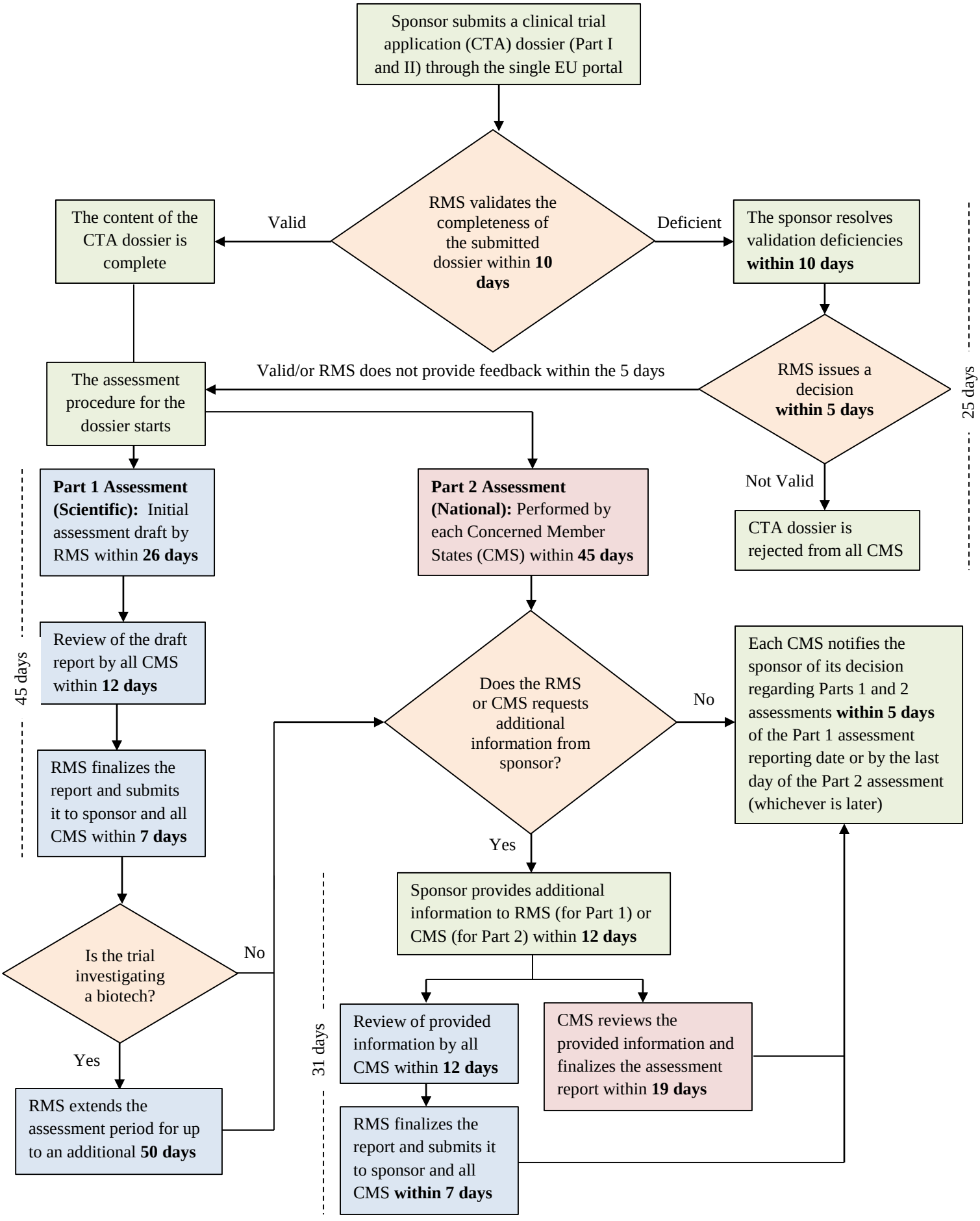
Sponsor submits a clinical trial application (CTA) dossier (Part I and II) through the single EU portal
RMS validates the completeness of the submitted dossier within **10 days**
Valid
Deficient
The content of the CTA dossier is complete
The sponsor resolves validation deficiencies **within 10 days**
RMS issues a decision **within 5 days**
Valid/or RMS does not provide feedback within the 5 days
Not Valid
CTA dossier is rejected from all CMS
25 days
The assessment procedure for the dossier starts
Part 1 Assessment (Scientific): Initial assessment draft by RMS within **26 days**
Part 2 Assessment (National): Performed by each Concerned Member States (CMS) within **45 days**
45 days
Review of the draft report by all CMS within **12 days**
RMS finalizes the report and submits it to sponsor and all CMS within **7 days**
Does the RMS or CMS requests additional information from sponsor?
No
Each CMS notifies the sponsor of its decision regarding Parts 1 and 2 assessments **within 5 days** of the Part 1 assessment reporting date or by the last day of the Part 2 assessment (whichever is later)
Yes
Sponsor provides additional information to RMS (for Part 1) or CMS (for Part 2) within **12 days**
Is the trial investigating a biotech?
No
Yes
RMS extends the assessment period for up to an additional **50 days**
31 days
Review of provided information by all CMS within **12 days**
CMS reviews the provided information and finalizes the assessment report within **19 days**
RMS finalizes the report and submits it to sponsor and all CMS **within 7 days**

Figure 1. A flowchart for the authorization of clinical trials under the new EU Clinical Trial Regulation. A sponsor submits a single CTA dossier (containing Part 1 and 2) through the EU-Portal to all Concerned Member States (CMS) where the sponsor intends to conduct the trial. The sponsor proposes one of the CMSs as the Reporting Member State (RMS) which shall be responsible to validate the application and coordinate the assessment procedure. The RMS checks the completeness of the submitted dossier within 10 days. Incase deficiencies exist; the sponsor has 10 days to response followed by 5 days for the RMS to make a decision. The RMS then prepares a draft assessment report for Part 1 of the dossier within 26 days of validation, then the report is reviewed by CMSs within 12 days, and the RMS finalize the report considering issues raised by CMS and submit it back to CMSs and sponsor within 7 days with a conclusion (trial conduct is acceptable, acceptable subject to certain conditions, or not acceptable). If the RMS concludes that the trial is not acceptable, this shall be deemed to be the conclusion of all CMS, but not vice versa. The period may extend up to 31 days if the RMS requests additional information from the sponsor, plus an additional 50 days if the clinical trial involves an advanced therapy or biotech product. The Part 2 assessment will be conducted in parallel with Part 1 assessment and is done separately by each individual CMS within 45 days. The period may also extend up to 32 days if CMS requests additional information from sponsor. Each CMS notifies the sponsor via the portal of its decision regarding Parts 1 and 2 assessments within five days of Part 1 assessment report date, or by the last day of the Part 2 assessment, whichever is later. A CMS may still refuse to authorize a clinical trial and therefore participate in this trial protocol under the following circumstances: (i) where an ethics committee has issued a negative opinion which, in accordance with national law, is valid for the entire CMS; (ii) if it finds, on duly justified grounds, that the aspects of the Part 2 requirements are not complied with; or (iii) if it disagrees with the RMS's conclusion in Part 1 assessment report. If any CMS fails to issue a decision within the predetermined timeframe then the conclusion of the RMS part 1 assessment report will automatically be considered as this CMS decision on the application. If parts 1 and 2 of the dossier are not submitted together, part 1 may be submitted first for assessment, followed by the part 2 up to 2 years after the part 1 assessment is completed. It should be noted that if the sponsor failed to respond to additional information requests at any stage within the predefined timelines, the application will be considered withdrawn from all CMSs. *ATMP: Advanced Therapy Medicinal Product; RMS: Reporting Member State; CMS: Concerned Member State*