Info Session on The Clinical Trials Regulation – 15 December 2021

Transition of a Clinical Trial from the Clinical Trials Directive (CTD) to the Clinical Trials Regulation (CTR): advantages and disadvantages

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Agenda

- Introduction

- Advantages of transitioning

- Disadvantages of transitioning

- Particular case : VHP

- Additional considerations

Introduction

- CTR foresees a transition period
- During one year after CTR go life, initial dossiers may still be submitted according to the Directive process
- Clinical trials already authorised under the Directive may continue in the Directive until the end of the trial or until the end of the 3 years transition period (31 January 2025)
- The application to transition a trial still ongoing after 31 January 2025 needs to be submitted in CTIS at least 60 days before 31 January 2025

Advantages of transitioning

- Allows the sponsor to only submit only one dossier within CTIS for all member states and ethics committees concerned for the subsequent substantial modifications

- Transitioning to CTR will avoid that more protocol differences between member states will arise due to staying within the framework of the Directive

- Opportunity to start submissions within CTIS with a more “easy”/straight forward dossier, without time pressure

Advantages of transitioning

- Once a clinical trial with an IMP has been submitted according to CTR, for competent authorities ASR must only be submitted within CTIS

- Once all clinical trials with the same products have been transitioned to CTR, CT3 must not be respected anymore

  => ASR only submitted to CTIS

- In Belgium, submission according to the CTR will be free of charge

Disadvantages of transitioning

- Transition is not automatic and the trial must be compliant with the Regulation before transition
- Protocol must be harmonised between all member states
- A substantial amendment have to be submitted following Directive process to make the trial compliant if needed
- A submission dossier for transition of the trial has to be prepared and submitted

Conclusion

This is really up to the sponsor to balance what would be the best option, taking into account the expected length of the trial, if this is a trial with frequent adaptations and therefore submissions of modifications, …

Particular case : VHP dossiers

Question 11.9 of the CTR Q&A in Eudralex volume 10

"In order to benefit from the advantages of harmonization, a sponsor should transition VHP trials as soon as possible after the entry into application of the Regulation, and at the latest before any new submission concerning a trial".

⇒ if possible VHP trials should be transitioned as soon as possible after implementation of CTR and substantial modifications submitted afterwards within CTIS

VHP : Voluntary Harmonisation Procedure

Particular case : VHP dossiers

Classical VHP dossiers

If it would not be possible to wait for the implementation of the CTR and the switch of the trial from the Directive to the CTR, the substantial amendments must be submitted nationally according to the Directive process and separately in each member state concerned.

Particular case : VHP dossiers

VHP plus dossiers

If this is not possible to wait for the implementation of CTR because the substantial modification is urgent, it can be submitted following the CTR pilot (non-VHP plus) usual process, and it will be processed by the FAMHP and the independent EC".

Additional considerations - Safety reporting

What about the safety reporting (SUSARs, ASRs/DSURs, etc.) during the transition period ? Does it also depend on the choice of the trial submitted (CTD or CTR)? Does this mean that trials submitted in CTR during transition period no longer need to submit SUSARs and DSURs?

ASR

Question 7.49 of the CTR Q&A in Eudralex volume 10

How to submit ASRs during the transition period from the EU Directive 2001/20 to the Clinical Trials Regulation (EU) 536/2014?

"In case one clinical trial is ongoing in alignment with the Clinical Trials Regulation (EU) 536/2014 while others are under the Directive 2001/20/EC, an ASR should be submitted to the database specified in the regulation. Sponsors are allowed to name all MSs concerned for all ongoing CTs in EU/EEA within Directive as well as Clinical Trials Regulation".

Additional considerations Safety reporting

Question 7.50 of the CTR Q&A in Eudralex volume 10
How to report SUSARs during transition time from Directive 2001/20/EC to EU Clinical Trials Regulation (EU) 536/2014?
"**SUSARs** must be submitted in Eudravig (EV) database and double reporting should be avoided.
In addition, despite reporting to NCAs via EV, the reporting obligations as of CT-3 still need to be respected, especially reporting to Ethics Committees according to national legislations in MSs for all IMPs/CTs within Directive 2001/20/EC as well as reporting to investigators (CT-3 Article 109)"

Links of interest

- CTFG Best Practice guide for transition of multinational trials
- CTR Q&A document in Eudralex volume 10
- EMA will publish a new training module specifically dedicated to transition of the trials from the CTD to the CTR : expected in January 2022

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