

NEED FOR SPEED – Accelerating Centralized Monitoring

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Introduction

Centralized monitoring applications enables 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 JMP® Clinical for statistical monitoring and Qlik 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.

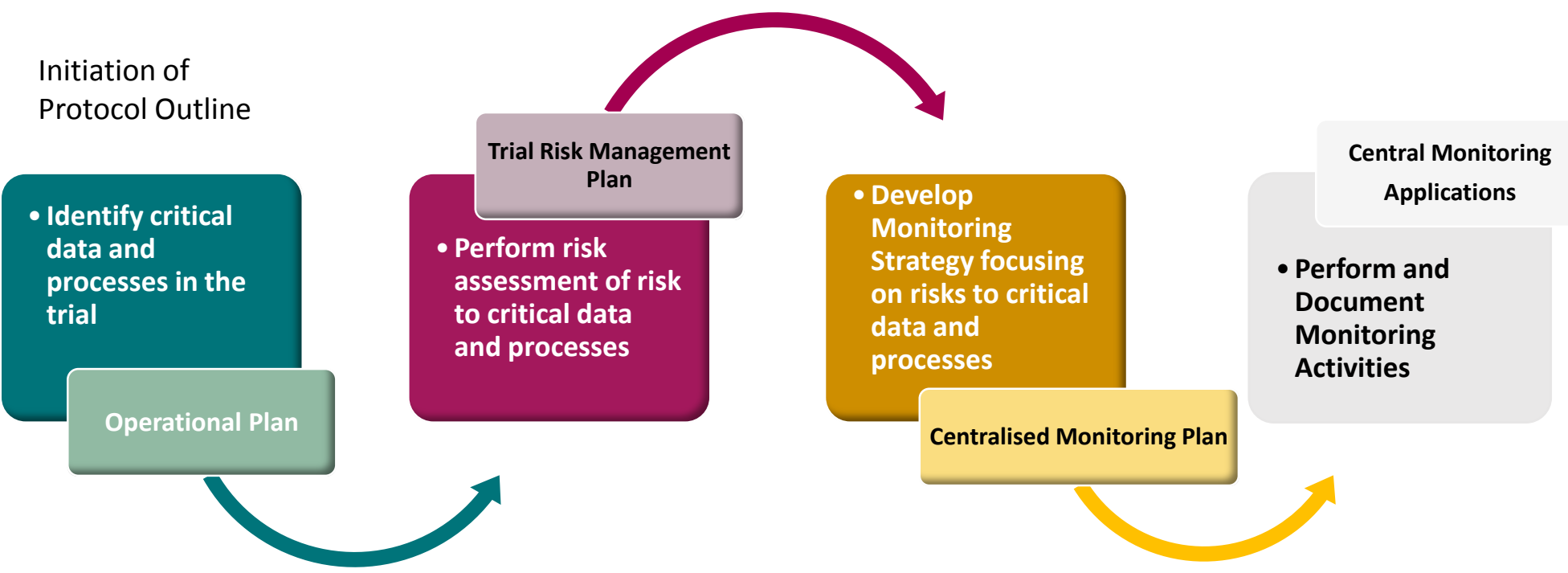
The Solution

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 those processes and data that are critical to ensure human subject protection and the reliability of trial results.

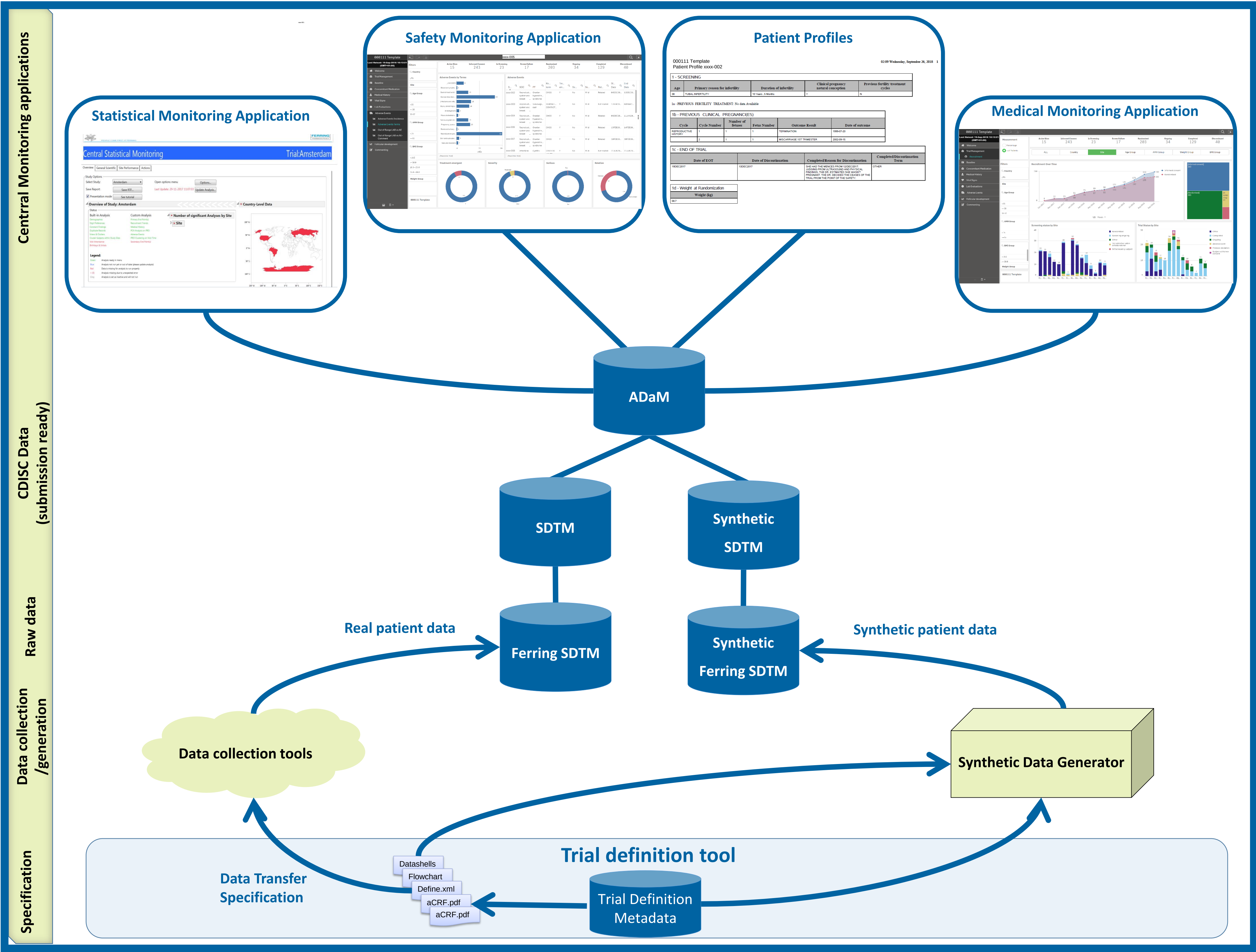
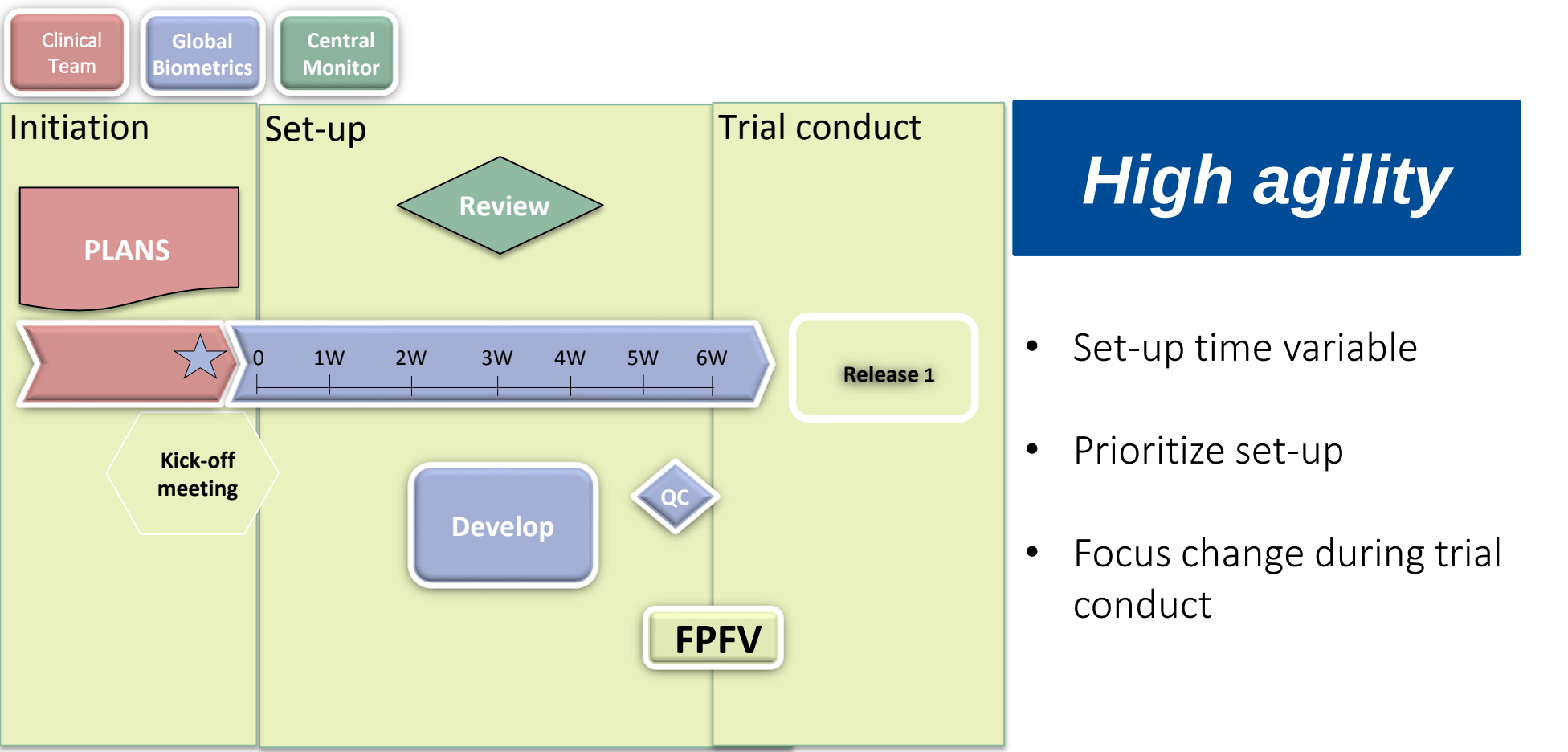


Centralized monitoring plan

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

Setting up Centralized monitoring applications

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



Specification

- The Trial definition tool (TDT) is a Ferring proprietary tool for setting up the eCRF and the 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 SDTM+).
- 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 SDTM+). 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 Ferring SDTM a set of standard macros generates the SDTM data,
- 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 JMP® 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 Qlik Sense® allowing the monitors to review the data from a medical/scientific perspective. The applications allow on the fly drill down in the data in case of any important finding

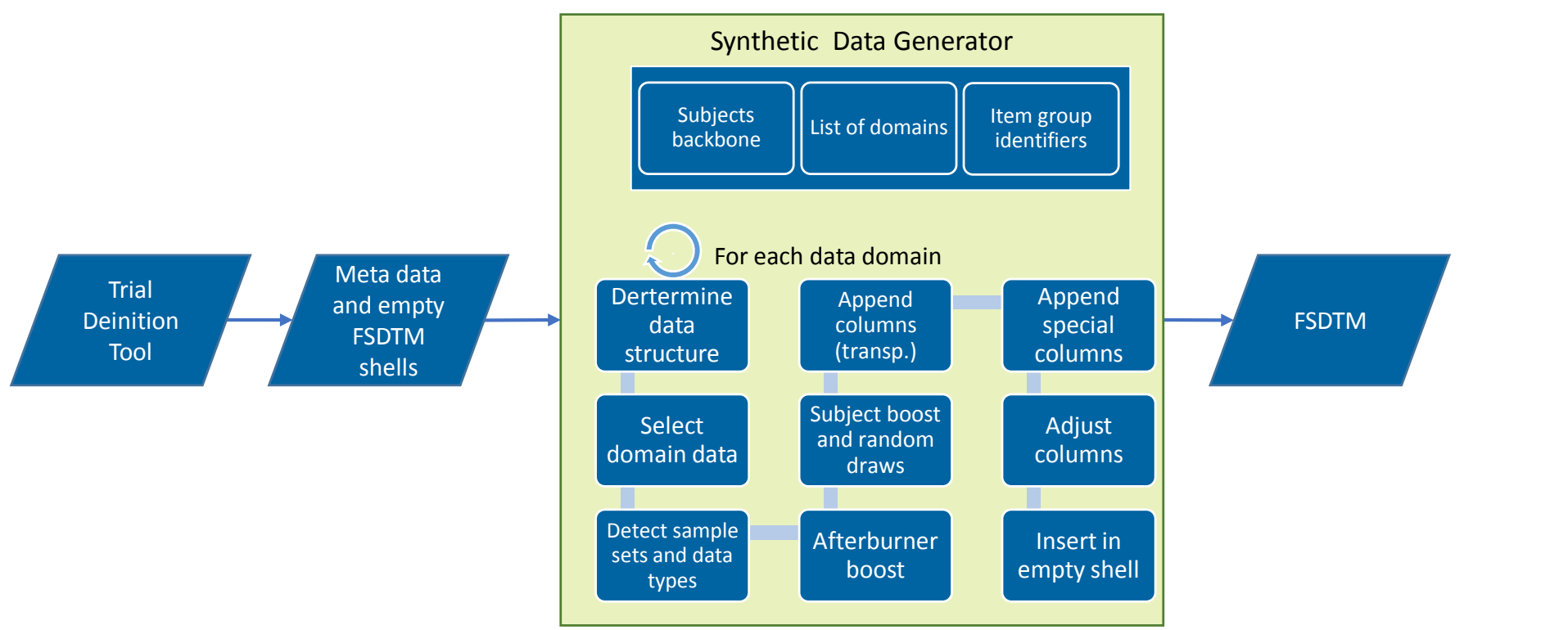
Safety monitoring is performed using Qlik Sense® with focus on adverse event and potentially adverse event of special interest allowing early detection of any safety issue

Patient profiles are linked to the medical and safety applications allowing the monitors direct access to all data collected for a given subjects 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 records according to 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 (e.g. SUBJID and SITEID)
- 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. DSDECOD and DSTERM or VISIT and VISITNUM)
- Fine-tune selected columns (e.g. dates and endpoint variables)
- Insert the synthetic data into empty domain shell

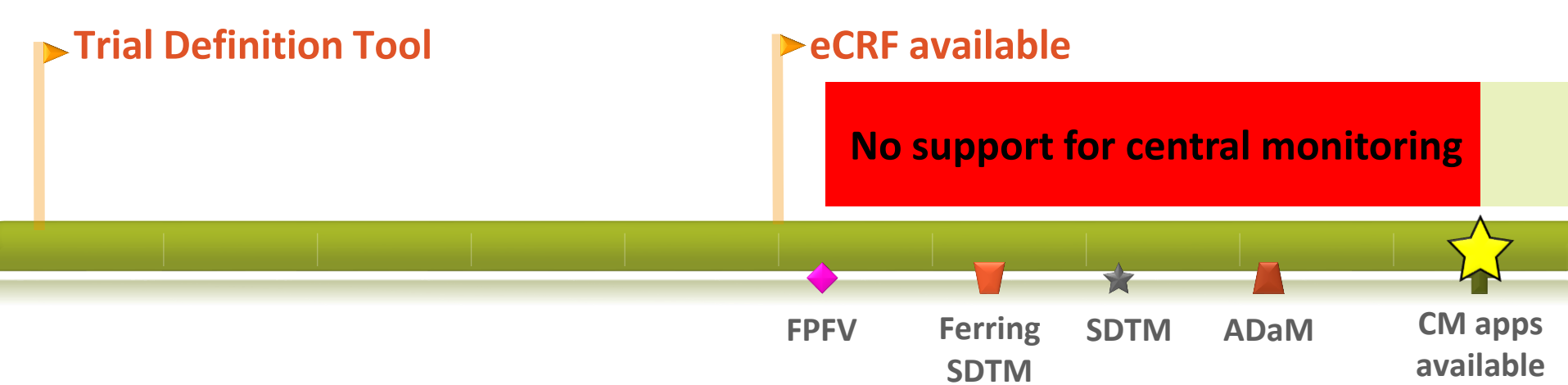
Conclusion

Ferring utilize information from the trial definition tool to generate synthetic data. The synthetic data is based directly on the meta data and empty SDTM shells and generates SDTM 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 trail
- Early 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



Timelines using the synthetic data generator

