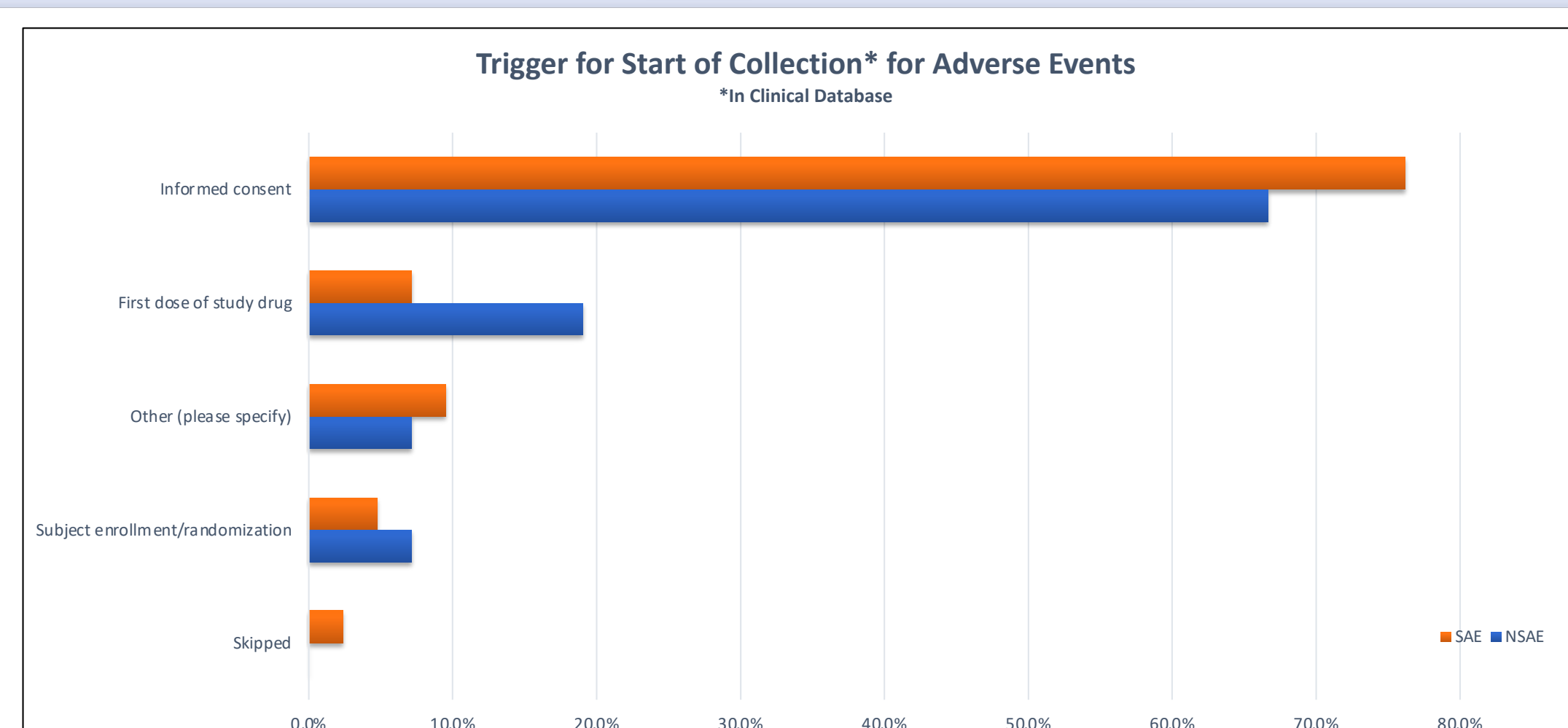


Primary Authors: Aimee Basile, Otsuka Pharmaceuticals (aimee.basile@otsuka-us.com), Mary Nilsson, Lilly (nilsson_mary_e@lilly.com) and the members of the PHUSE Adverse Event Collection Recommendations Project Team

The PHUSE Adverse Event Collection Recommendations Project Team will be releasing a white paper detailing best practices for AE collection in order to reduce variability in the collection of adverse events in the industry. This poster outlines the key topics of the new paper.*

Begin collecting AEs (both serious and non-serious at time of informed consent)

Majority of survey respondents start collecting serious and non-serious adverse events at informed consent
Additionally, most collect events that start after informed consent on the Adverse Events CRF



Serves as a baseline for treatment emergent determination, but does not mean these events will be considered treatment emergent

Facilitates the ability to comply with reporting expectations by some regulatory agencies (eg, serious events related to study procedures)

Easier for sites if all medical events after informed consent are recorded in one place

Do not collect investigator assessment of relatedness for non-serious AEs

Not required for non-serious events per regulations
- 2010 FDA Clinical Reviewer Template²
- 2005 CIOMS VI³

Some documents show optional AE relatedness summary tables, but discussions with some of those authors indicate they were not intended to endorse the collection of the assessment by the investigator for non-serious events

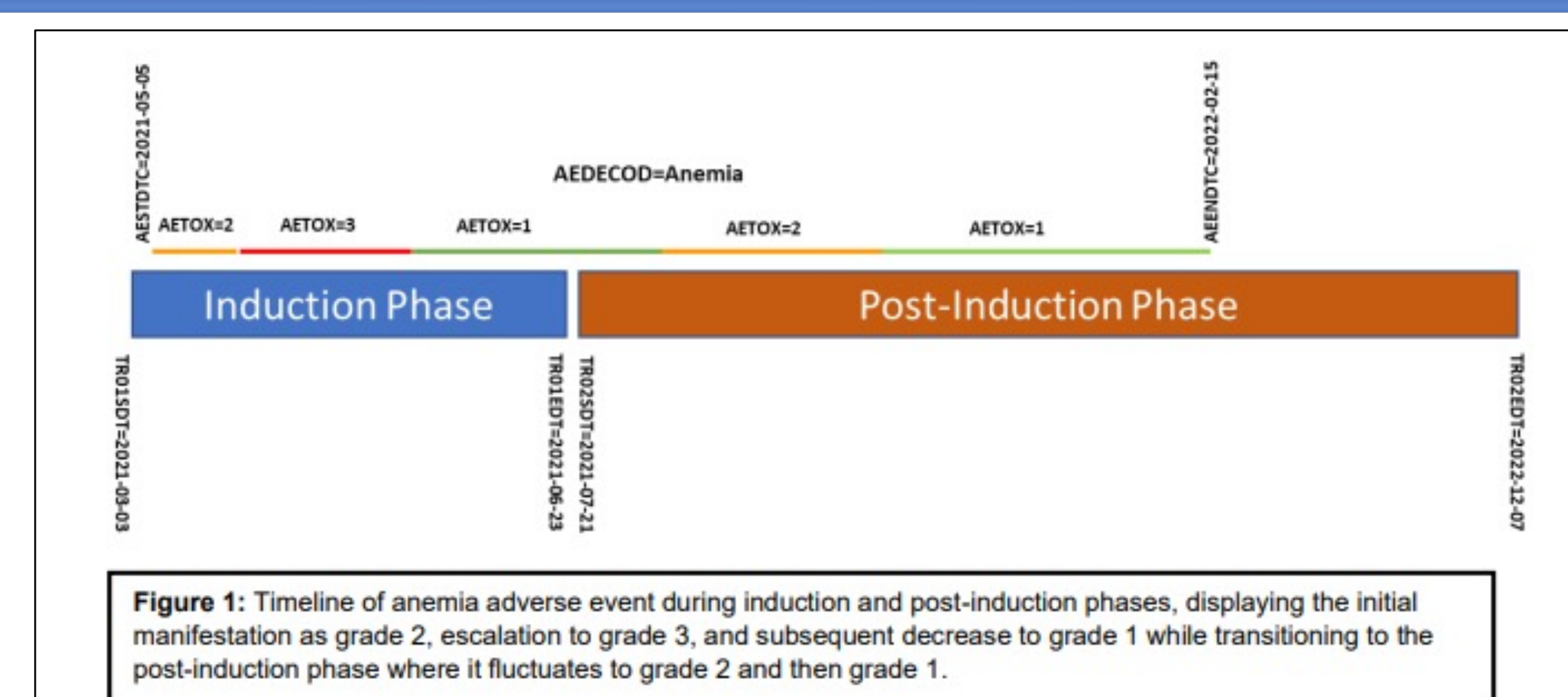
- PMDA labels often include percentages of events considered related by the investigator
- EMEA Plain Language Summaries implementation guide have proposed using investigator relatedness summary tables⁴
- FDA standard tables and figures (currently in draft) included an optional table for investigator relatedness assessment⁵

CDISC SDTM Implementation Guide shows investigator assessment of relatedness to study drug is permissible, meaning it can be blank for non-serious AEs

Collect both worsening and improvements to severity and seriousness

Capturing the entire pattern of an AE over time is best for flexibility in treatment emergence determination, especially where studies have multiple phases/analysis timepoints

Example showing changes to AE severity over time¹:
How can treatment emergent AE be determined for post-induction phase if these changes are not captured in the data?



In order to prevent over-counting of AEs, the changes can be reported in SDTM findings about (FA) domain and/or use AE Group ID (AEGRPID) to combine records

CDASH SAE supplement⁶ shows how to present changes to an event over time, specifically using serious start date (SASTDAT) and end date (SAENDAT)

Does not necessarily add to clinical site burden:

- Dynamic CRFs can be used to capture all changes to a single event without re-entering much of the adverse event data
- Focus group of clinical site coordinators indicated that all changes to adverse events are already documented in source notes, regardless of sponsor instructions

Provide CRF completion guidelines for intermittent events

If the CCG is silent on this topic, sites might be confused and could introduce unnecessary variability in AE collection.

Example CRF completion guideline instruction:

Whether to consider an event as an intermittent event (e.g., with a single start and stop date) versus multiple events (with each occurrence having a corresponding start and stop date) requires medical judgement. Per medical judgement, if it's the same event that is simply waxing and waning over time, it should be considered a single intermittent event. Alternatively, if the events are considered separate, it should be entered as separate events.

* Scope is for Phase 2 and 3 clinical trials

¹ Papasani, Madhusudhan Reddy, "Paper DH05: Addressing Challenges in Structuring CDISC-SDTM and ADaM Datasets to Report Adverse Events Spanning Two Treatment Periods," PHUSE US Connect 2024, Bethesda, Maryland (February 2024). https://phuse.s3.eu-central-1.amazonaws.com/Archive/2024/Connect/US/Bethesda/PAP_DH03.pdf

² US Food and Drug Administration Center for Drug Evaluation and Research. (2005). Review Guidance: Conducting a Clinical Safety Review of a New Product Application and Preparing a Report on the Review. <https://fda.report/media/71665/Conducting-a-Clinical-Safety-Review-of-a-New-Product-Application-and-Preparing-a-Report-on-the-Review.pdf>

³ CIOMS Working Group VI. (2005). Management of safety information from clinical trials. Geneva: Council for International Organizations of Medical Sciences. https://cioms.ch/wp-content/uploads/2017/01/Mgmt_Safety_Info.pdf

⁴ Clinical Trials Expert Group. (2021, October). 2021 Good Lay Summary Practice. https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-10/glsop_en.pdf

⁵ Center for Drug Evaluation and Research (CDER) and Biomedical Informatics and Regulatory Review Science (BIRRS) Team. (2022). Advancing Premarket Safety Analytics Workshop Meeting Material Standard Safety Tables and Figures Integrated Guide. <https://www.regulations.gov/document/FDA-2022-N-1961-0002>

⁶ CDISC SAE Development Team. (2021). CDASH Serious Adverse Event Supplement. https://www.cdisc.org/system/files/members/standard/foundational/CDASH_SAE_Supplement_v2.0_0.pdf