Paper TA07

Journey of Reactogenicity Data from EDC to SDTM to Analysis Datasets

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ABSTRACT

Vaccines, the necessity of the recent times, play a major role in the prevention of infectious diseases. Vaccine development is a complex process and is continuously evolving to optimize efficacy and minimize reactogenicity and safety issues. The main safety assessment in vaccine development is reactogenicity analysis, which outlines anticipated short-term reactions to vaccines. In clinical trials, reactogenicity is measured by collecting sets of injection site and systemic signs and symptoms that are solicited from study participants over a specified time after vaccination. These symptoms may include pain, redness, swelling for injected vaccines, and systemic symptoms, such as fever, headache, or rash. The collection of these symptoms from subjects is done through various sources like study site Investigator, participant Diary etc. The challenge is how to gather all these data from various sources and transform into standardized Reactogenicity data in SDTM and Analysis datasets, which will be covered in this paper.

INTRODUCTION

Vaccine safety is regularly assessed, starting with clinical trials and ending with post-authorization/post-licensure research. Following authorization, pharmacovigilance activities are carried out by the vaccine manufacturer, regulatory bodies, and independent researchers to monitor the safety of the vaccine. These activities include the review of spontaneous reports of adverse events (AEs) that are received from healthcare professionals, laypeople, and regulatory agencies worldwide. In focused safety studies carried out after licensure, the investigation of certain AEs of interest may continue.

Although there is little evidence to support the widely held belief that reactogenic reactions following vaccination are indicative of a healthy immune response, this belief is nonetheless widely held. Vaccine reactogenicity, which can include injection site and systemic symptoms, is the term used to describe the outward manifestation of an inflammatory response to a vaccine. These symptoms that do occur early after vaccination are usually mild and self-limiting and rarely have serious medical consequences.

Certain symptoms, such as body temperature, redness, swelling, and heart rate, may be evaluated objectively. While other symptoms are ill-defined and subjective, and their perception varies based on many circumstances these variables may include one's attitude, the existence of additional medical illnesses or symptoms, the environment, one's personal pain threshold, etc. It is also challenging to quantify the impact of symptoms on a person's quality of life and physical functioning, decreased productivity at work, or usage of medical services or prescription drugs.

This document discusses the data that was gathered for these reactogenicity events, how it was standardized, and how it was transformed for analysis.

REACTOGENICITY EVENTS

Reactogenicity events, 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. The symptoms recorded and the duration of data collection vary depending on the vaccine under investigation and the specific objectives of the individual studies. Solicited reactions, obtained through active questioning of participants, generally result in higher reported frequencies compared to unsolicited symptoms, where participants are asked to spontaneously report any symptoms they experience. These events are useful to make informed decisions on the selection of better tolerated vaccines.

Reactogenicity events can be classified as either administration site or systemic events.

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. Another term, localized event, is used to denote adverse events that have a localized manifestation, but not necessarily at the administration site (e.g., rash that is considered a systemic event, whose manifestation can be localized).

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.

Manifestations of reactogenicity typically assessed in vaccine trials include pain, tenderness, itching, bruising, erythema/redness, induration, and swelling at the administration site; and fever, fatigue, malaise, myalgia, arthralgia, headache, and nausea for systemic events. Some manifestations are typically associated to a specific sub-population, for example, vomiting, abnormal crying, drowsiness, appetite loss, or irritability for infants and toddlers.

Severity of the reactogenicity event may be assessed by the subject, the investigator, or both. When the investigator assesses the severity, it is common to use a standard toxicity grading scale such as the FDA Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials.

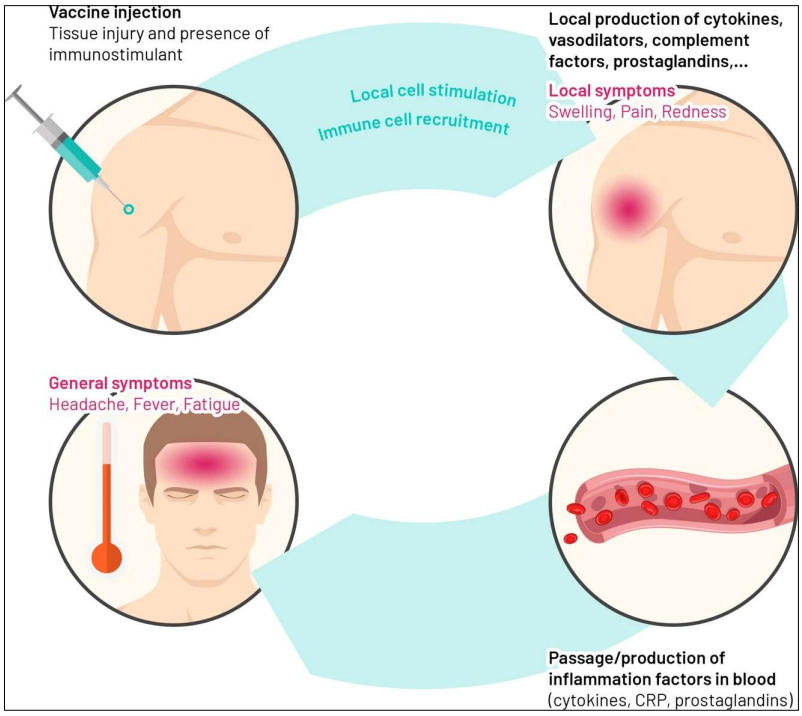

Figure 1. Reactogenicity

NEED FOR REACTOGENICITY EVENTS ASSESSMENTS

Vaccines need to be proven safe for the general population and reactogenicity is part of the safety profile of the vaccine. The more detailed term ‘safety’ profile refers to all adverse events (AEs) that could potentially be caused/triggered or worsened at any time after vaccination, and includes AEs such as anaphylactic reactions, diseases diagnosed after vaccination and autoimmune events. Understanding the range of symptoms that vaccination might cause is important for the person receiving the vaccine, for caregivers making healthcare decisions on behalf of the participants and for

healthcare professionals who recommend and administer vaccines. Reactogenicity can contribute to a person's willingness to be vaccinated.

The recent FDA, Center for Biologics Evaluation and Research (CBER) Guidance for Industry on the Emergency Use Authorization for Vaccines to Prevent Coronavirus disease 2019 (COVID-19) necessitates vaccines studies to collect local and systemic solicited AEs in an adequate number of participants to characterize the reactogenicity profile in each age group participating in the trial.

HOW DOES REACTOGENICITY EVENTS HAPPENS

Vaccines contain antigens that induce an immune response capable of providing specific protection from disease. Depending on the composition of the vaccination, individual vaccine antigens may cause innate immune responses that vary in quality or quantity but nevertheless result in a robust adaptive immunological response.

ADMINISTRATIVE SITE EVENTS

Upon vaccination, inflammation is triggered by innate immune activation of pattern-recognition receptors (PRR) including Toll-like receptors (TLRs) that recognize and bind antigens and potential immune enhancers present in the vaccine formulation. Resident immune cells, mast cells, monocytes and macrophages are activated within minutes of injection and release soluble factors (proinflammatory cytokines, chemokines, effectors of the complement cascade) and vasodilators, that allow cell recruitment from blood but also lead to the development of redness and swelling symptoms.

SYSTEMIC EVENTS

The main step in the development of systemic symptoms after vaccination is thought to be the presence of inflammatory markers in the bloodstream, which signal at the blood-brain barrier level and induce influenza-like symptoms.

FACTORS CAUSING REACTOGENICITY EVENTS

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 and pre-existing immunity, and vaccine administration and composition factors, such as route and site of administration, injection technique, type of antigen, vaccine formulation, and type of adjuvant.

COLLECTION INSTRUMENTS FOR THE REACTOGENICITY DATA

In most vaccine clinical trials, the vaccine recipients, caregivers, or study staff collect the daily record information of reactogenicity events using paper or electronic diary cards (eDCs). Diary cards (DCs) completion level should be checked during a face-to-face or telephone contact between the trial participant/caregiver and study staff, who may provide further instructions to improve compliance and data quality.

The use of electronic methods such as eDCs allows fast, remote collection of reactogenicity events, compliance checks and follow-up, and it is particularly useful in a pandemic context where visits to physicians are not recommended except for medical emergencies. However, the use of eDCs may not be feasible in resource-limited settings or in populations with low levels of technical expertise.

The reactogenicity eDCs allows recording of these assessments each day, thus providing the accurate representation of the participant's experience. Data on local reactions and systemic events reported in the reactogenicity eDCs will be transferred electronically to a third-party vendor, where they will be available for review by investigators and the clinicians at all times via an internet-based portal.

The study CRF collects the follow up of the reactogenicity events and the unplanned assessments corresponding to these events.

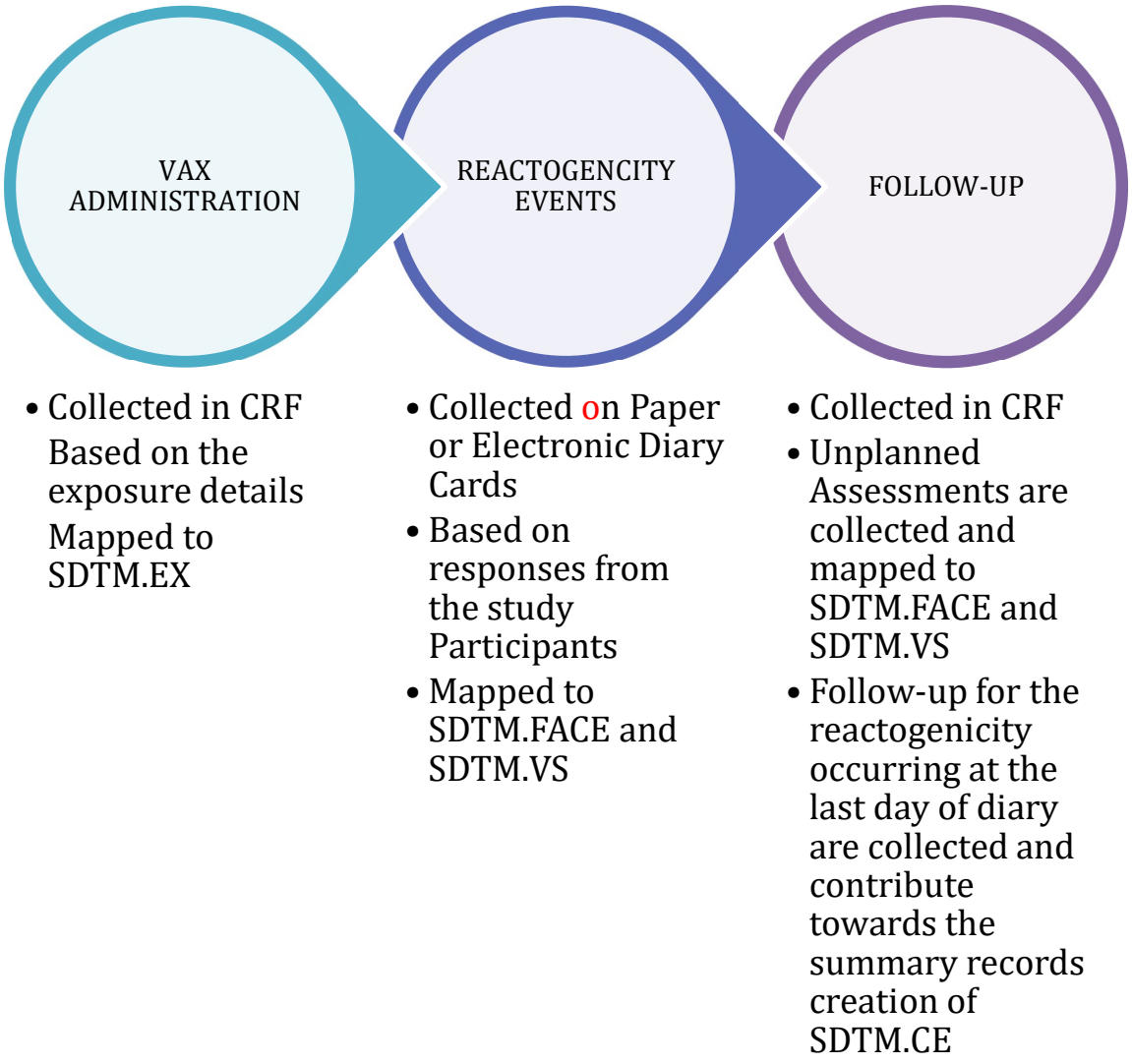

Figure 2. Collection Timelines of Reactogenicity Events

APPROACHES FOR MAPPING REACTOGENICITY DATA

The three strategies used in this guide are described below:

- ✓ **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.

The studies using electronic diary information tend to use strategy 1 since all of the diary information is easily loaded into the sponsor database and there is no manual data entry required for the subject diary. This paper discusses the flat model implementation of the reactogenicity data.

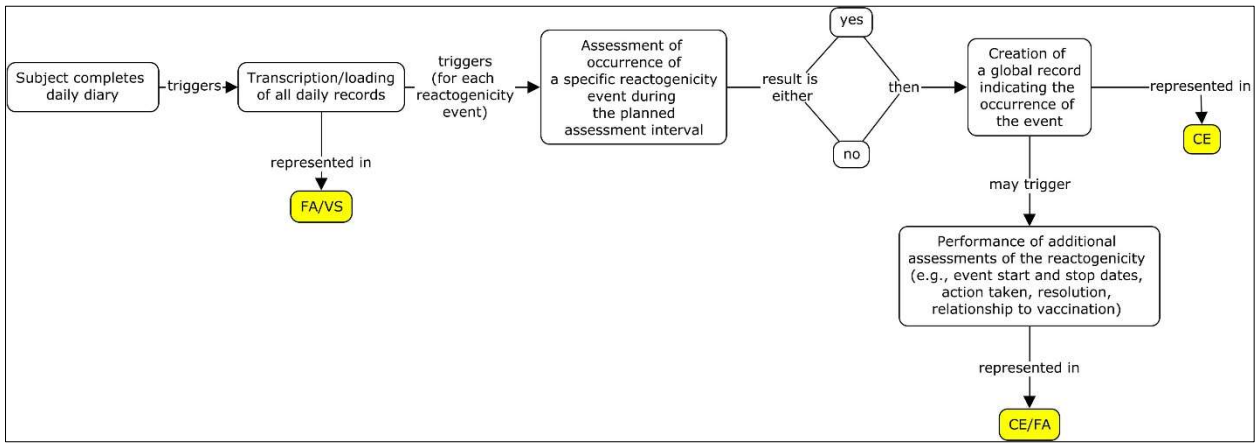

Figure 3. Flat Model Implementation

INPUTS FOR THE REACTOGENICITY DATA

The inputs for the reactogenicity data are as follows:

1. Vaccination Symptom Diary - Paper or Electronic Diary Cards
2. Symptom resolution Dates – Follow-up for the reactogenicity Events
3. Unplanned Assessment for the Reactogenicity Events
4. Additionally, general AE data (unsolicited AEs) will be searched for the reactogenicity Events.

SDTM DATASETS FOR THE REACTOGENICITY DATA

VITAL SIGNS (VS)

VS Dataset will contain the body temperature findings from the daily diary and any unplanned assessments of temperature from CRF data. “NOT DONE” records in VS are created for all missing diary days per subject, per vaccination, per day. Additionally, the unsolicited adverse events pertaining to AEDECOD denoting Pyrexia will be added as a derived record in VS with VSSTRESC = FEVER, as daily records based on the AE start and end dates, where the AE start date lies within the diary period.

The daily records will be created based on the AE start and end dates, even if the AE end date is more than the diary period. in case of unsolicited AE being an ongoing event, the daily records will be created up to diary period starting within the AE start date. The severity and relationship will be captured in supplementary VS dataset.

The SAS Code Snippet is to create the daily record for unsolicited AEs when both AE start and end dates are available.

```
data ae_vs;
set ae_reacto_;
do i = _aestdtc_n to _aeendtc_n;
if i = _aestdtc_n then diadt = _aestdtc_n;
else diadt + 1;
DDAY = diadt - _aerftdtc_n + 1;
output;
end;
run;
```

Note

The Severity and the relationship to the administration will be retained for each daily records in the parent VS Dataset in SUPPVS

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	

Table 1. Unsolicited AE Meeting Reactogenicity Criteria

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

Table 2. SDTM VS Dataset Showing the Reactogenicity Data

SUBJID	QNAM	QLABEL	QVAL
12345678	VSSEV	Fever Severity	MILD
12345678	VSREL	Fever Relation	RELATED
12345678	VSSEV	Fever Severity	MILD
12345678	VSREL	Fever Relation	RELATED
12345678	VSSEV	Fever Severity	MILD
12345678	VSREL	Fever Relation	RELATED
12345678	VSSEV	Fever Severity	MILD
12345678	VSREL	Fever Relation	RELATED

Table 3. Supplementary VS Dataset

FINDINGS ABOUT (FACE)

FACE Dataset will contain the daily diary (except temperature) records plus findings from Unplanned Assessment of Reactogenicity (CRF). “NOT DONE” records in FA (with FATESTCD=OCCUR) are created for all missing diary days per subject, per vaccination, per event, per day.

General/Unsolicited adverse event data will also be searched for potential reactogenicity events and added here with FACAT = “‘REACTOGENICITY – UNPLANNED ASSESSMENT”. FAEVAL is used to identify who reported the data (STUDY SUBJECT or INVESTIGATOR). When AEENRTPT is ONGOING, records are created for every day of the event in FACE (FATESTCD=OCCUR/SEV/REL) until the last day of the diary period. On the last day of diary, FAENRTPT will be as ‘ONGOING’ denoting the ongoing event.

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

Table 4. Unsolicited Adverse Event Showing Ongoing Criteria

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						

Table 5. SDTM FACE Dataset

CLINICAL EVENTS (CE)

CE will have the global records, summarizing whether each symptom occurred for each subject following each vaccination. Global records are created using the diary data, Symptom Resolved Dates CRF, and Unplanned Assessment CRF. If the entire diary was not completed, then a set of global summary records will additionally be created in the CE domain with CESTAT = “NOT DONE” and CEREASND = “SUBJECT DID NOT COMPLETE ELECTRONIC DIARY”. In these cases where the entire record was derived, additionally SUPPCE.CEDRVFL = “Y” (derived flag) will be created.

CEOCCUR
Assign 'Y' if any FAORRES = 'Y' when FATESTCD = 'OCCUR' (based on diary data); else 'N’. When CESTAT = 'NOT DONE' then CEOCCUR will be null. Assign ‘Y’ if any event captured in unplanned assessments (AE/Unplanned) during diary period.

CESTDTC
Start date of the event will be derived by the least date when the event has occurred. First FACEVD.FADTC (date portion) when FATESTCD=OCCUR and FAORRES=Y and FADTC should be within the diary assessment period (EXSTDTC <= FADTC <= EXSTDTC + x - 1), where EXSTDTC is the exposure date and the FADTC is the date of reactogenicity assessments.

CEENDTC
Stop date of the event in the global summary record in the CE domain will be based on the last date reported for that event (latest diary date where symptom occurred or stop date from Symptom Resolved Dates CRF). In a multi-dose vaccine study (> 1 vaccination, administered at different visits), if an event is continuing past the next vaccination date, then the event stop date will be set to the next vaccination date.

CEDUR
Duration of event in the CE domain will be derived as CEENDTC – CESTDTC + 1. Any gaps are ignored.

CESEV/CEREL

Both the severity and the relationships will be derived for the global CE record for each symptom, based on the 'worst' case scenario. The point to be noted is that within diary period if the unplanned assessments Severity is worse than original severity collected in the diary, then update (if worse) with the Severity from unplanned assessments.

SUPPCE.CEDIFFRS/SUPPCE.CEEVAL

When the investigator's assessment overrides the subject's, SUPPCE.CEEVAL should be "INVESTIGATOR", otherwise assign evaluator as "STUDY SUBJECT". The overridden value (subject's worst reported severity) should then be mapped to SUPPCE.CESEV1 (Severity/Intensity 1) along with an additional supplemental qualifier SUPPCE.CEDIFFRS (Reason Investigator Changed Assessment), assigned as "INVESTIGATOR ASSESSED AS MORE SEVERE DURING UNPLANNED ASSESSMENT".

USUBJID	CETERM	CEEVAL	Start Date_Diary	Ocuur_ Diary	EndDate_Diary	Severity _Diary
12345678	DIARRHEA	STUDY SUBJECT	2021-12-15	Y	2021-12-15	MILD

USUBJID	CETERM	CEEVAL	Start Date_Inv	Occur_ Inv	End Date_Inv	Severity _Inv
12345678	DIARRHEA	INVESTIGATOR	2021-12-15	Y	2021-12-17	MILD

Table 6. The Summary Records from the Diary and the Investigator Assessment

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

Table 7. CE Dataset - Global Summary Record

ADAM DATASETS FOR REACTOGENICITY DATA

FACE ANALYSIS DATSET

The SDTM datasets – FACE and VS are the core datasets for creating the FACE Analysis Dataset. This analysis dataset follows the BDS ADAM structure as prescribed by the CDISC. The temperature measurements in the SDTM.VS are used to create the FEVER records based on the condition – if VSSTRESC>=38 and VSSTRESU='C' or VSSTRESC="FEVER" assign as 'Y', else 'N'.

The AVLAC/AVALN are mapped based on the FASTRESC/FASTRESN. The maximum temperature parameter is derived based on the higher temperature measured during the diary period. Similarly maximum diameter parameter for Redness/Swelling Symptoms and Maximum severity for other Symptoms. The following table shows the parameter details used in the FACE analysis dataset.

FATESTCD	FAOBJ	PARAMCD	PARAM
DIAMETER	Redness	DIARE	Concatenation of FAOBJ, FATEST, FALOC, FALAT
DIAMETER	Swelling	DIASW	Concatenation of FAOBJ, FATEST, FALOC, FALAT
OCCUR	Fever	OCFEVER	Concatenation of FAOBJ, FATEST, FALOC, FALAT
SEV	Fatigue	SEVFATI	Concatenation of FAOBJ, FATEST, FALOC, FALAT
	Fatigue	MAXSFAT	Concatenation of FAOBJ, FATEST, FALOC, FALAT
OCCUR	Fatigue	OCFATIG	Concatenation of FAOBJ, FATEST, FALOC, FALAT

Table 8. PARAM Lookup

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
123456789	FA	OCCUR	OCHEAD	Headache occurrence indicator	HEADACHE	REACTOGENICITY	SYSTEMIC	Y	.		DAY 7	VACCINATION 1
123456789	VS	MAXTEMP	MAXTEMP	Fever maximum temperature	FEVER	REACTOGENICITY	SYSTEMIC		38	MAXIMUM		VACCINATION 1

Table 9. FACE Analysis Dataset

CE ANALYSIS DATASET

The clinical events analysis dataset is created on the core SDTM datasets – FACE/VS/CE. the summary records are created based on the analysis points as detailed in the SAP. The maximum severity for the events is done based on the worst-case scenario, similar to the SDTM CE Dataset. Additionally, duration for the maximum severity and lesser severity are created separately.

The known values flags are created which when set to “Y” indicates that a value is known for at least one day for that subject, for that treatment group, location and Vaccination phase. The EVENTFL flag will indicate that the subject reported the symptoms at least for a day in the diary period.

USUBJID	CETERM	CEOCCUR	CESEV	CEEVAL	CEDIFFRS	CEDUR	ADURU	ADURN	ASTDT	AENDT	ONGNXVIS	CEENRTPT	CEENTF
12345678	VOMITING	N						.	.	.			
12345678	SWELLING	N						.	.	.			
12345678	REDNESS	N						.	.	.			
12345678	PAIN AT INJECTION SITE	Y	MILD	INVESTIGATOR	REACTOGENICITY SYMPTOM WAS OVERRIDEN BY INVESTIGATOR AS UNPLANNED ASSESSMENT	P15D	DAYS	15	44545	44559		ONGOING	DAY 7
12345678	NAUSEA	N						.	.	.			
12345678	MUSCLE PAIN	N						.	.	.			
12345678	JOINT PAIN	N						.	.	.			
12345678	HEADACHE	Y	MILD			P1D	DAYS	1	44549	44549	N		
12345678	FEVER	N						.	.	.			
12345678	FATIGUE	Y	MODERATE			P7D	DAYS	7	44543	44549	N		

Table 10. CE Analysis Dataset

CONCLUSION

This paper addresses 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. It 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. It also contains FDA, CBER, and other regulatory bodies' recommendations and remarks regarding the application of the flat model.

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