

Collaborating on Standards: An Approach to Harmonizing Vaccine Regulatory Submissions

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on behalf of the Vaccine Standards Industry Group

Various Companies

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Disclaimer Slide

- The views and opinions expressed in this presentation are our own and do not necessarily reflect those of Moderna and Merck, and the Vaccine Industry User Group Organizations or any other company we are affiliated with.
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- Any references to company-specific processes or experiences are for illustrative purposes and do not imply endorsement or official policy.
- The information presented is intended for general discussion and should not be considered as regulatory or legal advice.

Overview of the Presentation

Background and Motivation

Formation of the Vaccine Industry Standards
Group (VISG)

Challenges in Regulatory Submissions

Outcomes and Collaborations

Future Goals

Conclusions and Impact

Background

1. Vaccine Trial Considerations

- **Safety:** Emphasis on solicited and unsolicited reactogenicity data collection and adverse event monitoring to ensure participant safety
- **Efficacy:** Tracking disease prevention outcomes and confirming diagnoses via laboratory testing

2. Regulatory Guidance and Standards

- Diverse requirements from global health authorities (FDA, EMA, PMDA, CDE...)
- Importance of CDISC standards for consistency and transparency.



Background



3. Challenges in Data Collection and Submission

- Contradictions between existing guidance documents (e.g., CDISC vs. OVR).
- 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

Formation of VISG

Genesis and Goals of VISG

Sharing Challenges and
Feedback

Standardizing Data Collection
and Submission

Enhancing Public Health
Outcomes

Feedback from the health
authorities (FDA, EMA, MHRA,
PMDA etc)

Membership

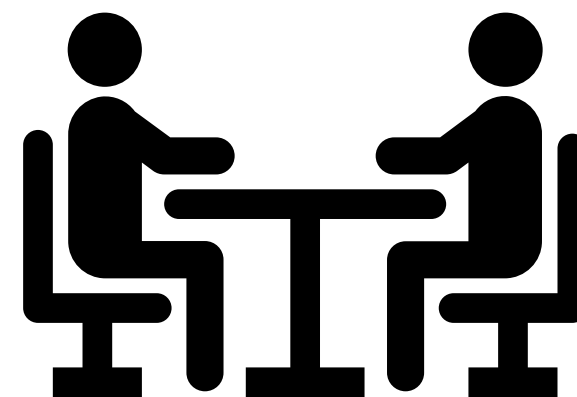
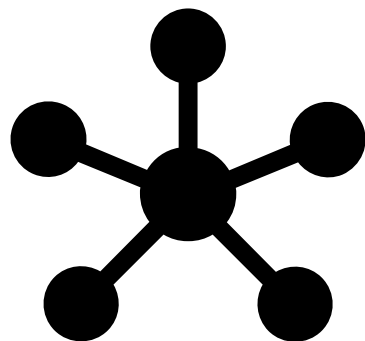
Seven Key Companies (Trying to
get “everybody”)



VISG Collaboration Model

Monthly Meetings and Shared Resources

- Rotating Leadership and Recordkeeping
- Centralized platforms for collaboration:
 - Cloud based collaboration tools opened for cross Sponsor use



Key Areas of Discussion

- **Reactogenicity Data Models:** Exploring methods for data collection and submission
 - **Investigator's Assessment Approaches:** Harmonizing evaluation practices
- **CBER Feedback and Industry Examples:** Sharing regulatory insights to align interpretations

Key Challenges Addressed by VISG

Contradictory Guidance

- SDTM vs. Derived Data Expectations: Misalignment between regulatory guidance and CDISC standards.

Outdated Guidance

- Vaccine TAUG Misalignment: Inconsistencies with current regulatory requirements.
- OVRG Guidance / Technical specification on submitting Datasets to CBER
 - Reactogenicity example

Limited Guidance

- Undefined handling of efficacy data, such as:
 - Reporting multiple primary efficacy endpoints.
 - Differentiating confirmed vs. suspected cases.

Evolving Expectations

- Compliance metrics and ad-hoc feedback from regulators.

Global Complexity

- Variations in health authority requirements across regions.

Case Study: Reactogenicity Data

Challenges

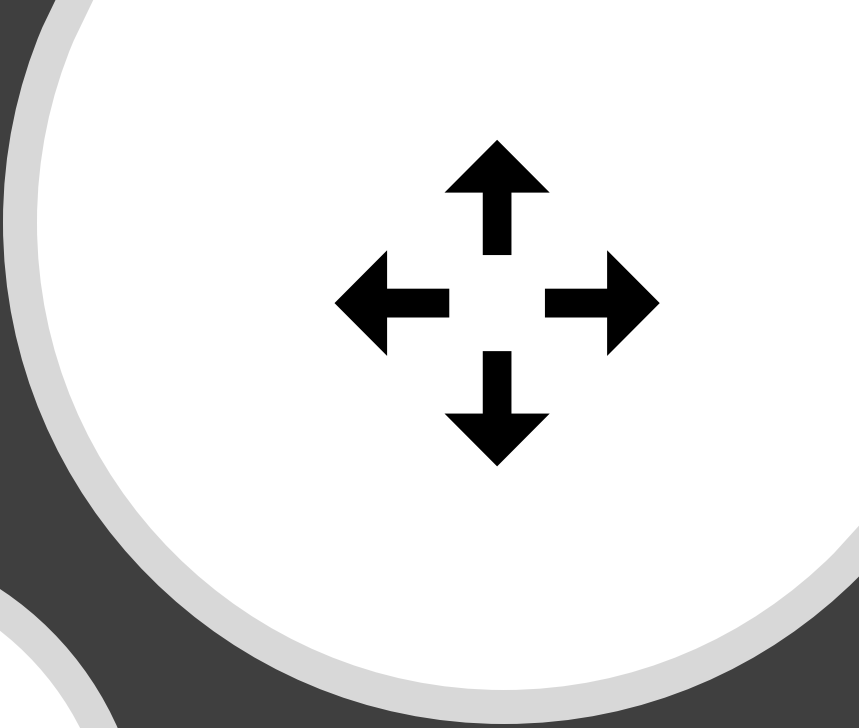
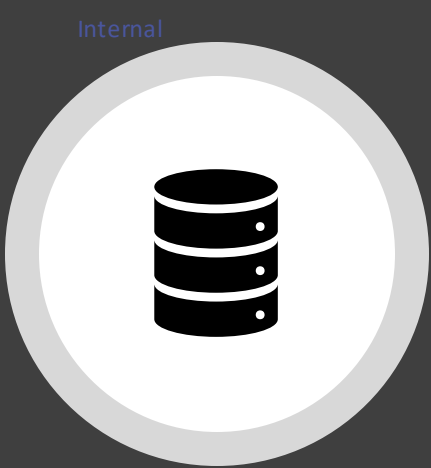
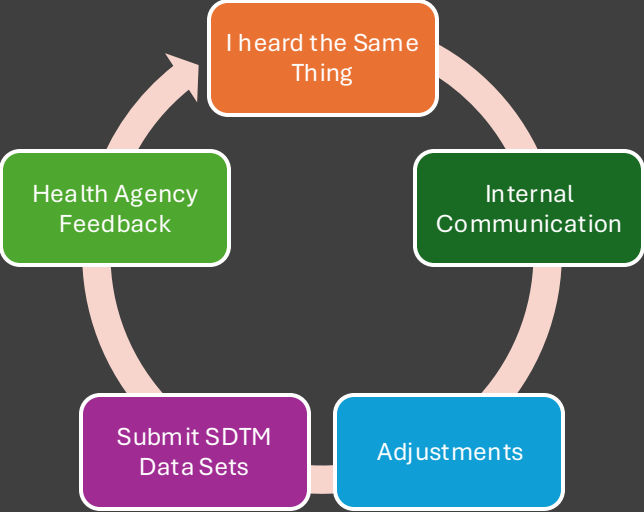
- Flat vs. Nested Models: Discrepancies in data modeling approaches.
- Derived Variables (--DUR): Misalignment between expected data submissions and SDTM standards.

Case Study: Reactogenicity Data CDISC TAUG

- Three suggested models for providing Reactogenicity Data.
- Company A: Nested
- Company B: Flat
- Company C: Flat
- Company D: Highly Nested

1. 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 (**flat model**) .
2. 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 (**nested model**) .
3. 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 (**highly nested model**) .

Case Study: Reactogenicity Data



Understanding the –DUR Variable: OVR vs. CDISC Guidance

OVR Guidance

- Expects the –**DUR** variable to be derived in SDTM datasets.
- Assumes durations should be included, even if start and end dates/times are captured.

CDISC Guidance

- –**DUR** is only used if:
- Duration was directly collected.
- Start and end dates/times are **not** captured.
- Aligns with the principle of avoiding derived data in SDTM.

Impact on Reactogenicity Events

- For reactogenicity events:
- Start and end dates are **always captured**.
- As per CDISC, –**DUR** is **not expected** in SDTM datasets.
- This misalignment creates challenges for sponsors submitting to FDA/CBER.

Case Study: Reactogenicity Data

- VISG Solution
 - Adoption of Flat Model: Aligned on the flat data model for consistency in submissions.
 - Shared Examples for Clarification: Provided regulatory examples to ensure alignment and clarity.

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Row	STUDYID	DOMAIN	USUBJID	FASEQ	FALNKGRP	FATESTCD	FATEST	FAOBJ	FACAT	FASCAT	FAORRES	FAORRESU	TAETORD	EPOCH	FADTC	FADY	FADY2
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3	ABC	FA	ABC-1001	3	1	EPSDNUM	Number of Episodes	Vomiting	REACTOGENICITY	SYSTEMIC	0		2	TREATMENT	2015-01-12	3	E D.
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Impact of Collaboration



Key Outcomes of VISG Collaboration

Improved Data Quality and Consistency:

- **Standardized approaches** reduced errors and discrepancies.



Streamlined Submission Processes:

Aligned interpretations of regulatory guidance minimized rework.



Proactive Anticipation of Regulatory Feedback:

Shared insights from member companies helped address **potential issues** before submission.



Reduction in Errors and Rework:

Clear, **unified strategies** saved time and resources.



Shared Learning Across Companies:

Open discussions fostered a culture of continuous improvement.

Future Goals of VISG



Deepened Collaboration with Regulators

- Build stronger partnerships with Health Regulatory and Standard Agencies starting with **FDA/CBER** and **CDISC**.
- Advocate for updated guidance to reflect current needs.



Specific Focus Areas

- Participant-Reported Diary Data: Ensure **harmonization in collection and analysis**.
- Reactogenicity and Efficacy Alignment: Standardize reporting methods across trials.



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

- Establish a **regular cadence of communication** with Health Authorities to ensure alignment on expectations, and update guidance.
- Develop a **dedicated communication channel** for VISG to discuss standards-level questions, separate from product-specific issues.
- Present consolidated voice to regulators for structured discussions.



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.



Focus on Standards-Level Questions

- Differentiate between product-specific feedback and **general standards-level issues**.
- Consolidate feedback to identify common challenges across sponsors, ensuring clarity for regulators.
- Highlight examples where **a comment to one sponsor reflects broader regulatory expectations**.



Regulator Presence at Discussions

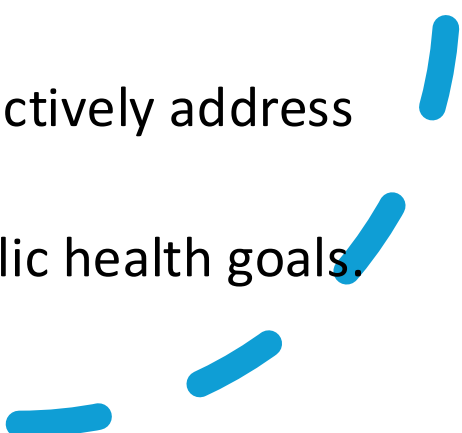
- Advocate for regulator participation in VISG discussions to foster transparency and mutual understanding.
- Create a feedback loop where regulators can address collective questions efficiently.

Conclusion

VISG as a Model for Success

- Demonstrates the power of collaboration in harmonizing regulatory submissions.
- Aligns Organizations to create consistent standards and streamline vaccine development.
- Accelerates timelines while maintaining data quality and compliance.

Call to Action

- Expand the collaborative model to other therapeutic areas.
 - Continue engaging with regulators to proactively address challenges.
 - Foster partnerships to advance global public health goals.
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