Collaborating on Standards: An Approach to Harmonizing Vaccine Regulatory Submissions

Médéric Celle (Sanofi) and Estella Sani (GSK)

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Meet the Speakers

Médéric Celle

Title: Statistical Programming Standards

Organization: Sanofi

Médéric Celle is part of the Global Biostatistics Science in the Vaccines Therapeutic Area of Sanofi and has 16 years of experience in SDTM, ADaM, TLF and programming. In his current role, he leads the development, maintenance and management of the standard specifications and programs of SDTM, ADaM and TLF, for vaccine studies. Médéric also provides support in responding to Health Authority comments related to SDTM, ADaM and TLF standards. He has served as chairman of the Vaccines Industry Standards Group (VISG) for the past 2 years.

Estella Sani

Title: Principal Lead, Data Standards

Organization: GSK

Estella Sani is part of the Data Standards team at GSK. In her current role, she is responsible for the development and management of the global data standards used for pipeline delivery, including CDASH, SDTM, Controlled Terminology, and Value Level Definition. With 20 years of experience in Clinical Data Management and Data Standards, Estella serves as a subject matter expert for the Vaccines therapeutic area and SDTM.

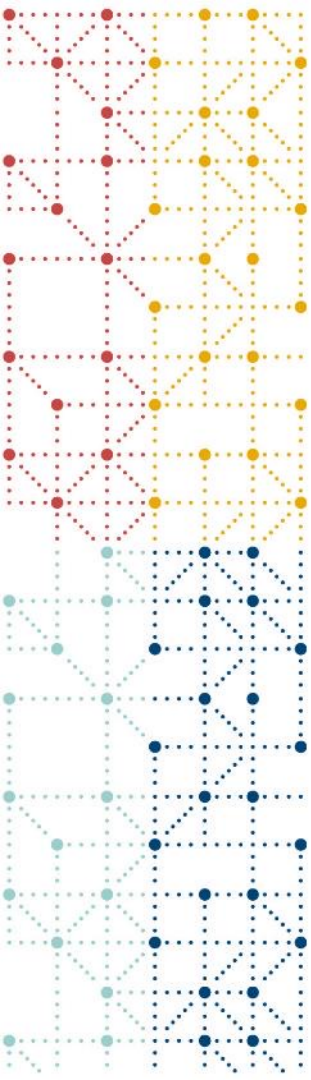
Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC or the participating organizations.*

- *The authors may hold shares and/or stock options in their respective companies.*

Agenda

1. Introduction
2. The Vaccines Industry Standards Group (VISG)
3. Challenges
4. Impact of Collaboration
5. Future Goals and Areas for Collaboration
6. Conclusion



Introduction

Background

1. Vaccine Trial Considerations

- **Safety**: Monitoring Adverse Event (AEs) to ensure participant safety, including reactogenicity data (solicited events) and unsolicited AE data collection
- **Efficacy**: Tracking disease prevention outcomes and confirming diagnoses via laboratory testing
- **Immunogenicity**: Assessing the body's response to a vaccine

2. Regulatory Guidance and Standards

- Diverse requirements from global health authorities
- Importance of CDISC standards for consistency and transparency

Background

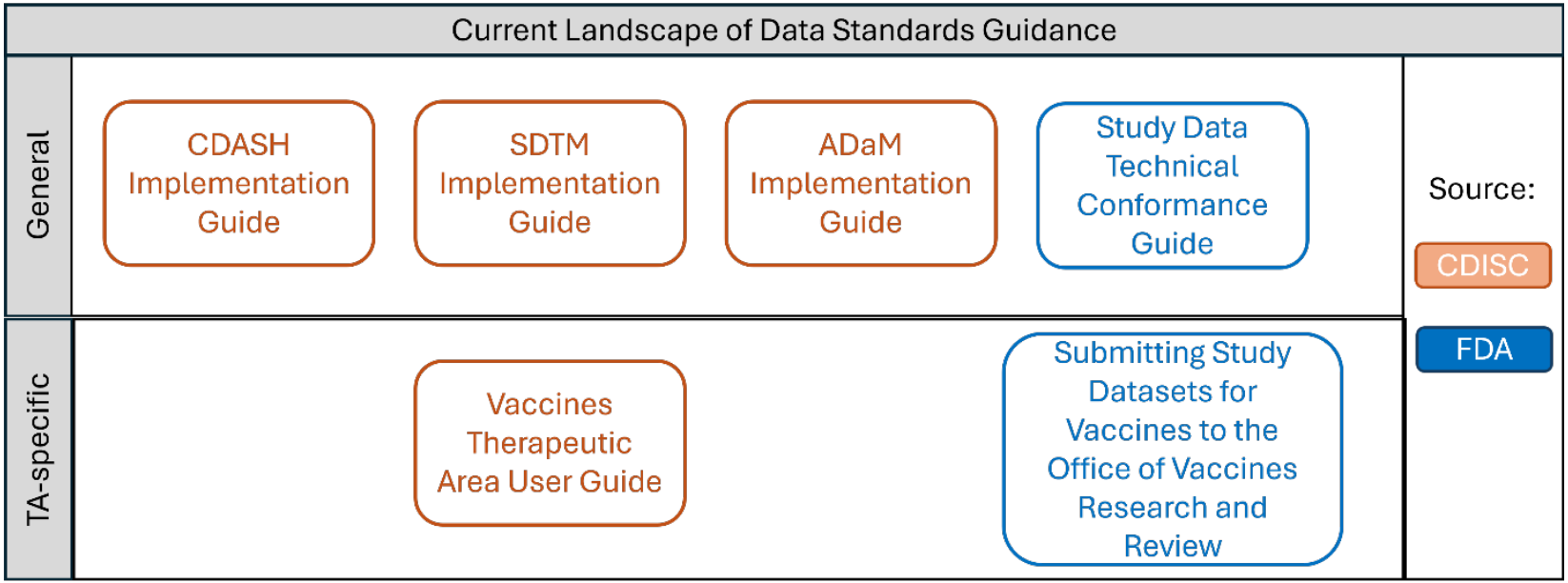
3. Challenges in Data Collection and Submission

- Inconsistencies between existing guidance documents (e.g., CDISC vs. OVRR)
- Need for **harmonization** to streamline submissions and reduce errors

4. Why Collaboration is Key

- Tackling shared challenges across companies in interpreting and implementing guidance
- Improving regulatory submission quality through collaborative efforts

Background


Current Landscape of Data Standards Guidance
General
CDASH Implementation Guide
SDTM Implementation Guide
ADaM Implementation Guide
Study Data Technical Conformance Guide
TA-specific
Vaccines Therapeutic Area User Guide
Submitting Study Datasets for Vaccines to the Office of Vaccines Research and Review
Source:
CDISC
FDA

The Vaccines Industry Standards Group (VISG)

Formation of Vaccines Industry Standards Group (VISG)

Genesis

Created in Q1 2023

Organizations recognized the value of a collaboration

Enhancing Public Health Outcomes

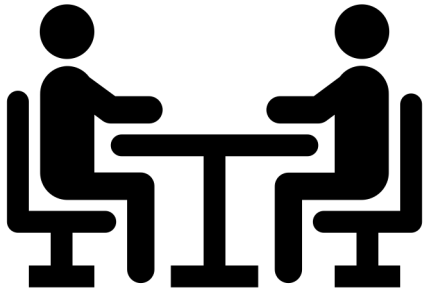
Membership

Seven Key Companies
(Trying to get “everybody”)

VISG Collaboration Model

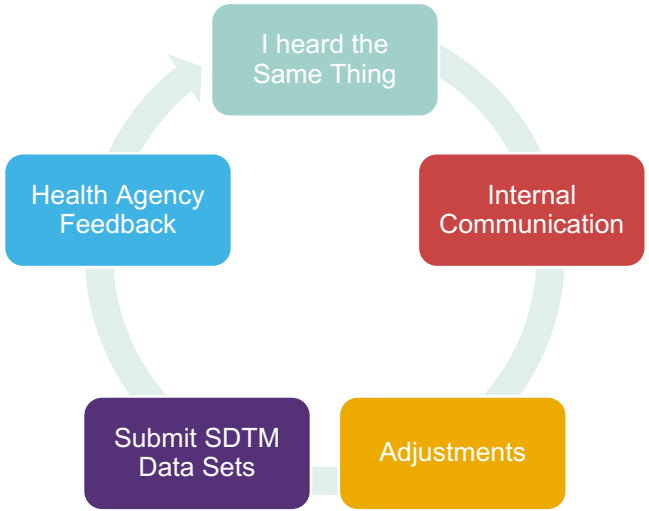
Monthly Meetings and Shared Resources:

- Led by a chairman
- Agenda based on topics shared by the organizations before the meeting for mature discussion
- Rotating notetaker
- Centralized platforms for collaboration:
  - Cloud based collaboration tools opened for cross Sponsor use



Objectives of the VISG

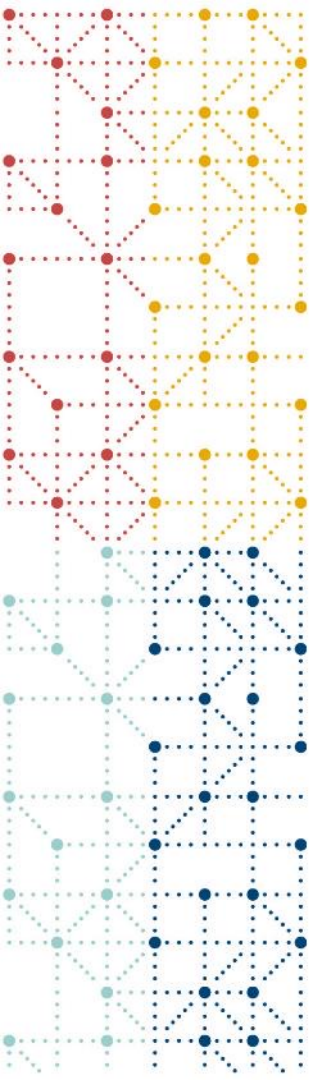
- **Sharing Challenges** and Feedback
- **Discussing** the Understanding of Feedback/Guidance
- Be an open forum to share and discuss implementation plans (pros and cons of each option)



Areas of focus

- Vaccines Therapeutic Area
- Data collection, SDTM, ADaM and Statistical Analysis

- Example topics of discussion:
  - Reactogenicity Data Models: Exploring methods for data collection and submission
  - Other Safety data
  - Efficacy data
  - Health authority feedback



Challenges

Common challenges faced by the organizations

Outdated Guidance

The CDISC Vaccines TAUG (last revised in April 2018) does not align with current regulatory requirements

Example:

- The CDISC Vaccines TAUG illustrates three possible models for reactogenicity data: flat, nested, or highly nested
- The OVRR guidance expects the flat model to be used for submitting reactogenicity data

Evolving Expectations

Some CBER expectations evolved over time but are not reflected in the OVRR guidance

Example:

- The guidance indicates that reactogenicity events continuing beyond the protocol-defined assessment period should be reported in both the CE and AE domains in SDTM
- More recent feedback from CBER instructed that reactogenicity events should only be reported in the SDTM CE domain

Limited Guidance

The OVRR guidance does not provide detailed instructions on certain points, which leaves them open to interpretation and makes implementation challenging

Example:

The guidance offers limited details on handling efficacy data, presenting only a basic scenario and no detailed examples of common industry situations

- No clear guidance on generating the CDECASE “clinical disease endpoint case” flag in SUPPDM for a trial with multiple primary efficacy endpoints
- No clear guidance on how to report confirmed and suspected cases

Inconsistent Guidance

Inconsistency between regulatory guidance and CDISC standards

Example 1:

- CBER expects the variable ARMNRS to be included in trials following SDTM IG version 3.2, while this variable was not introduced by CDISC until SDTM IG version 3.3
- Implementing this request introduces CDISC compliance issues and duplicates information that is already available in the DM domain

Inconsistent Guidance

Inconsistency between regulatory guidance and CDISC standards

Example 2:

- According to CDISC, the --DUR variable should only be used if the duration is collected and only when start and end dates/times are not collected
- The OVRR guidance expects the --DUR variable to be derived in SDTM for reactogenicity events where duration is not collected

Inconsistent Guidance

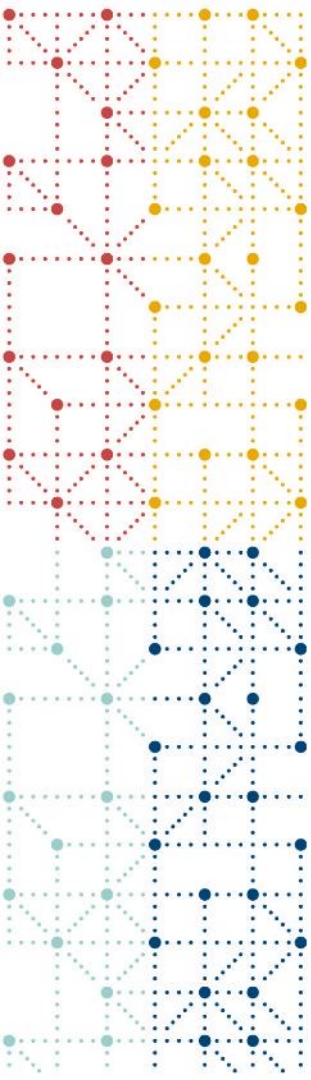
- CBER expectation for certain derived (and potentially complex) information to be included in SDTM creates a paradox for organizations striving to comply with submission guidelines while adhering to the core principles of SDTM
- The inclusion of derived data in SDTM not only deviates from its intended purpose but also introduces complexities in data collection and downstream processes (e.g. duplicated derivations in SDTM and ADaM)

Variations in Regulatory Feedback

Variations in feedback make it difficult to discern whether it originates from individual reviewers or an agency's preferences

This uncertainty poses a challenge in determining whether feedback for a specific study or submission should be applied universally to all vaccine studies

It would be beneficial if agencies updated their guidance to reflect current preferences, ensuring consistent application across all vaccine studies and submissions



Impact of Collaboration

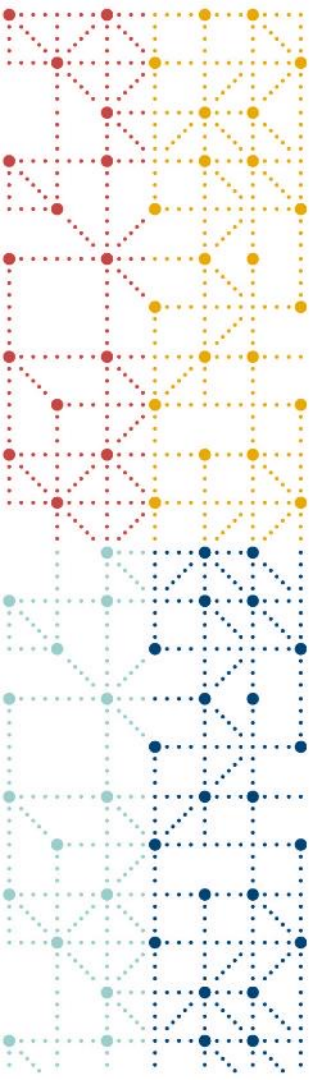
Key Outcomes

Aligned interpretations of regulatory requirements & expectations
Consensus on best practices
Shared learning across companies - fosters a culture of continuous improvement
Shared insights from member companies - address potential issues before submission

By sharing knowledge, discussing practices, aligning interpretations, and evaluating outcomes, member organizations can critically evaluate their methodologies and explore innovative solutions to enhance operational processes

Practical Benefits for Member Organizations

Streamlined submission processes
Proactive anticipation of regulatory feedback
Reduction in discrepancies and rework
Improved data quality and consistency
Enhancement of the overall effectiveness of practices
Enrichment of the collective knowledge base



Future Goals and Areas for Collaboration

Future goals of VISG and areas for collaboration

Deepened Collaboration with Health Authorities and Standards Organizations (Win-Win collaboration)

- Build stronger partnerships starting with **FDA/CBER** and **CDISC**
- Advocate for updated guidance to reflect current needs, starting with the Vaccines Therapeutic Area User Guide

Advocacy for Industry-Wide Adoption

- **Expand the VISG model** to other therapeutic areas
- Promote consistent standards and transparent communication

Blueprint for Broader Collaboration

Engagement with Health Authorities / Standards Organizations

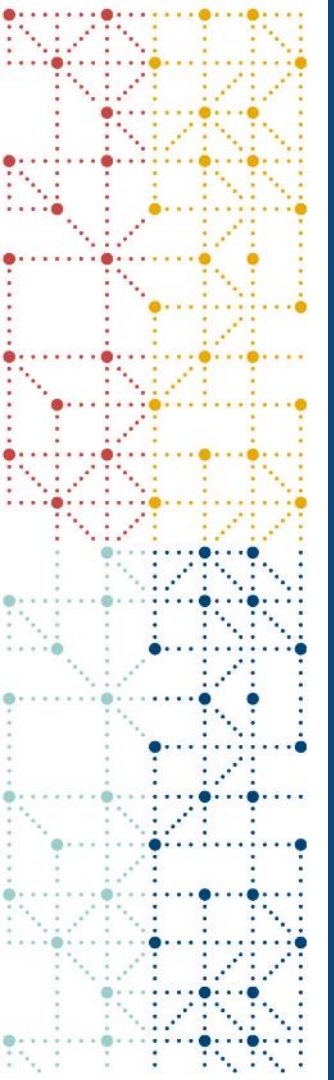
- Develop a **dedicated communication channel** between all parties to discuss standards-level questions
- Present a consolidated voice for structured discussions, ensuring clarity in communications
- Highlight examples where **a comment to one sponsor reflects broader regulatory expectations**
- Establish a **regular cadence of communication** to ensure alignment on expectations, and update guidance

Timeline and Planning

- Define a timeline for formal engagement with agencies, including milestones for identifying key questions and concerns at the standards level, preparing a unified feedback document, scheduling roundtable discussions with regulators

Regulator Presence at Discussions

- Advocate for regulator participation in VISG discussions to foster transparency and mutual understanding
- Create a feedback loop where regulators can address collective questions efficiently



Conclusion

Conclusion

VISG as a Model for Success

- Open sharing and discussions on feedback and challenges
- Help Organizations to proactively anticipate regulatory feedback
- Accelerate timelines while maintaining data quality and compliance
- Win-Win collaboration for Organizations

Call to Action

- Win-Win Collaboration with Health Authorities and Standards Organizations
- Update of the CDISC guideline Vaccines Therapeutic Area User Guide
- Foster partnerships to advance global public health goals

Reference

- PhUSE US Connect 2025: Collaborating on Standards: An Approach to Harmonizing Vaccine Regulatory Submissions

Thank You!