NEED FOR SPEED – Accelerating Centralized Monitoring
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Introduction
Centralized monitoring applications enable the clinical team to monitor critical data and processes during trial conduct ensuring high-quality databases. To ensure proper and timely oversight the central monitoring applications should be available as early as possible after first patient first visit.

At Ferring centralized monitoring is performed using SAS ADaM® Clinical for statistical monitoring and DAS Sense® for medical and safety monitoring. These central monitoring applications and deliverables are based on ADaM® datasets ensuring consistency across the applications and ultimately consistency with the end of trial deliverables.

The Challenge
To shorten the time interval between first patient first visit and go-live of the central monitoring applications ideally having all applications available at first patient first visit. In order to achieve this the ADaM® datasets needs to be available shortly after—or even before—first patient first visit.

The Solution
Using synthetic data it is possible to develop the ADaM® datasets as soon as the eCRF specification is available, i.e. before first patient first visit. Based on the synthetic ADaM® datasets the central monitoring applications can be developed. When the real data starts flowing in, the synthetic records are excluded in a controlled manner, allowing centralized monitoring on real data from first patient first visit. Synthetic data is a system-generated data that mimics real data. This poster gives an overview of the process used at Ferring.

Prerequisites
Timely planning of monitoring activities is essential. In line with ICH E6(R2) the plans for central monitoring at Ferring are initiated already during protocol development by identifying processes and data that are critical to ensure human subject protection and the reliability of trial results.

Setting up Centralized monitoring applications
The Centralized Monitoring Plan serves as the specification for setting up the centralized monitoring applications. A high-level overview of the process and the standard timelines is given below.

Centralized monitoring plan
The Centralized Monitoring Plan is a trial-specific cross-disciplinary document detailing how to conduct centralized data monitoring including responsibilities for each activity.

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Specification
• The trial specific ADaM® specification for setting up the ADaMs for Ferring SDTM database.

Data collection/generation
• The data collection tools are based on the metadata from the TDT ensuring consistency across collection tools and that data is collected in Ferring SDTM (similar to SDTMv). The Synthetic Data Generator uses the metadata from the TDT to generate the synthetic patient data.

Raw data
• The output from the Synthetic Data Generator is Ferring SDTM (similar to SDTMv). Since the synthetic data is based on the TDT in the same manner as the data collection tools the data will have the same structure as the real patient data.

CDISC Data (submission ready)
• Based on the trial specific ADaM® specification the ADaMs can then be developed.

Central monitoring applications based on ADaM®
Statistical monitoring is based on a customizable SAS ADaM® clinical template with the aim of identifying statistical significant trends. In addition the application can detect anomalous data patterns, such as lack of variation, odd correlation structures, high or low incidences, digit preferences, and incorrect dates.

Medical monitoring is performed using DAS Sense® allowing the monitors to review the data from a medical/scientific perspective. The applications allow on the fly drill down into the data in case of any important finding

Safety monitoring is performed using DAS Sense® with focus on adverse event and potentially adverse event of special interest allowing early detection of any safety issue

Patient profiles are linked to the medical and safety applications allowing the monitors direct access to all data collected for a given subject without opening the eCRF.

All applications are refreshed daily throughout the duration of the trial

Synthetic data generator
The synthetic data generator is a set of macros called by a driver program. It generates synthetic data with meta-rules according to the characteristics of each variable as defined in the study definition (metadata) to create Ferring SDTM for all required domains.

Synthetic data generator step by step
• Initialization
  • Create subject level core variables to be used across all the domains
  • Create patient identifiers
  • Identify domains required in a trial
• Identify type of each domain and create unique item group identifiers
• Loop for each domain:
  • Identify sample set and/or data type for all variables
  • Assign values to all variables for all subjects
  • Identify dependency variables and enforce relation rules (e.g. DSECDDD and SDTMv or VISIT and VISITNM)
  • Few/two selected columns (e.g. data and endpoint variables)
  • Insert the synthetic data into empty domain shell

Conclusion
Ferring utilize information from the trial definition tool to generate synthetic data. The synthetic data is based directly on the meta data and empty SDTMv shells and generates SDTMv datasets which are identical to what will be obtained during the trial. This allows the statistical programmer to develop the ADaM® datasets before first patient first visit.

Benefits
• Central monitoring applications can be released at first patient first visit
• The clinical team can monitor critical data and processes throughout the trial
• Daily detection and correction of issues ensuring high-quality databases
• Integrity of the trial database leading to high confidence in trial conclusions
• Compliance with ICH E6(R2)

Timelines without using the synthetic data generator

Time line - Trial Definition Tool
- ADaM® Data generator
- Ferring SDTM (submission ready)
- Directly available

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Full support for central monitoring

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