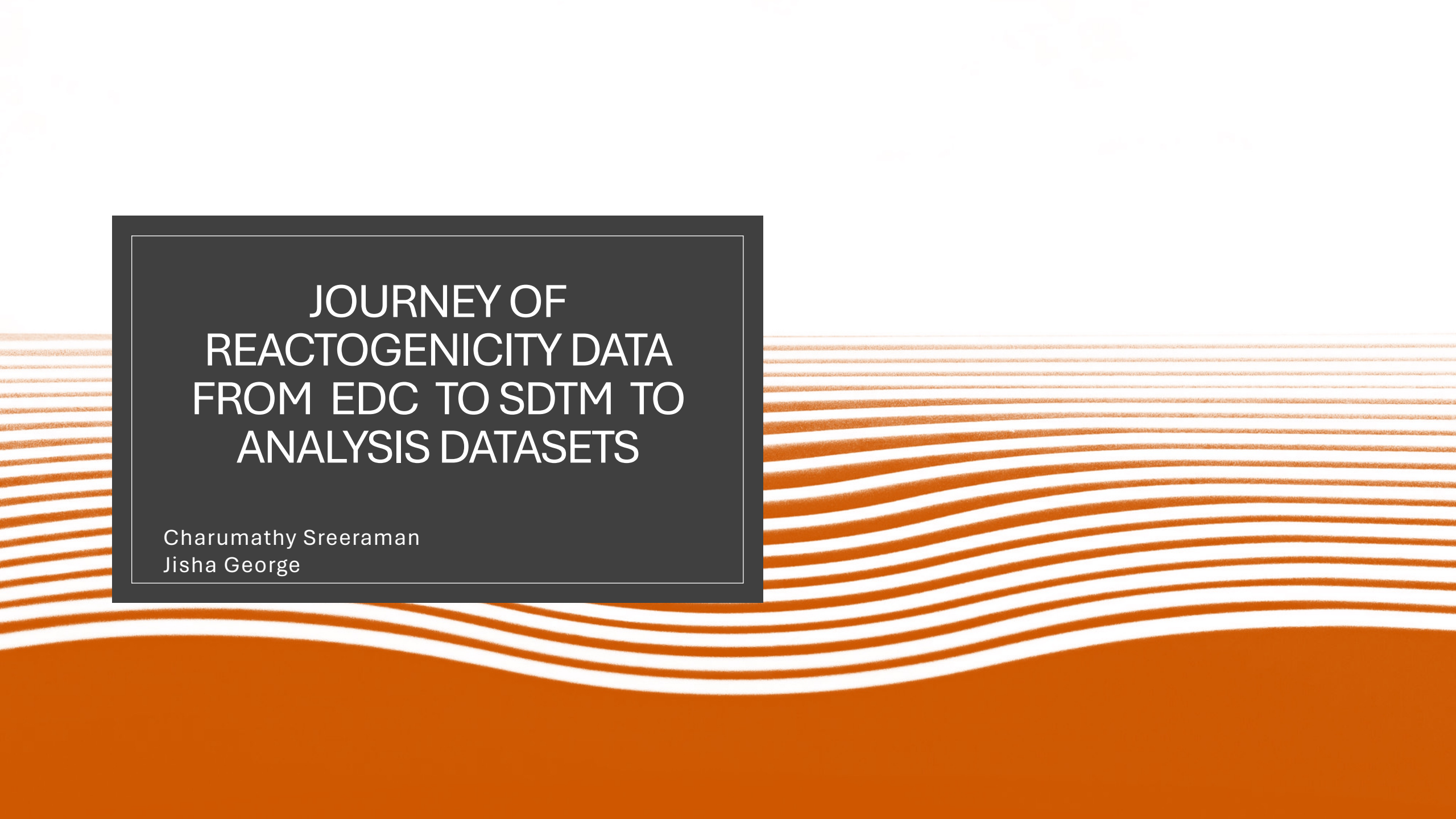


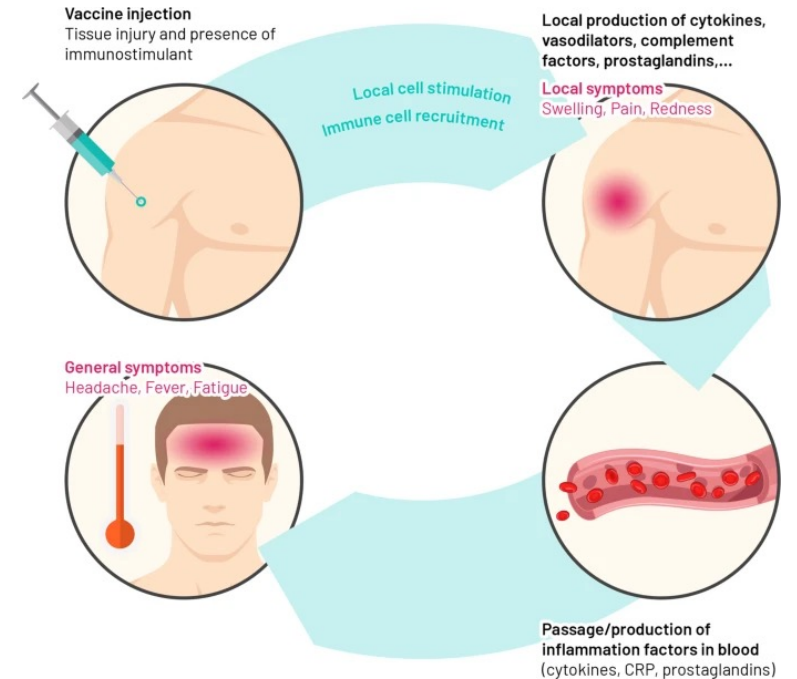


# JOURNEY OF REACTOGENICITY DATA FROM EDC TO SDTM TO ANALYSIS DATASETS

Charumathy Sreeraman  
Jisha George

# Reactogenicity Events – An Intro

- Also known as **solicited adverse events** or reactions, refer to a predetermined set of adverse events collected during a specific timeframe.
- These events are typically assessed in clinical trials by gathering information on both local injection site reactions and systemic signs and symptoms from study participants.
  - **Administration site events** are those occurring at or around the vaccine's administration site. The term local is also commonly used to refer to events at or around the administration site.
  - **Systemic reactogenicity** events are those affecting an entire system or body. These reactogenicity events can be non-localized (e.g., fatigue or fever) or they can have localized manifestations (e.g., rash), where the localization cannot be pre-specified or predicted.



# Reactogenicity Events – Why assess?

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- Forms a part of safety profile of the vaccine
- Understanding the range of symptoms that vaccination might cause is important for:
  - The person receiving the vaccine,
  - The caregivers making healthcare decisions for others,
  - The healthcare professionals who recommend and administer vaccines.
- Reactogenicity can contribute to a person's willingness to be vaccinated.



# Reactogenicity Events – How does it happen?

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Vaccines contain antigens that induce an immune response capable of providing specific protection from disease.

Individual vaccine antigens induce innate immune responses that may differ qualitatively or quantitatively according to the vaccine composition, but that induce a good adaptive immune response.



# Reactogenicity Events – Factors affecting

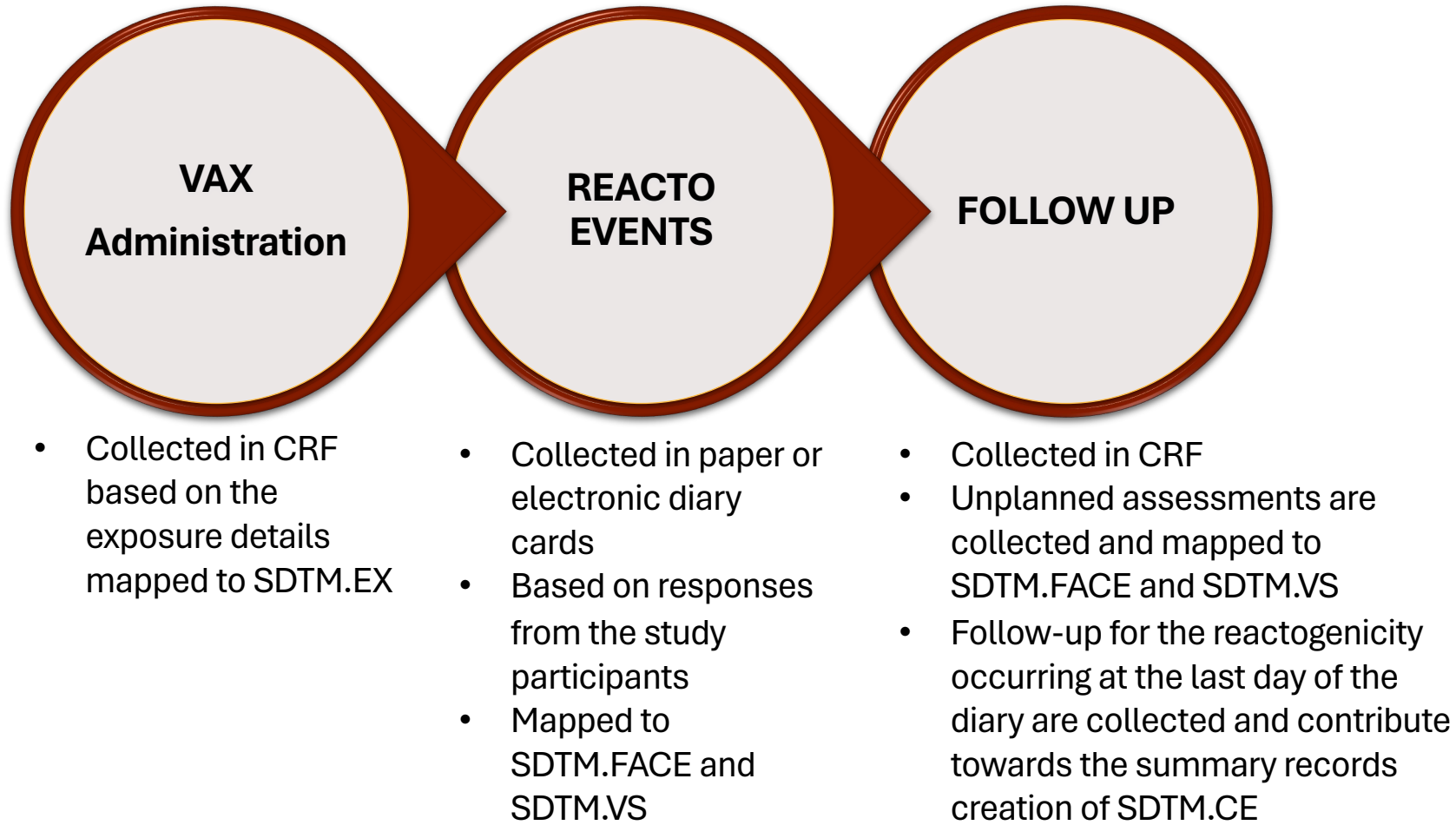
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- Extrinsic and intrinsic factors can impact the reactogenicity profile, tolerability, and immunogenicity of vaccines in a given individual. They include:
  - **Host characteristics**, such as age, gender, race/ethnicity, body mass, general health & pre-existing immunity
  - **Vaccine administration and composition factors**, such as route and site of administration, injection technique, type of antigen, vaccine formulation, and type of adjuvant.



# Collection of Reactogenicity events

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# Data mapping approaches

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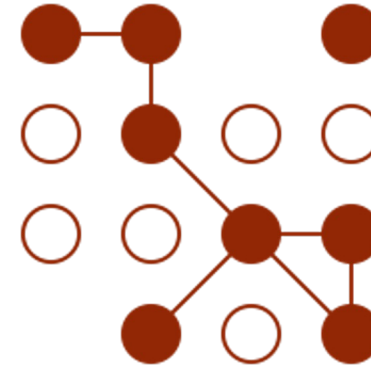
## Flat Model

All of the daily assessments are transcribed/loaded from the diary card and a global event record is created, whether or not a reactogenicity event occurred during the three-day assessment interval.



## Nested Model

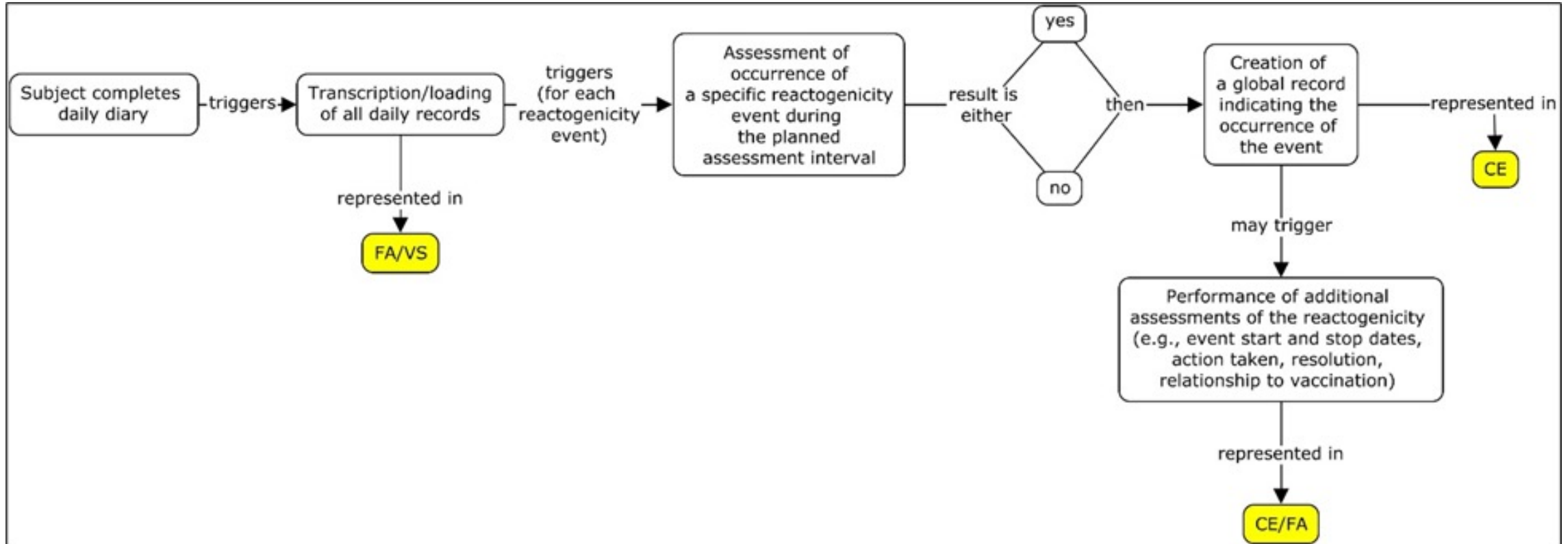
A global record is created for each reactogenicity event that is assessed; the daily assessment records for an event are transcribed/loaded only if the event occurred during the three-day assessment interval).



## Highly Nested Model

A global record is created for each type of reactogenicity category that is assessed (i.e., systemic and site administration events). If an event occurred in one of the categories, additional global records for all the events assessed in that category are created. Daily assessment records for an event are transcribed/loaded only if the event occurred during the three-day assessment interval.

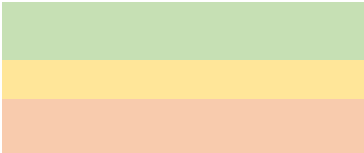
# Flat Model



# VS Dataset

| SUBJID   | AETERM           | AEDECOD | AEREL   | AETOXGR | AESTDTC    | AEENDTC    | AETPTREF      | AERFTDTC            | AEENRTPT |
|----------|------------------|---------|---------|---------|------------|------------|---------------|---------------------|----------|
| 12345678 | High Temperature | Pyrexia | RELATED | 1       | 2022-09-25 | 2022-09-28 | VACCINATION 1 | 2022-09-23T13:24:00 |          |

| SUBJID   | VSTESTCD | VSCAT                      | VSORRES | VSSTRESC | VSEVAL        | VSDTC               | VSTPT | VSRFTDTC            |
|----------|----------|----------------------------|---------|----------|---------------|---------------------|-------|---------------------|
| 12345678 | TEMP     | REACTOGENICITY             |         |          |               | 2022-09-24          | DAY 1 | 2022-09-23T13:24:00 |
| 12345678 | TEMP     | REACTOGENICITY             |         |          |               | 2022-09-25          | DAY 2 | 2022-09-23T13:24:00 |
| 12345678 | TEMP     | REACTOGENICITY             |         |          |               | 2022-09-26          | DAY 3 | 2022-09-23T13:24:00 |
| 12345678 | TEMP     | REACTOGENICITY             | 35.7    | 35.7     | STUDY SUBJECT | 2022-09-27T18:27:07 | DAY 4 | 2022-09-23T13:24:00 |
| 12345678 | TEMP     | REACTOGENICITY             | 39      | 39       | STUDY SUBJECT | 2022-09-28          | DAY 5 | 2022-09-23T13:24:00 |
| 12345678 | TEMP     | REACTOGENICITY - UNPLANNED |         | FEVER    | INVESTIGATOR  | 2022-09-25          | DAY 2 | 2022-09-23T13:24:00 |
| 12345678 | TEMP     | REACTOGENICITY - UNPLANNED |         | FEVER    | INVESTIGATOR  | 2022-09-26          | DAY 3 | 2022-09-23T13:24:00 |
| 12345678 | TEMP     | REACTOGENICITY - UNPLANNED |         | FEVER    | INVESTIGATOR  | 2022-09-27          | DAY 4 | 2022-09-23T13:24:00 |
| 12345678 | TEMP     | REACTOGENICITY - UNPLANNED |         | FEVER    | INVESTIGATOR  | 2022-09-28          | DAY 5 | 2022-09-23T13:24:00 |



Unsolicited AEs as daily records

Diary Data

Derived records for missing Diary Days

# FACE Dataset

| SUBJID   | AETERM   | AEDECOD  | AEREL       | AETOXGR | AESTDTC    | AEENDTC | AETPTREF      | AERFTDTC            | AEENRTPT |
|----------|----------|----------|-------------|---------|------------|---------|---------------|---------------------|----------|
| 12345678 | Headache | Headache | NOT RELATED | 2       | 2022-09-25 |         | VACCINATION 1 | 2022-09-23T13:24:00 | ONGOING  |

| SUBJID   | FATESTCD                         | FAORRES     | FAEVAL        | FADTC               | FATPT | FARFTDTC            | FAENRTPT |
|----------|----------------------------------|-------------|---------------|---------------------|-------|---------------------|----------|
| 12345678 | OCCUR                            | N           | STUDY SUBJECT | 2022-09-23T18:24:00 | DAY 1 | 2022-09-23T13:24:00 |          |
| 12345678 | OCCUR                            | N           | STUDY SUBJECT | 2022-09-24T18:24:00 | DAY 2 | 2022-09-23T13:24:00 |          |
| 12345678 | OCCUR                            | N           | STUDY SUBJECT | 2022-09-25T18:01:38 | DAY 3 | 2022-09-23T13:24:00 |          |
| 12345678 | OCCUR                            | Y           | STUDY SUBJECT | 2022-09-26T18:27:07 | DAY 4 | 2022-09-23T13:24:00 |          |
| 12345678 | SEV                              | MILD        | STUDY SUBJECT | 2022-09-26T18:27:07 | DAY 4 | 2022-09-23T13:24:00 |          |
| 12345678 | OCCUR                            | Y           | STUDY SUBJECT | 2022-09-27T19:01:00 | DAY 5 | 2022-09-23T13:24:00 |          |
| 12345678 | SEV                              | MILD        | STUDY SUBJECT | 2022-09-27T19:01:00 | DAY 5 | 2022-09-23T13:24:00 |          |
| 12345678 | OCCUR                            | Y           | INVESTIGATOR  | 2022-09-25          | DAY 3 | 2022-09-23T13:24:00 |          |
| 12345678 | OCCUR                            | Y           | INVESTIGATOR  | 2022-09-26          | DAY 4 | 2022-09-23T13:24:00 |          |
| 12345678 | OCCUR                            | Y           | INVESTIGATOR  | 2022-09-27          | DAY 5 | 2022-09-23T13:24:00 | ONGOING  |
| 12345678 | SEV                              | MODERATE    | INVESTIGATOR  | 2022-09-25          | DAY 3 | 2022-09-23T13:24:00 |          |
| 12345678 | SEV                              | MODERATE    | INVESTIGATOR  | 2022-09-26          | DAY 4 | 2022-09-23T13:24:00 |          |
| 12345678 | SEV                              | MODERATE    | INVESTIGATOR  | 2022-09-27          | DAY 5 | 2022-09-23T13:24:00 | ONGOING  |
| 12345678 | REL                              | NOT RELATED | INVESTIGATOR  | 2022-09-25          | DAY 3 | 2022-09-23T13:24:00 |          |
| 12345678 | REL                              | NOT RELATED | INVESTIGATOR  | 2022-09-26          | DAY 4 | 2022-09-23T13:24:00 |          |
| 12345678 | REL                              | NOT RELATED | INVESTIGATOR  | 2022-09-27          | DAY 5 | 2022-09-23T13:24:00 | ONGOING  |
|          | Unsolicited AEs as daily records |             |               |                     |       |                     |          |
|          | Diary Data                       |             |               |                     |       |                     |          |

# FACE Analysis Dataset

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| USUBJID   | SRCDOM | FATESTCD | PARAMCD | PARAM                        | FAOBJ   | PARCAT1        | PARCAT2  | AVALC    | AVALN | DTYPE   | ATPT  | ATPTREF       |
|-----------|--------|----------|---------|------------------------------|---------|----------------|----------|----------|-------|---------|-------|---------------|
| 123456789 | VS     | OCCUR    | OCFEVER | Fever occurrence indicator   | FEVER   | REACTOGENICITY | SYSTEMIC | N        | .     | DERIVED | DAY 7 | VACCINATION 1 |
| 123456789 | VS     | OCCUR    | OCFEVER | Fever occurrence indicator   | FEVER   | REACTOGENICITY | SYSTEMIC | N        | .     | DERIVED | DAY 5 | VACCINATION 1 |
| 123456789 | VS     | OCCUR    | OCFEVER | Fever occurrence indicator   | FEVER   | REACTOGENICITY | SYSTEMIC | N        | .     | DERIVED | DAY 4 | VACCINATION 1 |
| 123456789 | VS     | OCCUR    | OCFEVER | Fever occurrence indicator   | FEVER   | REACTOGENICITY | SYSTEMIC | N        | .     | DERIVED | DAY 3 | VACCINATION 1 |
| 123456789 | VS     | OCCUR    | OCFEVER | Fever occurrence indicator   | FEVER   | REACTOGENICITY | SYSTEMIC | N        | .     | DERIVED | DAY 2 | VACCINATION 1 |
| 123456789 | VS     | OCCUR    | OCFEVER | Fever occurrence indicator   | FEVER   | REACTOGENICITY | SYSTEMIC | N        | .     | DERIVED | DAY 1 | VACCINATION 1 |
| 123456789 | VS     | OCCUR    | OCFEVER | Fever occurrence indicator   | FEVER   | REACTOGENICITY | SYSTEMIC | N        | .     | DERIVED | DAY 6 | VACCINATION 1 |
| 123456789 | FA     | SEV      | SEVFATI | Fatigue severity/intensity   | FATIGUE | REACTOGENICITY | SYSTEMIC | MILD     | 1     |         | DAY 3 | VACCINATION 1 |
| 123456789 | FA     | SEV      | SEVFATI | Fatigue severity/intensity   | FATIGUE | REACTOGENICITY | SYSTEMIC | MODERATE | 2     |         | DAY 7 | VACCINATION 1 |
| 123456789 | FA     | SEV      | SEVFATI | Fatigue severity/intensity   | FATIGUE | REACTOGENICITY | SYSTEMIC | MILD     | 1     |         | DAY 1 | VACCINATION 1 |
| 123456789 | FA     | OCCUR    | OCFATIG | Fatigue occurrence indicator | FATIGUE | REACTOGENICITY | SYSTEMIC | Y        | .     |         | DAY 7 | VACCINATION 1 |
| 123456789 | FA     | OCCUR    | OCFATIG | Fatigue occurrence indicator | FATIGUE | REACTOGENICITY | SYSTEMIC | N        | .     |         | DAY 5 | VACCINATION 1 |
| 123456789 | FA     | OCCUR    | OCFATIG | Fatigue occurrence indicator | FATIGUE | REACTOGENICITY | SYSTEMIC | N        | .     |         | DAY 4 | VACCINATION 1 |
| 123456789 | FA     | OCCUR    | OCFATIG | Fatigue occurrence indicator | FATIGUE | REACTOGENICITY | SYSTEMIC | Y        | .     |         | DAY 3 | VACCINATION 1 |
| 123456789 | FA     | OCCUR    | OCFATIG | Fatigue occurrence indicator | FATIGUE | REACTOGENICITY | SYSTEMIC | N        | .     |         | DAY 2 | VACCINATION 1 |
| 123456789 | FA     | OCCUR    | OCFATIG | Fatigue occurrence indicator | FATIGUE | REACTOGENICITY | SYSTEMIC | Y        | .     |         | DAY 1 | VACCINATION 1 |

# CE Dataset

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| USUBJID  | CETERM   | CEEVAL        | Start<br>Date_Diary | Ocuur_<br>Diary | EndDate_Diary | Severity<br>_Diary |
|----------|----------|---------------|---------------------|-----------------|---------------|--------------------|
| 12345678 | DIARRHEA | STUDY SUBJECT | 2021-12-15          | Y               | 2021-12-15    | MILD               |
|          |          |               |                     |                 |               |                    |
| USUBJID  | CETERM   | CEEVAL        | Start<br>Date_Inv   | Occur_<br>Inv   | End Date_Inv  | Severity<br>_Inv   |
| 12345678 | DIARRHEA | INVESTIGATOR  | 2021-12-15          | Y               | 2021-12-17    | MILD               |

| USUBJID  | CETERM   | SUPPCE_CEEVAL | CEOCCUR | CESTDTC    | CEENDTC    | CESV | SUPPCE_CEDIFFRS                                                              |
|----------|----------|---------------|---------|------------|------------|------|------------------------------------------------------------------------------|
| 12345678 | DIARRHEA | INVESTIGATOR  | Y       | 2021-12-05 | 2021-12-17 | MILD | INVESTIGATOR<br>ASSESSED AS MORE<br>SEVERE DURING<br>UNPLANNED<br>ASSESSMENT |

# CE Analysis Dataset

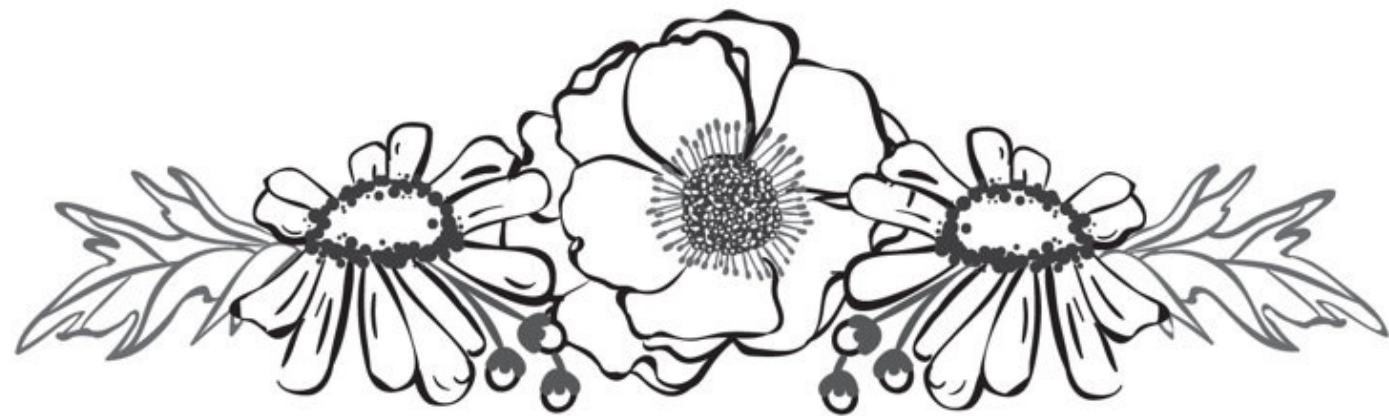
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| USUBJID   | CETERM                 | CESCAT              | CEOCCUR | CESEV    | ASEV | KNOWVFL | ADURU | ADURN | ASTDT      | ASTDTM             | AENDT      | EVENTFL | AVISIT | AVISITN | ADURTN | ADURTU |
|-----------|------------------------|---------------------|---------|----------|------|---------|-------|-------|------------|--------------------|------------|---------|--------|---------|--------|--------|
| 123456789 | VOMITING               | SYSTEMIC            | N       |          |      | Y       |       | .     | .          | .                  | .          | N       | Dose 1 | 1       | .      |        |
| 123456789 | SWELLING               | ADMINISTRATION SITE | N       |          |      | Y       |       | .     | .          | .                  | .          | N       | Dose 1 | 1       | .      |        |
| 123456789 | REDNESS                | ADMINISTRATION SITE | N       |          |      | Y       |       | .     | .          | .                  | .          | N       | Dose 1 | 1       | .      |        |
| 123456789 | PAIN AT INJECTION SITE | ADMINISTRATION SITE | Y       | MILD     |      | Y       | DAYS  | 15    | 2021-12-15 | 15DEC2021:00:00:00 | 2021-12-29 | Y       | Dose 1 | 1       | 15     | DAYS   |
| 123456789 | NAUSEA                 | SYSTEMIC            | N       |          |      | Y       |       | .     | .          | .                  | .          | N       | Dose 1 | 1       | .      |        |
| 123456789 | MUSCLE PAIN            | SYSTEMIC            | N       |          |      | Y       |       | .     | .          | .                  | .          | N       | Dose 1 | 1       | .      |        |
| 123456789 | JOINT PAIN             | SYSTEMIC            | N       |          |      | Y       |       | .     | .          | .                  | .          | N       | Dose 1 | 1       | .      |        |
| 123456789 | HEADACHE               | SYSTEMIC            | Y       | MILD     |      | Y       | DAYS  | 1     | 2021-12-19 | 19DEC2021:18:23:02 | 2021-12-19 | Y       | Dose 1 | 1       | 1      | DAYS   |
| 123456789 | FEVER                  | SYSTEMIC            | N       |          |      | Y       |       | .     | .          | .                  | .          | N       | Dose 1 | 1       | .      |        |
| 123456789 | FATIGUE                | SYSTEMIC            | Y       | MODERATE |      | Y       | DAYS  | 7     | 2021-12-13 | 13DEC2021:18:01:00 | 2021-12-19 | Y       | Dose 1 | 1       | 3      | DAYS   |
| 123456789 | DIARRHEA               | SYSTEMIC            | N       |          |      | Y       |       | .     | .          | .                  | .          | N       | Dose 1 | 1       | .      |        |

# Conclusion

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- The management of different data collection input sources, such as CRF pages, Subject Diary cards, Unplanned Assessments, and filtering out Adverse Events data that satisfies the reactogenicity criteria, in order to generate the flat model strategy adapted Reactogenicity datasets.
- Describes how the reactogenicity data moves from the EDC to being standardized using TAUG techniques, and then how the BDS and event format analysis datasets prepare it for study.
- Also contains FDA, CBER, and other regulatory bodies' recommendations and remarks regarding the application of the flat model.



THANK YOU

