LEARNINGS FROM AN EMA IT INSPECTION

Karin Gembert, Senior Director Data Management & Programming

Topics to cover

	Inspection Background
	A few Statistics from the Inspection
	Scope of the Inspection
	Vendor communication
	Questions and Discussion

Personal Introduction

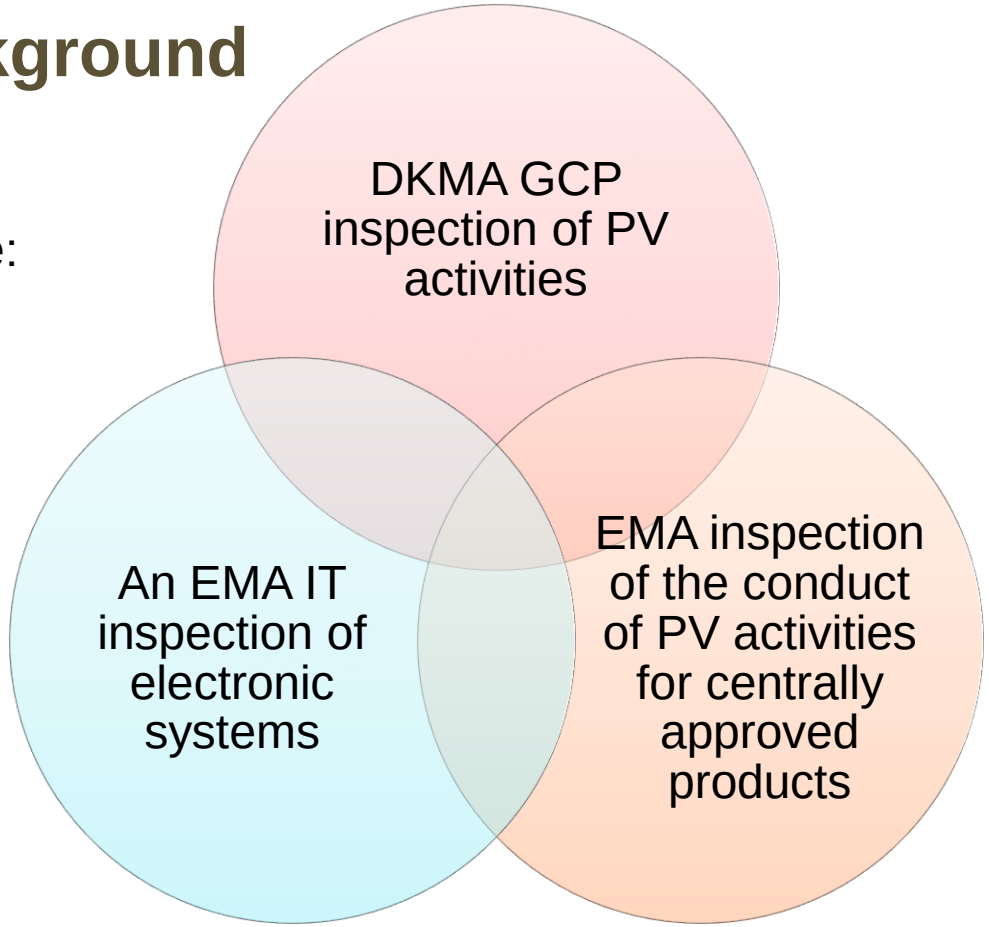
- Karin Gembert,
- Senior Director, Lundbeck, Valby Denmark

- Clinical Research & Development
- Data handling, analysing and reporting of data from Clinical Trials
- Department of Data Management and Programming

Ensure quality and consistency of the clinical database.
Ensure that our clinical data is provided in a standard format

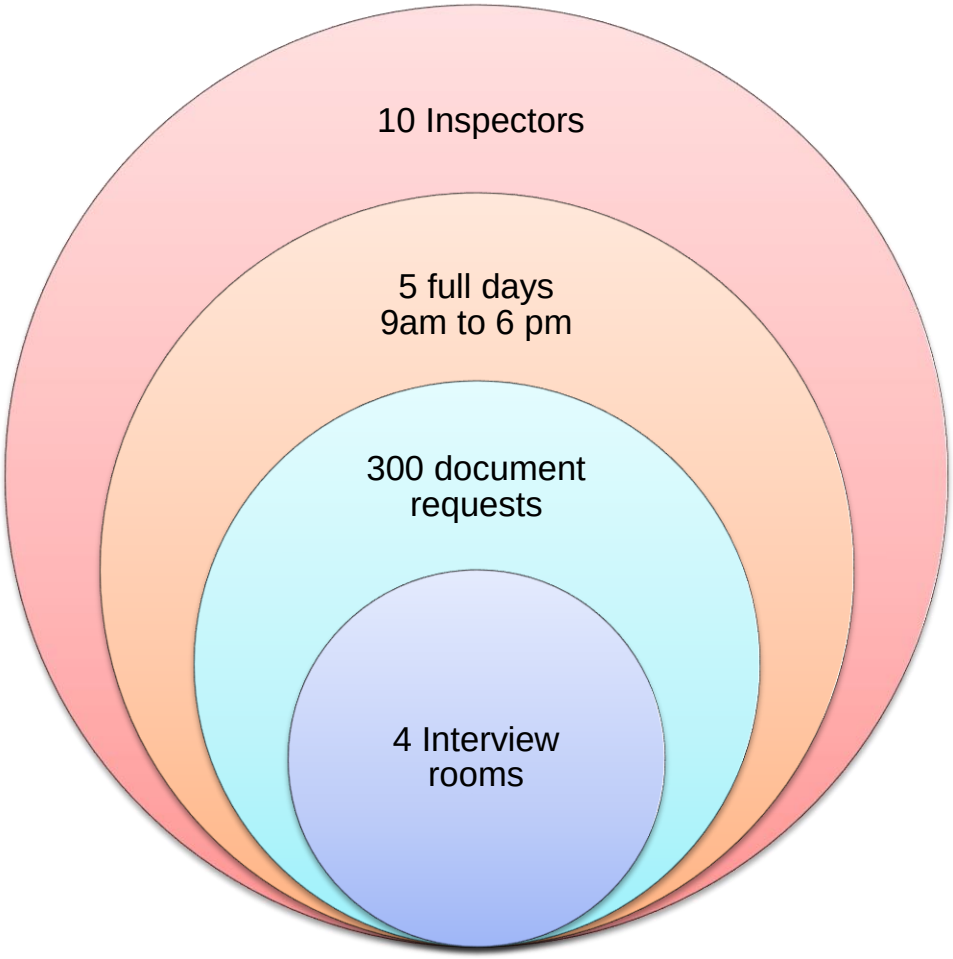
Inspection Background

Three inspections in one:



Agenda was provided in advance for the DKMA GCP and for the EMA PV inspection
No agenda was provided in advance for the EMA IT inspection

Inspection Statistics



Pre-inspection requests for the IT inspection

- Prior to the inspection, the inspectors requested the following to be available on the first day of the inspection:

A list of electronic systems used in pharmacovigilance and clinical trials

A list of all SOPs related to the electronic systems

A copy of each of the SOPs

All contracts relating to the electronic systems

Focus areas during the IT inspection

- ***EDC -*** *Electronic Data Capture System*
- A global Web Based Data Capture System used for capturing, managing and reporting data from clinical trials. It is a commercially available configurable standard software package. The system and its database is being provided and hosted.

- ***ePRO/eCOA*** - *E-patient related outcome (ePRO) and e-clinical outcome assessment (eCOA) devices*
- A scale provided on a tablet used for capturing and managing outcome assessment data from clinical trials.

Electronic Data Capture System

The validation activities at Lundbeck are limited

The scope of Lundbeck validation activities has been to show that the system fulfils regulatory requirements.

Validation activities have already been performed by the vendor.

Validation activities performed by the vendor has been made available to sponsor via the vendors validation portal.

During the inspection, test documentation was requested from vendor and provided and reviewed during the inspection.

ePRO/eCOA Devices

None of the validation activities have been performed by Lundbeck

The activities have been contracted out

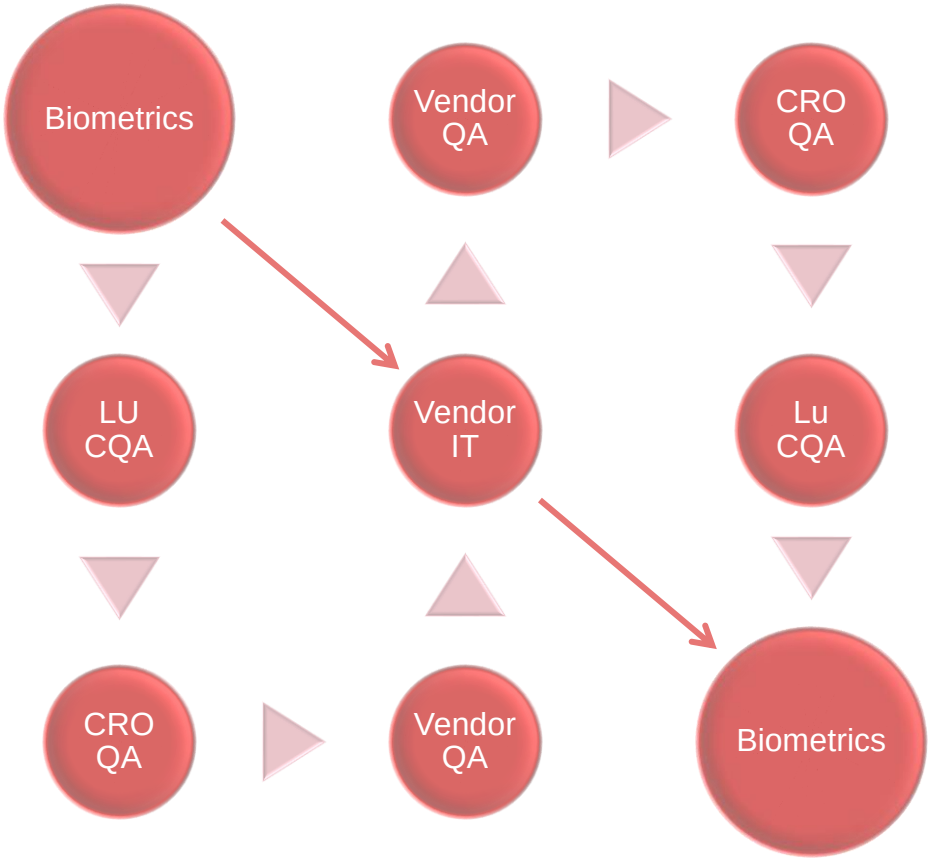
Some have been performed via further sub-contracting

Requests

- Information requested related to ePRO/eCOA included
  - documentation that Lundbeck has reviewed/accepted relevant documentation before implementation in a trial
  - audit trail for specific data for each trial and associated Data Clarification Forms
  - documentation for specific trial subjects demonstrating time stamped audit trails for data entry and upload to CRF/database
  - definition of source
  - password/authentication rules
  - attributability of records
  - inbuilt autosave/autologout
  - data transfer arrangements/plans
  - investigator access to read data
  - process for cleaning/encrypting devices
  - process for review of audit trail
- Very short timelines for responding

Communication process during the IT inspection

- Communication flow under high time pressure:



Comments due to communication complexity

- Unfortunately, due to very late availability of requested documentation, only a sample of the provided documentation has been reviewed.

- Please note that some of these comments/deviations could be the same for the other systems, since not all documentation has been inspected for all systems.

- Due to the above comments which are all potential deviations, the lack of time during this inspection and the incomplete documentation, the issue will be raised in a future GCP-inspection

ICH E6 R2

5.5.3 Electronic Trial Data Handling

Risk based validation approach

5.2.2 Transferred trial-related duty

Ensure oversight

Questions and Considerations regarding IT vendor oversight?

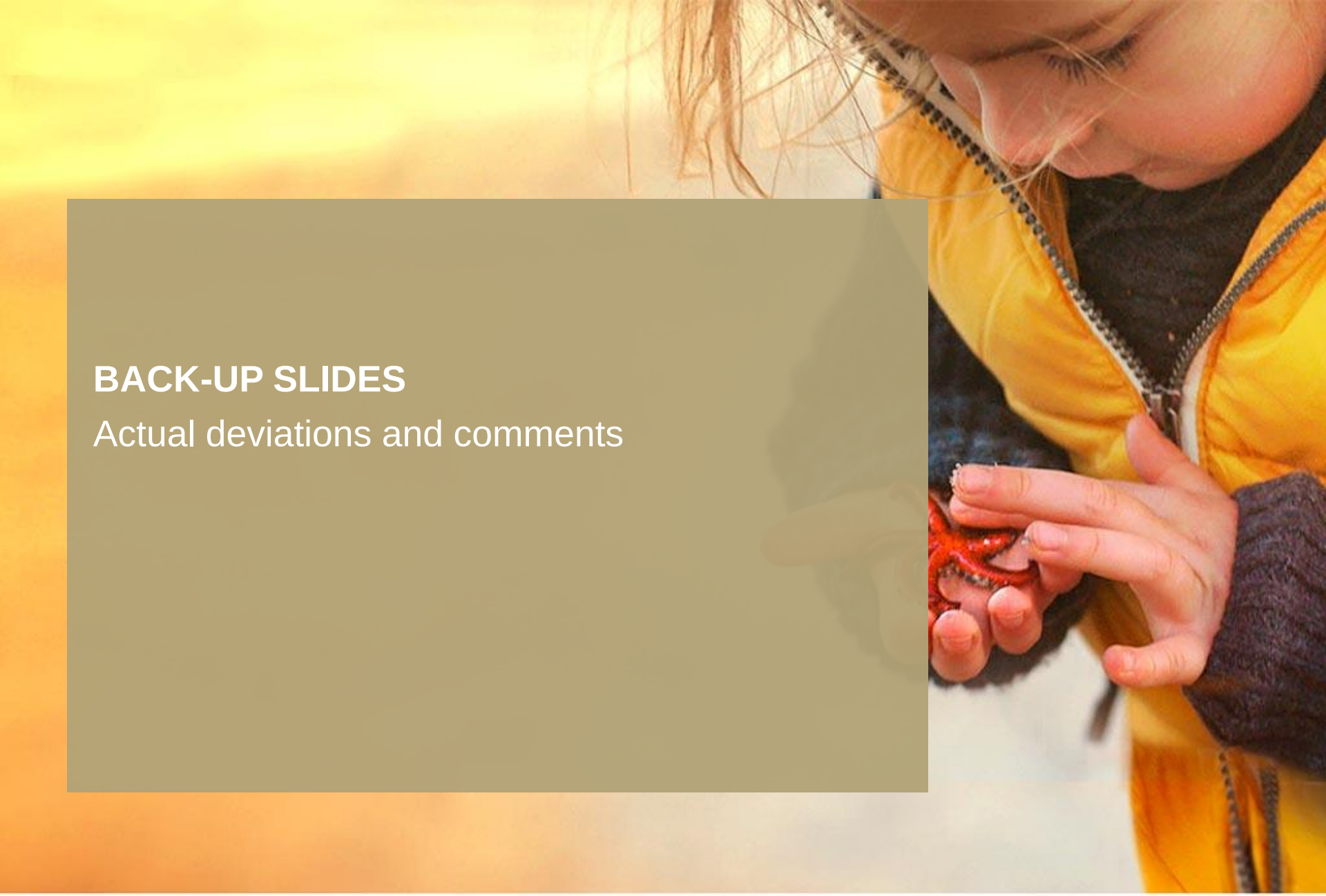
- Vendor Validation & Sponsor User Acceptance Test
  - Is adequate validation performed and documented?
  - What need to be performed by sponsor?
  - What is the sufficient level of oversight?

- Documentation available for Lundbeck – when and how?

- Sub-contracting and the obligation of the contracted CRO
  - What can be left in the hand of the contracted CRO?
  - What have to be controlled by sponsor?

Audit of eCOA vendors
- Before first contract?
- By whom?

QUESTIONS



BACK-UP SLIDES

Actual deviations and comments

Comments related to eCOA in the report (1/2)

- Vendor / PAERS:
  - The scale is used for patient assessments as well as rater assessments. The rater is logging on to the device for all processes so it is not clear from the documentation from the electronic system that the trial subject has done the rating. This is questionable and requires extremely robust procedures at site. Due to the scope of this inspection not being trial specific, it is only stated as a comment here. <u>This could potentially be a deviation, depending on site procedures.</u>
  - Data changes can only be performed via backend changes by the vendor, which requires extremely robust procedures to ensure site acceptance.

Comments related to eCOA in the report (2/2)

- Vendor / PANSS:
  - The reasons for change are not always clear or self-explanatory. Please comment if reasons for changes can be found elsewhere, for instance when duration (in seconds) is changed. It also seems that the audit trail provided for SCI-PANSS does not contain the actual symptoms assessments. This should be explained.

- Vendor / AISRS:
  - The Audit trail and change log for study xxxxxA, AISRS only contains data for a few actual changes and not the full audit trail for the data set.

Deviations related to ePRO/eCOA

- ePRO/eCOA
  - Major: Vendor / PANSS: the provided audit trail does not show original entry only changes made. Audit sequence number starts with 2.
  - Minor: Vendor / PANSS: it is stated that investigator access to review can be granted upon request. This is not acceptable, since the investigator should have access to patient data unless required by the protocol to be blinded.

- Please note that some of these comments/deviations could be the same for the other systems, since not all documentation has been inspected for all systems. Due to the above comments which are all potential deviations, the lack of time during this inspection and the incomplete documentation, <u>the issue will be raised in a future GCP-inspection</u>