

Almost 3 years under CTR

EORTC's experience

12 November 2024

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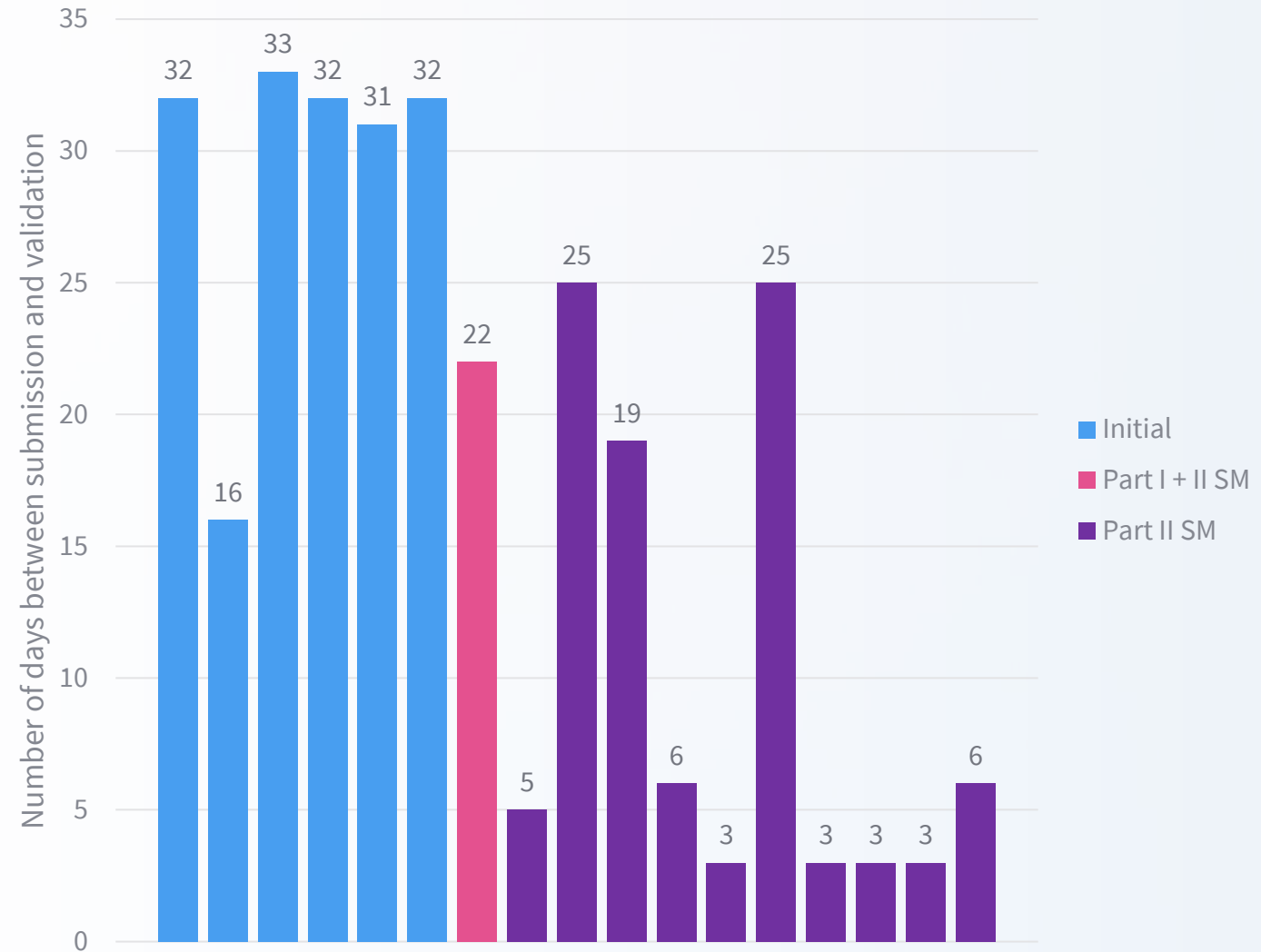
Our experience is based on...

- 10 initial submissions (1 low interventional)
 - 9 full applications
 - 1 mixed application
- 12 trials that were transitioned to CTR; 1 under evaluation

Timelines

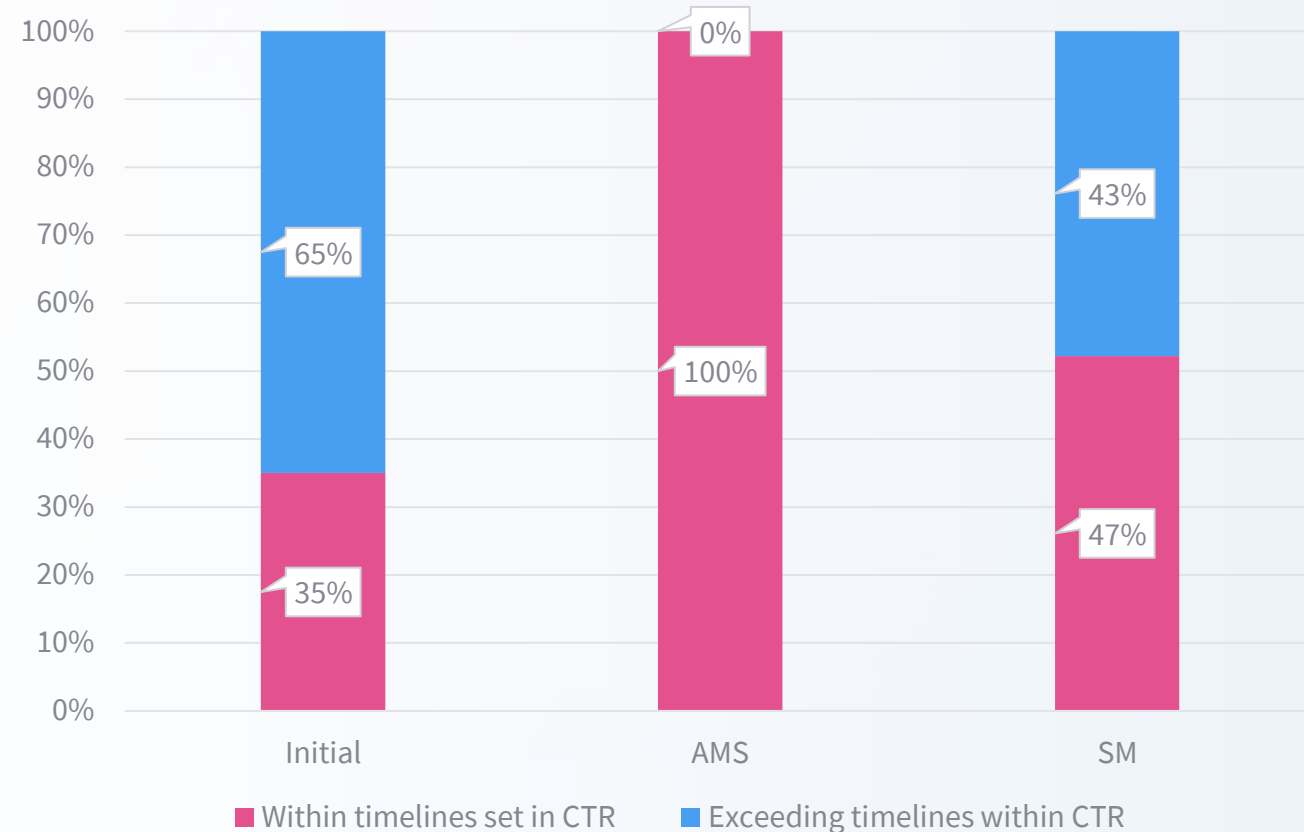
Validation timelines

- Initial application (CTR art. 5):
 - Up to 25 days from submission
 - RMS selection within 6 days from submission**
- Substantial modification (CTR art. 17 & 20):
 - Up to 21 days from submission



Timelines

- Initial application (CTR art. 5-8):
 - Up to 106 days from submission
- Addition of MSC (CTR art. 14):
 - Up to 95 days from submission
- Substantial modification (CTR art. 17-23):
 - Up to 90 days from submission



*Based on 23 initial decisions; 8 AMS decisions; 21 SM decisions

CTIS



Clinical Trial Information System (CTIS)

- Several bugs:
 - Need to log in several times
 - MSC was not seeing our reply whereas from our side all was submitted
 - Issues when several users working on the same trial
 - Problems with saving changes in Part I/II
 - When trying to delete an IMP, another IMP would disappear
 - IMPD section disappearing
 - Validation step expired → application had to be withdrawn and resubmitted

Clinical Trial Information System (CTIS)

- Notices and alerts and RFI tabs not always user friendly
- No notices and alerts for ad hoc assessment RFIs
- Information/documents from CTIS not always appearing in the public portal
- In case of staggered and mixed application, no Part I or Part II SM can be submitted until all MSCs received the Part II dossier
- No NSM can be submitted in case of an ongoing Part II SM in another MSC

Country requirements

Country requirements

- Completion of local portals to obtain site suitability form (for Spain and Italy)
- Only submitted what is mandatory (ICF, country docs, ...)
 - When recommended we do not submit unless requested in an RFI
- Requests for different documents in various Member States in an unpredictable and inconsistent way out of scope of the CTR requirements (Annex I)
 - National requirements are often only published on local websites in the national language and are also inconsistently applied – especially by ECs

Q-IMPD only application

IMPD-Q-only application

- EORTC is not the product owner
 - IMPD-Q-only application is a good short-term solution
 - Administrative burden of the “IMPD-Q-only application” for the company
 - Send to the company a download of Part I application: avoid mistakes
 - Part I RFIs: all IMPD-Q considerations were also included in the sponsor RFIs
 - Addition of a subsequent member state to the "sponsor trial" requires a resubmission "IMPD-Q-only application” with all MSCs based on CTR Q&A paragraph 125
- ➔ With simplification of CTIS Sponsor Roles, CT Admin will not have access to IMPD-Q anymore

RFIs



RFIs: what we observed...

- Monitor CTIS as no separate communication is sent (some MSCs still informed us via e-mail: Sweden, Italy, Denmark, Belgium)
- RFI received via e-mail from local EC that was not raised as RFI in CTIS
- Timing of Part II RFIs are unpredictable and at any moment from validation
 - Several rounds possible
 - Conclusion Part II can be received prior to receiving Part I RFIs
 - Some MSCs raised/we asked some MSCs to raise a second round of RFIs to allow us to implement changes following Part I RFIs
 - Concerns if Part I RFIs lead to Part II changes => Part II SM (ICF, recruitment arrangements, etc.) needed prior to activation

RFIs: what we observed...

- RFIs asking the same (Part I and Part II)
- Several RFIs concerning a specific document submitted as one RFI (up to 20 RFIs in one)
- ECs in one country are not harmonised
- Not always well compiled → contact CTR contact points for clarifications
- Part I acceptable with condition conclusion concerning removal of phrase in ICF, which was not expected as Part II acceptable conclusions were received
- Winter clock stop: we received RFIs on 27th December but with deadline to reply after the clock stop

After obtaining decisions

After obtaining decisions

- Local approvals required after obtaining decision (for The Netherlands)
- List of approved documents:
 - Participating sites often request a list of approved documents
 - Decision supporting document sometimes contains a list of approved documents
 - Assessment reports often contain a statement referring to the documents in CTIS portal
 - CTIS public portal does not display the documents correctly
 - Downloading a zip-folder with the documents from CTIS portal is not sufficient for sites
 - Currently, screenshots are the only option

Final remarks



If we could dream...

- For country requirements, a harmonized use of EU templates instead of country templates
- Add functionality to search with LOC-ID when adding trial sites and third parties
- For submissions:
 - RMS selection in parallel of validation
 - No Part II conclusion should be received prior to Part I RFIs to allow sponsors to implement Part II changes following Part I RFIs
 - Part I or Part II applications in parallel, if they concern different sections
 - This was allowed under CTD in several countries
 - e.g. Part I IMPD-Q SM and Part I protocol SM; Part II change of PI and Part II SIS and ICF SM in the same MSC
 - Highlight fields that were updated in a certain colour when replying to RFIs and submitting SMs/NSM

If we could dream...

- User management:
 - Download general list of roles/permissions
 - Part II viewer role per MSC
- For notices and alerts:
 - Automated e-mails
 - Show protocol number and/or trial title
- Download list of approved documents per MSC per application

In conclusion

We know:

- CTIS is not yet optimal
- Lack of harmonisation among MSCs

We believe we are still in a learning curve and in a period of adjustment:

- Positive updates of the transparency rules (removal of deferrals, simplifications of documents becoming publicly available)
- Continuous updates in CTIS
- Continuous updates to the Q&A
- Continuous updates to the training material
- Continuous updates to templates
- EMA informing us of technical issues or updates
- EMA Helpdesk: very helpful!!!
- CTR contact points

THANK YOU

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