

Adverse Events of Special Interest (AESI) Tabulation

ChuanFeng Shih
GlaxoSmithKline

Adverse Events of Special Interest (AESI) Tabulation

Definition of Adverse event of special interest (AESI)

An adverse event of special interest (serious or nonserious) is one of scientific and medical concern specific to the sponsor's product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate.

Adverse Events of Special Interest (AESI) Tabulation

Definition of Adverse event of special interest (AESI) (Cont.)

Such an event might warrant further investigation in order to characterize and understand it. Depending on the nature of the event, rapid communication by the trial sponsor to other parties (e.g., regulators) might also be warranted.

(Based on CIOMS VI)

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How to Identify AESI?

- PTs
- Pre-defined SMQs that can be extracted using MedDRA PTs.
- CQs that are specific to a study but are not pre-defined within MedDRA.
- Adjudication process with medical/clinical confirmation.
- Captured on CRF.

Adverse Events of Special Interest (AESI) Tabulation

AESI Adjudication

- Spreadsheet output created through specific searches of safety data
- Spreadsheets in specific structure that contain adequate information like Subject ID, AE sequence number, verbatim term, PT, SOC, onset date, resolved date, severity, seriousness, SMQs, CQs, ..., etc.

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Standardized MedDRA Queries (SMQs)

- SMQs are **groupings of pre-defined list of MedDRA terms**, ordinarily at the **Preferred Term (PT) level** that relate to a defined **medical condition or area of interest**.
- SMQs are intended to aid in the **identification and retrieval of potentially relevant** individual case safety reports.

Standardised MedDRA Queries (SMQs) (Cont.)

- The included terms may relate to **signs, symptoms, diagnoses, syndromes, physical findings, laboratory and other physiologic test data, etc.**
- The only Lowest Level Terms (LLTs) represented in an SMQ are those that **link to a PT** used in the SMQ; all others are excluded.

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Standardised MedDRA Queries (SMQs)

Currently, over 100 SMQs have been created. The following are a small sampling of SMQs that are available to users today:

- Anaphylactic reaction
- Central nervous system vascular disorders
- Convulsions
- Depression and suicide/self-injury
- Drug abuse, dependence and withdrawal
- Hyperglycaemia/new onset diabetes mellitus
- Hypersensitivity
- Ischaemic heart disease
- Lack of efficacy/effect
- Medication errors
- Severe cutaneous adverse reactions

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Customized Queries (CQs)

- CQs are typically **study-by-study** or **compound** base, and may not be pre-defined.
- CQs group adverse events by **study-specific rules**.

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Customized Queries (CQs) (Cont.)

- CQs can be determined by list of SMQs with study-specific modifications.
- CQs can be a list of PTs provided by clinician.
- CQs can also be programmatically defined with criteria provided by clinician, or as specified in Program Safety Analysis plan (PSAP) or Reporting and Analysis Plan (RAP).

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**Table 3.2.9.1 Standardized MedDRA Query Variables
from CDISC ADaM Occurrence Data Structure (OCCDS) (Version 1.0)**

Variable Name	Variable Label	Type	Codelist / Controlled Terms	Core
SMQzzNAM	SMQ zz Name	Char		Cond
SMQzzCD	SMQ zz Code	Num		Perm
SMQzzSC	SMQ zz Scope	Char	BROAD, NARROW	Cond
SMQzzSCN	SMQ zz Scope (N)	Num	1, 2	Perm
CQzzNAM	CQ zz Name	Char		Cond

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**Table 3.2.9.1 Standardized MedDRA Query Variables
from CDISC ADaM Occurrence Data Structure (OCCDS) (Version 1.0)**

Variable Label	CDISC Notes
SMQzzNAM	The standardized MedDRA queries name. Would be blank for terms that are not in the SMQ. Therefore this variable could be blank for all records if no terms within the study were included in the SMQ. Conditional on whether SMQ analysis is done.
SMQzzCD	The standardized MedDRA queries number code.
SMQzzSC	The search strategy for SMQs can be narrow or broad. The preferred terms that are narrow in scope have high specificity for identifying events of interest while the broad terms have high sensitivity. By definition, all narrow terms are also considered within the broad scope. Therefore, to summarize all broad terms, terms with either narrow OR broad would be considered. Will be null for terms that do not meet the criteria. Conditional on whether SMQ analysis is done.
SMQzzSCN	Will be null for terms that do not meet the criteria.
CQzzNAM	The customized query (CQ) name or name of the AE of special interest category based on a grouping of terms. Would be blank for terms that are not in the CQ. Conditional on whether CQ analysis is done. Examples: "DERMATOLOGICAL EVENTS" "CARDIAC EVENTS", "IARS (INFUSION ASSOCIATED

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AESI Tabulation

Adverse Events of Special Interest (AESI) Tabulation

AE Analysis Display Example Layout

Adverse Events by MedDRA System Organ Class and Preferred Term

SYSTEM ORGAN CLASS	Blinded		
Preferred Term [1]	(N=xxx)		
	#AEs	n	(n/N%)

ANY EVENT	xxxx	nnn	(xx.x%)
INFECTIONS AND INFESTATIONS			
At least one event	xxxx	nnn	(xx.x%)
Upper respiratory tract infection	xxxx	nnn	(xx.x%)
Urinary tract infection	xxxx	nnn	(xx.x%)
Nasopharyngitis	xxxx	nnn	(xx.x%)
Gastroenteritis	xxxx	nnn	(xx.x%)
Herpes zoster	xxxx	nnn	(xx.x%)
Bronchitis	xxxx	nnn	(xx.x%)

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AESI Analysis Display Example Layout #1

Anaphylactic/Hypersensitivity Reactions per
Anaphylactic Reaction SMQ algorithmic search

SYSTEM ORGAN CLASS Preferred Term	Treatment A (N=xxx)			Treatment B (N=xxx)		
	#AEs	n	(n/N%)	#AEs	n	(n/N%)

ANY EVENT	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
IMMUNE SYSTEM DISORDERS						
Any event	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Drug hypersensitivity	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Hypersensitivity	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
. . .						

Adverse Events of Special Interest (AESI) Tabulation

AESI Analysis Display Example Layout #2

Adverse Events of Special Interest

	Treatment A			Treatment B		
	(N=xxx)			(N=xxx)		
	#AEs	n	(n/N%)	#AEs	n	(n/N%)

MALIGNANT NEOPLASM						
All Malignancies Excluding NMSC	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
All Malignancies Including NMSC	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Solid Tumor	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Hematology	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Skin (All)	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
NMSC	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Excluding NMSC	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Tumours of Unspecified Malignancy Adjudicated as Malignant	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
INFUSION/ANAPHYLAXIS/HYPERSENSITIVITY REACTIONS						
Infusion-related Reactions/ Hypersensitivity per Anaphylactic Reaction SMQ narrow search	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Infusion-related Reactions/ Hypersensitivity per Anaphylactic Reaction SMQ broad search	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Infusion-related Reactions/ Hypersensitivity per Anaphylactic Reaction SMQ algorithmic search	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Anaphylaxis per Sampson Criteria (Adjudicated AEs)	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Anaphylaxis/ Hypersensitivity Reactions (Adjudicated AEs)	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
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AESI Analysis Display Example Layout #2

Adverse Events of Special Interest

	Treatment A			Treatment B		
	(N=xxx)			(N=xxx)		
	#AEs	n	(n/N%)	#AEs	n	(n/N%)

All Infections						
All infections (OI, HZ, Sepsis) per Preferred	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Term Definition						
Serious infections	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Opportunistic Infections (Adjudicated AEs)	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Opportunistic Infections	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
(Adjudicated AEs)						
Herpes Zoster per Preferred Term Definition	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Herpes Zoster	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Recurrent (Adjudicated AEs)	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Recurrent	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Disseminated (Adjudicated AEs)	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Disseminated	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Sepsis	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Sepsis	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
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Adverse Events of Special Interest (AESI) Tabulation

AESI Dataset

Adverse Events of Special Interest (AESI) Tabulation

USUBJID	AESQ	AEDECOD	AESOC	AESER	CQ06NAM	CQ06CFL	CQ07NAM
ABC01.001	3	Herpes zoster	Infections and infestations	Y	Opportunistic Infections	N	Herpes zoster

CQ06NAM: Customized Query 06 Opportunistic Infections

CQ06CFL: Customized Query 06 Opportunistic Infections Adjudication Flag

CQ07NAM: Customized Query 07 Herpes Zoster

All Infections

All infections (OI, HZ, Sepsis) per Preferred Term Definition

Serious infections

Opportunistic Infections (Adjudicated AEs)

Serious Opportunistic Infections (Adjudicated AEs)

Herpes Zoster per Preferred Term Definition

Serious Herpes Zoster

Recurrent (Adjudicated AEs)

Serious Recurrent

Disseminated (Adjudicated AEs)

Serious Disseminated

Sepsis

Serious Sepsis

Adverse Events of Special Interest (AESI) Tabulation

Adding:

AESI Category: (AESICAT/AESICACD)

AESI Sub-category: (AESIDECD/AESICOD)

Adverse Events of Special Interest (AESI) Tabulation

USUBJID	AESEQ	AEDECOD	AESOC	AESER	CQ06NAM	CQ07NAM
ABC01.001	3	Herpes zoster	Infections and infestations	Y	Opportunistic Infections	Herpes zoster



AESI Category/
AESI Sub-category

All Infections	[AESICACD=003]
All infections (OI, HZ, Sepsis) per Preferred Term Definition	[AESICOD=3001]
Serious infections	[AESICOD=3002]
Opportunistic Infections (Adjudicated AEs)	[AESICOD=3003]
Serious Opportunistic Infections (Adjudicated AEs)	[AESICOD=3004]
Herpes Zoster per Preferred Term Definition	[AESICOD=3005]
Serious Herpes Zoster	[AESICOD=3006]
Recurrent (Adjudicated AEs)	[AESICOD=3007]
Serious Recurrent	[AESICOD=3008]
Disseminated (Adjudicated AEs)	[AESICOD=3009]
Serious Disseminated	[AESICOD=3010]
Sepsis	[AESICOD=3011]
Serious Sepsis	[AESICOD=3012]

Adverse Events of Special Interest (AESI) Tabulation

USUBJID	AESEQ	AEDECOD	AESOC	AESER	CQ06NAM	CQ07NAM
ABC01.001	3	Herpes zoster	Infections and infestations	Y	Opportunistic Infections	Herpes zoster



USUBJID	AESEQ	AEDECOD	AESOC	AESER	CQ06NAM	CQ07NAM
ABC01.001	3	Herpes zoster	Infections and infestations	Y	Opportunistic Infections	Herpes zoster
ABC01.001	3	Herpes zoster	Infections and infestations	Y	Opportunistic Infections	Herpes zoster
ABC01.001	3	Herpes zoster	Infections and infestations	Y	Opportunistic Infections	Herpes zoster
ABC01.001	3	Herpes zoster	Infections and infestations	Y	Opportunistic Infections	Herpes zoster

USUBJID	AESEQ	AESICACD	AESICAT	AESICOD	AESIDECD
ABC01.001	3	003	All Infections	3001	All infections (OI, HZ, Sepsis) per Preferred Term Definition
ABC01.001	3	003	All Infections	3002	Serious infections
ABC01.001	3	003	All Infections	3005	Herpes Zoster per Preferred Term Definition
ABC01.001	3	003	All Infections	3006	Serious Herpes Zoster

Adverse Events of Special Interest (AESI) Tabulation

Adverse Events of Special Interest

	Treatment A			Treatment B		
	(N=xxx)			(N=xxx)		
	#AEs	n	(n/N%)	#AEs	n	(n/N%)

All Infections						
All infections (OI, HZ, Sepsis) per Preferred	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Term Definition						
Serious infections	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Opportunistic Infections (Adjudicated AEs)	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Opportunistic Infections	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
(Adjudicated AEs)						
Herpes Zoster per Preferred Term Definition	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Herpes Zoster	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Recurrent (Adjudicated AEs)	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Recurrent	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Disseminated (Adjudicated AEs)	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Disseminated	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Sepsis	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
Serious Sepsis	xxx	xxx	(xx.x%)	xxx	xxx	(xx.x%)
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USUBJID	AESEQ	AEDECOD	AESOC	AESER	SMQ01NAM	CQ12NAM
ABC01.002	12	Suicide attempt	Psychiatric disorders	Y	Suicide/self-injury	Suicide/Self-injury



USUBJID	AESEQ	AEDECOD	AESOC	AESER	SMQ01NAM	CQ12NAM
ABC01.002	12	Suicide attempt	Psychiatric disorders	Y	Suicide/self-injury	Suicide/Self-injury
ABC01.002	12	Suicide attempt	Psychiatric disorders	Y	Suicide/self-injury	Suicide/Self-injury

USUBJID	AESEQ	AESICACD	AESICAT	AESIDECD	AESICOD
ABC01.002	12	004	Depression/suicide/self-injury	4003	Suicide/self-injury
ABC01.002	12	004	Depression/suicide/self-injury	4004	Serious Suicide/self-injury

Adverse Events of Special Interest (AESI) Tabulation

AESI Category/ AESI Sub-category		Treatment A (N=xxx)		
		#AEs	n	(n/N%)

DEPRESSION/SUICIDE/SELF-INJURY	[AESICACD=004]			
Depression	[AESICOD=4001]	xxx	xxx	(xx.x%)
Serious Depression	[AESICOD=4002]	xxx	xxx	(xx.x%)
Suicide/self-injury	[AESICOD=4003]	xxx	xxx	(xx.x%)
Serious Suicide/self-injury	[AESICOD=4004]	xxx	xxx	(xx.x%)

Adverse Events of Special Interest (AESI) Tabulation

CONCLUSION

By using the expanded structure of ADAESI dataset:

- AESI can be grouped specifically for easier identification
- AESI can be tabulated to meet different reporting requirements.
- Need corresponding computational method and controlled terminology to support the dataset metadata.
- Formats for AESI category and sub-category to support the tabulation.