



Complexity and Magnitude of Participant Reactogenicity Data

PHUSE Presentation 1-4 May 2022

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Vaccines

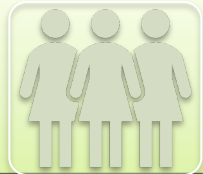
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Melinda, *Tree of Life*
Melinda's artwork reflects
her journey living with HIV.

Presentation topics



Introduction



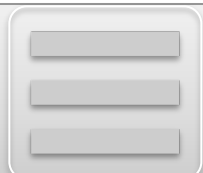
Data collection methods



Participant Diary versus Investigator Assessment



Data structure and important notes



Conclusion

Introduction

Introduction



Vaccines

An injection of an antigen (the vaccine) **mimics a pathogen**, without causing severe disease & **provokes an immune response to protect the organism from future exposure.**



Symptoms

Vaccines may cause **symptoms** such as

Local injection site reactions e.g. Redness, Pain/Tenderness, Swelling

Systemic reactions e.g. Fatigue, Headache, Nausea, Myalgia, Vomiting, Diarrhea and Fever

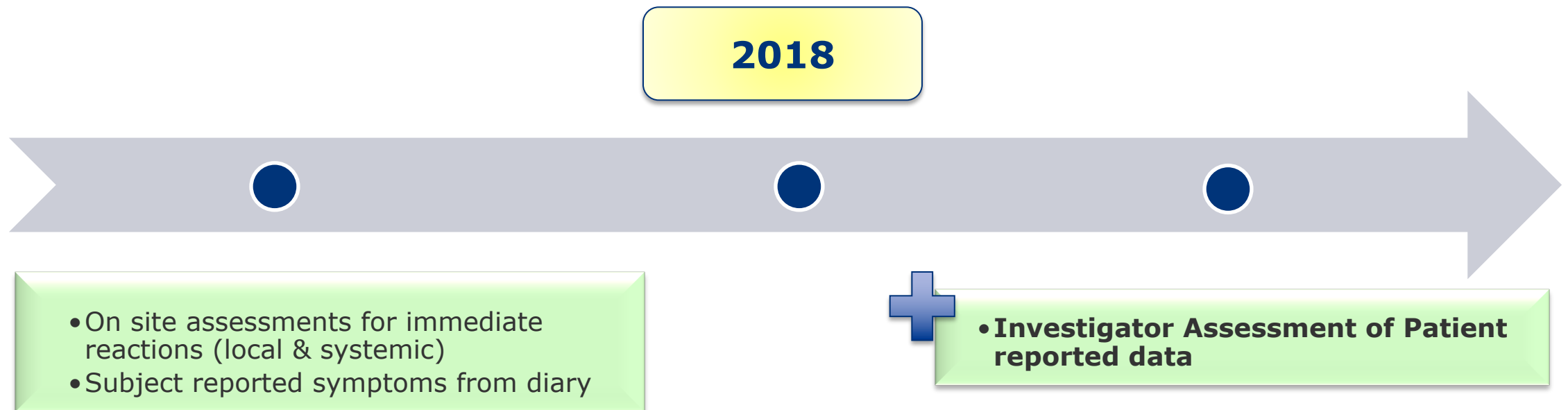


Reactogenicity

Prespecified symptoms in the protocol (post-vaccination) for which **occurrence & severity are captured** on a daily basis by the participant for a specified period & followed up until resolution

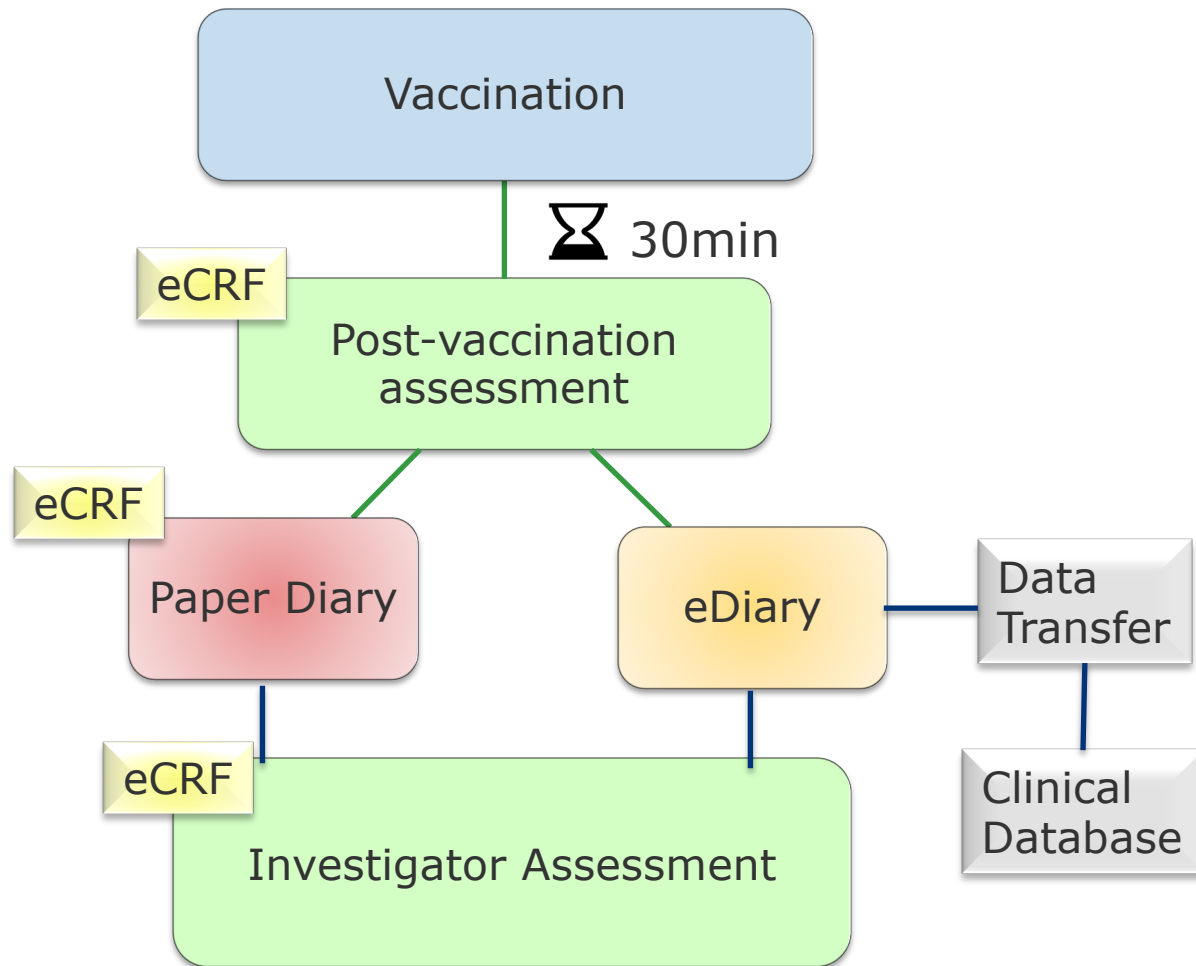
Introduction

- **Reactogenicity data are primary/secondary endpoints** in vaccine studies & **can pause vaccine development** to reassess the tolerability of the vaccine
- **Reactogenicity data collection evolved** after the release of **TAUG** (Therapeutic Area User Guide) and **OVRR** (Office of Vaccines Review and Research)



Data Collection Methods

Data Collection Methods



Vaccination Participant XXX

~8 assessments on-site

~8*8 assessments per subject

+/-13 questions per symptom
Investigator Assessment for each symptom

-> 8*13 responses

Total:
+/- 200 responses per vaccination/subject

Data Collection Methods



Paper Diary

- **Participant** discretion/dedication for timely **completion**
- **Adaptations/corrections** possible
- Transcribed by site staff in eCRF



Possibility of missing data due to low compliance	Population not acquainted with eDevice
Additional workload for staff	Locations with unstable connection
Risk of data entry errors	Back-up



Program bugs/glitches	Time efficient
Vendor transfer capabilities	Close to real time access to data
Not possible to alter data	Accurate representation as per subject judgement



Participant Diary versus Investigator Assessment

Participant Diary versus Investigator Assessment



Participant Diary

- **Daily symptom assessment** by **participant**
- **Indication of** intake of **medication** or need of medical aid
- Assessment **until full resolution** of symptom
- Paper diary or eDiary

Investigator Assessment

- **Summary** record for each symptom assessed by **investigator**
- Assessment at the end of protocol defined follow up period
- Recorded in eCRF

Large responsibility for investigators to correctly represent their assessment and document differences with participant assessment

Participant Diary versus Investigator Assessment



Participant Diary

- **Toxicity** Grade on **daily** basis
- **Fluctuations in toxicity** gradings/symptom presence **are clear**
- Maximum toxicity grade to be given: **3**

Investigator Assessment

- **Reflection of maximum toxicity** per investigator following protocol defined toxicity tables
- **Indication of duration** of maximum toxicity
- Indication of **continuous or intermittent presence** of symptom
- Maximum toxicity grade to be given: **4**

Any difference between maximum toxicity grade assessment or symptom duration assessment is to be flagged

Data structure and important notes

Data structure and important notes



Participant Reported Diary Data

- Elaborate and **mapped to FACE** domain (temperature mapping in VS)
- **Traceability for protocol** defined **follow up** period of reactogenicity
- **Not analysed by Statistics**

Investigator Assessment Data

- **Summary of reactogenicity** event in CE
- Differentiation of **immediate reactions**; identified by CEGRPID
- Summary record per symptom per vaccination
- Any differences in assessment to be flagged
- **Used in statistical analysis**

Data Structure and important notes

Crucial data for correct analysis



Reactogenicity data is a main focus in submission package review by authorities, which keeps a close eye on structure and completeness of the data

Difference Toxicity/Duration + Reason (SUPPCE)
Event Start and End date (CESTDTC, CEENDTC)
Symptom occurred intermittently (CEPATT)
Maximum Toxicity grade
Outcome (CEOUT) and Relationship (CEREL)
Continuing beyond evaluation period (CEENRTPT)

Conclusion

Conclusion



Reactogenicity data are considered as primary and/or secondary endpoints in executing vaccine studies and can cause pauses in vaccine development in order to reassess the tolerability of the vaccine



Ongoing efforts to alleviate data entry burden for site, without impacting data quality and integrity



Large responsibility for investigators to correctly represent their assessment and document differences with participant assessment



As early indicators of safety and tolerability, correct interpretation and analysis is crucial for further development of the compound



Main focus in submission package review by authorities, which keeps a close eye on structure and completeness of the data



Thank you

Contact information

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Thank you

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Back-up slides

Useful links

- Therapeutic Area User guide for Vaccines:

<https://www.cdisc.org/standards/therapeutic-areas/vaccines/vaccines-therapeutic-area-user-guide-v1-1>

- Office of Vaccines Review and Research (OVRR)

<https://www.fda.gov/media/112581/download>



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