Results of 2022 Industry SEND Survey

Janice Fiori, Lilly
Mike Harwood, Instem
Tania Smith, Labcorp

Introduction

- 60 responses were received
- Representing CROs, Sponsors, and IT suppliers
- An increase of 33% over last year

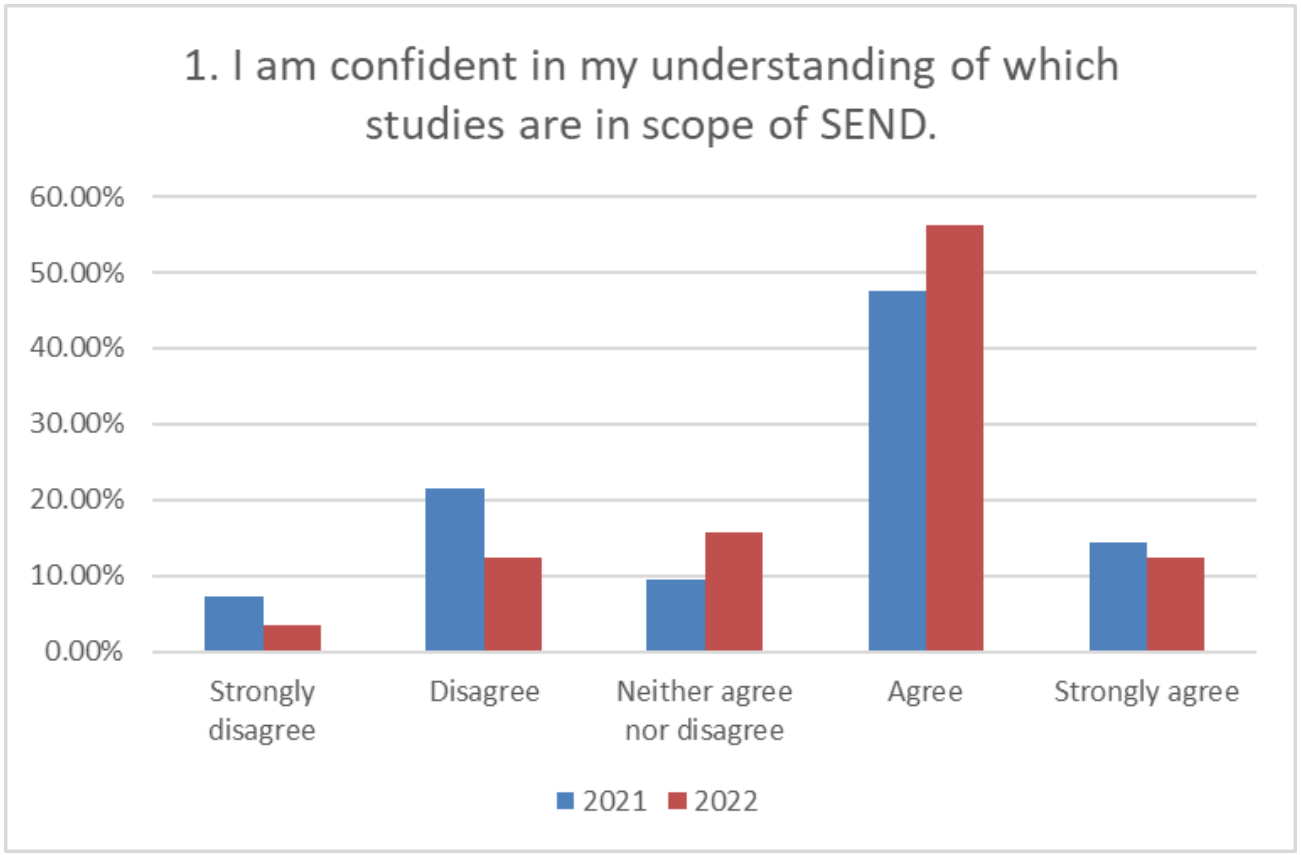
Scope this Year

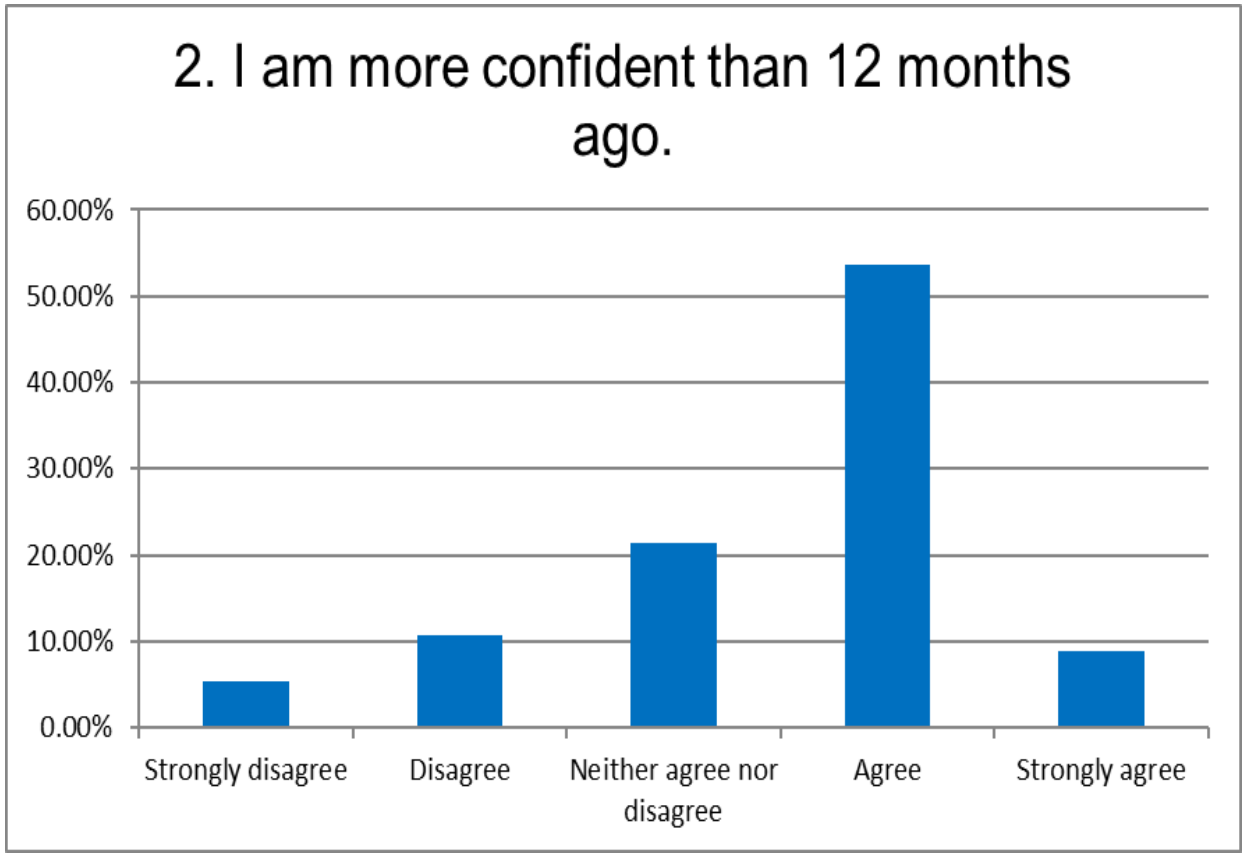
Topics:

- Scope of SEND
- Implementing flexibility in SEND
- Manual edits
- Non-CDISC initiatives
- Automation opportunities

Scope of SEND

Scope of SEND n=57



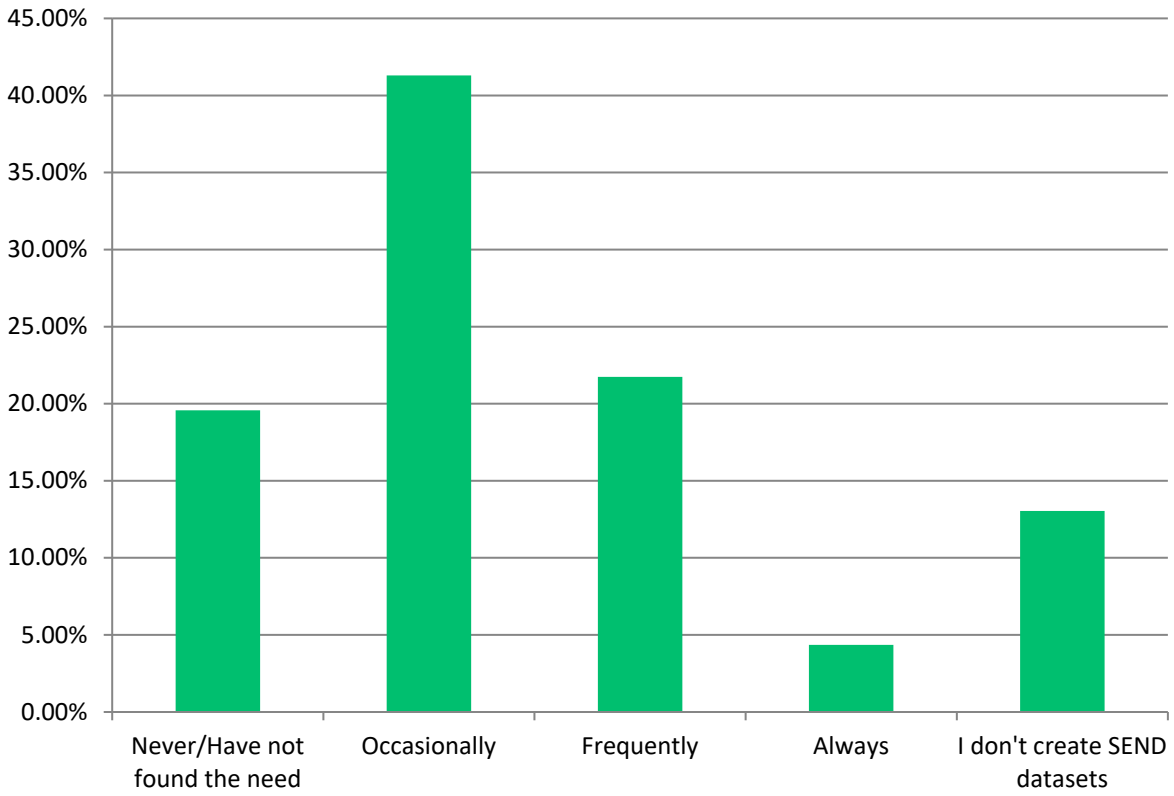


Implementing Flexibility

Summary of Flexibility

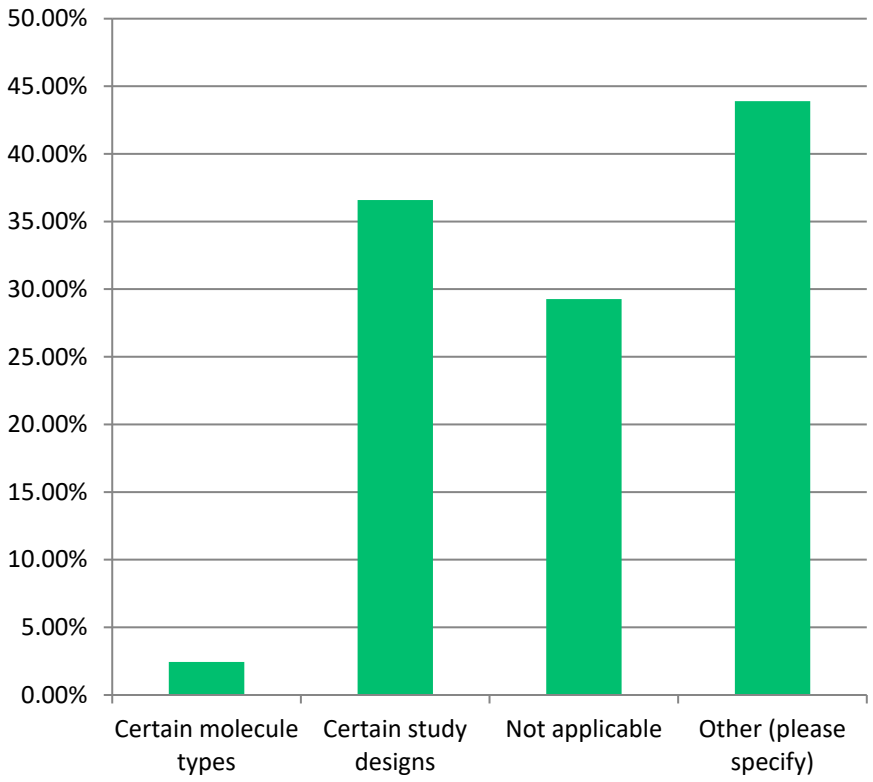
- Many have implemented permissible variables or have developed internal rules for creating SEND
- Driven by conformance, consistency, clarity and accuracy goals
- Trail domains, PC/PP, and LB require the most attention.

Q3. When creating SEND or requesting datasets, do you specify additional/more stringent rules than are specified in the SENDIG? For example, do you require permissible variables or specified terms for variables that do not require controlled terminology? n=46



- **CLSTRESC;** non-neo terms for **MI**
- Use of **timing variables,** STINT, ENINT, etc. Use of all timing variables in datasets DTC, DY and NOMDY
- Depends upon request from **Sponsor**, as we are performing a service for them.
- The standard for the **SEND provider**.
- If indicated by the Technical **Conformance** Guide
- To conform to the Study Data Technical **Conformance** Guide or FDA rules.
- Assumptions or expectations from **SENDIG** not specified in validation rules. Additional rules ensure that TRC are followed.
- To accommodate internal **systems processes**,
- **trial design details** for quality control and consistency purposes.
- As **warehousing** SEND data, certain additional permissible variables required for use with internal API tool developed

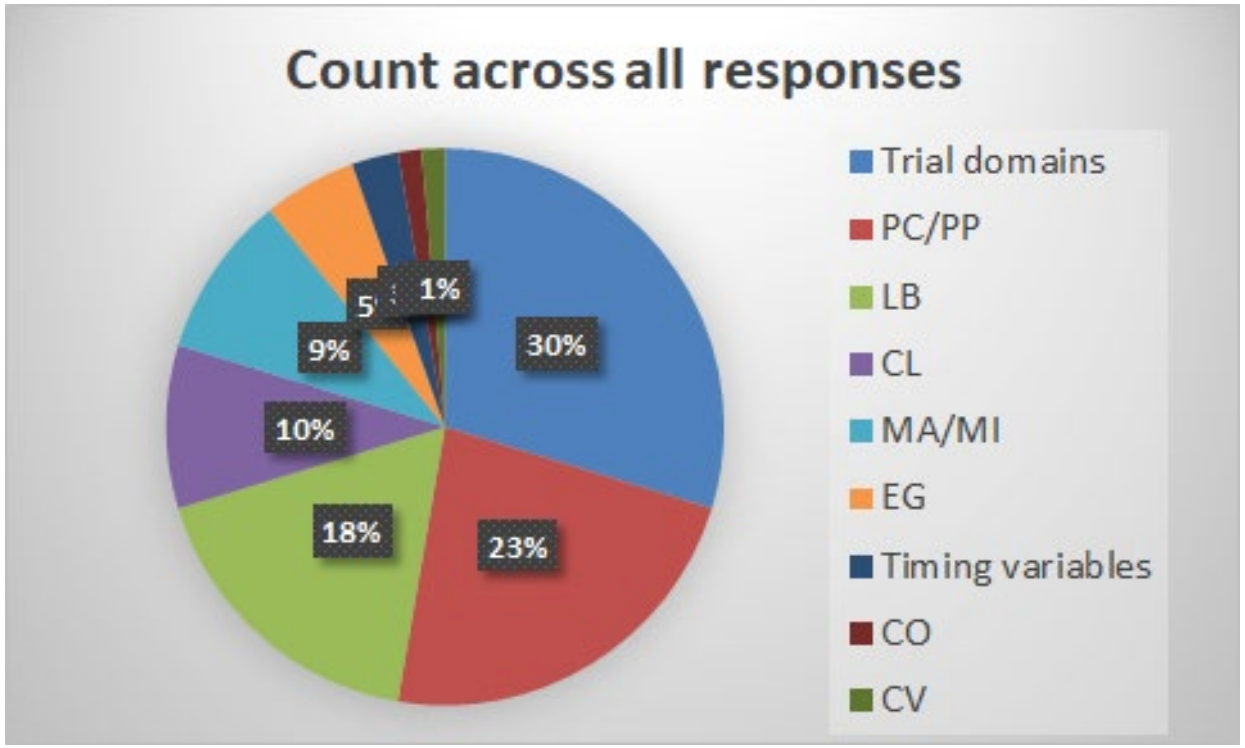
4. What drives your need to add this additional requirement? (Select all that apply.) n=41



1	conformance	Industry best practices, TCG and eCTC requirements
1	conformance	Rules developed based on suggestions from FDA and TRC. Also to ensure consistency of timing and controlled terminology.
1	conformance	Study Data Technical Conformance Guide and FDA rules.
2	consistency	As above, we need to accomodate internal systems processes as well as standardize trial design details for quality control and consistency.
2	consistency	Business-procedure consistency
2	consistency	consistency of study identifiers with submission documents
2	consistency	Consistency purposes + Specific Client Requirements
3	Customer	Sponsor preferences
3	Customer	Sponsor's request, very rare
4	collect details	equipment, measurement, or something like that in Findings domain
4	collect details	Provide more details
4	study design	FOCID could be triggered by certain study designs, --LAT in case of separate examination of bilateral organs, label requirements to --TPTREF for Latin-square designs etc. Also, if describe by the TCG (e.g., PCCALCN), we would request/require it.
4	to match report	If information available in report, we attend to map it in SEND.
5	automate mapping	Ability to get the information into the dataset electronically. If it is easily mapped in the system, we like to provide as much data as possible.
6	accurate presentation of data	When creating regulatory documents like CTD and Investigators Brochure, we always feel difficulty in aggregating clinical signs, for example, from study reports on the same compound but outsourced to different CROs; they often use different dictionaries/glossaries which makes the situation very complicated (i.e., different terms for the same symptom).
6	clarity of data	To make the datasets clear and concise
7	warehousing	Warehousing efforts internally

5. What are the top three domains/variables where your organization uses local rules most often? N=29

Count for Top Slot	
Domain/variable	Count
Trial domains	13
LB	5
PC	4
CL, EG, MA, MI, NOMLBL, timing variables	1 each



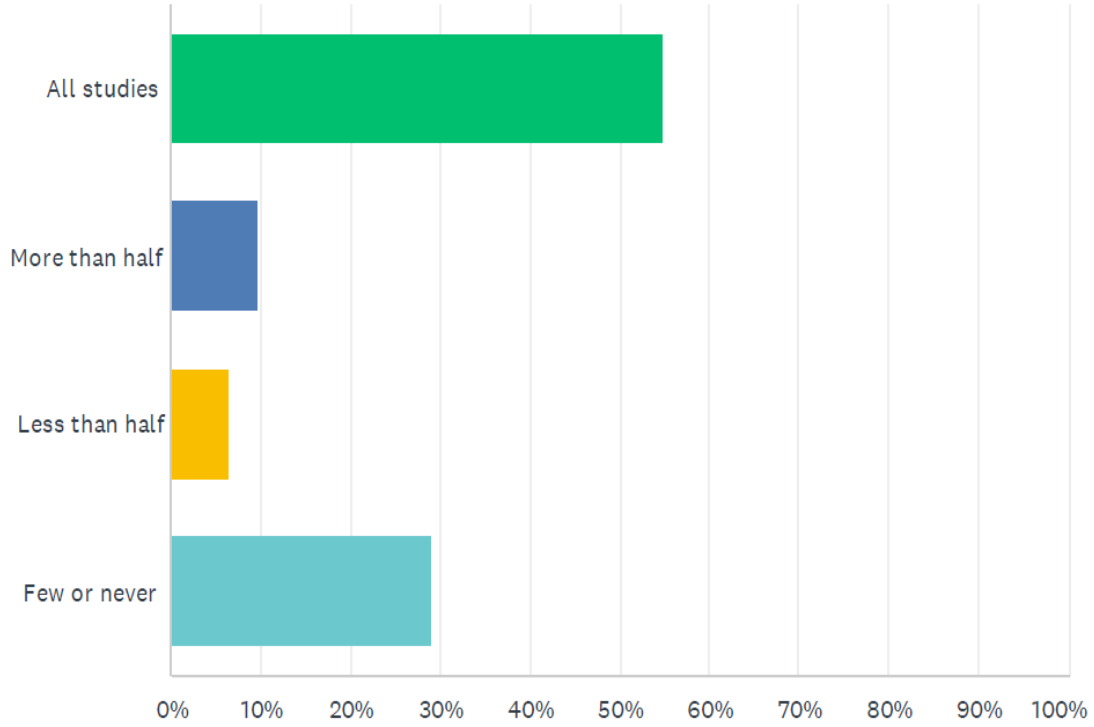
Domain/Variable	Count
Trial domains	22
PC/PP	17
LB	13
CL	7
MA/MI	7
EG	4
Timing variables	2
CO	1
CV	1

Manual Edits

Summary of Manual Edits

- Manual edits are typically conducted.
- LIMS systems appear to be a contributing factor.
- Significant touch and cycle time is common.
- 80+% labs have changed working practises for SEND
  - 50+% made significant changes

Q6 - How often do you perform manual editing to convert data into SEND? N=31



#	COMMENT:
1	We are not a LIMS provider, but we routinely generate and quality check SEND using our processes, including software that converts, transforms, and harmonizes data from disparate sources into an invariant Universal Data Model and corrects validation warnings and inconsistencies. Automatic LIMS to SEND software is not sufficient to create an error-free SEND dataset.
2	Amount depends on study design and endpoints
3	PC, PP, EG, CV, RE data are collected in an external system and manually loaded to SENDLIMS
4	Only limited to internal studies. For outsourced studies, we will ask them to edit as necessary.
5	Mostly trial design domains incl. CO domain, sometimes finding domains
6	All Trial Design domains, DM and SE are always done manually.

Q7 - Which three study designs require the most manual entry? N=22

Study type	Count
Latin square	6
Safety Pharmacology	5
Carcinogenicity	4
Dose escalation	3
Parallel	2
Cardiovascular	2
TK studies	2
DART	2
Multi-phase	2

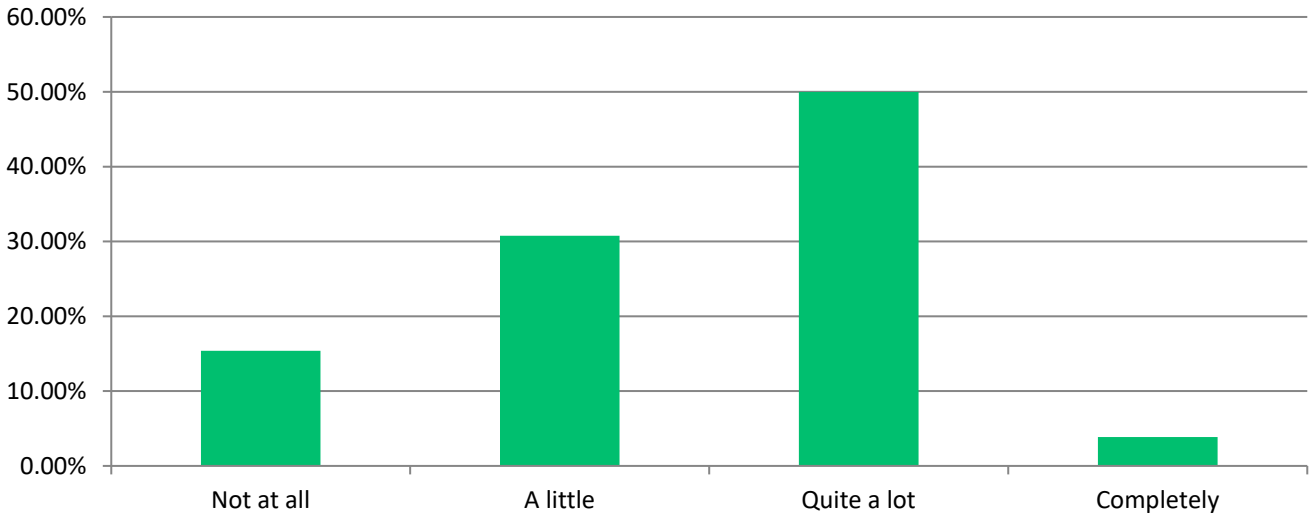
Q8 - Thinking about all the studies your organisation runs, which three domains/variables are manually edited most often? N=30

Domains/Variables	Count
Trial design	18
Timing variables	8
CL	6
Pharmacokinetics	6
MA/MI	5
EX	4
LB	3
SE	3
DM	2
EG	2

Influence of SEND on Labs

n=26

24. How much have data collection processes at the lab level changed in your organisation because of the SEND requirement?



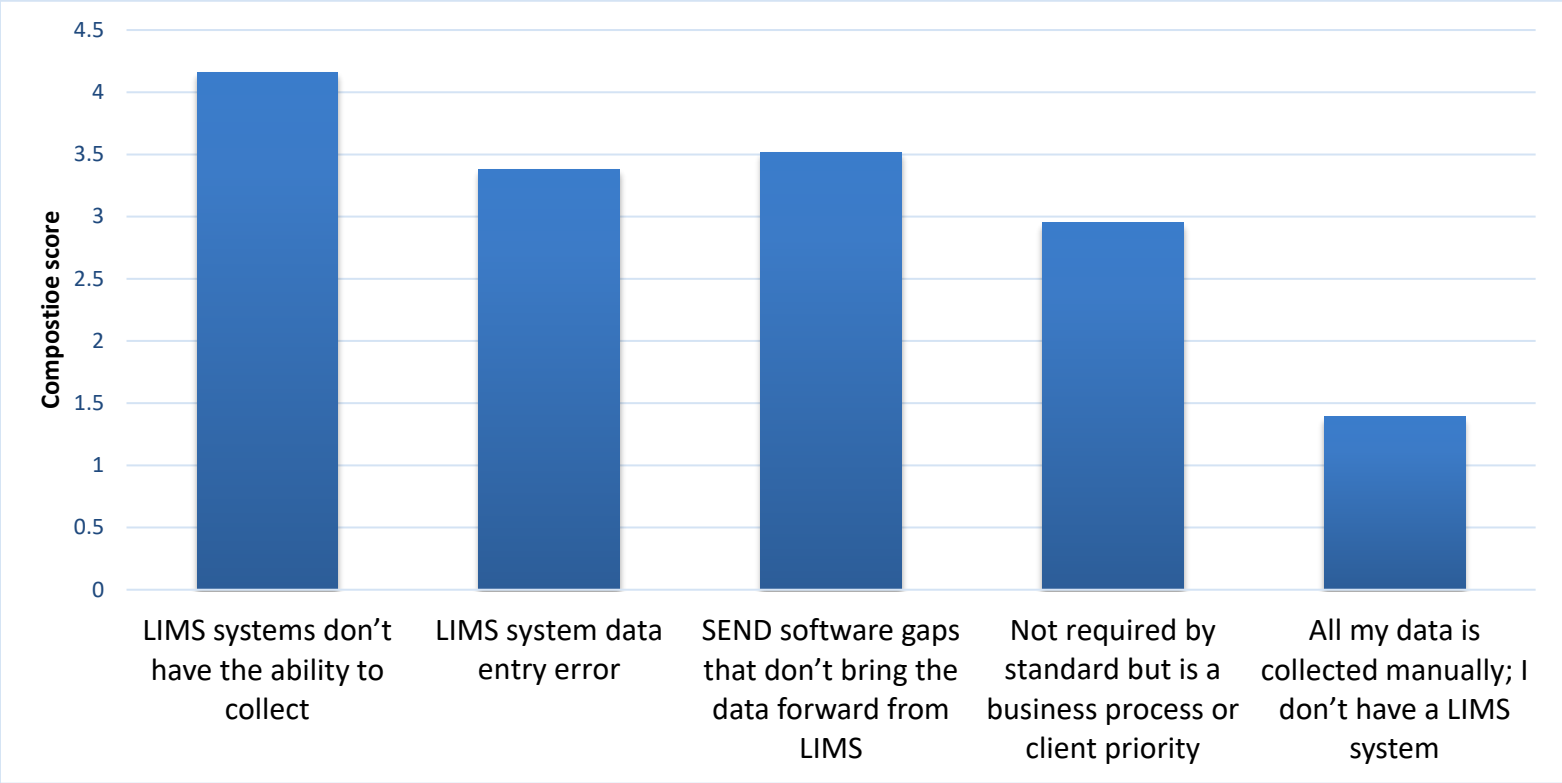
Comments

- Primarily there has been a move to record everything digitally and in real time. Paper recording of data is a serious impediment to SEND production. The standard has also influenced the choice of systems purchased and used, in particular whether the system has SEND capability or not.

- Labs had to adapt to SEND in the way parameters are created, how results are record, how comment are entered... Because not everything appears in the tox report but everything is present in SEND

- Since 2015 (one year before first FDA requirement of SEND in Dec 2016) data collection has changed a lot. All new versions of sdTCG (bi-annual) require an evaluation, mostly changes in SEND dataset generation procedures and sometimes changes on a lab level. New versions of SENDIG require mostly implementing new technology and/or process changes from lab level up to SEND data generation. After all, the SEND data standard evolved and continues to evolve through the years, so we have to adapt. And adaptation is key to evolution.

Q9 - What are the causes of manual edits of the SEND domains? (Rank in frequency, 1 being most often.) n=27



Q9. Raw Scores

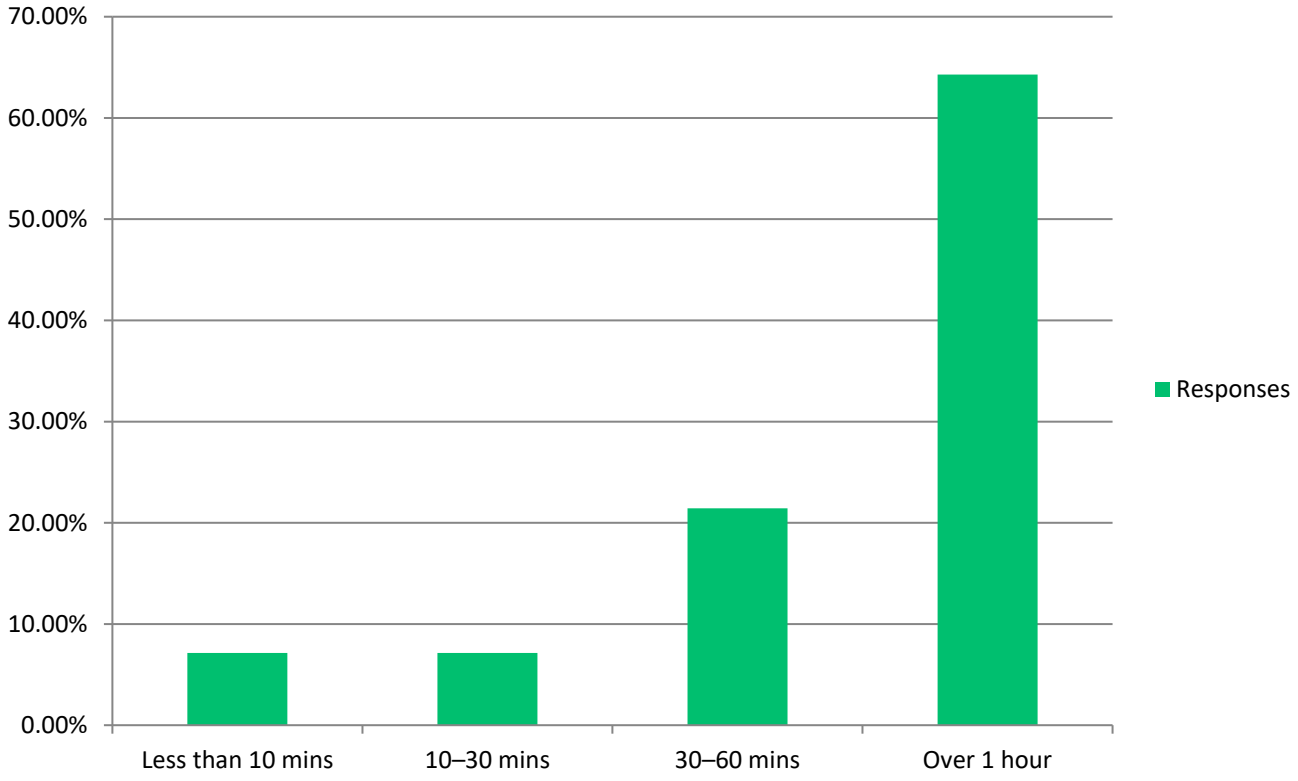
9. What are the causes of manual edits of the SEND domains? (Rank in frequency, 1 being most often.)

	1		2		3		4		5		Total	Score
LIMS systems don't have the ability to collect	48.00%	12	28.00%	7	16.00%	4	8.00%	2	0.00%	0	25	4.16
LIMS system data entry error	16.67%	4	33.33%	8	20.83%	5	29.17%	7	0.00%	0	24	3.38
SEND software gaps that don't bring the data forward from LIMS	21.74%	5	34.78%	8	21.74%	5	17.39%	4	4.35%	1	23	3.52
Not required by standard but is a business process or client priority	19.05%	4	4.76%	1	38.10%	8	28.57%	6	9.52%	2	21	2.95
All my data is collected manually; I don't have a LIMS system	5.56%	1	0.00%	0	5.56%	1	5.56%	1	83.33%	15	18	1.39
											Answered	27

Q9a- Causes of Manual Edits: Comments

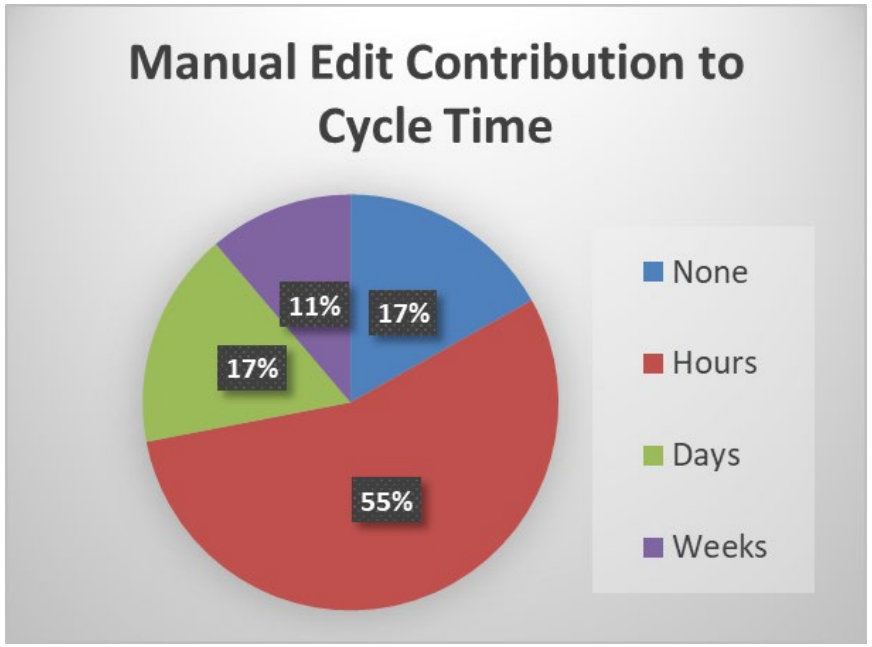
#	Responses
1	None
2	ADA, biomarkers, etc. usually not collected by LIMS systems.
3	A greater ability by LIMS systems to collect all required data to easily translate to SEND would drastically cut down on manual entry/missing data
4	LIMS SEND reporting error correction or limited functionality prevents full standardization as intended by SENDIG
5	NA
6	Most of the time it's that the data from LIMS system is not up to SEND Standards
7	NA
8	Limited LIMS setup to accommodate SEND trial design, followed by limited or incorrect mapping from LIMS entries to SEND output
9	N/A
10	Most of the time the data comes in PDF or scanned images
11	Information incorrectly entered in protocol causing the wrong information to be entered in TS
12	ECG/CV/RE data generated outside of In-life LIMS, difficulties in connection between tools and additional information only contained in report/study plan

Q10. How much touch time per study, on average, do manual edits take (not including QC time)? n=12



Over 60% of respondents reported manual edits requiring over one hour of touch time per study.

Q11. Contribution of manual edits to cycle time n=26



Q11. How much cycle time do manual edits add to the time to delivery? (Distribute 100% across the choices.) Example: 30% of studies add hours, 1% of studies add weeks, 69% no additional time.

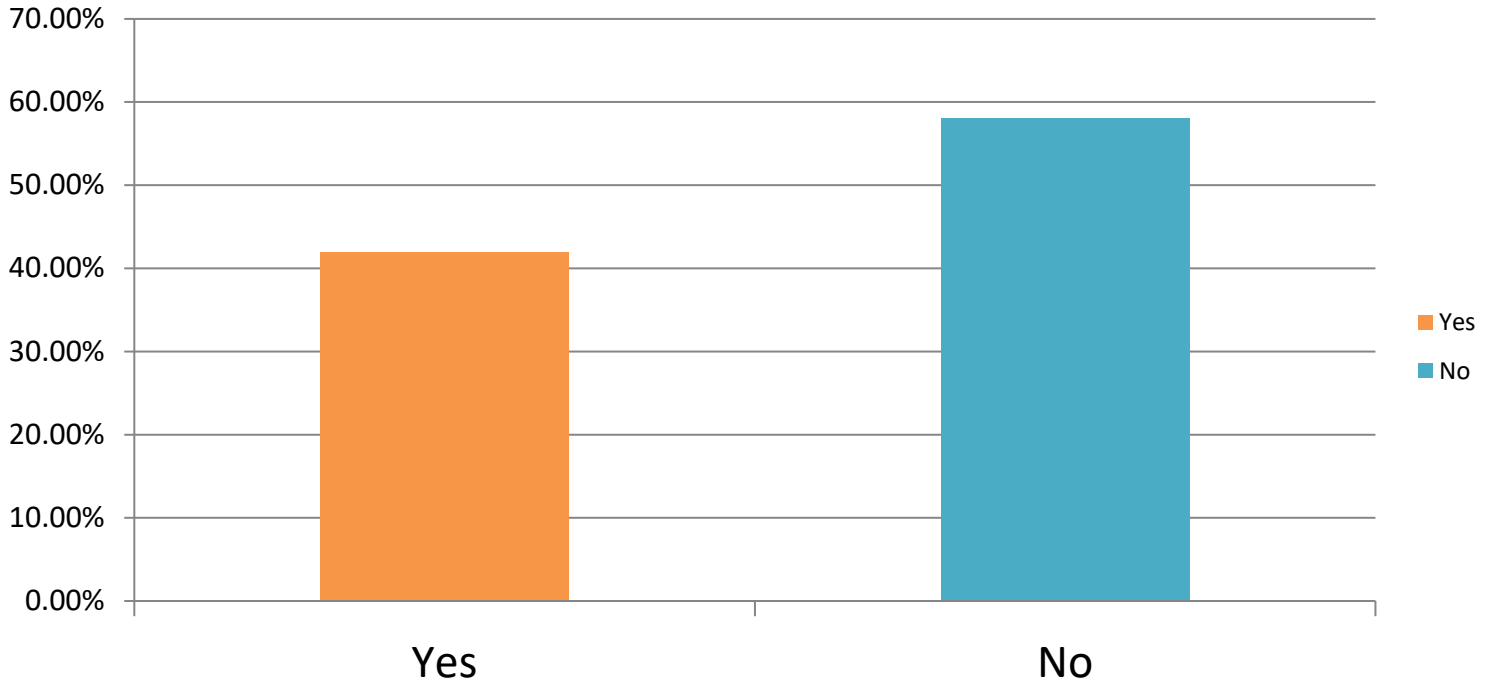
No additional cycle time	Hours	Days	Weeks	total
100				100
70		30		100
50	30	15	5	100
5	90	5		100
5	80	10	5	100
5	45	45	5	100
	100			100
	100			100
	99	1	0	100
	80	19	1	100
	70	25	5	100
	70	20	10	100
	50	50	0	100
	10	70	20	100
	10	45	45	100
			100	100
			100	100
	2	0	0	2
		5		5
		2		2

Non-CDISC Initiatives

Summary of non-CDISC Initiatives

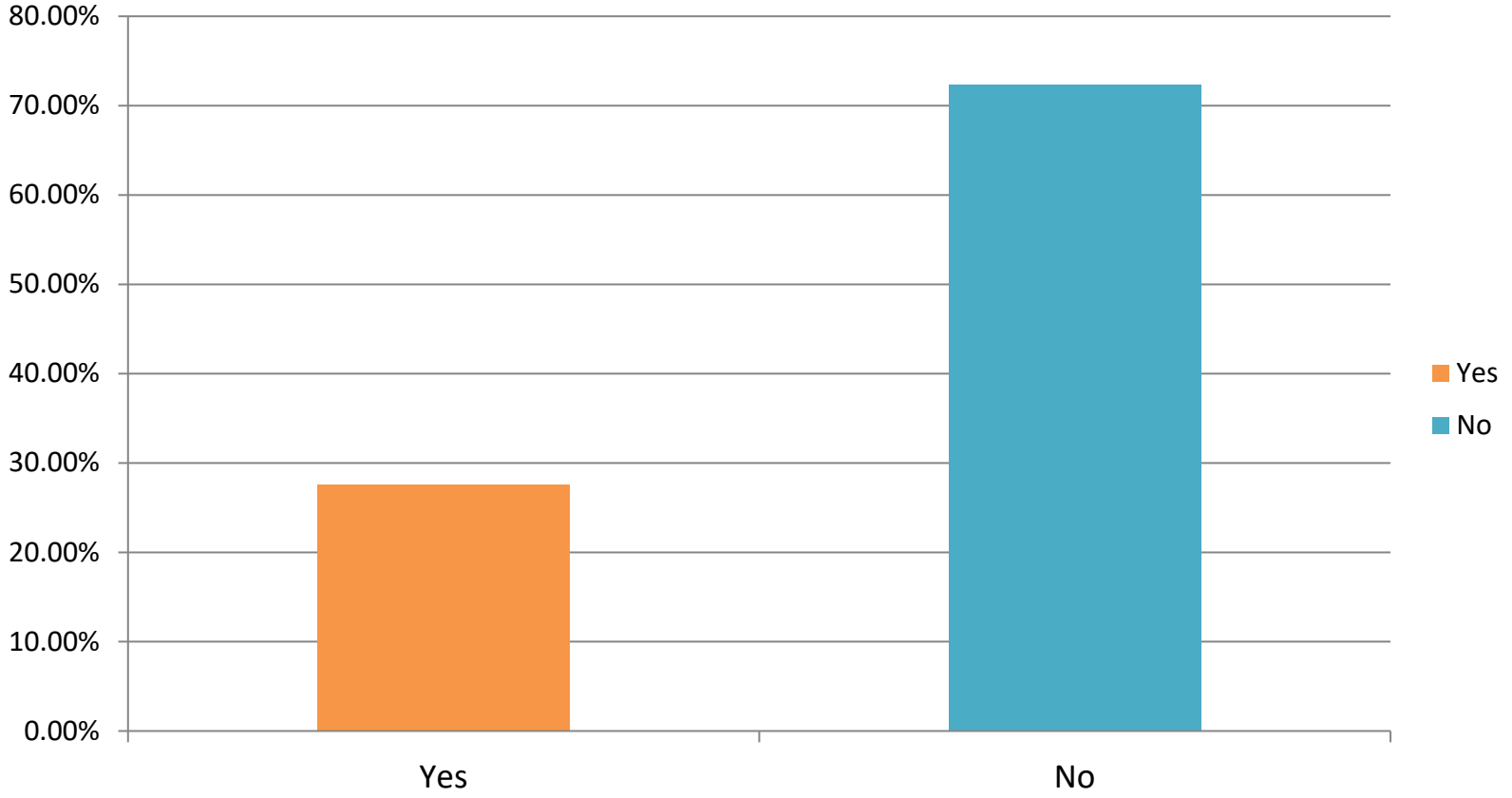
- A significant portion of respondents create multiple SEND outputs
- Over 25% of respondents are implementing non-CDISC proposals
- Customer Demand was cited most frequently as the primary driver for implementation
- There is no consensus on standardization of non-CDISC proposals

Q12. Do you have different/multiple SEND outputs for different end uses for the same study, e.g., submission vs internal uses? n=31

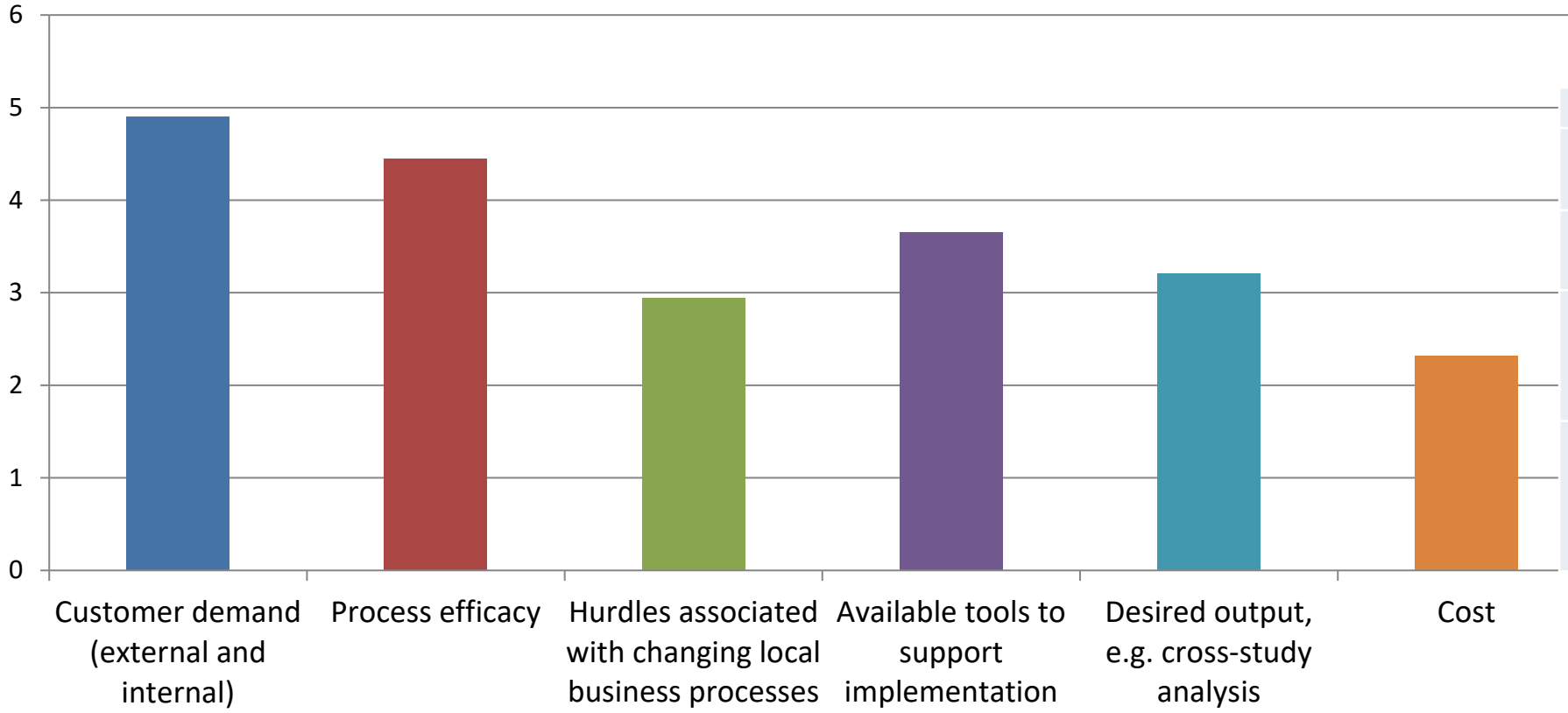


#	COMMENT:
1	different set for data mining
2	Draft outputs for data verification/mapping/client feedback vs. final outputs for client deliverables
3	Generate near-SEND format for legacy studies not intended for later regulatory submission
4	We can do just an extract without manual edit for internal use only for example
5	BioCelerate contributions have different requirements
6	We go by the highest denominator - the SEND output that we deliver will fit all needs.

Q13. Are you currently adopting non-SENDIG/non-TCG harmonisation proposals from PHUSE, BioCelerate or other organisations? n=29



Q14. How do you prioritise the implementation of non-SENDIG/non-TCG proposals? Rank 1–7 from most to least important in your organisation. n=21



#	Comment
1	would be better if they were the standard though.
2	only based on customer demand
3	Additionally, harmonization /standardization results of PHUSE / BioCelerate projects
4	Generally, just the customer demand. if the customer wants it, we find a way to deliver it.

Q15. Should these non-CDISC/non-TCG proposals be incorporated into the SEND standard? n=23

Q15 – Full Responses

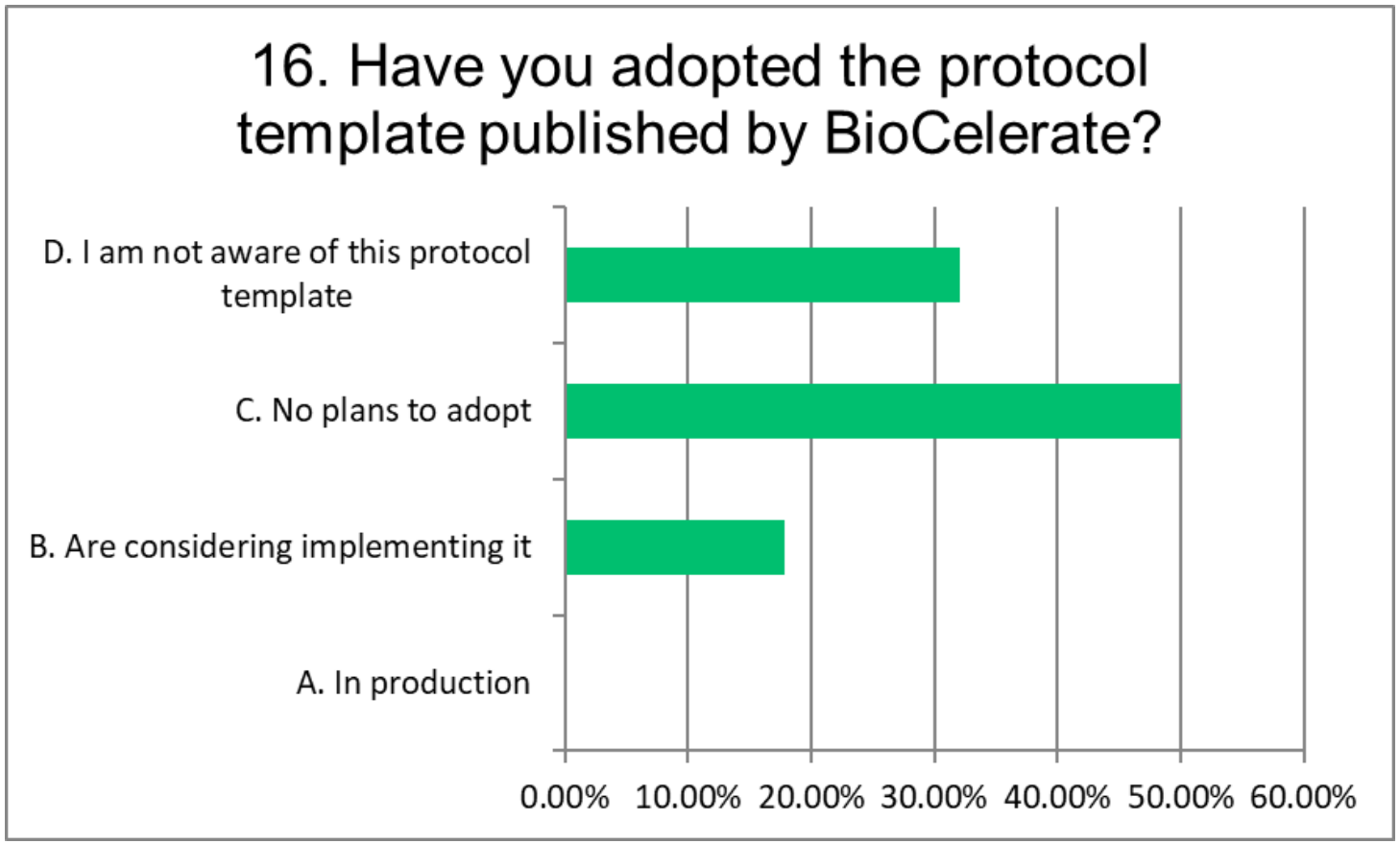
Response	Reason for your answer:
No	We do not see much use for a templated study report because the need in the industry is for study data, analysis summary data and the essential metadata along with the study protocol as reported in the Study Report to be placed in a digital columnar tabulation that is machine readable. SEND is an exchange standard that is still not familiar to or being taken up by Study Directors, toxicologists or even Reviewers. A digital version of the Study Report in its native terminology and units will go a long way to improving adoption.
No	There is a lot of other thing to incorporate first into SEND standard. Improving granularity of EX domain for example
No	We should separately think such "additional rules" depending on the purpose.
No	Currently, the SEND model is still evolving and work is still needed to improve and expand the model. Adding these types of requests takes time away from model development and adds complications that are not a priority for FDA review.
No	implementation/automation must be readily supported by SEND system vendors or else they're difficult to apply
No	Unless expected by FDA, I do not recommend adding additional requirements to SEND
No	Not all suggested proposals are universally helpful to on-going activities with SEND and often take time to implement
Yes	decreased variability
Yes	We are using SEND two-fold, one for regulatory requirement obligations and the other for data warehousing where we are wanting and needing to provide access to the data to our scientist enabling them to make quicker and better project decisions
Yes	other proposal should be checked by CDISC/TCG expert.
Yes	These implementations represent progress. In large part, they are going to be in future versions of the SEND standard anyways and are already in draft form in v3.2.
Yes	If it is important, it absolutely should be incorporated into the standard to ensure implementation across the board.
Yes	Unsure for my answer, but enough companies are doing these / requesting these then I think we should come to a consensus on these items.
Yes	More clarification and guidance on cross-study analysis and harmonization of variables / codelists across domains in SEND datasets would be appreciated
Yes	Structured Protocol would be useful and between organizations. Many BioCelerate proposals are being considered by the CDISC SEND team already.
Yes	Maybe not as is, but they represent industry needs and should as such be prioritized high by the SEND team. These proposals are the key to the industry getting some benefits from the standard, not just regulatory reviewers. By discarding industry requests with 'but FDA does not have that need', will eventually stall the use and implementation of the standard for business needs. (foot meet bullet).
Yes	However, it would depend on the specific proposal

Automation opportunities

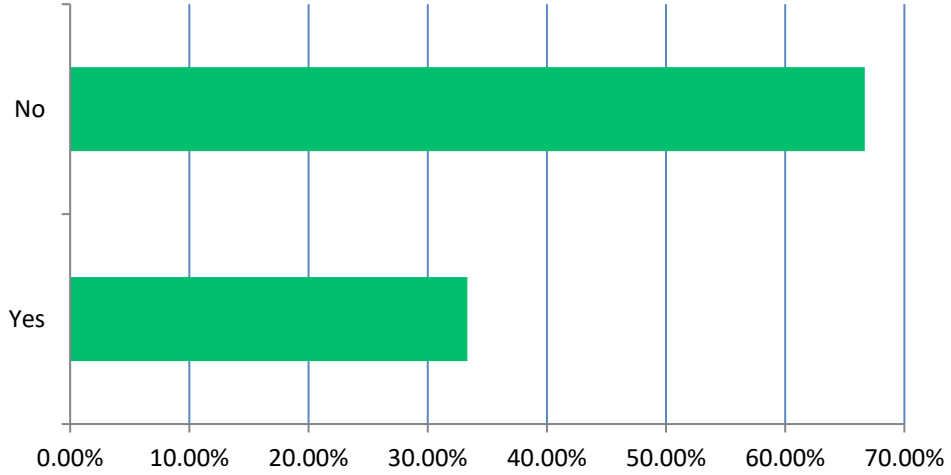
Summary of Automation Opportunities

- Protocol Template
  - Strong support for a machine-readable protocol template
    - Rich feedback on desirable features
  - Currently, low uptake for BioCelerate template
- Interest in CDISC CORE adoption
  - some caution until tools available and acceptable

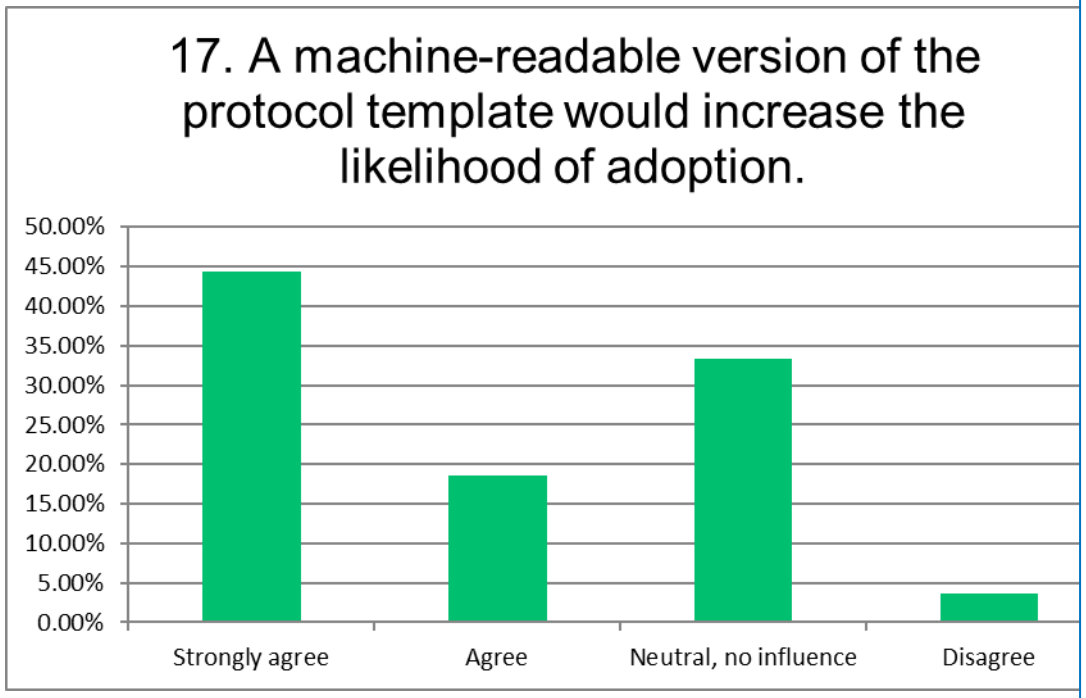
Q16. Biocelerate protocol template



16a. If you selected A or B, did you/will you make any changes to adapt the template to your own needs? n=6



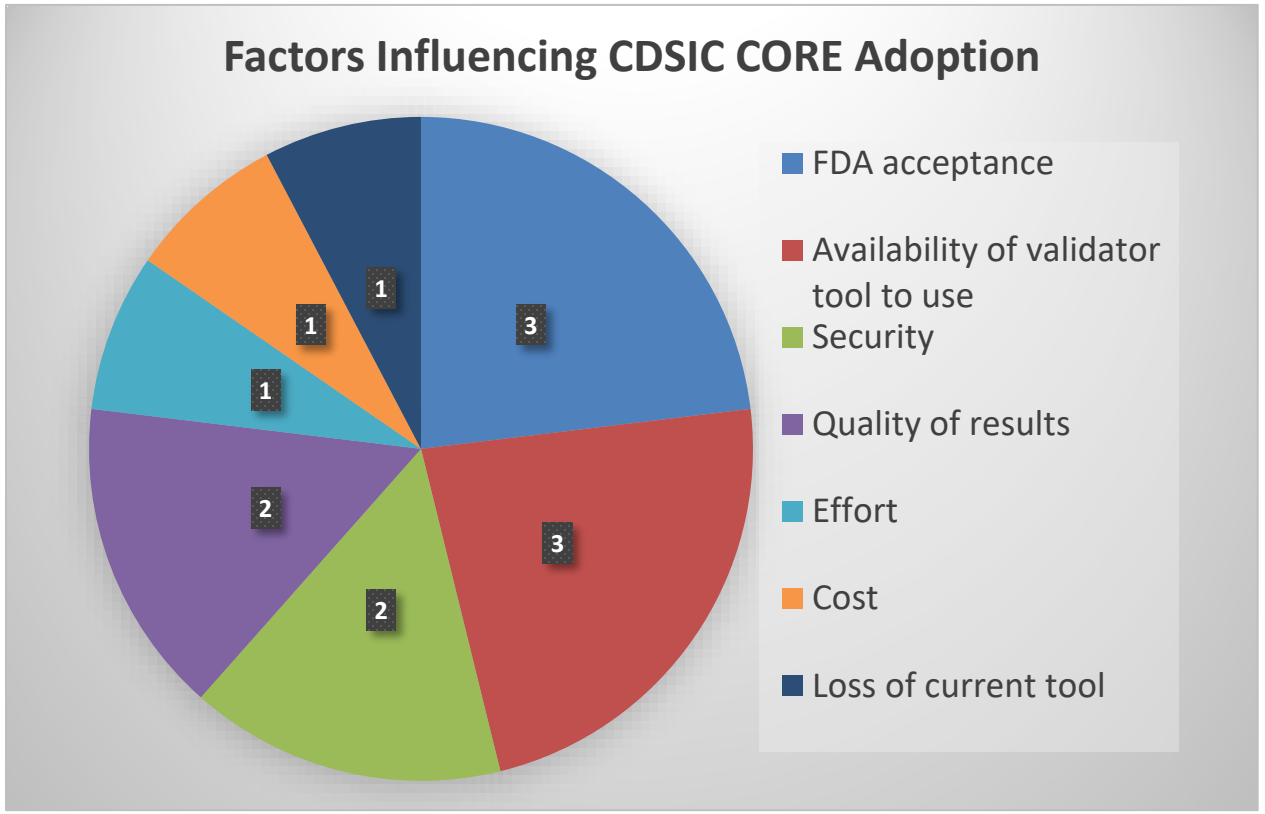
Machine Readability Features Summary



- Integration
  - Open source code where details could be used to populate SEND Trial Domains.
  - **compatibility with SEND systems** (e.g., to populate **TS and nSDRG**)
  - easily accessible
  - **If readable by data collection LIMS**, …
  - **Once tools are enhanced to leverage** the machine-readable version…
  - **ability to populate certain SEND variables** that might available via LIMS.
- Domains of interest
  - populate into the **TS domain** and **Trial Design**
  - populate **TS and nSDRG**
  - regarding **timed measurements** that are expected
  - automating **trial design**,
  - Distinguishable **trial design** grouping
  - Well defined **data endpoint categories** for collection and timepoints associated
  - **METHOD, NOMDY, TESTCD/TEST, SPEC**
  - population of **define file** content (user defined codelists),
  - study metadata for data warehousing libraries
- Controls
  - All terms should not permit interpretation to avoid doubt
  - One protocol for one study type
- Other
  - Required extensive amount of data to frame the machine-readable protocols
  - Global acceptance and adoption of this protocol
- Cons
  - If the protocol is being standardized it still leaves out the essential metadata about the study that is required later in SEND. …it is more important to **digitize the Study Report into a columnar tabulation…**

19. What factors will influence adoption by your organization of the CDISC CORE open rules engine (conformance rules checker) currently under development? N=19

- Several factors influencing acceptance
- Some active interest
  - Neutral 7
  - Embracing 3



Q19. All responses

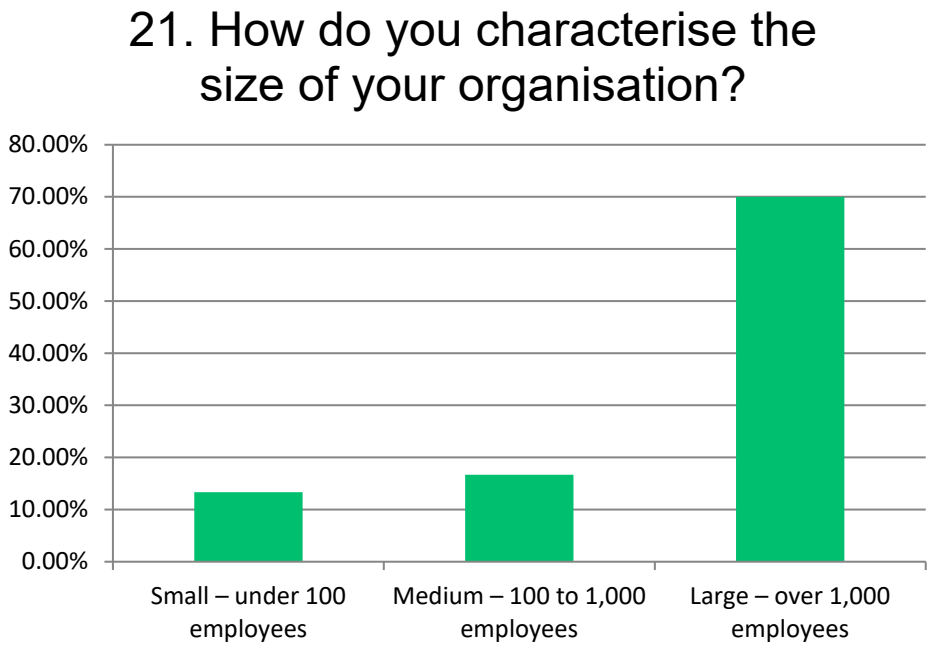
Responses:

- will likely use instead of alternative
- Accuracy of validation, usability, comparison to Pinnacle/eData Validator, ability to influence functionality if it is needed
- We have started using the CDISC SEND conformance rules as part of our in-house validation tool. We remain supportive of the open-source initiative.
- We will need to test it and compare the results against our actual tool
- Organization is looking forward to incorporation of the CDISC CORE open rules engine to decrease reliance on a company that has a monopoly on the market and that engages in shady business practices.
- We would need more information about CDISC CORE to fully understand how we could implement it
- Don't know.
- Our organization plans to adopt these rules when available.
- use by Pinnacle 21 community validator
- Not familiar with CDISC CORE.
- Whether Pinnacle21 will cost a fortune to use now after being acquired.
- Ease of access
- As far as I understood CDISC CORE creates machine readable validator rules. With this in mind: 1. Interface of machine-readable validator rules to existing available validator tools 2. Open source validator tool (PHUSE, CDISC, BioCelerate, etc.) that can interpret those rules
- Availability of end-user tools to perform validation. FDA's endorsement would have a great impact.
- If it will reduce a manually QC burden without generating an additional burden on weeding out true positives. If we can customize the engine with our own rules (since we are already running two validation tools, we will likely not adopt a third but rather build new rules into our own tool unless the CDISC Core proves a superior tool). Our process is dynamic and continuously evolving, we will only adopt a tool if it can keep up with evolving internal and external requirements.
- If the FDA use it as part of their review process and how it uses/stores data
- Sponsor data security, Expected to be a more efficient tool than Pinnacle21 or in-house tools, Global acceptance including FDA
- Not sure
- If P21 community is unsuitable going forward. Cloud based solution - need to assess potential data security risks

Demographics

Type of Organization

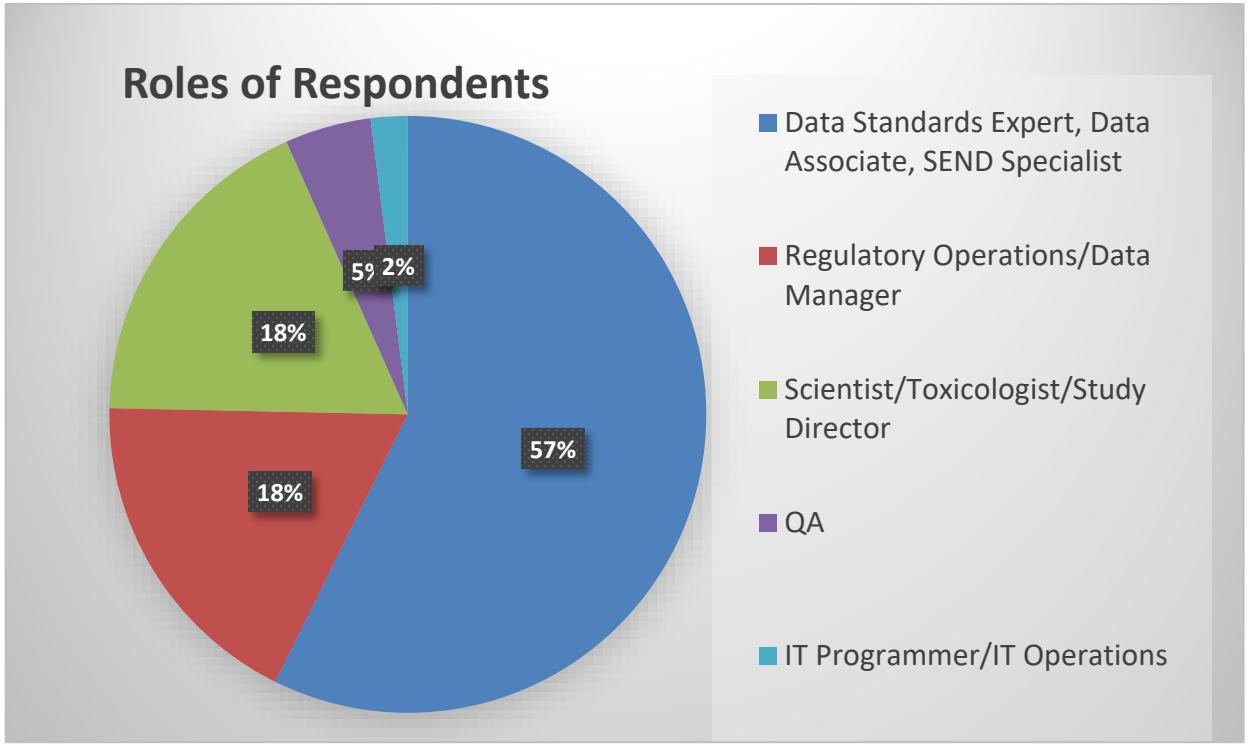
Answer Choices	Responses	
Sponsor	40.00%	12
Contract Research Organisation (CRC	33.33%	10
Software/service provider	20.00%	6
Other	6.67%	2
Government	0.00%	0
Consortium	0.00%	0
	Answered	**30**
	Skipped	**30**



Global Representation, n=29

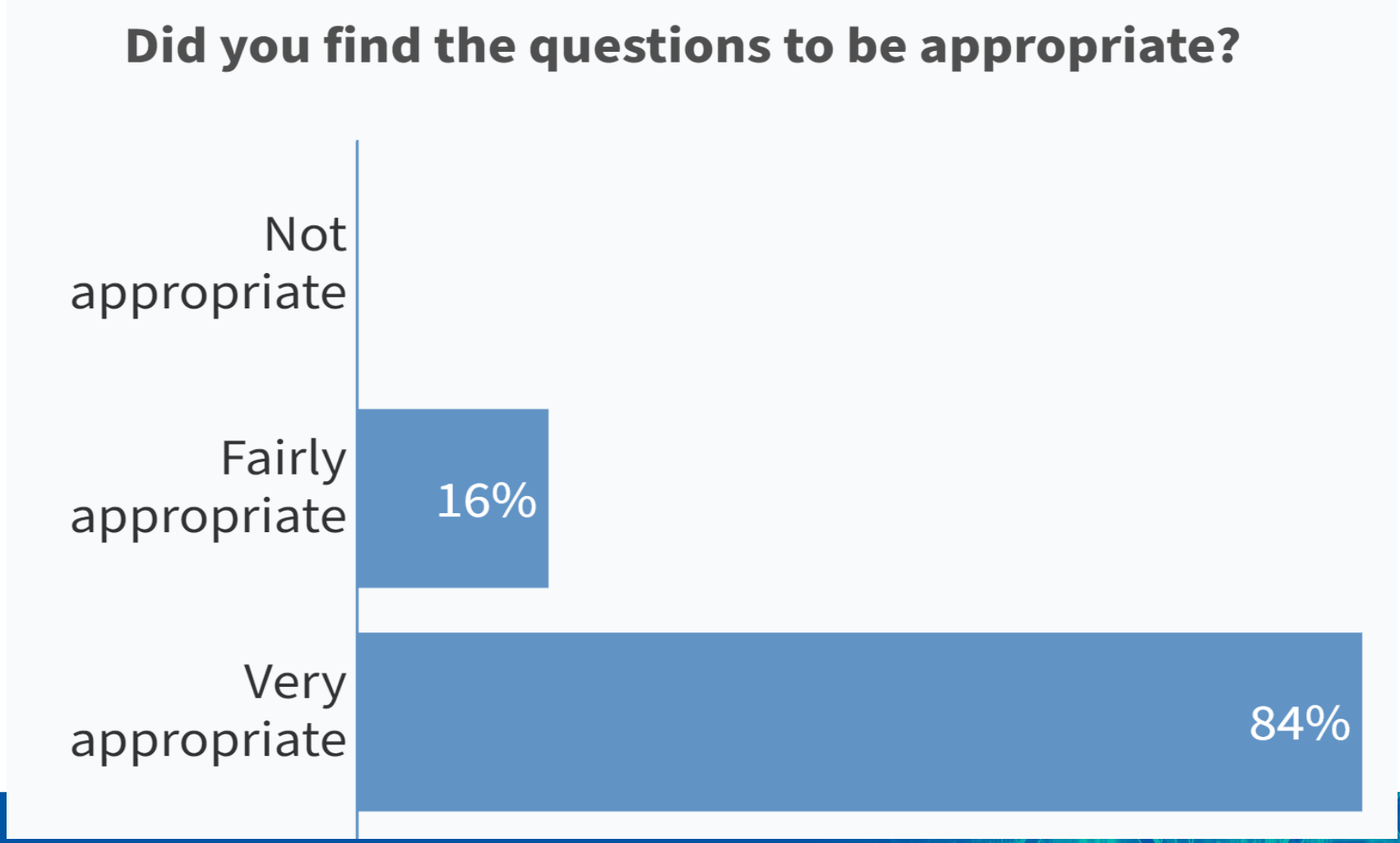
Denmark, France,
Germany, India,
Japan, Multi,
Switzerland, Taiwan,
UK 6, US 14

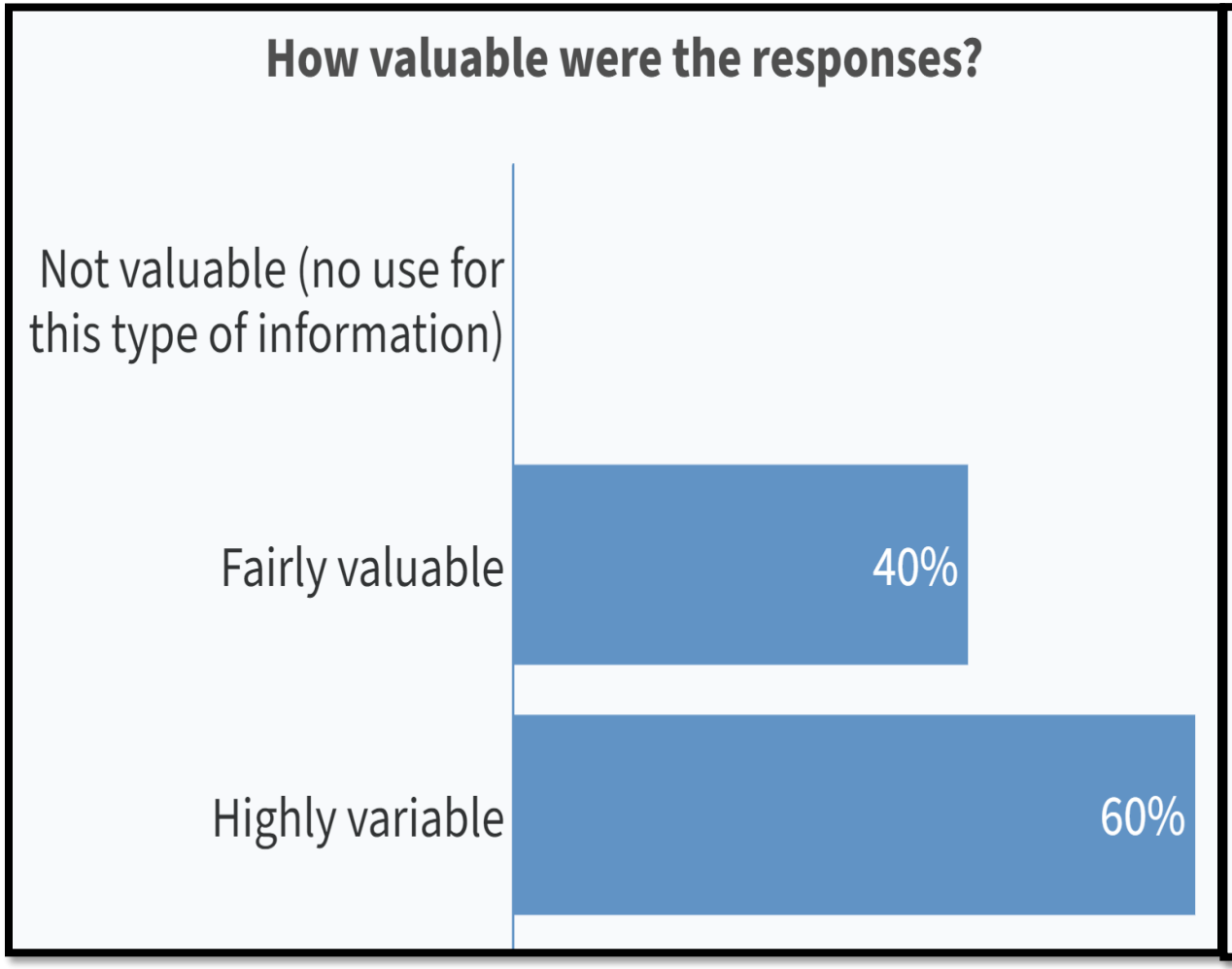
23. How do you characterize your role in your organization? (Select all that apply.)

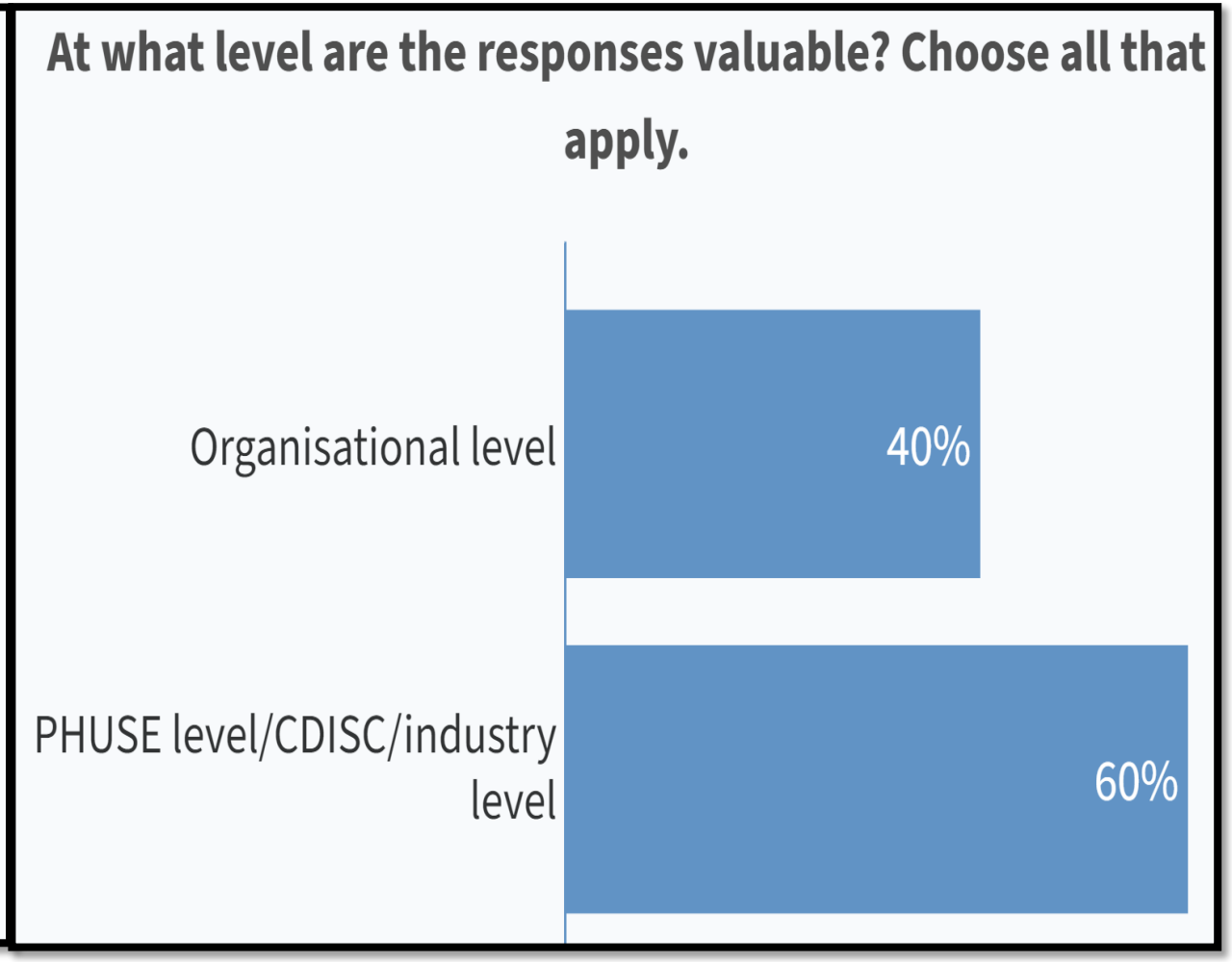


"…the SEND data standard evolved and continues to evolve through the years, so we have to adapt. And adaptation is key to evolution."

Results of CSS WG audience poll




How valuable were the responses?
Not valuable (no use for this type of information)
Fairly valuable
40%
Highly variable
60%


At what level are the responses valuable? Choose all that apply.
Organisational level
40%
PHUSE level/CDISC/industry level
60%

Other feedback, topics of interest, interest in joining the team, etc.

- Great set of information provided by respondents
- Better connection with clinical data
- Manual edits time, would like to see more information on amount of time needed. I would like to join this team. I am particularly interested in SEND QC Practices and how to handle permissible variables
- Interested in the improvement of LIMS systems to reduce manual edits.
- Topics: cross study analysis; is the idea of reporting directly from SEND data.
- I think the next set of survey questions should take into account that CBER will go online next year and ask some questions to tease out the level of understanding for CBER focused companies
- More specificity behind some of the answers regarding LIMS systems or area of data that need manual intervention would be useful.
- How some people are spending need than an hour in manual edits.
- Really looking forward to going through results more thoroughly.
- Need to look at results in more detail
- Data mining/warehousing, best practices transforming historical data in SEND, long term storage solutions