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Health Products Regulatory Authority

The new Clinical Trial Regulation (CTR) explained-

Authorisation – Session 1, November 22, 2021

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MSC and RMS

- Member States Concerned (MSC) - any member state where an application for the authorisation of a clinical trial has been submitted.
- Reporting Member State (RMS) - The MSC responsible for conducting the primary assessment of the part 1 submission and compiling the assessment report for circulation to the other MSC.
- Choice of RMS
  - A MSC is nominated to serve as RMS by the Sponsor at the time of application
  - If a MSC other than that proposed is willing to be RMS or the MSC nominated does not wish to be RMS, this is notified to all MSC and Sponsor through CTIS
  - If more than one MSC expresses willingness, RMS chosen by MSC taking into consideration recommendations from CTAG.
  - If there is no agreement among MSC, RMS role reverts to that nominated by Sponsor

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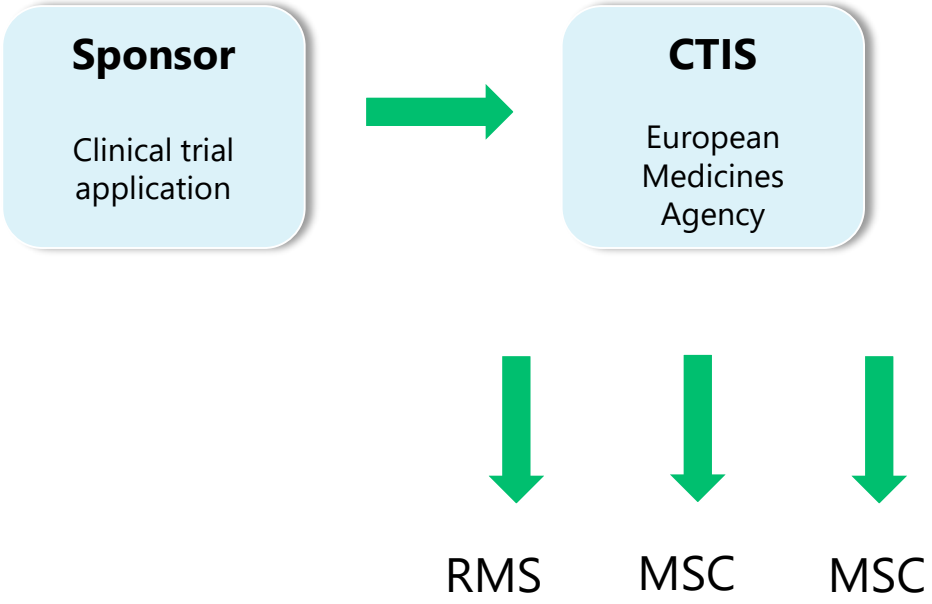
The authorisation process

Article 5 - Submission of an application



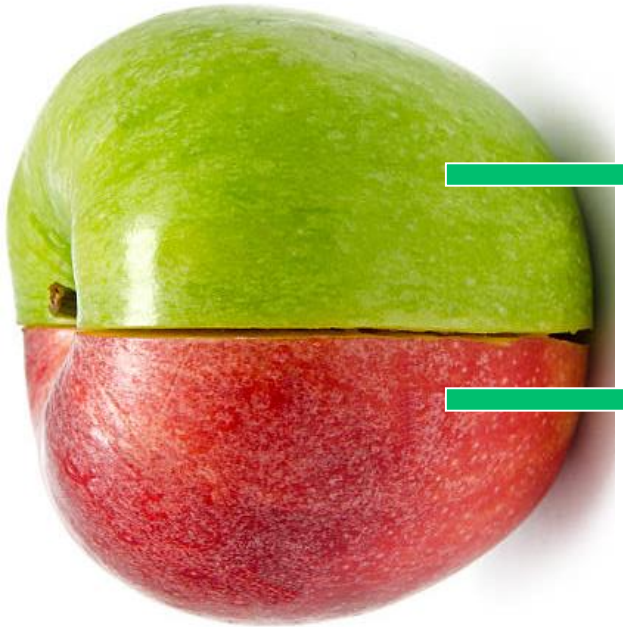
The sponsor selects Member States Concerned **(MSCs)**

The sponsor shall propose the **reporting** Member State **(RMS)"leading"MS**

Other MSs can volunteer (within 3 days)

RMS prepares the assessment report and leads an assessment

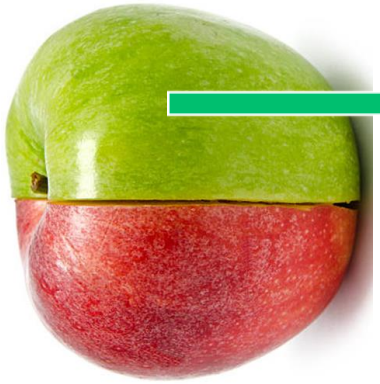
Application – Part I and Part II



Part I - scientific part, common for all MSCs, coordinated review

Part II – national/local part – ethical review

Article 6 - Assessment report – Aspects covered by Part I

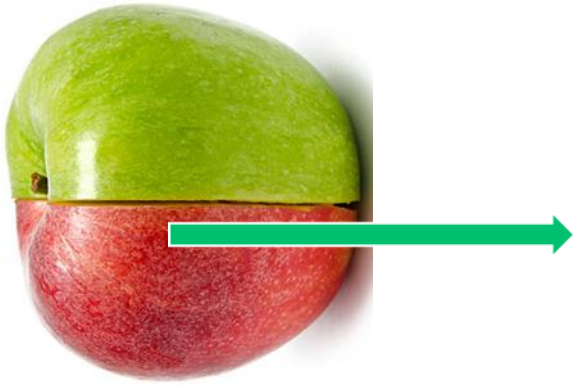


Part I - scientific part, common for all MSs

Aspects covered by Part I:

- Whether the clinical trial is **low-interventional**
- The anticipated therapeutic and public health **benefits**
- The **risks** and inconveniences for the subject
- Compliance with the requirements concerning the **manufacturing and importation** of IMP
- Compliance with the **labelling** requirements
- The completeness and adequateness of the **investigator's brochure.**

Article 7 - Assessment report – Aspects covered by Part II



Part II – national/local part – ethical review

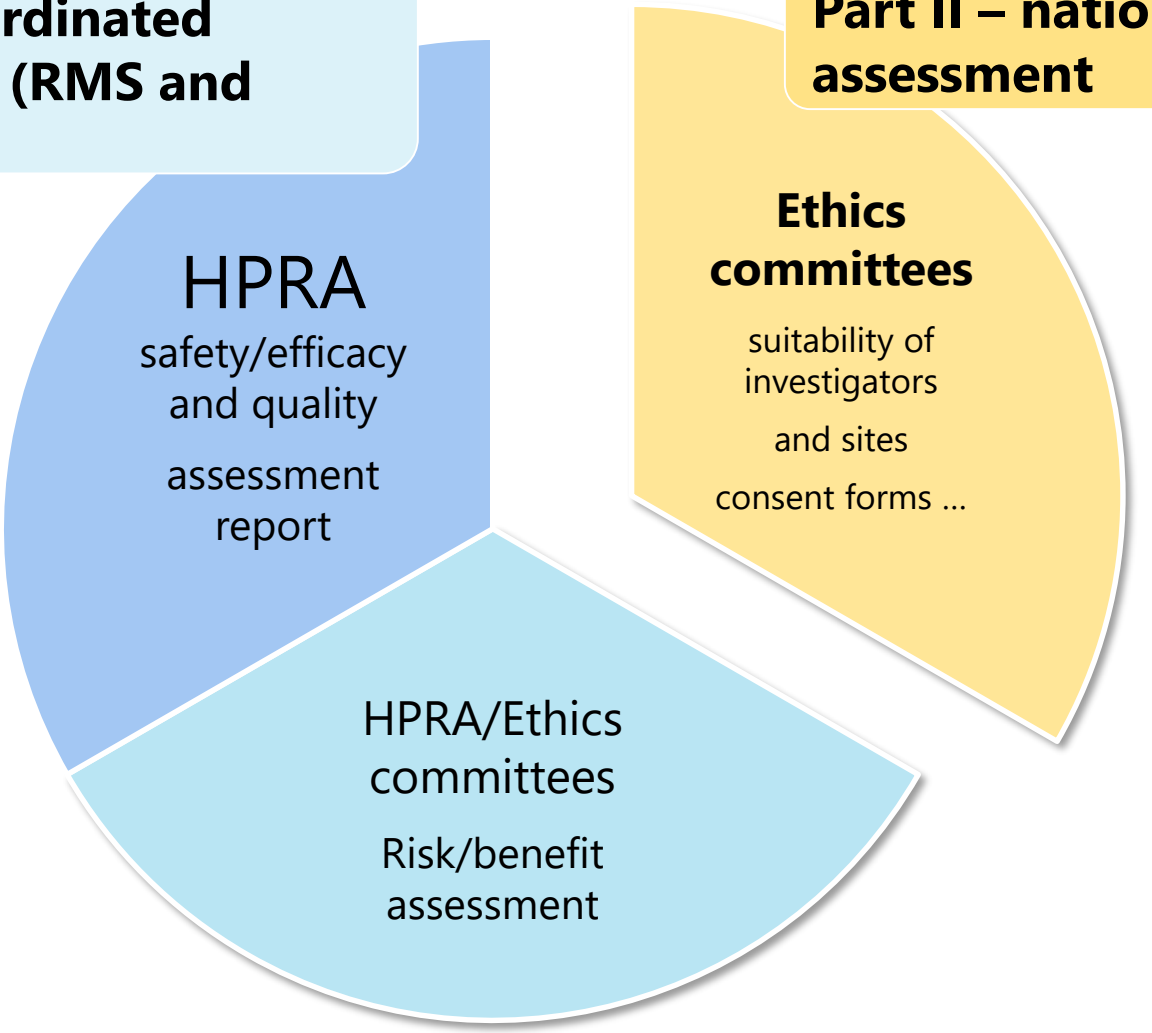
Aspects covered by Part II:

- **Informed consent**
- Arrangements for rewarding or compensating investigators and subjects
- Arrangements for recruitment of subjects
- Suitability of investigators and **trial sites**
- **Damage compensation**
- Collection, storage and future use of biological samples of the subject.

Who will assess what ?

Part I – co-ordinated assessment (RMS and MSC)

Part II – national assessment



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Timelines

Assessment timelines – Part I

Validation	Assessment	Final decision
10 days	45 days	5 days

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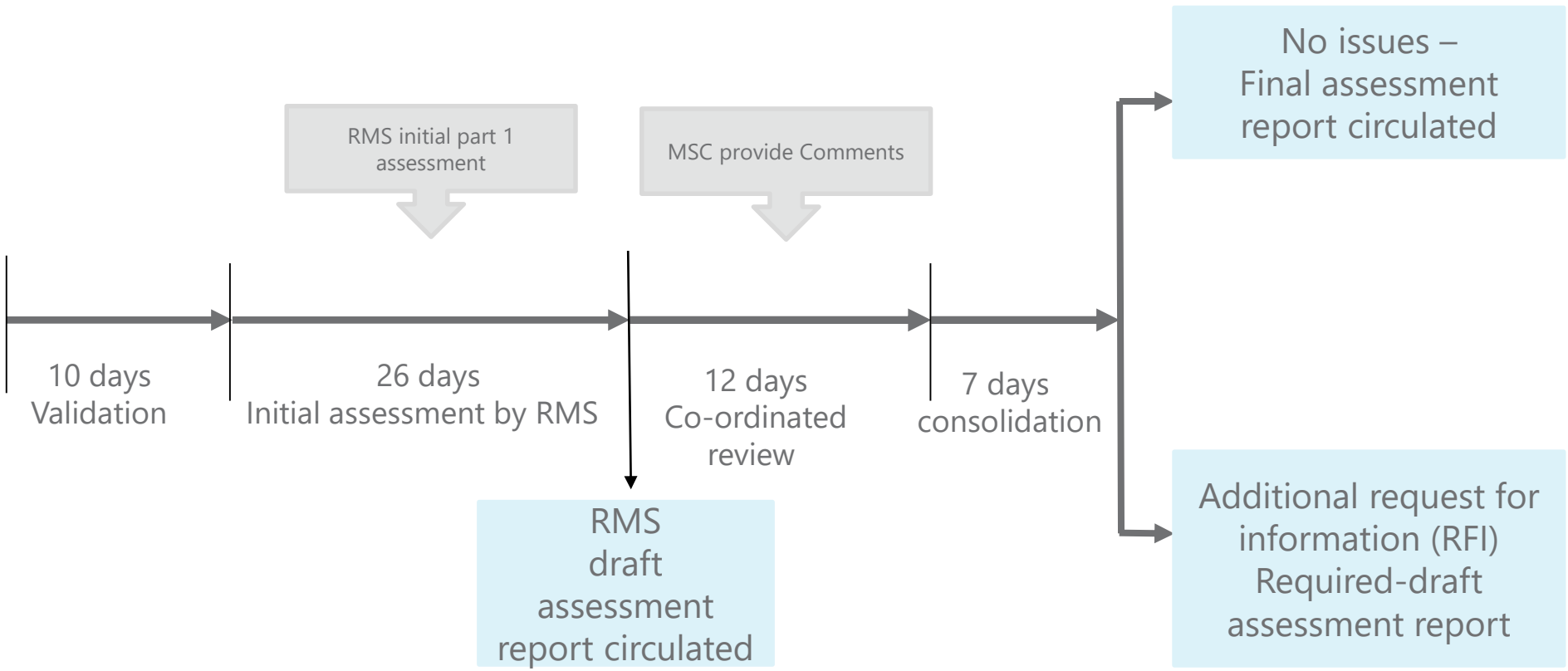

Assessment timelines – Part I

Validation	Assessment	Final decision
10 days	45 days	5 days

In the case of requests for further information, timelines can be extended to a maximum outlined below:

Validation	Assessment	Final decision
25 days 10+10+5	76 days 45+12+12+7	5 days

Assessment of Part I

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- Short timeline, extensions are not permitted
- Tacit approval – if no response from RMS.
- Application lapse – if response to RFI from sponsor not received within deadline.
- Transparency - Final assessment report publically available
- Collaboration between the HPRA and NREC in the assessment of Part I

Article 7 - Aspects covered by Part II

- **Each Member State** shall assess **Part II** and prepare an assessment report within 45 days from the validation date.

Validation	Assessment + notification
10 days	45 days

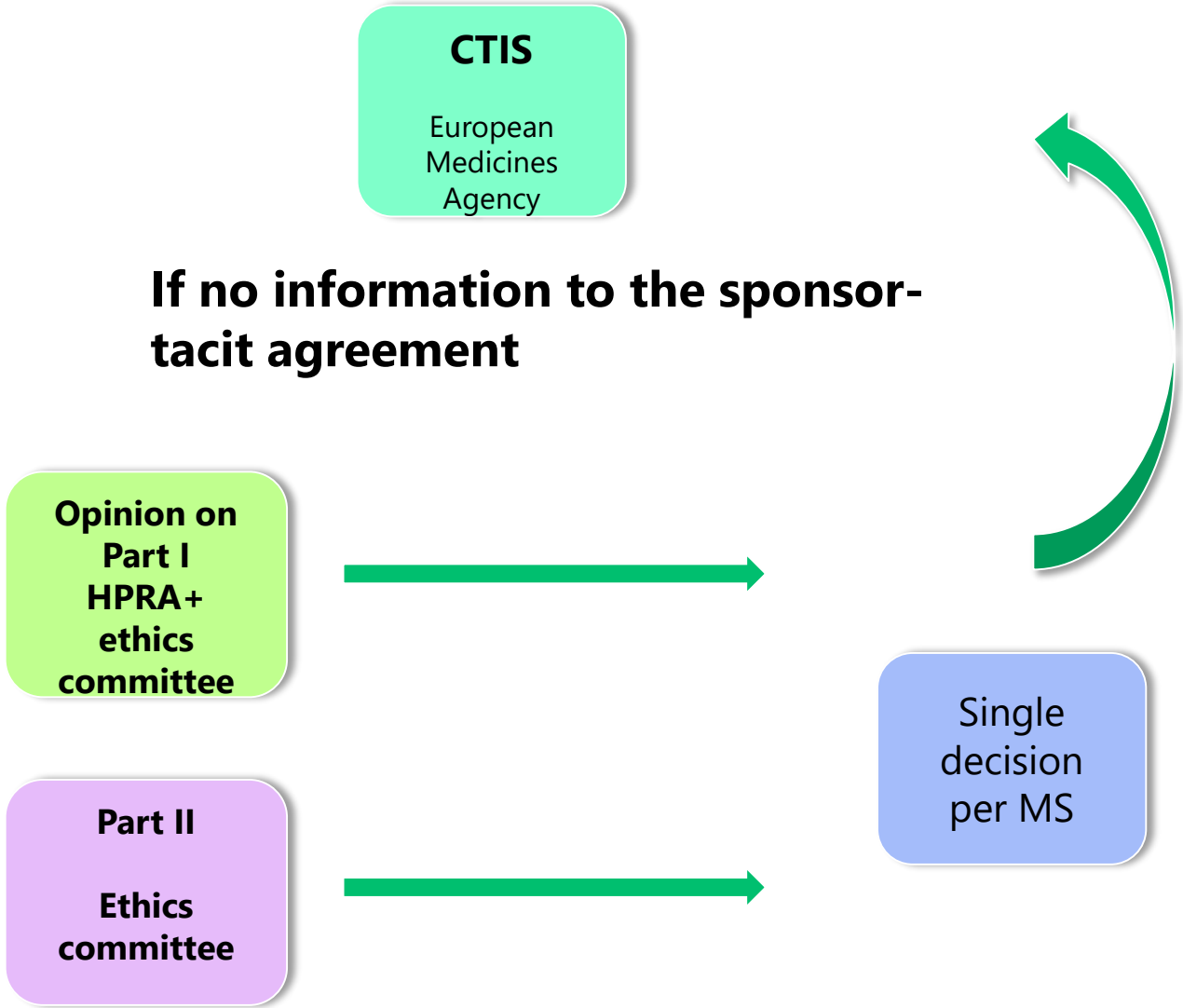
In the case of requests for further information, timelines can be extended to a maximum outlined below:

Validation	Assessment + notification
25 days 10+10+5	76 days 45+12+19

Article 8 - Decision on the clinical trial

- Each Member State concerned shall notify the sponsor through **CTIS** as to whether the clinical trial is:
  - authorised;
  - authorised subject to conditions;
  - or refused
- Notification shall be done by way of **one single decision** within five days from the Part I reporting date or the last day of part II assessment – whichever is later
- Any disagreement with the RMS conclusions together with a detailed justification, needs to be communicated through CTIS, to the Commission, to all Member States, and to the sponsor.

Article 8 - Decision on the clinical trial



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Article 11 and Article 14 procedures

Article 11-Submission of applications limited to part I or part II

- At sponsors request, assessment of the CT can be limited to part I assessment.
- Sponsor can submit aspects related to part II up to 2 years following the notification of the conclusion of the part I assessment.

Article 14 – Subsequent addition of an MSC

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- Possible to add additional MSC after the authorisation of the initial clinical trial application.
- In the case of an initial Article 11 staggered submission, at go-live, only possible to add an MSC once all MSC to the original submission have notified a decision.
- Only possible provided there is no ongoing assessment of any Part I, or Part I and Part II substantial modification procedures in any MSC.
- Additional MSC shall notify the Sponsor through CTIS of the national single decision within 52 days of the submission of the application dossier.

Article 14 – Subsequent addition of an MSC

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- Additional MSC can discuss application with RMS and other MSC within these defined timelines.
- In some instances this may lead to RFI, only RMS may send additional RFI to Sponsor-in this case maximum timeline extended by 31 days (12+12+7).
- Additional MSC can disagree with the conclusion of the RMS part I AR as in an initial application, but this does not change the completed part I assessment.
- More than one Article 14 procedure can be run in parallel, but it is recommended to submit the addition on MS together.

Thank you!

Health Products Regulatory Authority

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