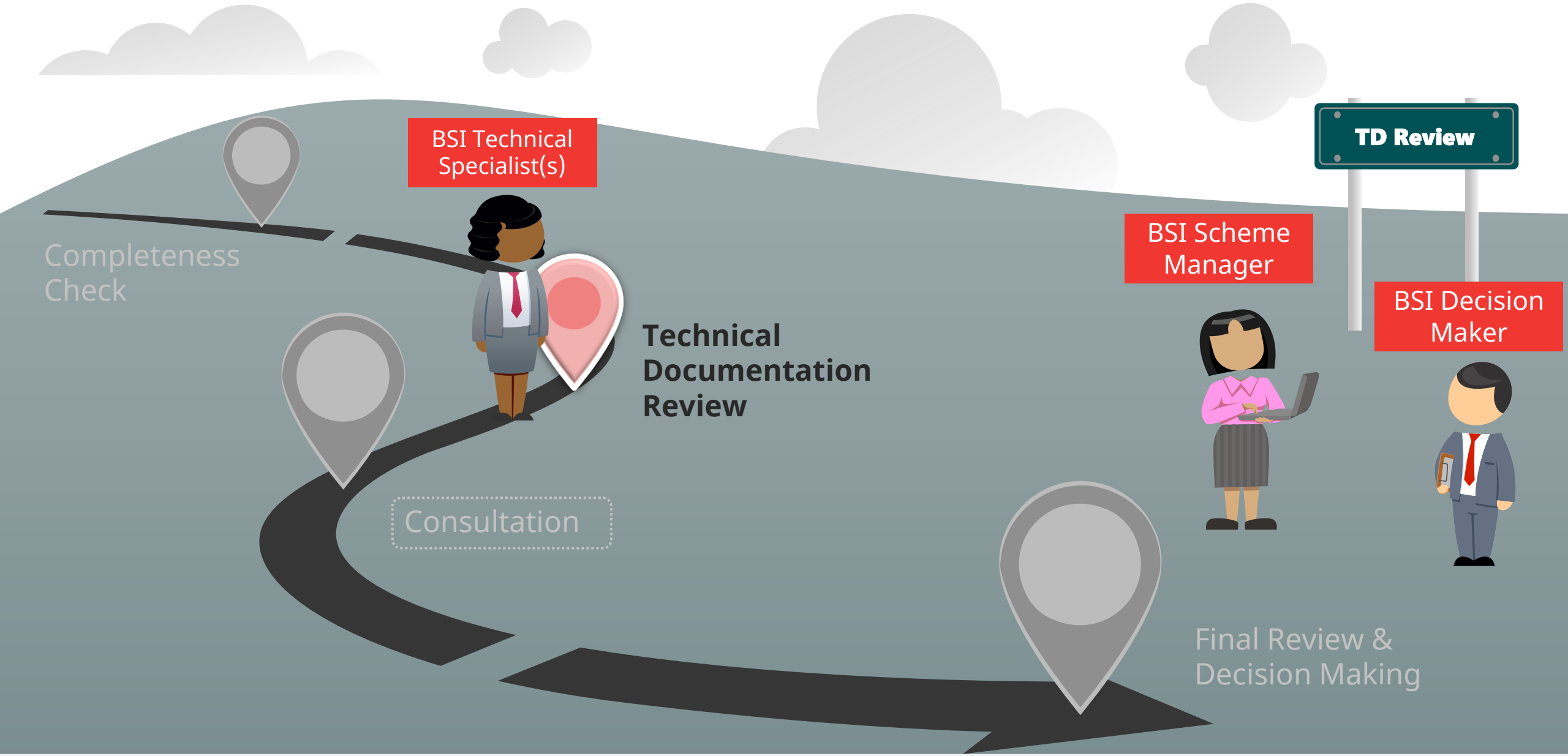
BSI IVD Project Management







- Manufacturer assembles technical documentation considering BSI Best Practice Guidelines
- Manufacturer submits the technical file & completed IVDR Technical Documentation Completeness Check Form to BSI
- BSI Technical Specialist verifies completeness of the technical documentation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Completeness Check
Technical Documentation Review
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Final Review & Decision Making

Summary of Technical Documentation (STED)

EU Declaration of Conformity

Instructions for Use (IFU)

Summary of Safety and Performance (SSP)

Performance Evaluation Plan (PEP)

Scientific Validity Report (SVR)

Analytical Performance Report (APR)

Clinical Performance Report (CPR)

Clinical Performance Study Plan (CPSP)

Clinical Performance Study Report (CPSR)

Performance Evaluation Report (PER)

Post-Market Surveillance Plan

Risk Management File

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Reference to previous and similar generations of the device (Annex II, Section 1.2)

- **Technological status of the device:**
  - **Original/Co-developed CDx:**
    - Version of the device was used in the pivotal clinical trial
    - Changes to the device since the pivotal trial and their impact
  - **Follow-on CDx**:
    - Reference to the original CDx
    - The reference device used to demonstrate clinical performance and justification for why is it appropriate
  - **Legacy device or new to market?**

STED IFU SSP PEP SVR APR CPR CPSP CPSR PER PMS PMPF

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Information in the instructions for use (Annex I – AKA GSPRs, Section 20.4.1)

- **The instructions for use shall contain the following particulars:**
  - The devices intended purpose:
    - Its function = Companion Diagnostic ***GSPR 20.4.1 (c)(ii)***
    - The specific information that is intended to be provided = CDx indications & target populations ***GSPR 20.4.1 (c)(iii)***
    - International Non-proprietary Name (INN) of associated medicinal product ***GSPR 20.4.1 (c)(viii)***
  - The devices analytical & clinical performance characteristics, etc. ***GSPR 20.4.1 (w – ab)***
    - Detailed information is expected ⇨ claim, acceptance criteria, materials & methods, statistical methods, results, conclusions

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Summary of Safety and Performance (Article 29)

- **The SSP shall include:**
  - Reference to previous generation(s) of the device, and description of the differences ***Article 29, section 2(e)***
    - Summary of the information provided in the STED
  - Summary of the performance evaluation (including scientific validity, analytical performance, clinical performance, and planned PMPF) ***Article 20, section 2(e)***
    - Detailed information is needed for CA or EMA to perform a qualified assessment on the suitability of the device in relation to the concerned medicinal product(s)
- **The MDCG 2022-9 SSP Template shall be used**

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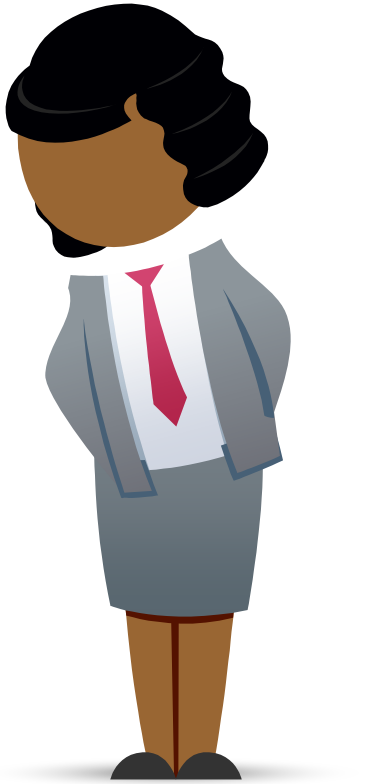
Performance Evaluation Plan (Annex XIII, section 1.1)

- **The performance evaluation plan shall include…an outline of the different development phases….**
  - **Original/Co-developed CDx:**
    - Alignment of the development phases of the CDx with the clinical development program of the medicinal product(s)
    - Identification of the development phases were scientific validity, analytical, and clinical performance were determined



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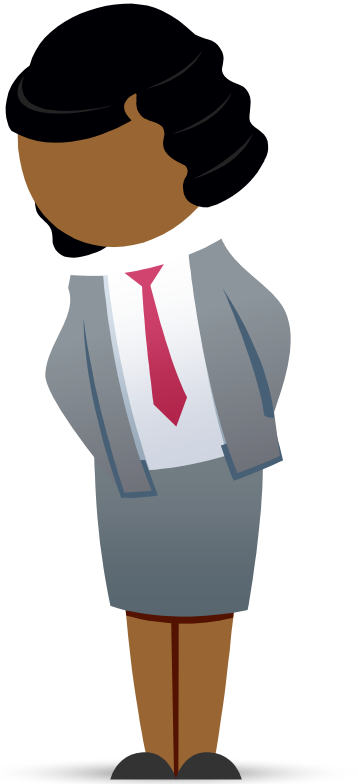

Scientific Validity Report (Annex XIII, section 1.2.1)

IVDR Definition:

- 'scientific validity of an analyte' means the association of an **analyte** with a **clinical condition** or a physiological state ***Article 2(38)***
    - **For CDx Devices:**
        - **Analyte** = CDx biomarker (i.e., BRAF V600E or BRAF V600K mutations in melanoma patients)
        - **Clinical Condition** = response to associated medicinal product (i.e., response to treatment with Mekinist -> INN=trametinib)
- For multiplex devices, scientific validity must be demonstrated for **every CDx biomarker**

Scientific Validity Report (Annex XIII, section 1.2.1)

- Mechanism of action for the corresponding medicinal product(s)
- CDx biomarker is established as a predicative biomarker for the associated medicinal product
- Marketing authorization of the corresponding medicinal product(s) in Europe
  - Name of the medicinal product, INN, and Agency Product Number, for example:
    - Name of the Medicinal Product: Mekinist
    - INN: trametinib
    - Agency Product Number: EMEA/H/C/002643
    - Therapeutic indications
  - The approved therapeutic indications of the medicinal product align with the intended purpose of the CDx

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STED IFU SSP PEP SVR **APR** CPR CPSP CPSR PER PMS PMPF

Analytical Performance Report (Annex XIII, section 1.2.2)

IVDR Definition:

- 'analytical performance' means the ability of a device to correctly detect or measure a particular analyte ***Article 2(40)***

For CDx Devices:

- The analytical performance for the applicable GSPR 9.1(a) characteristics will need to be demonstrated for **all CDx biomarkers** that the device claims to detect
  - i.e., BRAF V600E, BRAF V600K
- Attention will be given to the selection of the assay cut-off since it is of particular importance for the benefit/risk assessment of the medicinal product
- Detailed information on the acceptance criteria, materials & methods, statistical methods, results, conclusions shall be given

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Clinical Performance Report (Annex XIII, section 1.2.3)

IVDR Definition:
'clinical performance' means the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user ***Article 2(41)***

For a CDx the aim of clinical performance is to:

- Demonstrate that the CDx is able to detect the specified CDx biomarker(s) in patient samples and in the intended use environment
- Demonstrate that the CDx can identify the patient population who is expected to benefit from the corresponding medicinal product(s)

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Clinical Performance Report (Annex XIII, section 1.2.3)

Clinical performance must be demonstrated using one or a combination of the sources specified in IVDR Annex XIII, section 1.2.3

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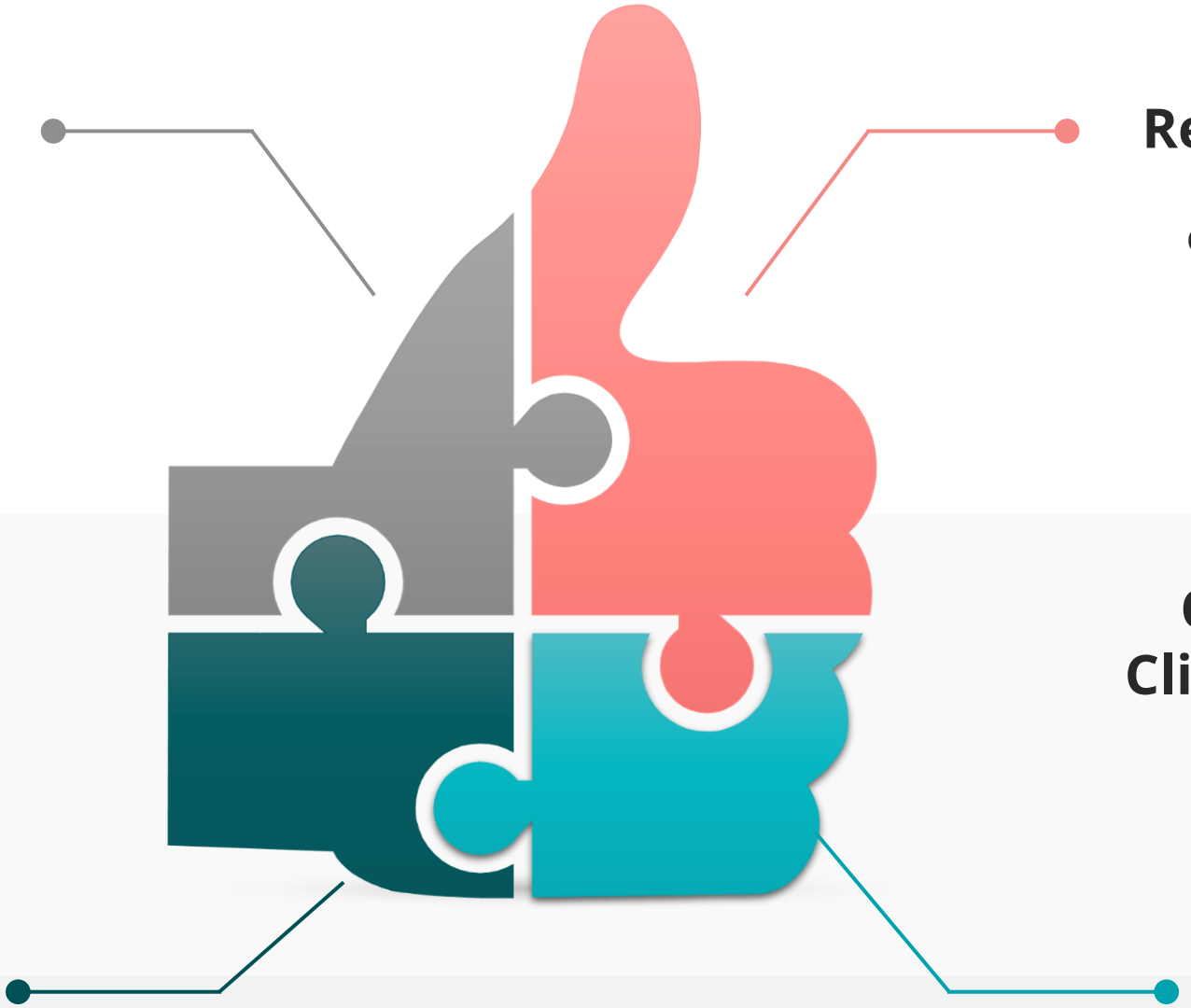
Approach used to demonstrate clinical performance

Clinical Performance Studies

IVDR Annex XIII, section 2

Scientific Peer Reviewed Literature

Data used to support clinical performance must be generated using the CDx device under review



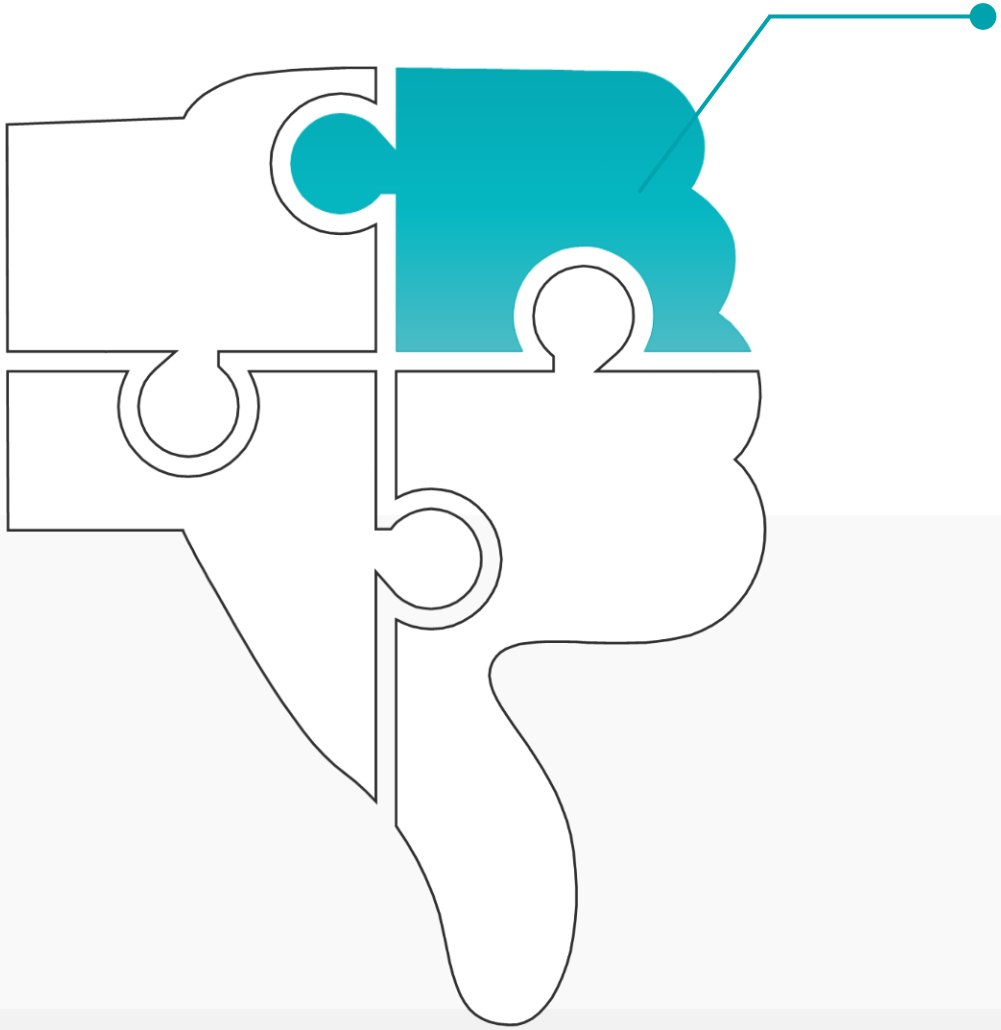
Published Experience Gained by Routine Diagnostic Testing

i.e., EQA data

Other Sources of Clinical Performance Data

i.e., data from pivotal clinical trial performed before the IVDR

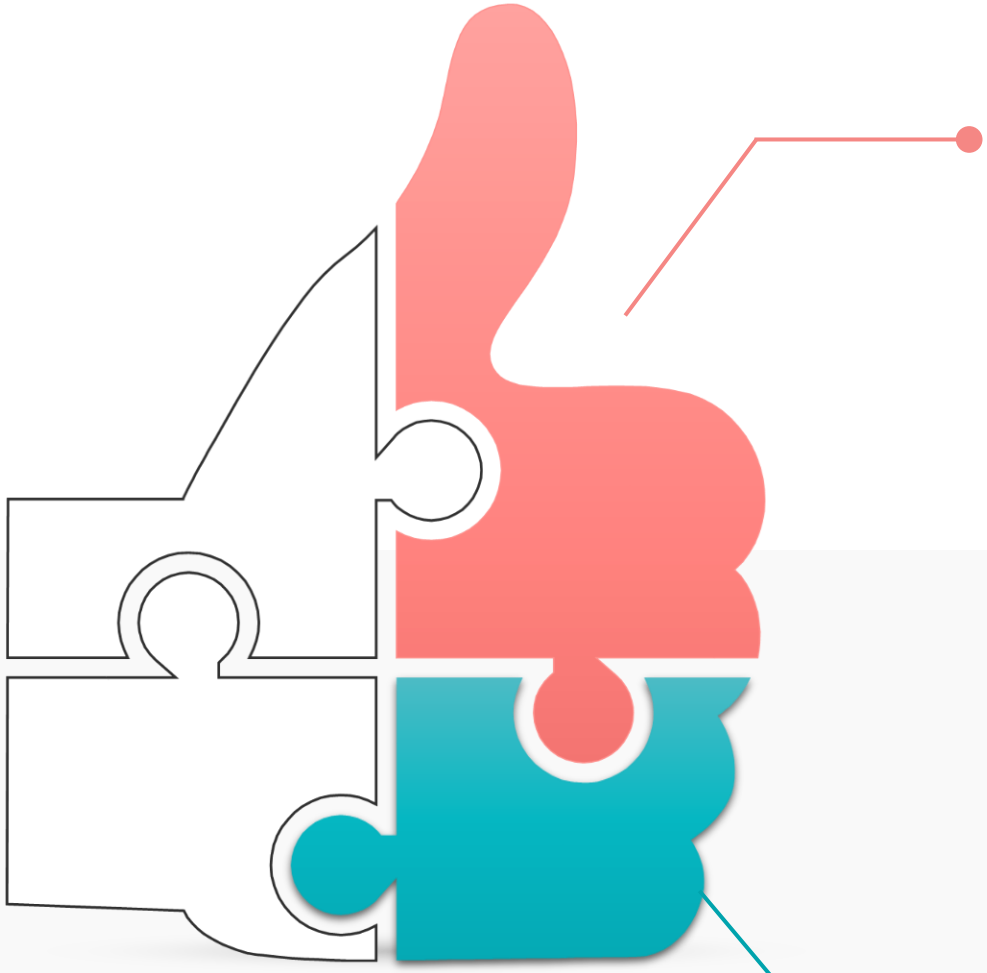
Approach used to demonstrate clinical performance



Other Sources of Clinical Performance Data

i.e., data from pivotal clinical trial performed before the IVDR

Approach used to demonstrate clinical performance



Scientific Peer Reviewed Literature

Data used to support clinical performance must be generated using the CDx device under review

Other Sources of Clinical Performance Data

i.e., data from pivotal clinical trial performed before the IVDR

Approach used to demonstrate clinical performance

Published Experience Gained by Routine Diagnostic Testing

i.e., EQA data

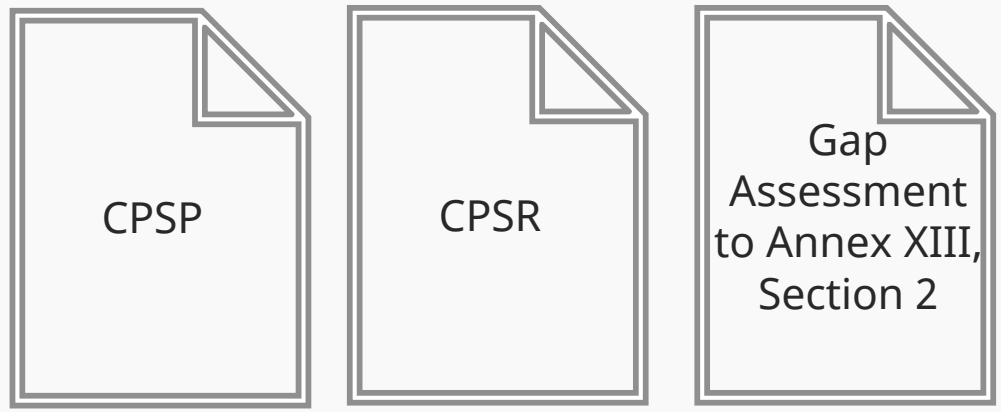
Other Sources of Clinical Performance Data

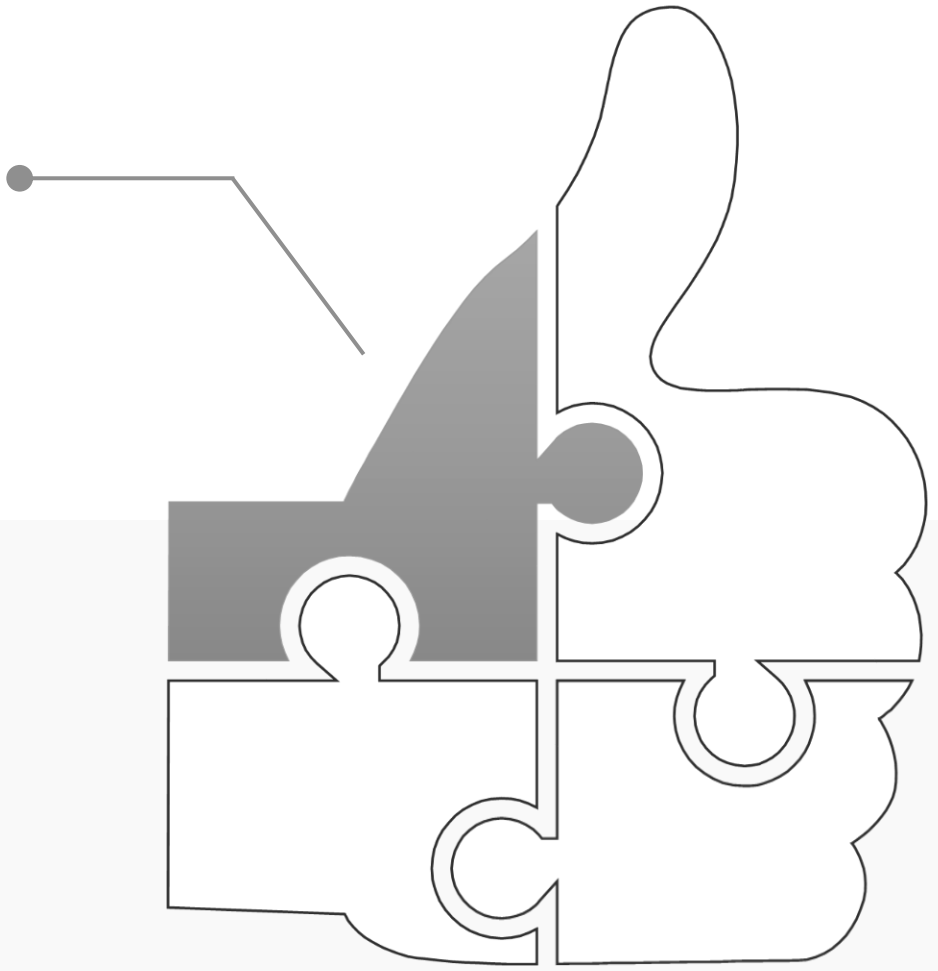
i.e., data from pivotal clinical trial performed before the IVDR

Approach used to demonstrate clinical performance

Other Sources of Clinical Performance Data Submitted as a Clinical Performance Studies

i.e., data from pivotal clinical trial performed before the IVDR





STED IFU SSP PEP SVR APR **CPR** CPSP CPSR PER PMS PMPF

Clinical Performance Report (Annex XIII, section 1.2.3)

Original/Co-developed CDx:

- Clinical performance is demonstrated via the use of the device to select patients for the pivotal clinical trial(s) for the corresponding medicinal product(s)
  - ⇨ Correlation with a clinical endpoint
  - ⇨ Applicable GSPR 9.1(b) clinical performance characteristics depend on the clinical trial design

Follow-on CDx:

- Clinical performance is demonstrated by a concordance study with a clinically valid reference assay (i.e., the original CDx)
  - ⇨ Applicable GSPR 9.1(b) clinical performance characteristics would include PPA, NPA, OPA

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Clinical Performance Study Plan (Annex XIII, Section 2.3.2)

- The clinical performance study plans corresponding to the clinical performance studies selected to demonstrate the clinical performance of the CDx device shall be provided
- Clinical performance study plans written retrospectively to meet the requirements of the IVDR will not be accepted

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STED IFU SSP PEP SVR APR CPR CPSP **CPSR** PER PMS PMPF

Clinical Performance Study Report (Annex XIII, Section 2.3.3)

- The CPSR corresponding to the clinical performance studies selected to demonstrate the clinical performance of the CDx device shall be provided
- CPSRs written retrospectively to meet the requirements of the IVDR will not be accepted
- CPSRs shall be signed by a medical practitioner or other person responsible
- CPSR ≠ CPR

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Performance Evaluation Report (Annex XIII, Section 1.3.2)

Documents the manufacturer's assessment of the clinical evidence against the applicable GSPRs and state of the art in medicine in Europe (i.e., medicinal product approval in Europe)

When the medicinal product is not yet approved the end of the CA/EMA consultation will close this loop. Therefore, the PER may need to be updated after the CA/EMA consultation

Post-Market Surveillance Plan (Annex III, Section 1)

The PMS plan should also monitor the medicinal product(s)

For example, are there changes to the indications of the medicinal product that impact the conclusion of the benefit-risk analysis for the CDx

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Post-Market Performance Follow-Up Plan (Annex XIII, Part B)

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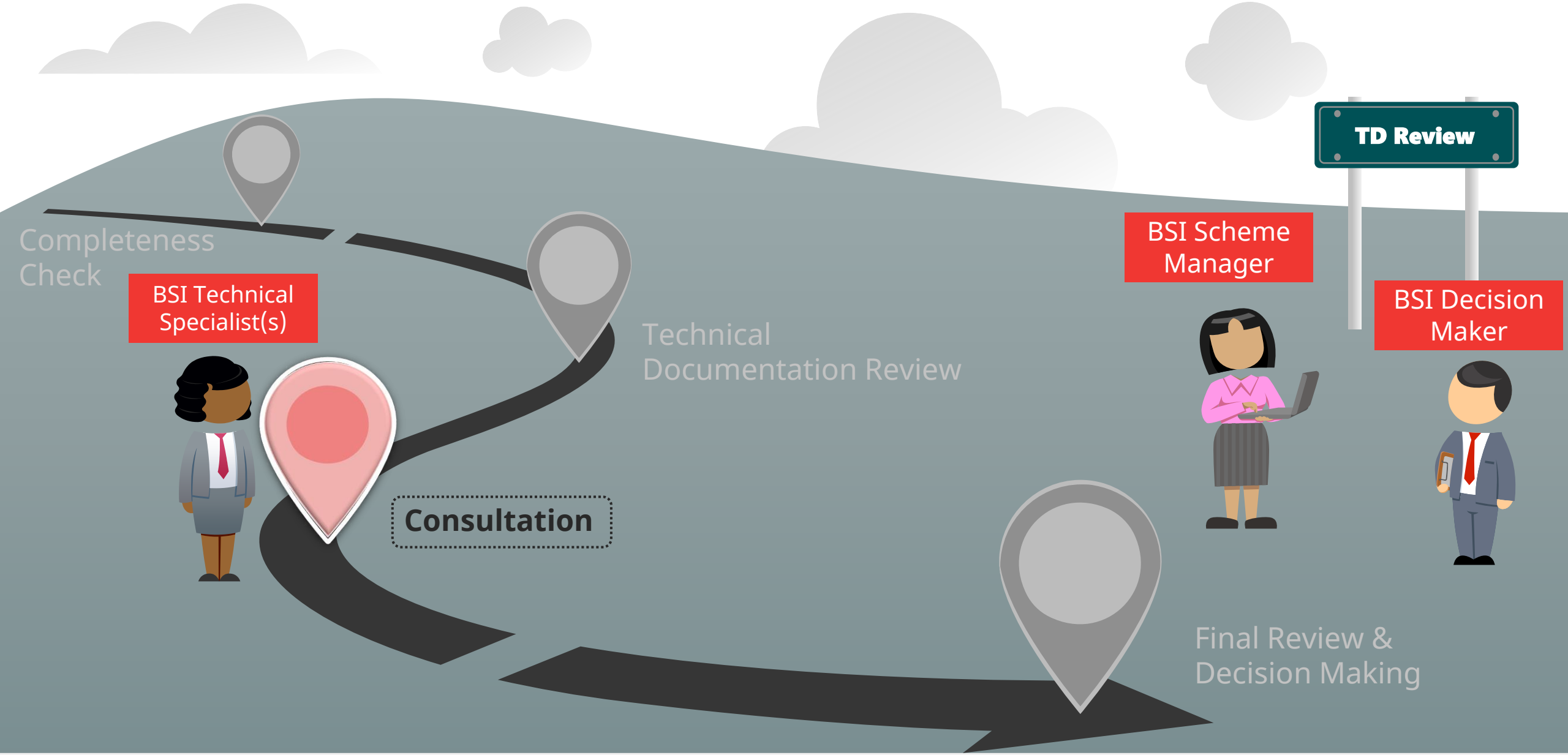
Are there any outstanding performance or safety issues that need to be addressed via PMPF studies?

Are there any PMPF studies planned to expand the CDx indications and sample types?


TD Review
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Final Review & Decision Making

Competent Authority or EMA Consultation

Consultation

BSI consults the authority that approved the medicinal product

Centralised Procedure

- Single marketing authorisation for EU via EMA

National Authorisation Procedure

- Individual Member States authorize medicines for use in their own territory

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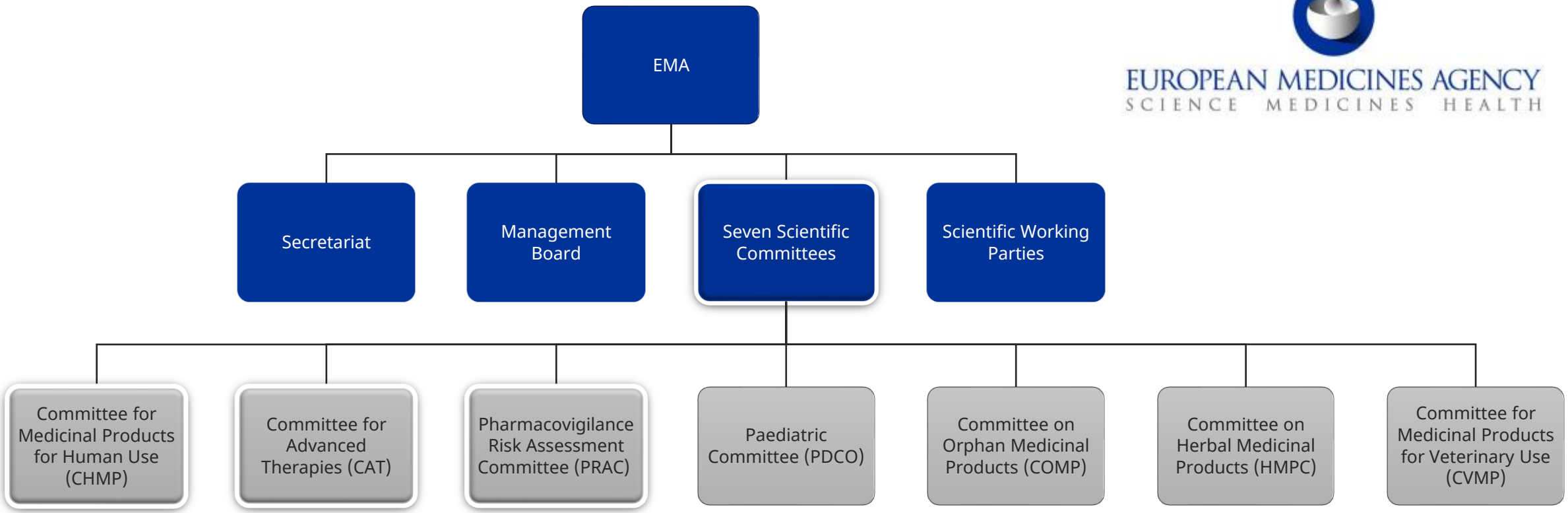
Centralised Marketing Authorisation via EMA

Allows companies to submit a single application to EMA to obtain a centralised marketing authorization from the European Commission

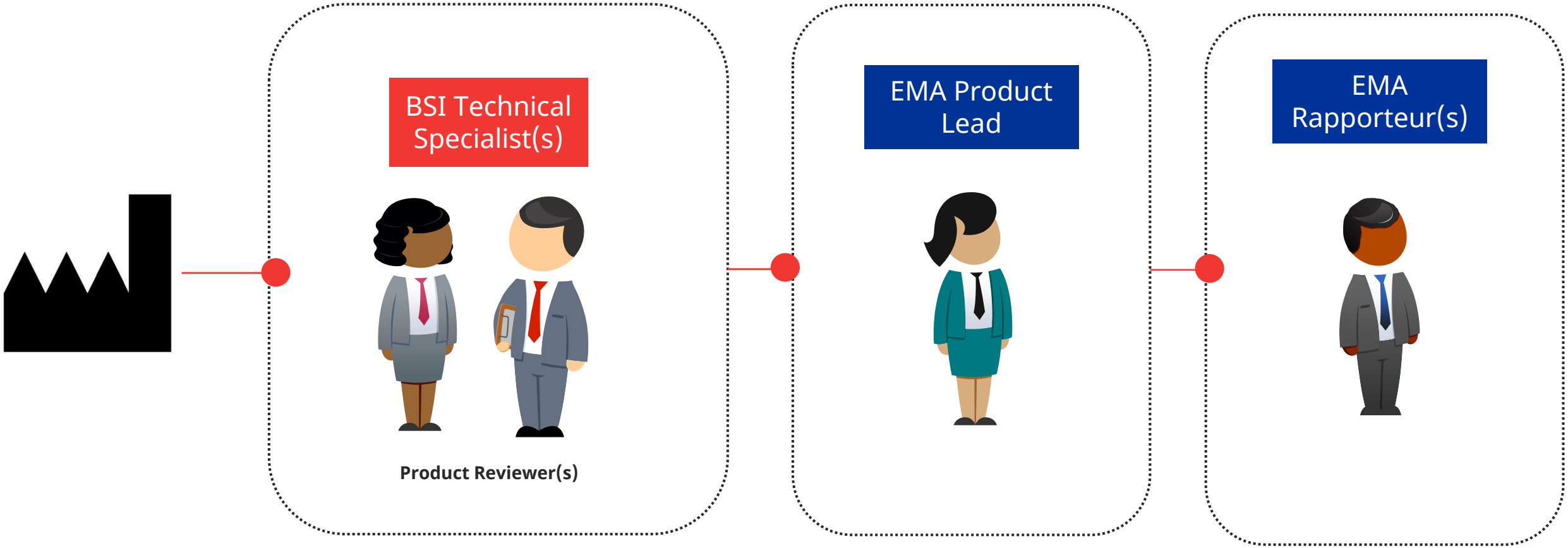
- Centralised marketing authorization is valid in EU member states, Iceland, Liechtenstein and Norway
- EMA performs assessment of medicinal product and makes recommendation for marketing authorization to the EU Commission
- EU Commission grants marketing authorization based on EMA’s recommendation

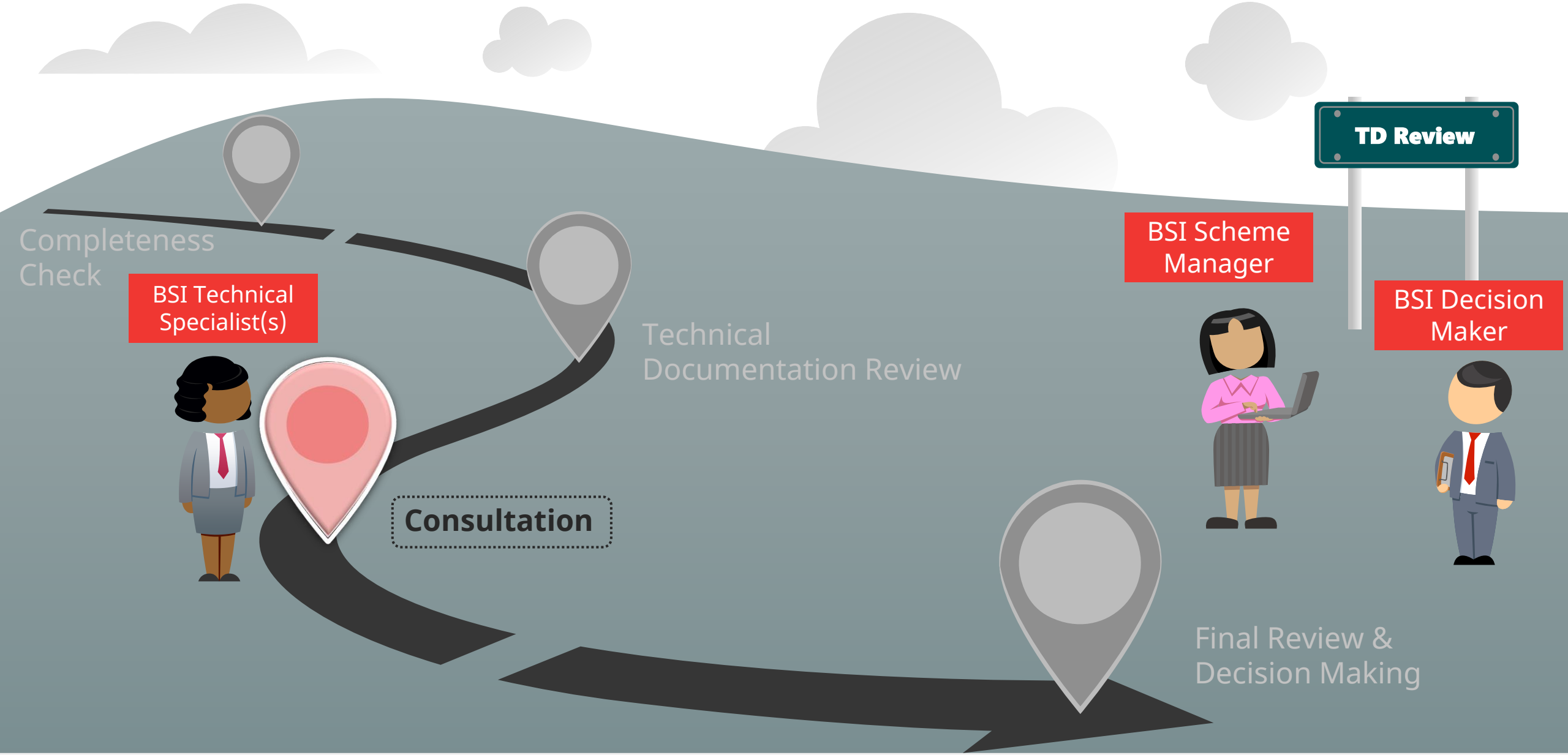
European Medicines Agency (EMA)

Agency in the EU in charge for evaluation and supervision of medicinal products



Roles and Responsibilities for EMA Consultation

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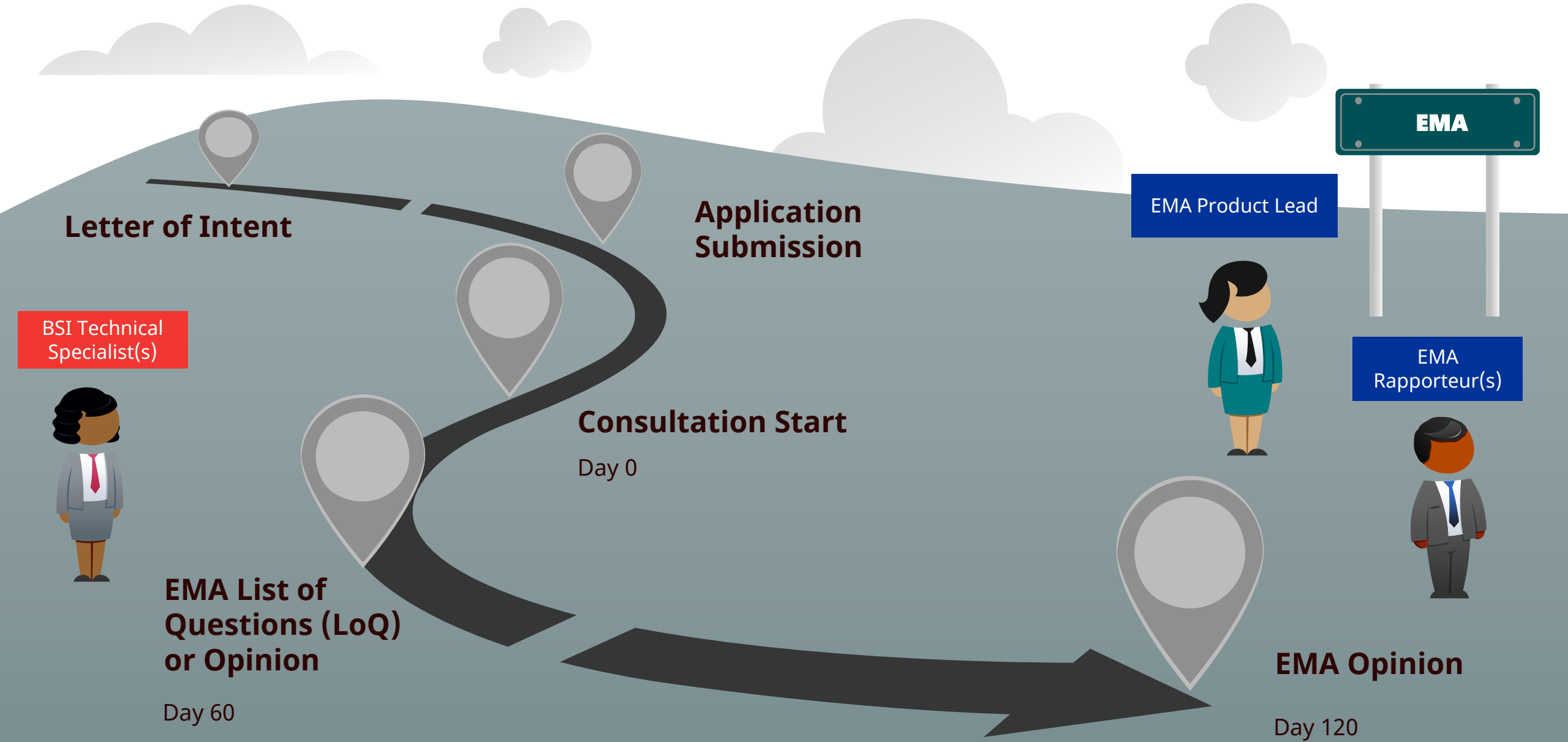
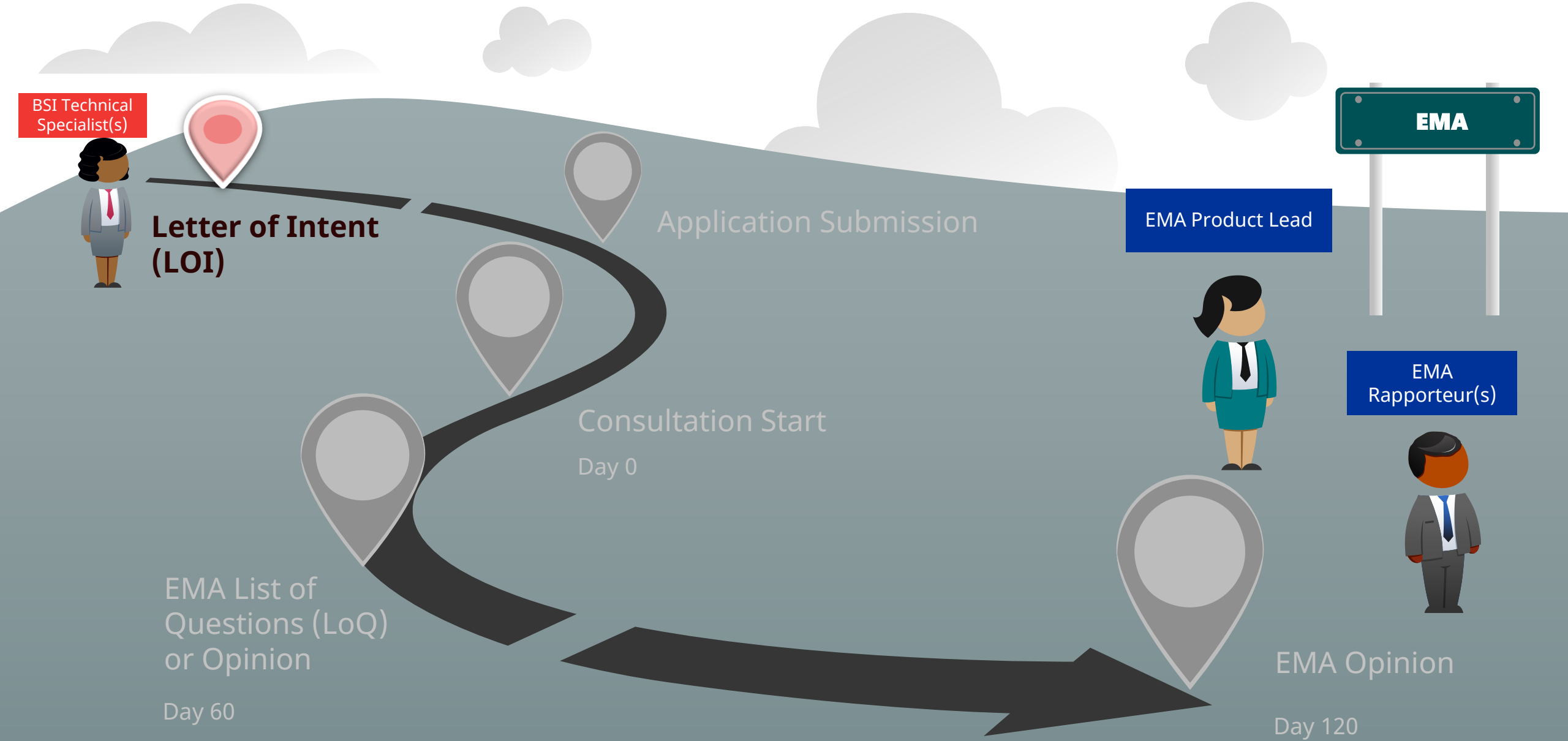
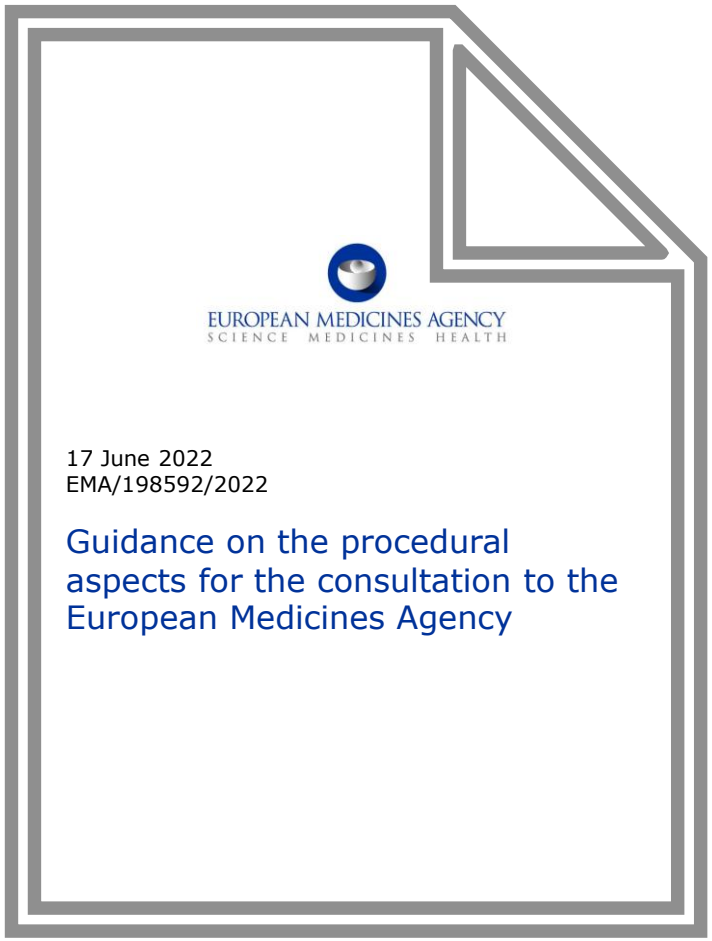

Letter of Intent
Application Submission
BSI Technical Specialist(s)
Consultation Start
Day 0
EMA
EMA Product Lead
EMA Rapporteur(s)
EMA List of Questions (LoQ) or Opinion
Day 60
EMA Opinion
Day 120


BSI Technical Specialist(s)
Letter of Intent (LOI)
Application Submission
Consultation Start
Day 0
EMA List of Questions (LoQ) or Opinion
Day 60
EMA Opinion
Day 120
EMA Product Lead
EMA Rapporteur(s)
EMA

- BSI Technical Specialist submits the letter of intent to EMA **once all technical review questions are closed**.
- Must be submitted **3 months** before the application for consultation.

EMA Consultation – Letter of Intent (LOI)



Pre-submission phase:

The notified body is expected to provide an **"intention-to-submit-letter"** to the EMA at least **3 months before the planned submission date** of request for a scientific opinion on the suitability of the CDx with the concerned medicinal product(s), using the **relevant template** that can be found on the European Medicines Agency website.

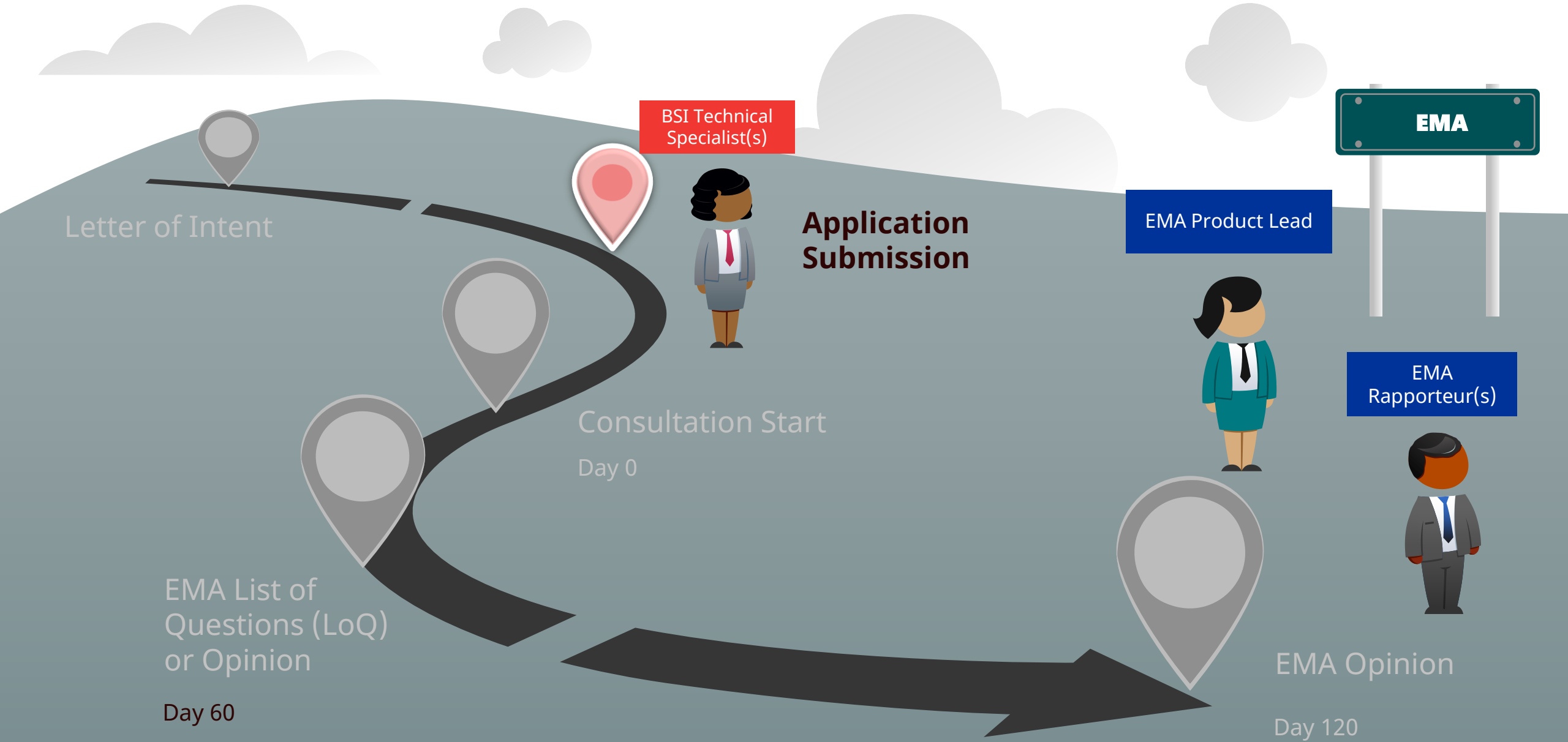
This intention to submit-letter also aims to trigger the timely **appointment of the rapporteur(s)**.

EMA Consultation – Letter of Intent (LOI)

The LOI shall be submitted using the template provided on EMA's website

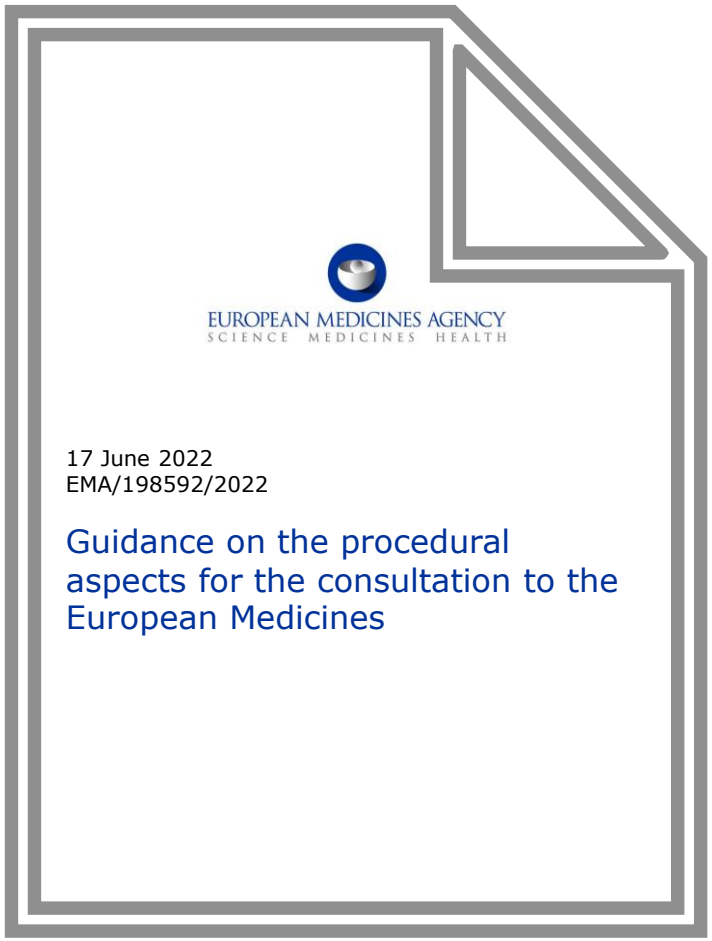
Letter of intent for the submission of a consultation to the European Medicines Agency by a notified body on a companion diagnostic in accordance with Regulation (EU) 2017/746
(DOCX/117.99 KB)

First published: 08/07/2022
Last updated: 31/07/2023
EMA/781233/2021


Letter of Intent
BSI Technical Specialist(s)
Application Submission
EMA
EMA Product Lead
EMA Rapporteur(s)
Consultation Start
Day 0
EMA List of Questions (LoQ) or Opinion
Day 60
EMA Opinion
Day 120

BSI Technical Specialist submits application to EMA

EMA Consultation – Application Submission



Submission Phase:

The application consists of a:

1. Cover Letter
2. Application Form
3. IFU (draft)
4. SSP (draft)

EMA Consultation – Application Submission

The Application shall be submitted using the application form template provided on EMA's website

Application form for initial consultation by a notified body on a companion diagnostic (DOCX/128.43 KB)

First published: 20/12/2021
Last updated: 01/07/2022

EMA Consultation Follows Published Procedural Timetables

Companion diagnostic consultation

Timetable: Companion diagnostic initial consultation (PDF/232.82 KB)

First published: 21/01/2022
Last updated: 11/05/2022
EMA/3932/2022 Rev.1

Timetable: Companion diagnostic initial consultation - ATMP (PDF/226.62 KB)

First published: 21/01/2022
Last updated: 28/04/2023
EMA/3933/2022 Rev.2

→ Initial Consultation

Timetable: Companion diagnostic follow-up consultation (PDF/139.08 KB)

First published: 08/12/2022
EMA/3932/2022

Timetable: Companion diagnostic follow-up consultation - ATMP (PDF/172.98 KB)

First published: 08/12/2022
EMA/3933/2022

→ Follow-up Consultation

bsi.

Initial submission assessment timetable

60-day timetable

	Deadline for Submission (*)	Start date	CHMP Rapporteur AR	Steps only applicable in case of PRAC involvement				Comments from CHMP (**)	Updated CHMP Rapporteur AR (***)	List of questions (LoQ) or Opinion
				PRAC Rapporteur AR	Comments from PRAC (**)	Updated PRAC Rapporteur AR (***)	PRAC outcome (~)			
A1	12/11/2021	29/11/2021	22/12/2021	03/01/2022	05/01/2022	06/01/2022	13/01/2022	17/01/2022	20/01/2022	27/01/2022
A2	26/11/2021	27/12/2021	25/01/2022	28/01/2022	02/02/2022	03/02/2022	10/02/2022	14/02/2022	17/02/2022	24/02/2022
A3	07/01/2022	24/01/2022	22/02/2022	25/02/2022	02/03/2022	03/03/2022	10/03/2022	14/03/2022	17/03/2022	24/03/2022
A4	02/02/2022	22/02/2022	22/03/2022	25/03/2022	30/03/2022	31/03/2022	07/04/2022	11/04/2022	13/04/2022	22/04/2022
A5	04/03/2022	21/03/2022	19/04/2022	22/04/2022	26/04/2022	28/04/2022	05/05/2022	10/05/2022	12/05/2022	19/05/2022
A6	08/04/2022	25/04/2022	24/05/2022	30/05/2022	01/06/2022	02/06/2022	10/06/2022	13/06/2022	16/06/2022	23/06/2022
A7	06/05/2022	23/05/2022	21/06/2022	24/06/2022	29/06/2022	30/06/2022	07/07/2022	11/07/2022	14/07/2022	21/07/2022

Letter of Intent

Application Submission

EMA

EMA Product Lead

EMA Rapporteur(s)

Consultation Start

Day 0

BSI Technical Specialist(s)

EMA List of Questions (LoQ) or Opinion

Day 60

EMA Opinion

Day 120

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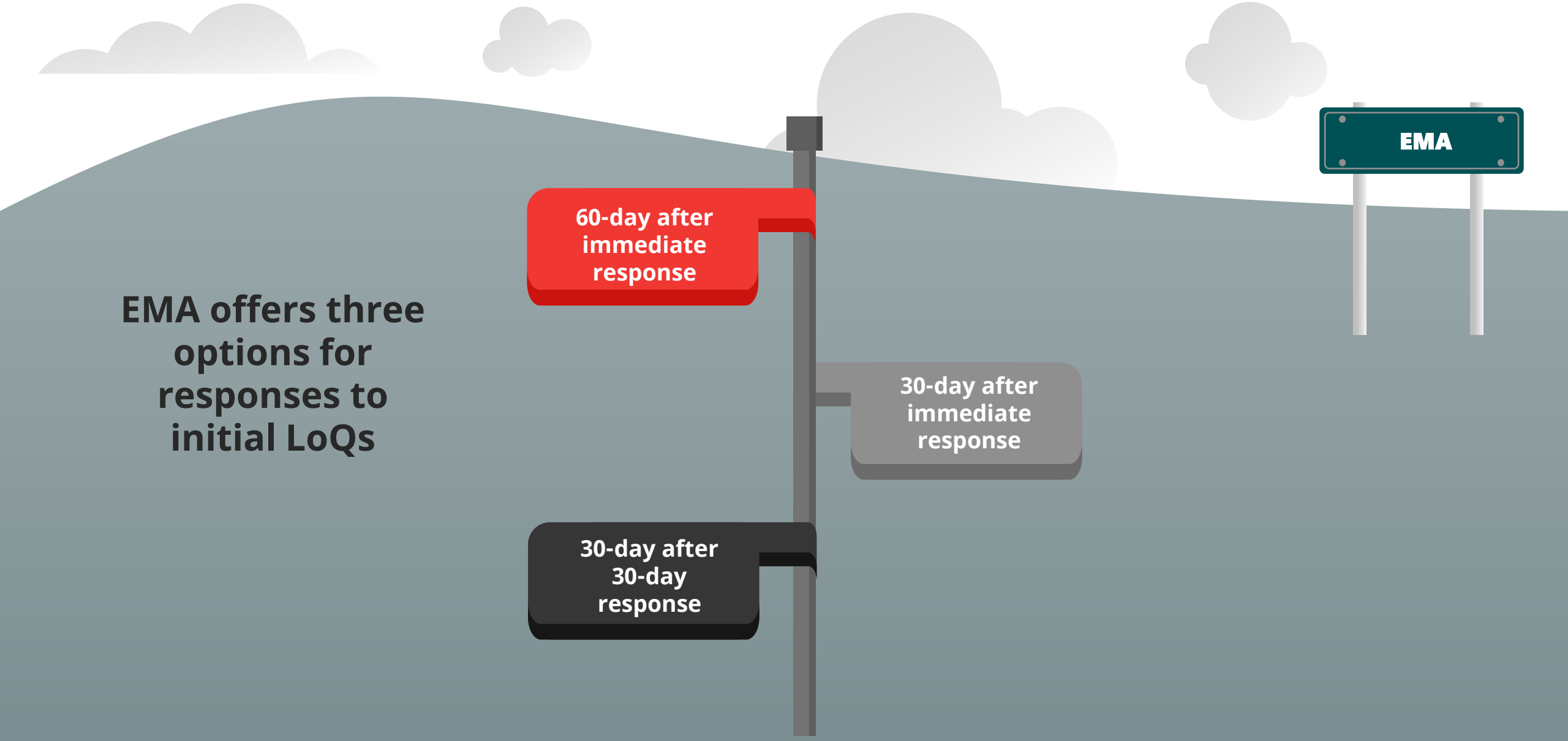
EMA offers three options for responses to initial LoQs



60-day after immediate response

Initial submission assessment timetable

60-day timetable

	Deadline for Submission (*)	Start date	CHMP Rapporteur AR	Steps only applicable in case of PRAC involvement				Comments from CHMP (**)	Updated CHMP Rapporteur AR (***)	List of questions (LoQ) or Opinion
				PRAC Rapporteur AR	Comments from PRAC (**)	Updated PRAC Rapporteur AR (***)	PRAC outcome (~)			
A1	12/11/2021	29/11/2021	22/12/2021	03/01/2022	05/01/2022	06/01/2022	13/01/2022	17/01/2022	20/01/2022	27/01/2022
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A3	07/01/2022	24/01/2022	22/02/2022	25/02/2022	02/03/2022	03/03/2022	10/03/2022	14/03/2022	17/03/2022	24/03/2022
A4	02/02/2022	22/02/2022	22/03/2022	25/03/2022	30/03/2022	31/03/2022	07/04/2022	11/04/2022	13/04/2022	22/04/2022
A5	04/03/2022	21/03/2022	19/04/2022	22/04/2022	26/04/2022	28/04/2022	05/05/2022	10/05/2022	12/05/2022	19/05/2022
A6	08/04/2022	25/04/2022	24/05/2022	30/05/2022	01/06/2022	02/06/2022	10/06/2022	13/06/2022	16/06/2022	23/06/2022
A7	06/05/2022	23/05/2022	21/06/2022	24/06/2022	29/06/2022	30/06/2022	07/07/2022	11/07/2022	14/07/2022	21/07/2022

Assessment of Responses to List of Questions (LoQ)

60-day timetable after immediate responses¬

	Deadline for Submission (*)	Restart	CHMP Rapporteur AR	Steps only applicable in case of PRAC involvement				Comments from CHMP (**)	Updated CHMP Rapporteur AR (***)	Opinion
				PRAC Rapporteur AR	Comments from PRAC (**)	Updated PRAC Rapporteur AR (***)	PRAC outcome (#)			
B1	08/12/2021	09/12/2021	22/12/2021	03/01/2022	05/01/2022	06/01/2022	13/01/2022	17/01/2022	20/01/2022	27/01/2022
B2	05/01/2022	06/01/2022	25/01/2022	28/01/2022	02/02/2022	03/02/2022	10/02/2022	14/02/2022	17/02/2022	24/02/2022
B3	02/02/2022	03/02/2022	22/02/2022	25/02/2022	02/03/2022	03/03/2022	10/03/2022	14/03/2022	17/03/2022	24/03/2022
B4	03/03/2022	04/03/2022	22/03/2022	25/03/2022	30/03/2022	01/04/2022	07/04/2022	11/04/2022	13/04/2022	22/04/2022
B5	30/03/2022	31/03/2022	19/04/2022	22/04/2022	26/04/2022	28/04/2022	05/05/2022	10/05/2022	12/05/2022	19/05/2022
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B8	27/07/2022	28/07/2022	16/08/2022	19/08/2022	24/08/2022	25/08/2022	01/09/2022	05/09/2022	08/09/2022	15/09/2022

bsi.

30-day after immediate response

Initial submission assessment timetable

60-day timetable

	Deadline for Submission (*)	Start date	CHMP Rapporteur AR	Steps only applicable in case of PRAC involvement				Comments from CHMP (**)	Updated CHMP Rapporteur AR (***)	List of questions (LoQ) or Opinion
				PRAC Rapporteur AR	Comments from PRAC (**)	Updated PRAC Rapporteur AR (***)	PRAC outcome (~)			
A1	12/11/2021	29/11/2021	22/12/2021	03/01/2022	05/01/2022	06/01/2022	13/01/2022	17/01/2022	20/01/2022	27/01/2022
A2	26/11/2021	27/12/2021	25/01/2022	28/01/2022	02/02/2022	03/02/2022	10/02/2022	14/02/2022	17/02/2022	24/02/2022
A3	07/01/2022	24/01/2022	22/02/2022	25/02/2022	02/03/2022	03/03/2022	10/03/2022	14/03/2022	17/03/2022	24/03/2022
A4	02/02/2022	22/02/2022	22/03/2022	25/03/2022	30/03/2022	31/03/2022	07/04/2022	11/04/2022	13/04/2022	22/04/2022
A5	04/03/2022	21/03/2022	19/04/2022	22/04/2022	26/04/2022	28/04/2022	05/05/2022	10/05/2022	12/05/2022	19/05/2022
A6	08/04/2022	25/04/2022	24/05/2022	30/05/2022	01/06/2022	02/06/2022	10/06/2022	13/06/2022	16/06/2022	23/06/2022
A7	06/05/2022	23/05/2022	21/06/2022	24/06/2022	29/06/2022	30/06/2022	07/07/2022	11/07/2022	14/07/2022	21/07/2022

Assessment of responses List of Questions (LoQ)

30-day timetable after immediate responses¬

	Deadline for Submission (*)	Restart	CHMP Rapporteur AR	PRAC Rapporteur AR (#)	Comments from CHMP (**)	Comments from PRAC (#)(**)	Updated CHMP Rapporteur AR (~)(***)	Updated PRAC Rapporteur AR (#)(~)(***)	List of Questions (LoQ) or Opinion
D1	22/12/2021	29/12/2021	12/01/2022	12/01/2022	17/01/2022	17/01/2022	20/01/2022	20/01/2022	27/01/2022
D2	01/02/2022	02/02/2022	09/02/2022	09/02/2022	14/02/2022	14/02/2022	17/02/2022	17/02/2022	24/02/2022
D3	01/03/2022	02/03/2022	09/03/2022	09/03/2022	14/03/2022	14/03/2022	17/03/2022	17/03/2022	24/03/2022
D4	30/03/2022	31/03/2022	06/04/2022	06/04/2022	11/04/2022	11/04/2022	13/04/2022	13/04/2022	22/04/2022
D5	26/04/2022	27/04/2022	04/05/2022	04/05/2022	10/05/2022	10/05/2022	12/05/2022	12/05/2022	19/05/2022
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D7	28/06/2022	29/06/2022	06/07/2022	06/07/2022	11/07/2022	11/07/2022	14/07/2022	14/07/2022	21/07/2022

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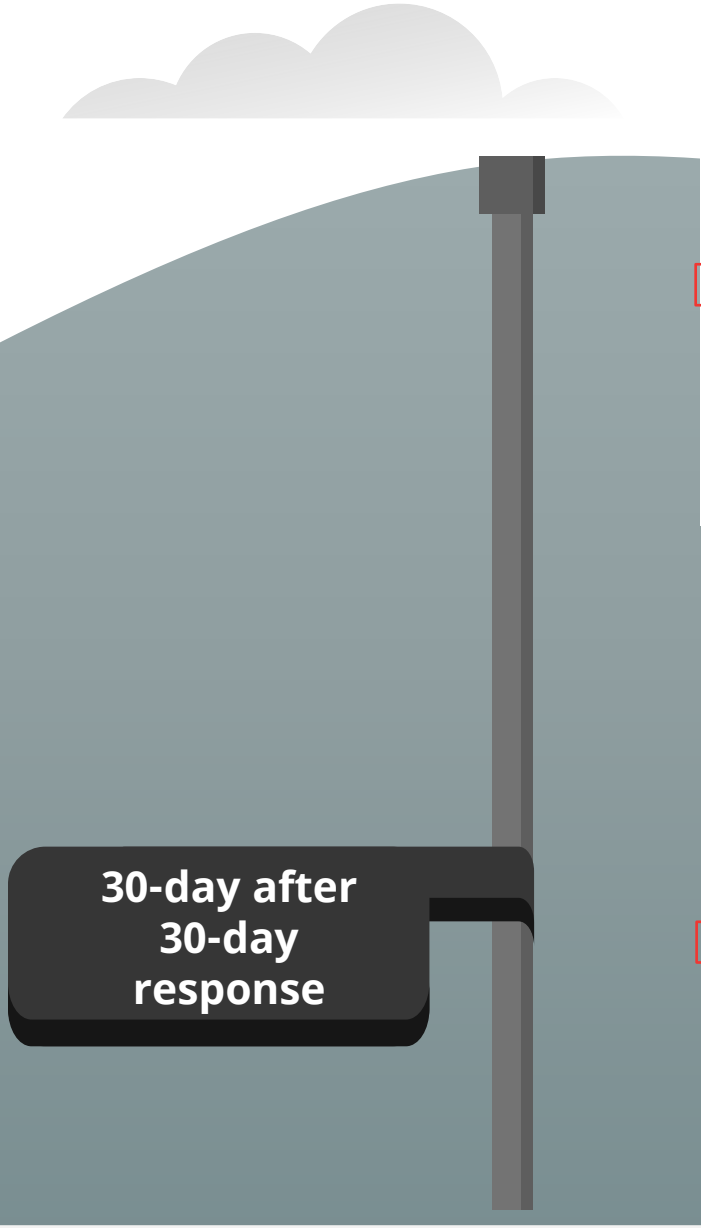

Initial submission assessment timetable

60-day timetable

	Deadline for Submission (*)	Start date	CHMP Rapporteur AR	Steps only applicable in case of PRAC involvement				Comments from CHMP (**)	Updated CHMP Rapporteur AR (***)	List of questions (LoQ) or Opinion
				PRAC Rapporteur AR	Comments from PRAC (**)	Updated PRAC Rapporteur AR (***)	PRAC outcome (~)			
A1	12/11/2021	29/11/2021	22/12/2021	03/01/2022	05/01/2022	06/01/2022	13/01/2022	17/01/2022	20/01/2022	27/01/2022
A2	26/11/2021	27/12/2021	25/01/2022	28/01/2022	02/02/2022	03/02/2022	10/02/2022	14/02/2022	17/02/2022	24/02/2022
A3	07/01/2022	24/01/2022	22/02/2022	25/02/2022	02/03/2022	03/03/2022	10/03/2022	14/03/2022	17/03/2022	24/03/2022
A4	02/02/2022	22/02/2022	22/03/2022	25/03/2022	30/03/2022	31/03/2022	07/04/2022	11/04/2022	13/04/2022	22/04/2022
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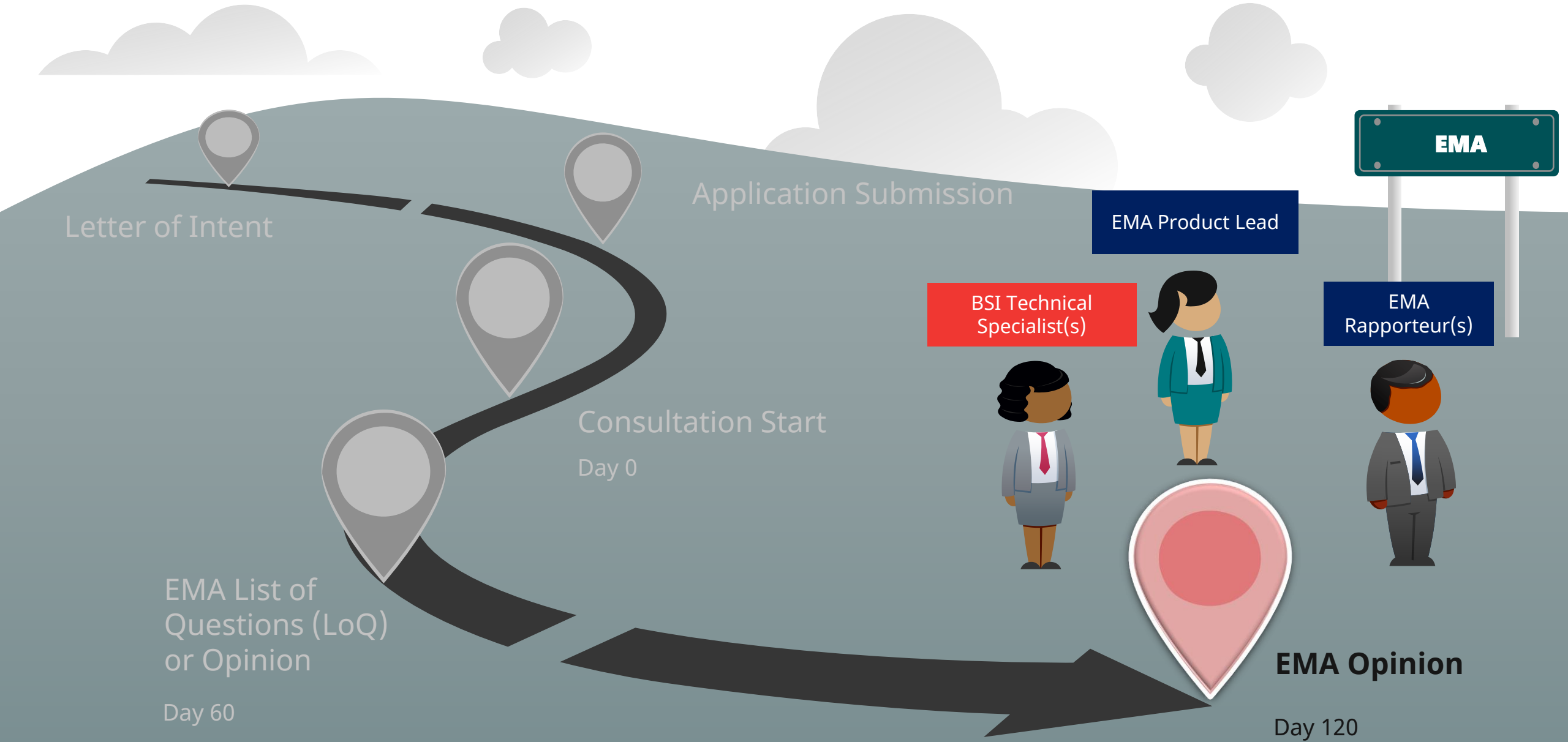
A6	08/04/2022	25/04/2022	24/05/2022	30/05/2022	01/06/2022	02/06/2022	10/06/2022	13/06/2022	16/06/2022	23/06/2022
A7	06/05/2022	23/05/2022	21/06/2022	24/06/2022	29/06/2022	30/06/2022	07/07/2022	11/07/2022	14/07/2022	21/07/2022

Assessment of responses to List of Questions (LoQ)

30-day timetable after 30-day response time

	Deadline for Submission (*)	Restart	PRAC Rapporteur AR (+)	Comments from PRAC (**)(+)	Updated PRAC Rapporteur AR (***)(+)	CHMP Rapporteur AR	PRAC outcome (#)(+)	Comments from CHMP (**)	Updated CHMP Rapporteur AR (~)(***)	Opinion
C1	22/12/2021	29/12/2021	03/01/2022	05/01/2022	06/01/2022	12/01/2022	13/01/2022	17/01/2022	20/01/2022	27/01/2022
C2	25/01/2022	26/01/2022	31/01/2022	02/02/2022	03/02/2022	09/02/2022	10/02/2022	14/02/2022	17/02/2022	24/02/2022
C3	22/02/2022	23/02/2022	28/02/2022	02/03/2022	03/03/2022	09/03/2022	10/03/2022	14/03/2022	17/03/2022	24/03/2022
C4	23/03/2022	24/03/2022	28/03/2022	30/03/2022	31/03/2022	06/04/2022	07/04/2022	12/04/2022	13/04/2022	22/04/2022
C5	19/04/2022	20/04/2022	25/04/2022	26/04/2022	28/04/2022	04/05/2022	05/05/2022	10/05/2022	12/05/2022	19/05/2022
C6	24/05/2022	25/05/2022	30/05/2022	01/06/2022	02/06/2022	08/06/2022	10/06/2022	13/06/2022	16/06/2022	23/06/2022
C7	21/06/2022	22/06/2022	27/06/2022	29/06/2022	30/06/2022	06/07/2022	07/07/2022	11/07/2022	14/07/2022	21/07/2022
C8	16/08/2022	17/08/2022	22/08/2022	24/08/2022	25/08/2022	31/08/2022	01/09/2022	05/09/2022	08/09/2022	15/09/2022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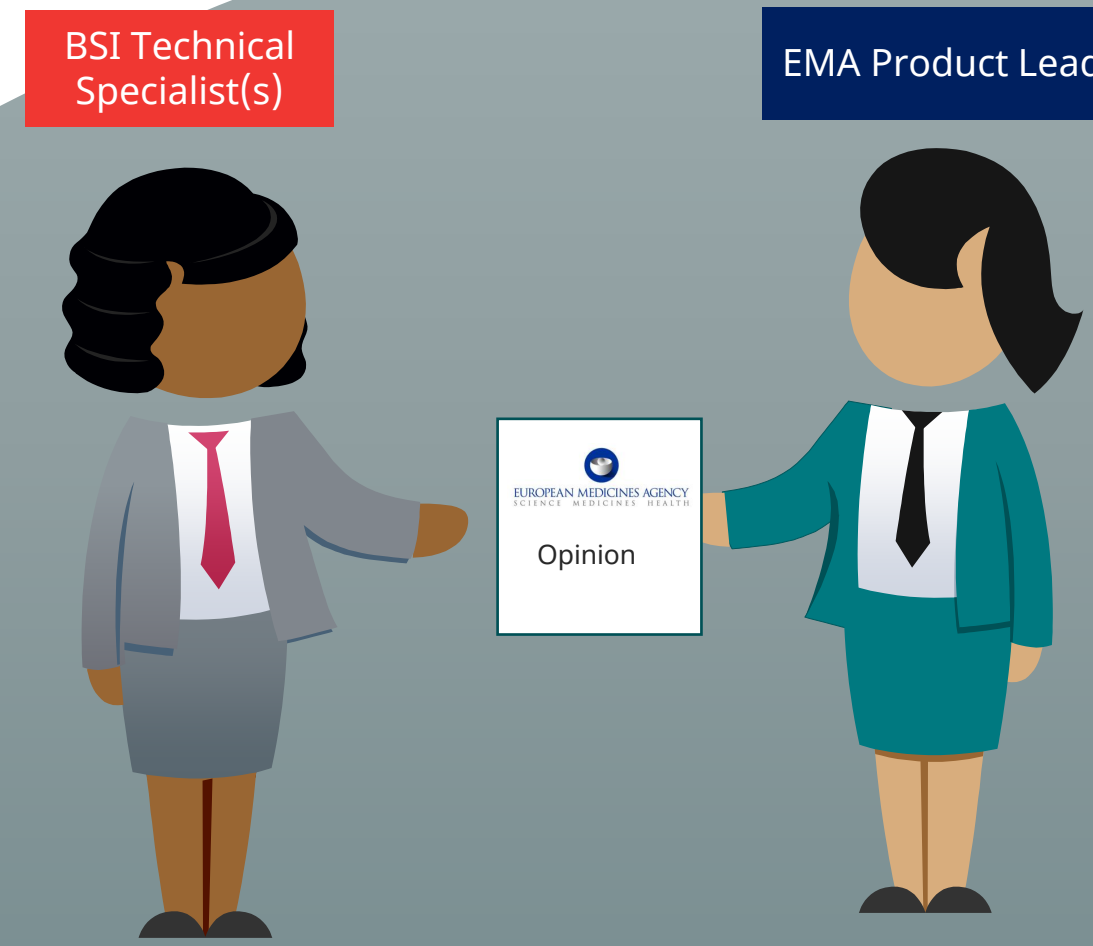


EMA Product Lead will provide BSI with EMA's opinion on the suitability of the CDx device in relation to the the corresponding medicinal product(s)

EMA Consultation – Opinion

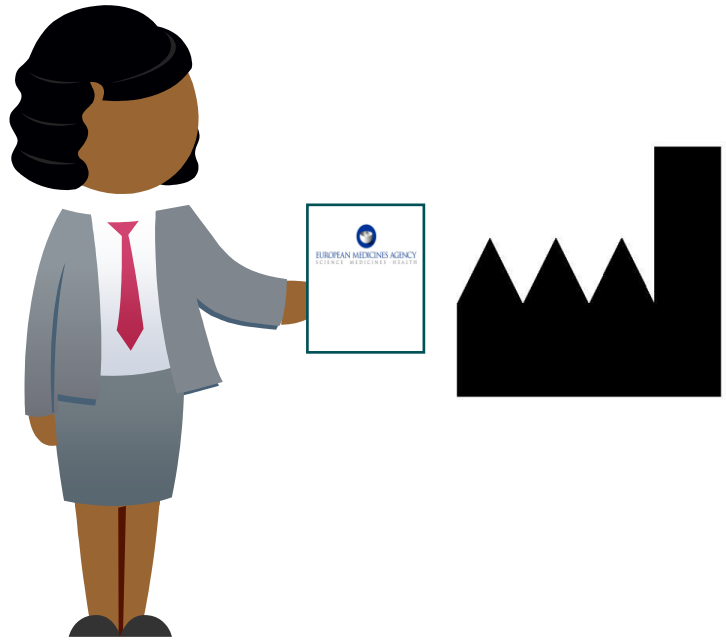
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

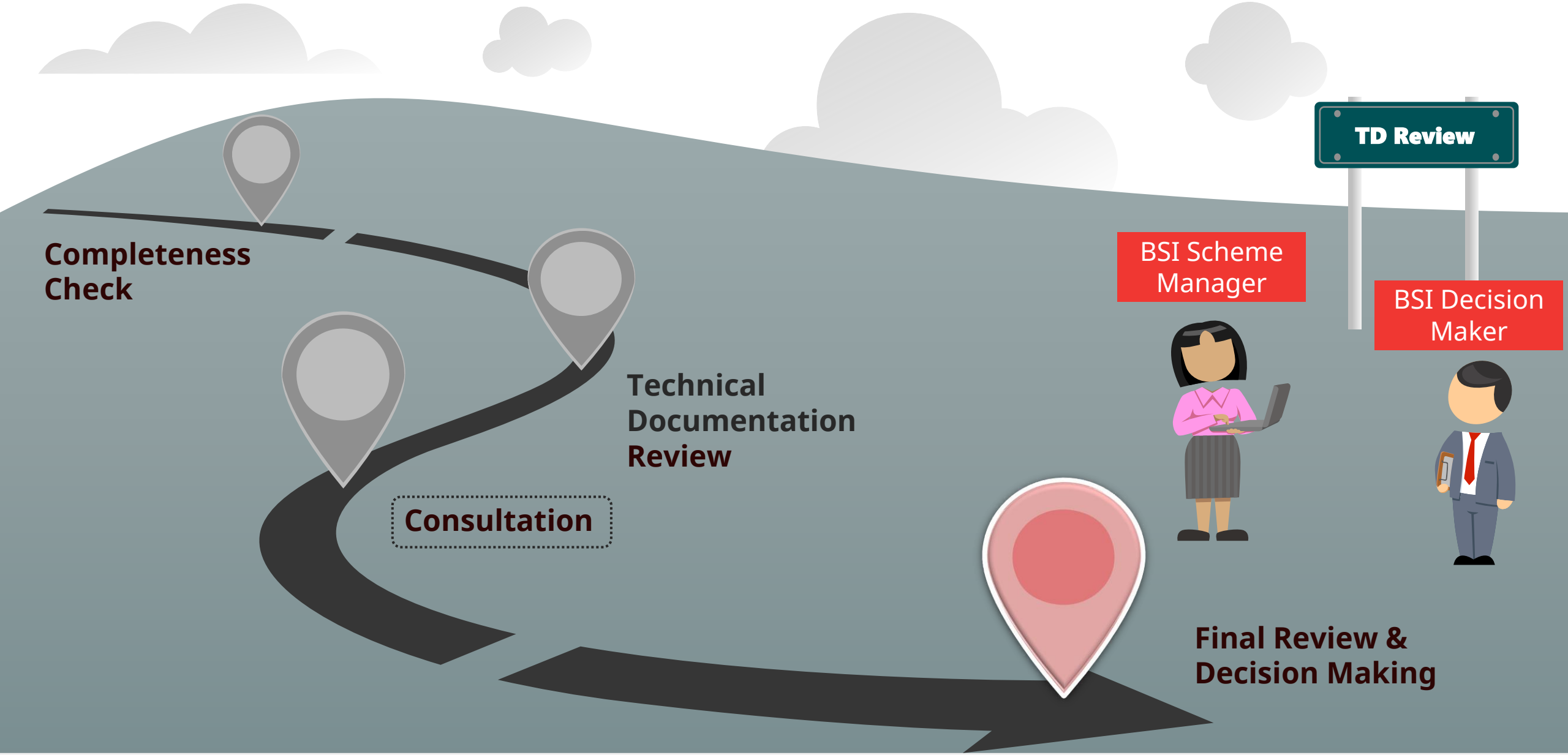
Opinion of the CHMP on the consultation procedure for a companion diagnostic

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

CHMP Assessment Report

BSI Technical Specialist(s)




TD Review
BSI Scheme Manager
BSI Decision Maker
Completeness Check
Technical Documentation Review
Consultation
Final Review & Decision Making

EU Quality Management System Certificate

Regulation (EU) 2017/746,

Annex IX Chapter I and III

EU Technical Documentation Assessment Certificate

Regulation (EU) 2017/746,

Annex IX Chapter II

CE

2797

bsi.

References (links to literature)

REGULATION (EU) 2017/746 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL (IVDR) **(Link)**

BSI IVDR Documentation Submission Best Practice Guidance **(Link)**

MDCG 2020-16 (rev.2) Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746 **(Link)**

MDCG 2022-9 Summary of safety and performance Template **(Link)**

European Medicines Agency – Medical Devices Landing Page **(Link)**

Links to:

- Guidance on procedural aspects for the consultation to European Medicines Agency by a notified body on companion diagnostics
- Q&A on the guidance document
- Letter of intent form
- Application forms for initial and follow-up consultation
- Assessment report template

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