
# The EU CTR and Its Impact on the TMF

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

# 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. Karla holds a Master of Arts in English and a Pharma Consultant Diploma.
She has spent over 14 years working with TMFs, starting her TMF career as a student in the paper TMF archive in a large pharmaceutical company in Denmark.
Since then, Karla has worked on both the CRO and Sponsor side and whithin Clinical Operations and Regulatory Affairs. Currently, Karla is working on creating submission processes under the EU CTR, keeping oversight of trial TMFs and is the chair of the Ascendis Pharma's eTMF Ambassador's Group.

# 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.*

- *The author(s) have no real or apparent conflicts of interest to report.*

# Agenda

1. The EU CTR, the TMF and Ascendis Pharma
2. Our Documents and the CTIS
3. New Document Requirements
4. Information Captured in the CTIS
5. Final Thoughts

# The EU CTR, the TMF and Ascendis Pharma

… a little background

# 15 November 2022

# The EU CTR about the TMF

*Article 57*

**Clinical trial master file**

The sponsor and the investigator shall keep a clinical trial master file. The clinical trial master file shall at all times contain the essential documents relating to that clinical trial which allow verification of the conduct of a clinical trial and the quality of the data generated, taking into account all characteristics of the clinical trial, including in particular whether the clinical trial is a low-intervention clinical trial. It shall be readily available, and directly accessible upon request, to the Member States.

The clinical trial master file kept by the investigator and that kept by the sponsor may have a different content if this is justified by the different nature of the responsibilities of the investigator and the sponsor.

*Article 58*

**Archiving of the clinical trial master file**

Unless other Union law requires archiving for a longer period, the sponsor and the investigator shall archive the content of the clinical trial master file for at least 25 years after the end of the clinical trial. However, the medical files of subjects shall be archived in accordance with national law.

The content of the clinical trial master file shall be archived in a way that ensures that it is readily available and accessible, upon request, to the competent authorities.

Any transfer of ownership of the content of the clinical trial master file shall be documented. The new owner shall assume the responsibilities set out in this Article.

The sponsor shall appoint individuals within its organisation to be responsible for archives. Access to archives shall be restricted to those individuals.

The media used to archive the content of the clinical trial master file shall be such that the content remains complete and legible throughout the period referred to in the first paragraph.

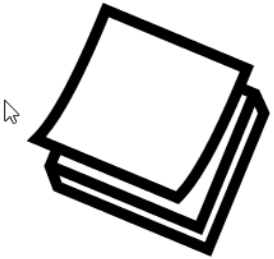
Any alteration to the content of the clinical trial master file shall be traceable.

# Setting the Scene

- 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,
    - Veeva Vault RIM
    - SharePoint Sites
    - BOX
- Challenging change management

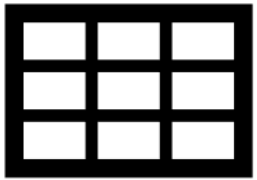
# The EU CTR Effect

Document storage



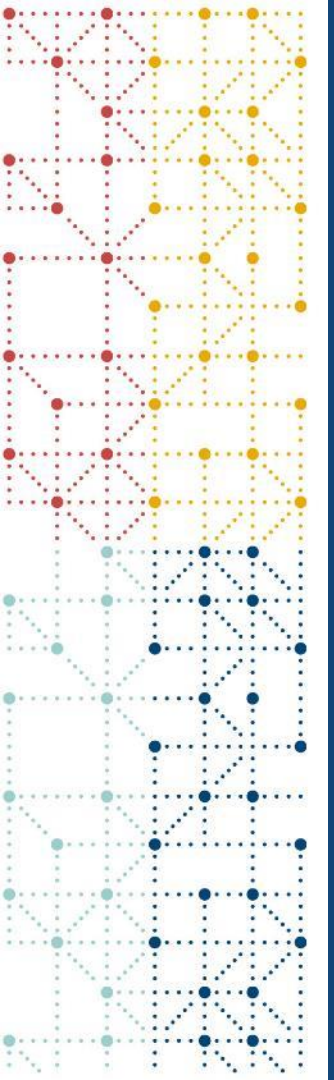
New documents

Redactions



Data fields

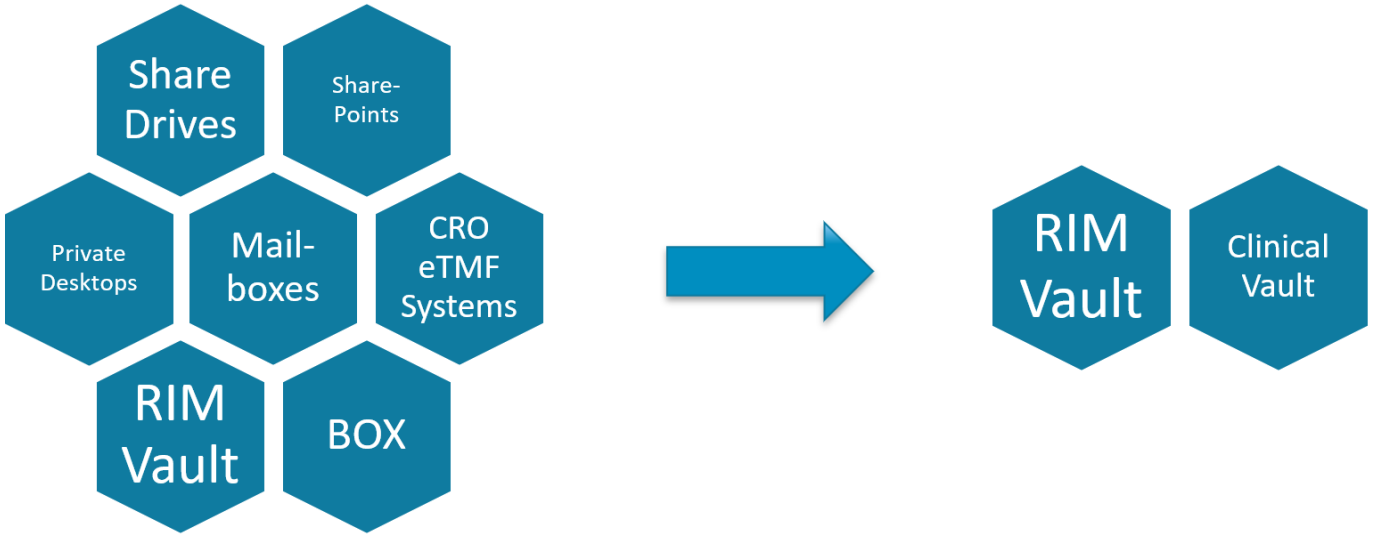
Approvals



# Our Documents and the CTIS

…getting into formation

# Where our Documents are Filed



# The Game Changer: CTIS

- CTIS: One Submission
- Work Instruction: Documents cannot be a part of the EU submission unless it is filed in the 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 timlines for Request for Information as motivator
- Updates to our TMF Structure

# New Document Requirements

…reinventing the wheel

# 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: Where We Filed Them

- Template statement on compliance Regul
- Compensation for trial partici
- Declaration of inte
- Site su

and patient recruitment procedure

liance with applicable rules for biological samples

All filed under Zone 04.01.01

# Implications

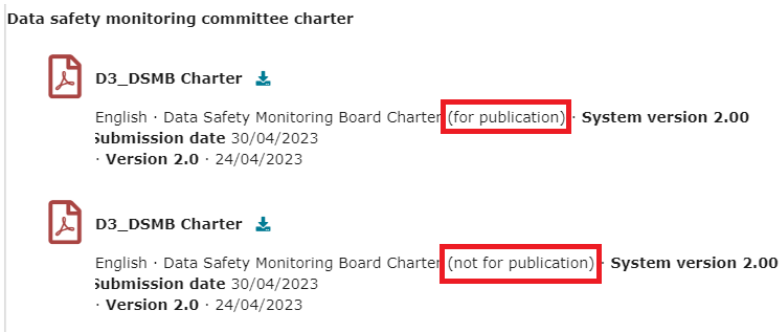
Move misfiled documents

Retrain stakeholders

Reupdate TMF Structure

# Redacted Documents

## Some documents will be public




## Example of a redacted document

**Statement of compliance with Regulation (EU) 2016/679 (GDPR)**

| | |
|---|---|
| Sponsor | Ascendis Pharma Growth Disorders A/S Tuborg Boulevard 12, DK-2900, Hellerup, Denmark |
| Title of the clinical trial | AttaCH: A Phase 2, Multicenter, Long-Term, Open Label Extension Trial Evaluating Safety, Tolerability, and Efficacy of Subcutaneous Doses of TransCon CNP Administered Once Weekly in Children and Adolescents with Achondroplasia |
| EU CT Number | 2022-502202-33-00 |

The sponsor declares that data have been and will be collected and processed in accordance with the General Data Protection Regulation (EU) 2016/679 (GDPR).

Date: [redacted]

Name and surname: [redacted]

Role in the sponsor organisation: **Vice President, Clinical Development**

# 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?

# Information Captured in the CTIS

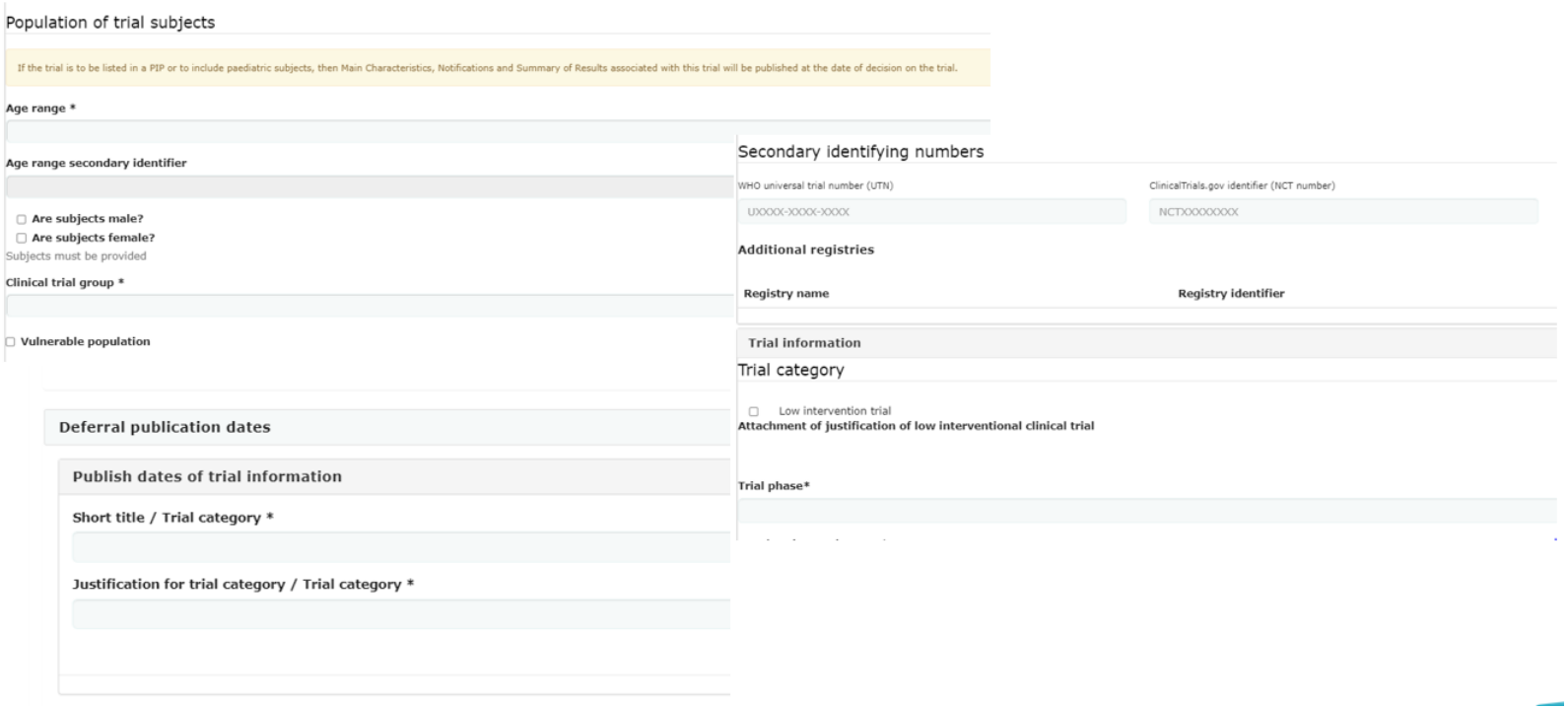
… and in the eTMF?

# Data Fields, Modifications and other Notifications

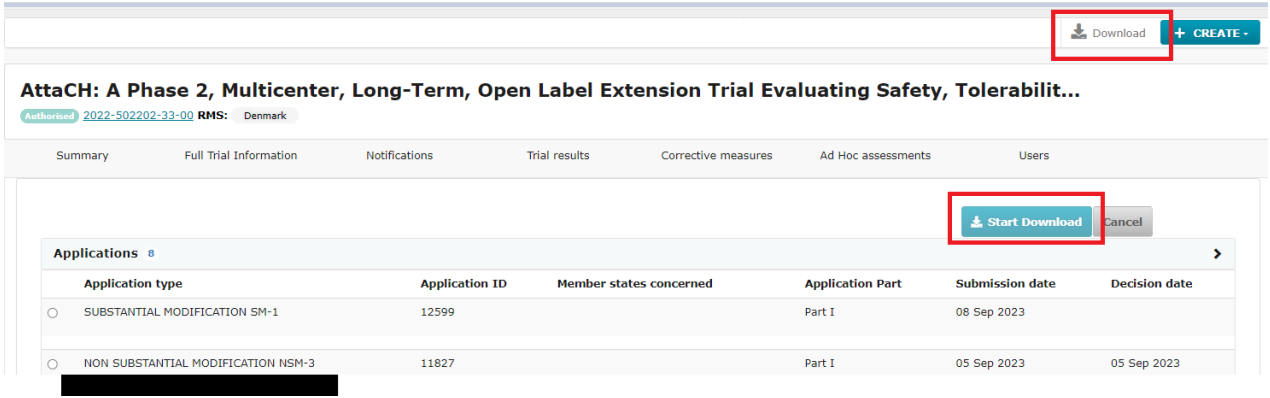
**APPLICATION AND NON-SUBSTANTIAL MODIFICATION**

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

# Data Fields


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
Secondary identifying numbers
WHO universal trial number (UTN)
U0000-0000-0000
ClinicalTrials.gov identifier (NCT number)
NCT00000000
Additional registries
Registry name
Registry identifier
Trial information
Trial category
Low intervention trial
Attachment of justification of low interventional clinical trial
Trial phase*
Deferral publication dates
Publish dates of trial information
Short title / Trial category *
Justification for trial category / Trial category *

# Downloading Information from the CTIS




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

# Approvals and List of Approved Documents

## Extract from an assessment report

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: [redacted]

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

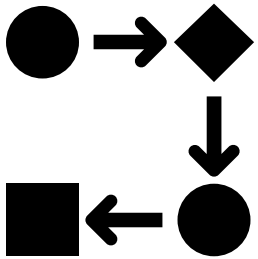
List of submitted documents can be accessed via Full Trial Information in CTIS.

# Challenges

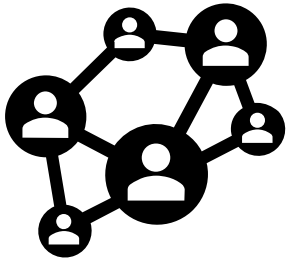
- “Submitted” not “Approved”
- ICH-GCP: Documented approval/favourable opinion of IRB/IEC (…)

  To identify the version number and date of the document(s)
- 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

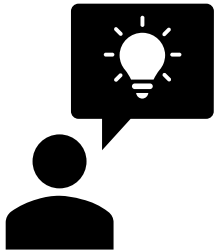
# In Conclusion



Change is not just challenges



Resources and network



Constantly give input

# Thank You!