



2024 CDISC + TMF
US INTERCHANGE

PHOENIX/SCOTTSDALE

23-24 OCTOBER: CONFERENCE & EXPO | 21, 22, 25 OCTOBER: TRAININGS

The EU CTR and Its Impact on the TMF

Presented by Karla Navera-Andersen, Clinical Trial Manager,
Clinical Operations, Ascendis Pharma



Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*



Meet the Speaker

Karla Navera-Andersen

Title: Clinical Trial Manager

Organization: Ascendis Pharma A/S

Karla Navera-Andersen is an eTMF Manager turned Clinical Trial Manager at Ascendis Pharma A/S.

Karla holds a Master of Arts in English and a Pharma Consultant Diploma. She has spent over 15 years working with TMFs, starting her TMF career as a student in the paper TMF archive in a large pharmaceutical company.

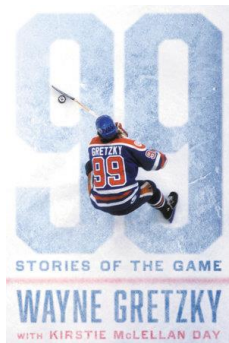
Since then, Karla has worked on both on the CRO and Sponsor side and within Clinical Operations and Regulatory Affairs. Currently, Karla is working as a Clinical Trial Manager, focusing on improving the quality and processes of TMF management within Clinical Operations and between Sponsor and CRO.



99

Articles in the EU Clinical Trials Regulation

Significance of 99





The EU Clinical Trials Regulation

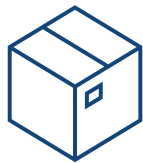
- Effective January 2022, replacing the EU Clinical Trials Directive
- Implementation of the Clinical Trials Information System - CTIS
- TMF only mentioned in two articles of the EU CTR
- Streamlining, efficiency, reducing administrative requisites



Ascendis Pharma

- Ascendis Pharma founded in 2006
- eTMF System implemented in the Summer of 2020
- First eTMF Managers hired in the Fall of 2021
- eTMF previously housed in multiple systems and locations
- Challenging change management

The EU CTR Effect



Document Storage



New Documents



Redactions



Data Fields



Approvals

TMF Documents in Ascendis

- TMF housed in multiple systems and locations
- Many different CRO collaborators
- The mess challenge mostly rooted in the CTA process



The Game Changer: CTIS



CTIS: One Submission



Work Instruction: Documents cannot be a part of the EU submission if not filed in eTMF



Submission documents to be **filed or cross-linked** to Clinical Vault/eTMF



CRO to get direct access to our eTMF for country and site documents



Short timelines for Request for Information as motivator



Updates to our TMF Index



New Required Documents

- Template statement on compliance Regulation (EU) 2016/679
- Compensation for trial participants
- Declaration of interest
- Site suitability form
- Informed consent and patient recruitment procedure
- Compliance with applicable rules for biological samples

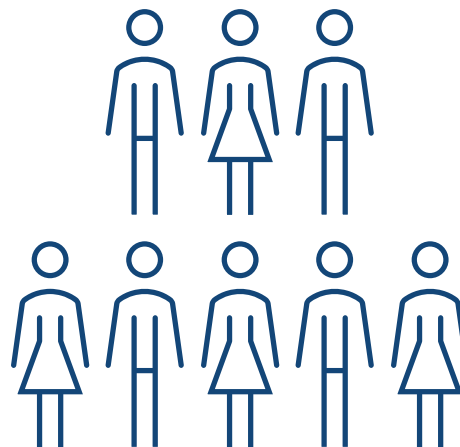
New Required Documents

- Template statement on compliance Regulation (EU) 679
- Compensation for trial participants
- Declaration of interest†
- Site suitability
- Informed consent and patient recruitment procedure
- Compliance with applicable rules for biological samples

All filed under Zone 04.01.01

The Danish TMF Network to the Rescue

- Network comprising 12-15 Danish pharmaceutical companies
- F2F meetings held every 6 months
- Mailing lists and LinkedIn group for random TMF questions and challenges
- Sharing knowledge from inspections, authorities and TMF Reference Model



Implications



Move misfiled documents



Reupdate TMF index



Retrain stakeholders

Redacted Documents

ASND0042 Protocol Version 1.0, 22-Mar-2024
Navepegritide and Lonapegsomatropin

Ascendis Pharma
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SPONSOR CONTACT

Medical Monitors

[REDACTED]
[REDACTED]
[REDACTED]
Ascendis Pharma
Tuborg Boulevard 12, DK-2900
Hellerup, Denmark
[REDACTED]

[REDACTED]
[REDACTED]
[REDACTED]
Ascendis Pharma
Tuborg Boulevard 12, DK-2900,
Hellerup, Denmark
[REDACTED]

Safety Reporting

Safety reporting should be primarily via the electronic safety adverse event (eSAE) reporting process directly through the Electronic Data Capture system (EDC) along with all relevant information within 24 hours of awareness.

If the EDC is unavailable, a completed safety report form / pregnancy report form should be uploaded to the Sponsor Safety Reporting Portal (safety.ascendispharma.com) within 24 hours of awareness, or for sites that cannot upload to the portal, the safety report form can be sent via Fax to: 1-844-307-5997.

The Sponsor may suggest an alternate route for reporting SAEs, adverse events of special interest (AESIs) and Special situation reports as applicable. Such alternate mechanisms will be clearly communicated to the sites with applicable guidance from the Sponsor.



D4_Patient facing documents SF-10_IE_Acute_UK **REDACTED**

English · Protocol **(for publication)** · System version 1.00
submission date 22/12/2023
· Version 1.0 · 13/01/2016



D4_Patient facing documents SF-10_IE_Acute_UK

English · Protocol **(not for publication)** · System version 1.00
submission date 22/12/2023
· Version 1.0 · 13/01/2016

Thoughts on Redacted Documents



Will the redacted versions crowd our eTMFs?



Are these at all eTMF documents?



Duplicates?



De facto submission document



Can we refer to CTIS for these versions?



“Nothing in the Regulation states that the redacted versions need to be stored in the TMF”

Data Fields, Modifications and other Notifications

APPLICATION AND NON-SUBSTANTIAL MODIFICATION

Type	ID	Parts	MSCs	Submission date	Decision date	Reason	Scope	Link	
Substantial modification	SM-1	Part I Part I Part I Part I Part I	IE(Under evaluation) DE(Under evaluation) PT(Under evaluation) DK(Under evaluation) AT(Under evaluation)	08/09/2023		+	+		+ INFO
Non-substantial modification	NSM-3	Part I Part I Part I Part I Part I	IE(Authorised) DE(Authorised) PT(Authorised) DK(Authorised) AT(Authorised)	05/09/2023	05/09/2023	-	-	-	
Additional MSC	AM-3	Part I (Translations) & Part II	PT(Authorised with condition)	08/06/2023	21/08/2023	-	-	-	+ INFO
Additional MSC	AM-2	Part I (Translations) & Part II	DE(Authorised with condition)	08/06/2023	21/08/2023	-	-	-	+ INFO
Additional MSC	AM-1	Part I (Translations) & Part II	AT(Authorised)	08/06/2023	04/09/2023	-	-	-	+ INFO
Non-substantial modification	NSM-2	Part I Part I	IE(Authorised) DK(Authorised)	07/06/2023	07/06/2023	-	-	-	
Non-substantial modification	NSM-1	Part I Part I	IE(Authorised) DK(Authorised)	31/05/2023	31/05/2023	-	-	-	
Initial	IN	Part I & Part II Part I & Part II	DK(Authorised with condition) IE(Authorised with condition)	08/02/2023	22/05/2023	-	-	-	+ INFO

Data Fields in CTIS

Population of trial subjects

If the trial is to be listed in a PIP or to include paediatric subjects, then Main Characteristics, Notifications and Summary of Results associated with this trial will be published at the date of decision on the trial.

Age range *

Age range secondary identifier

Are subjects male?

Are subjects female?

Subjects must be provided

Clinical trial group *

Vulnerable population

Deferral publication dates

Publish dates of trial information

Short title / Trial category *

Justification for trial category / Trial category *

Secondary identifying numbers

WHO universal trial number (UTN)

UXXXX-XXXX-XXXX

ClinicalTrials.gov identifier (NCT number)

NCTXXXXXXXX

Additional registries

Registry name

Registry identifier

Trial information

Trial category

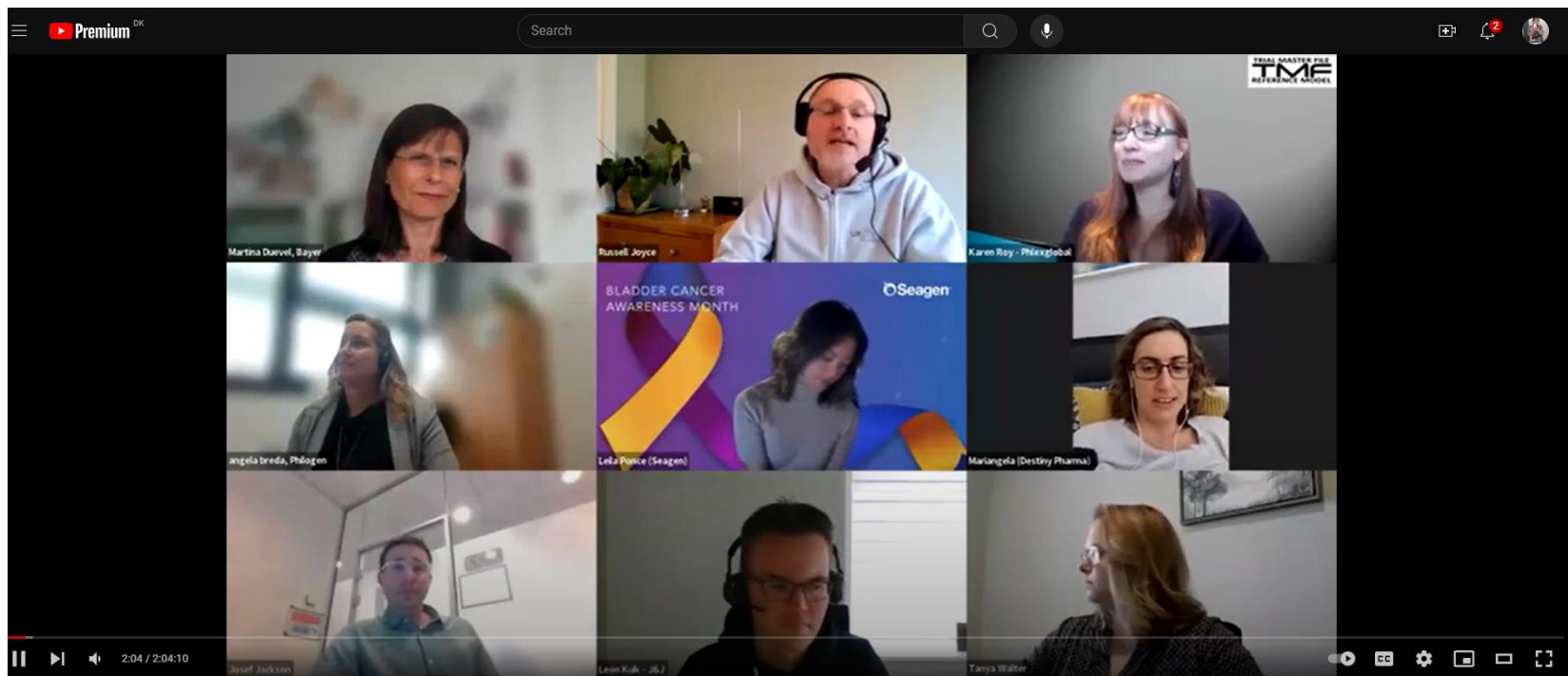
Low intervention trial

Attachment of justification of low interventional clinical trial

Trial phase*

Information in data fields are often already included in a submission documents

TMF Reference Model to the Rescue



Workshop - EU Clinical Trial Regulation and Impact on TMF Content and Process (07-Apr-2022)

Downloading Information from the CTIS

- Full submission / notification / modification packages
- Dates and structured data
- Assessment reports

The screenshot displays the CTIS interface for a trial titled "AttaCH: A Phase 2, Multicenter, Long-Term, Open Label Extension Trial Evaluating Safety, Tolerabilit...". The interface includes a navigation bar with tabs for Summary, Full Trial Information, Notifications, Trial results, Corrective measures, Ad Hoc assessments, and Users. A "Download" button is highlighted in a red box in the top right corner. Below the navigation bar, there is a "Start Download" button, also highlighted in a red box, and a "Cancel" button. The main content area shows a table of applications with the following data:

Application type	Application ID	Member states concerned	Application Part	Submission date	Decision date
<input type="radio"/> SUBSTANTIAL MODIFICATION SM-1	12599		Part I	08 Sep 2023	
<input type="radio"/> NON SUBSTANTIAL MODIFICATION NSM-3	11827		Part I	05 Sep 2023	05 Sep 2023

Approvals and List of Approved Documents

2022-502202-33-00

Please note that a committee member may have been absent from the meeting due to scheduling conflicts. Furthermore, if a committee member had a conflict of interest, they would thus not have participated in the discussion and assessment of the application.

If a sponsor requires a specific list of members who participated in the application, they may contact MREC for this information (kontakt@dvmk.dk).

The approval is valid for the following trial sites and investigators

Trial Site: Rigshospitalet, Principal investigator:

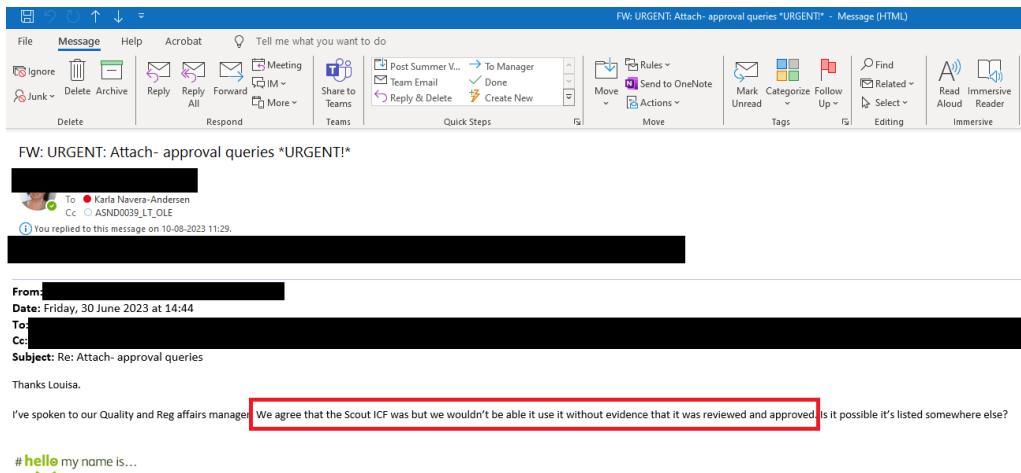
List of documents on the basis of which the decision was made

List of submitted documents can be accessed via Full Trial Information in CTIS.

Challenges of Assessment Reports

- “Submitted” not “Approved”
- Review of approved documents in eTMF against an approval letter
- Stakeholders lack reference for finding latest approved document
- Added workload and increase of mistakes in manual tracking
- Sites are accustomed to good ol’ fashioned approval letters listing date and version of patient facing documents and have no access to CTIS

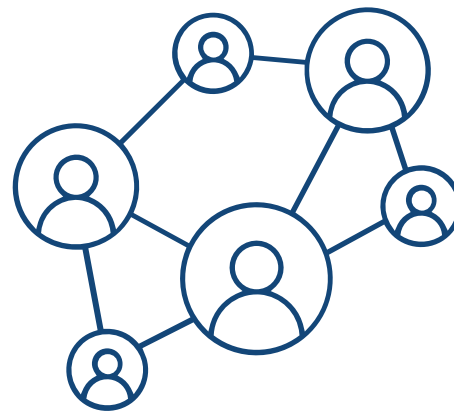
Story About an Irish Site



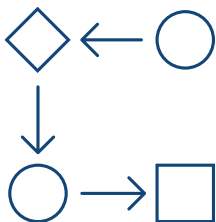
We agree that the Scout ICF was but we wouldn't be able it use it without evidence that it was reviewed and approved.

Input to the Authority to the Rescue

- CRO contacted NREC directly
- TMF Network discussion with the Danish HA regarding the issue
- Danish HA crowdsourced questionnaires for CTIS input



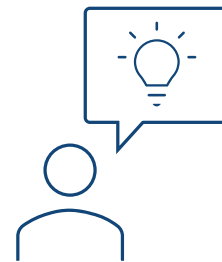
In Conclusion



Challenges brings upon
change for the better



Resources and
networking

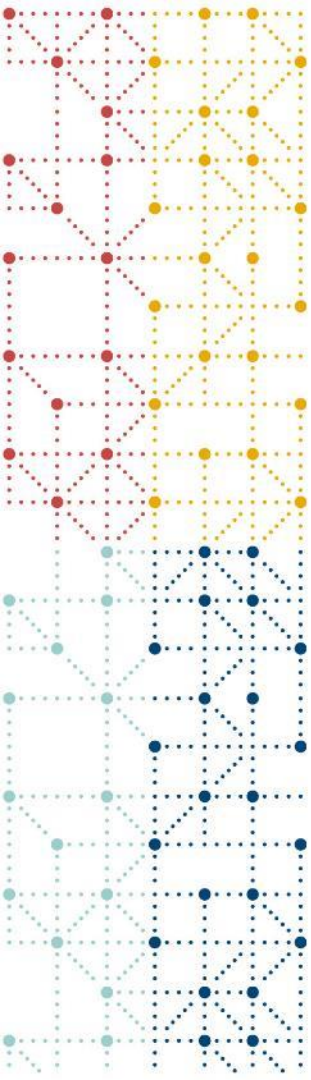


Constantly provide
input to authorities



I've got 99 problems but TMF ain't one

- Jay Z (not really)



Thank You!

