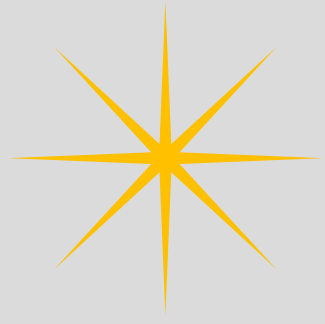




CLINICAL DISEASE ENDPOINT FLAG IMPLEMENTATION FOR VACCINE STUDIES

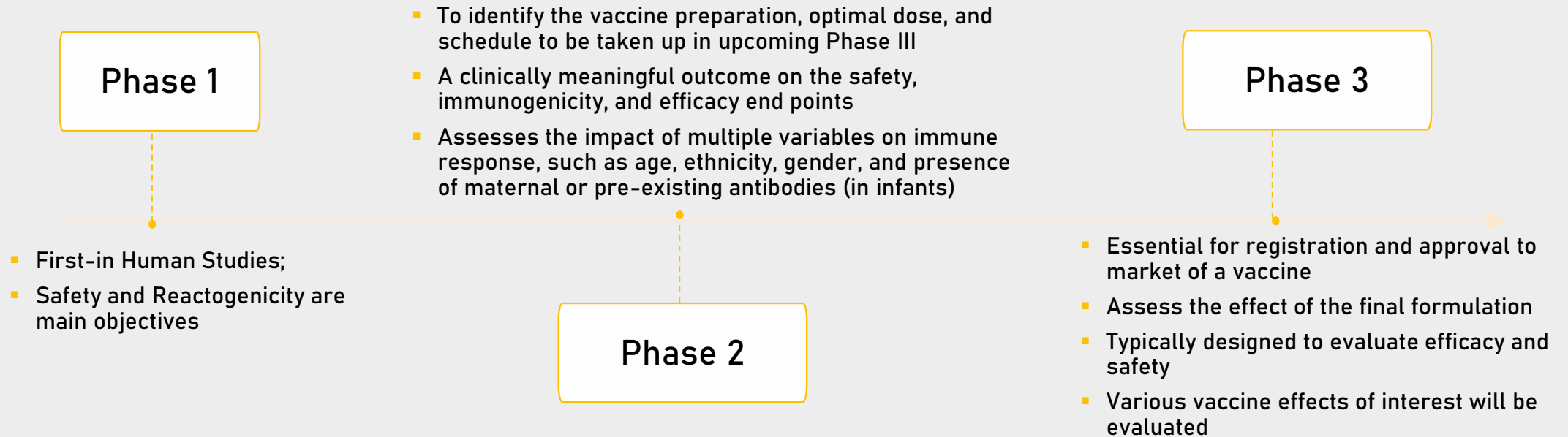
Charumathy Sreeraman



Introduction

- Multiple level of evaluations and assessments
- Vaccine Effectiveness – Pivotal role in Vaccine Approval
- Safety Concerns to be addressed

Development Of Vaccines

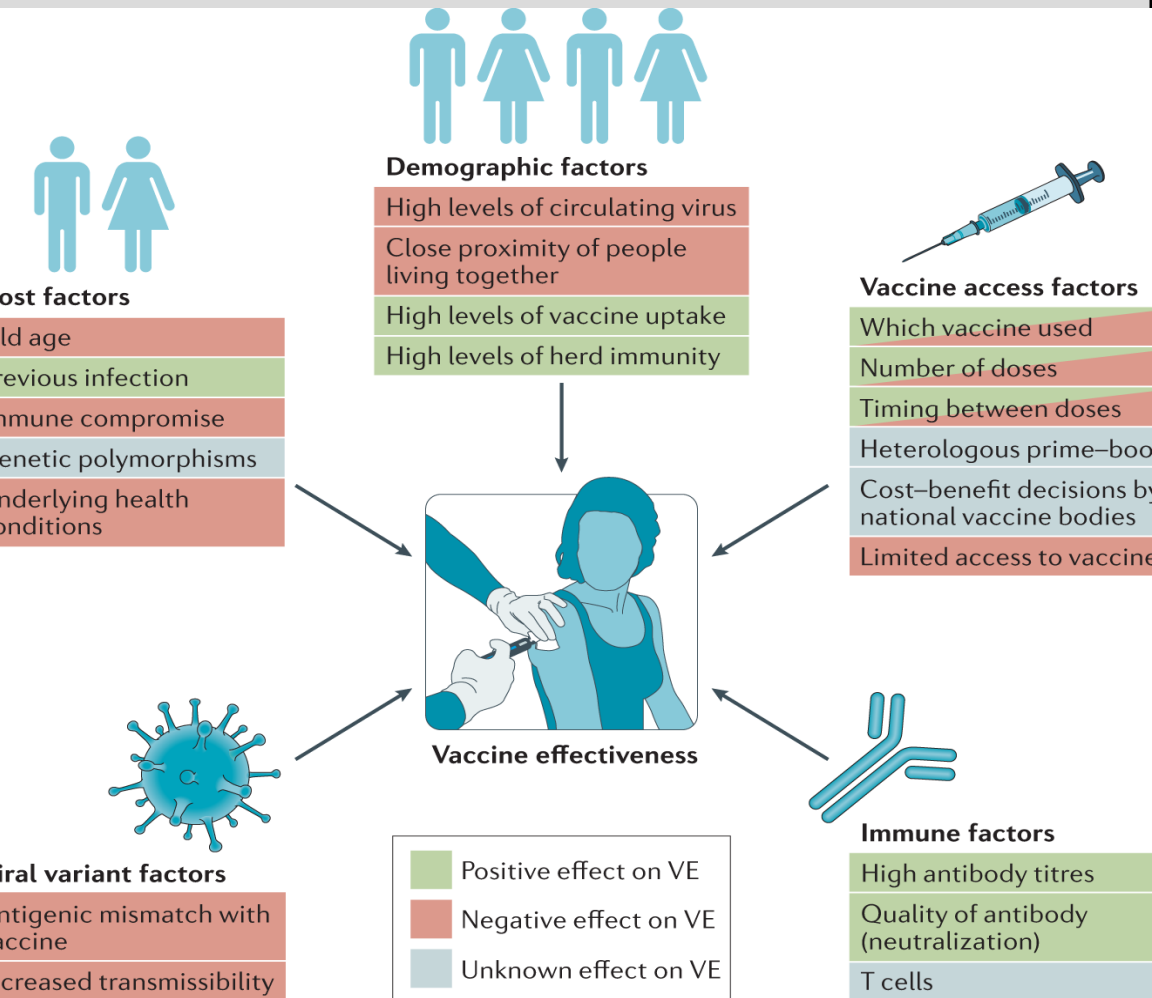


- A clinical endpoint is a measurable outcome or event in a clinical trial that determines the safety and efficacy of a treatment.
- Endpoints are objective tools that help guide clinical decision making.
- They are usually included in the study objectives and can vary depending on the nature of the trial.
- Crucial for determining the efficacy of vaccine candidates.



Clinical Disease Endpoint

Vaccine Effectiveness



- Vaccine efficacy is one of the major clinical endpoints for the vaccine trials.
- The US FDA proposed that laboratory-confirmed disease infection be adopted as the primary endpoint in vaccine effectiveness studies. Infection, severity, or transmission might be prevented with an effective vaccine.
- Vaccine Efficacy (VE) is defined as the percent reduction in incidence (of disease or infection) among the vaccinated.
- The CBER guidance “Submitting Study Datasets for Vaccines to the Office of Vaccines Research and Review” requests that a “clinical disease endpoint case flag” (CDECASE) be included in SDTM to flag confirmed cases of the disease of interest which are used to determine efficacy.
- In vaccine studies, with disease as the primary endpoint, the definition of trial endpoints with respect to efficacy depends on characteristics of the disease and the candidate vaccine.

- When the study is not submitted to showcase the effectiveness of the vaccines, CDECASE variable is created in the supplemental DM with QNAM = "CDECASE", QLABEL = "Clinical Endpoint Case Flag" and QVAL = "TBD".
- When the study is submitted for the evaluation of the effectiveness of the vaccines, if the disease of interest is confirmed, either by Clinical investigator or adjudication committee or using the information from a clinical assessment and the results of confirmatory tests, it should be flagged in a supplemental DM domain with QNAM = "CDECASE," (QLABEL) = "Clinical Endpoint Case Flag" and QVAL = "Y"
- If the disease of interest is not confirmed by either the clinical investigator or by an adjudication committee or the results of assessments it should be flagged in a supplemental DM domain with QNAM = "CDECASE" QLABEL = "Clinical Endpoint Case Flag" and QVAL = "N".



SDTM Domains - SUPPDM

SDTM Domains - MB

The MB domain will be collection of details on the assessments for the confirmation of the disease, through methods defined in the protocol.

Test results from assays conducted to confirm the presence of the microbe of interest (e.g., polymerase chain reaction (PCR), enzyme-linked immunosorbent assay (ELISA), cell culture, etc.) should be reported in the MB domain.

SDTM Domains - FACE

Symptoms	Symptom Present*
FEVER	
NEW OR INCREASED COUGH	
NEW OR INCREASED SHORTNESS OF BREATH	
CHILLS	
NEW OR INCREASED MUSCLE PAIN	
NEW LOSS OF TASTE OR SMELL	
SORE THROAT	
DIARRHEA	
VOMITING	

The signs and symptoms for the confirmation of the disease will be collected in the FACE with FACAT=EFFICACY.

SDTM Domain - CE

- The efficacy data will be primarily collected/reported in CE domain.
- To differentiate an efficacy clinical event (i.e., case of the disease of interest) from other clinical events, the variable CECAT should be utilized, and “efficacy” should be stated.
- Since efficacy is pre-specified, the variables CEOCCUR, Clinical Event Completion Status (CESTAT), and Clinical Event Reason Not Collected (CEREASND) should be included.
- The CETERM for the efficacy clinical event should be indicative of the disease, e.g., for an influenza vaccine, “influenza-like illness or ILI;” or for a human papillomavirus vaccine, “cervical intraepithelial neoplasia or CIN”.
- If hospitalization occurs during the clinical trial because of occurrence of the “disease of interest,” the CE domain variable Clinical Event Requires or Prolongs Hospitalization (CESHOSP) should be marked with “Y.” Additional data regarding the hospitalization and/or other healthcare encounter should be provided in the HO domain.



SDTM Scenario 1 - FACE

USUBJID	FATESTCD	FATEST	FAOBJ	FAORRES	VISITNUM	VISIT
ABCD 123 12345678	FSYDATE	First Symptom Date	Potential COVID-19	2021-09-20	901	COVID ILLNESS A
ABCD 123 12345678	FSYDATE	First Symptom Date	Potential COVID-19	2021-12-10	902	COVID ILLNESS B
ABCD 123 12345678	LSYDATE	Last Symptom Date	Potential COVID-19	2021-09-25	901	COVID ILLNESS A
ABCD 123 12345678	LSYDATE	Last Symptom Date	Potential COVID-19	2021-12-20	902	COVID ILLNESS B
ABCD 123 12345678	OCCUR	Occurrence Indicator	CHILLS	N	901	COVID ILLNESS A
ABCD 123 12345678	OCCUR	Occurrence Indicator	CHILLS	Y	902	COVID ILLNESS B



SUPPDM

With Placeholder

STUDYID	RDOMAIN	USUBJID	QNAM	QLABEL	QVAL	QORIG	QEVAL
ABCD	DM	ABCD 123 12345678	CDECASE	Clinical Disease Endpoint Flag	TBD	DERIVED	CLINICAL STUDY SPONSOR
ABCD	DM	ABCD 567 12345678	CDECASE	Clinical Disease Endpoint Flag	TBD	DERIVED	CLINICAL STUDY SPONSOR

CE

With Placeholder

DOMAIN	USUBJID	CETERM	CECAT	CEOCCUR	VISIT	CEDTC	CESTDTC	CEENDTC
CE	ABCD 123 12345678	COVID-19 like Illness	EFFICACY	N	COVID ILLNESS A			
CE	ABCD 123 12345678	COVID-19 Confirmed	EFFICACY					
CE	ABCD 123 12345678	COVID-19 like Illness	EFFICACY	Y	COVID ILLNESS B	2021-12- 20	2021-12-10	2021-12-20
CE	ABCD 123 12345678	COVID-19 Confirmed	EFFICACY					



CE with Placeholder

DOMAIN	USUBJID	CETERM	CECAT	CEOCCUR	VISIT	CEDTC	CESTDTC	CEENDTC
CE	ABCD 123 12345678	COVID-19 like Illness	EFFICACY	N	COVID ILLNESS A			
CE	ABCD 123 12345678	COVID-19 Confirmed	EFFICACY					
CE	ABCD 123 12345678	COVID-19 like Illness	EFFICACY	Y	COVID ILLNESS B	2021-12- 20	2021-12-10	2021-12-20
CE	ABCD 123 12345678	COVID-19 Confirmed	EFFICACY					

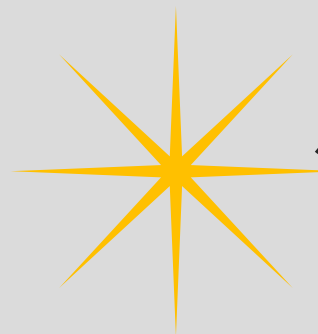


SUPPDM

STUDYID	RDOMAIN	USUBJID	QNAM	QLABEL	QVAL	QORIG	QEVAL
ABCD	DM	ABCD 123 12345678	CDECASE	Clinical Disease Endpoint Flag	Y	DERIVED	CLINICAL STUDY SPONSOR
ABCD	DM	ABCD 567 12345678	CDECASE	Clinical Disease Endpoint Flag	N	DERIVED	CLINICAL STUDY SPONSOR

CE

DOMAIN	USUBJID	CETERM	CECAT	CEPRES	CEOCCUR	VISIT	CEDTC	CESTDTC	CEENDTC
CE	ABCD 123 12345678	COVID-19 like Illness	EFFICACY		N	COVID ILLNESS A			
CE	ABCD 123 12345678	COVID-19 Confirmed	EFFICACY						
CE	ABCD 123 12345678	COVID-19 like Illness	EFFICACY		Y	COVID ILLNESS B	2021-12- 20	2021-12- 10	2021-12- 20
CE	ABCD 123 12345678	COVID-19 Confirmed	EFFICACY		Y	COVID ILLNESS B	2021-12- 20	2021-12- 10	2021-12- 20
CE	ABCD 123 12345678	CHILLS	EFFICACY	Y	Y	COVID ILLNESS B	2021-12- 20		



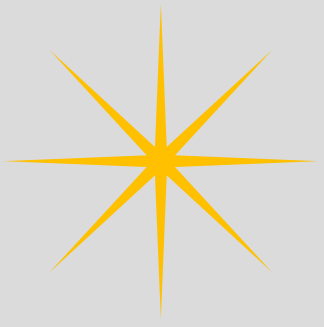
SDTM Scenario 2 - FACE

USUBJID	FATESTCD	FATEST	FAOBJ	FAORRES	VISIT
ABC 1234 12345678	FSYMDATE	First Symptom Date	RESPIRATORY ILLNESS	2020-10-20	RI_1
ABC 1234 12345678	LSYMDATE	Last Symptom Resolved Date	RESPIRATORY ILLNESS	2021-11-11	RI_1
ABC 1234 12345678	OCCUR	Occurrence Indicator	NEW OR INCREASED COUGH	Y	RI_1
ABC 1234 12345678	OCCUR	Occurrence Indicator	NEW OR INCREASED NASAL CONGESTION	Y	RI_1
ABC 1234 12345678	OCCUR	Occurrence Indicator	NEW OR INCREASED NASAL DISCHARGE	Y	RI_1
ABC 1234 12345678	OCCUR	Occurrence Indicator	NEW OR INCREASED SHORTNESS OF BREATH	N	RI_1



CE

USUBJID	CETERM	CECAT	CEPRES	CEOCCUR	VISIT	CEDTC	CESTDTC	CEENDTC
ABC 1234 12345678	ARI	EFFICACY	Y	Y	RI_1	2020-10-24	2020-10-20	2021-11-11
ABC 1234 12345678	ARI-RSV confirmed case	EFFICACY	Y	Y	RI_1	2020-10-24	2020-10-20	2021-11-11
ABC 1234 12345678	First evaluable LRTI-RSV with >=2 symptoms confirmed	EFFICACY	Y	Y	RI_1	2020-10-24	2020-10-20	2021-11-11
ABC 1234 12345678	First evaluable LRTI-RSV with >=3 symptoms confirmed	EFFICACY	Y	Y	RI_1	2020-10-24	2020-10-20	2021-11-11
ABC 1234 12345678	Exacerbation of Asthma	EFFICACY			RI_1	2020-10-21		
ABC 1234 12345678	NEW OR INCREASED COUGH	EFFICACY	Y	Y	RI_1	2020-10-24		
ABC 1234 12345678	NEW OR INCREASED NASAL CONGESTION	EFFICACY	Y	Y	RI_1	2020-10-24		
ABC 1234 12345678	NEW OR INCREASED NASAL DISCHARGE	EFFICACY	Y	Y	RI_1	2020-10-24		
ABC 1234 12345678	NEW OR INCREASED SHORTNESS OF BREATH	EFFICACY	Y	N	RI_1	2020-10-24		
ABC 1234 12345678	NEW OR INCREASED SORE THROAT	EFFICACY	Y	N	RI_1	2020-10-24		
ABC 1234 12345678	NEW OR INCREASED SPUTUM PRODUCTION	EFFICACY	Y	Y	RI_1	2020-10-24		
ABC 1234 12345678	NEW OR INCREASED WHEEZING	EFFICACY	Y	Y	RI_1	2020-10-24		
ABC 1234 12345678	TACHYPNEA	EFFICACY	Y	N	RI_1	2020-10-24		



THANK YOU

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