SEND Industry Feedback Survey 2021

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New Scope this Year

Topics:

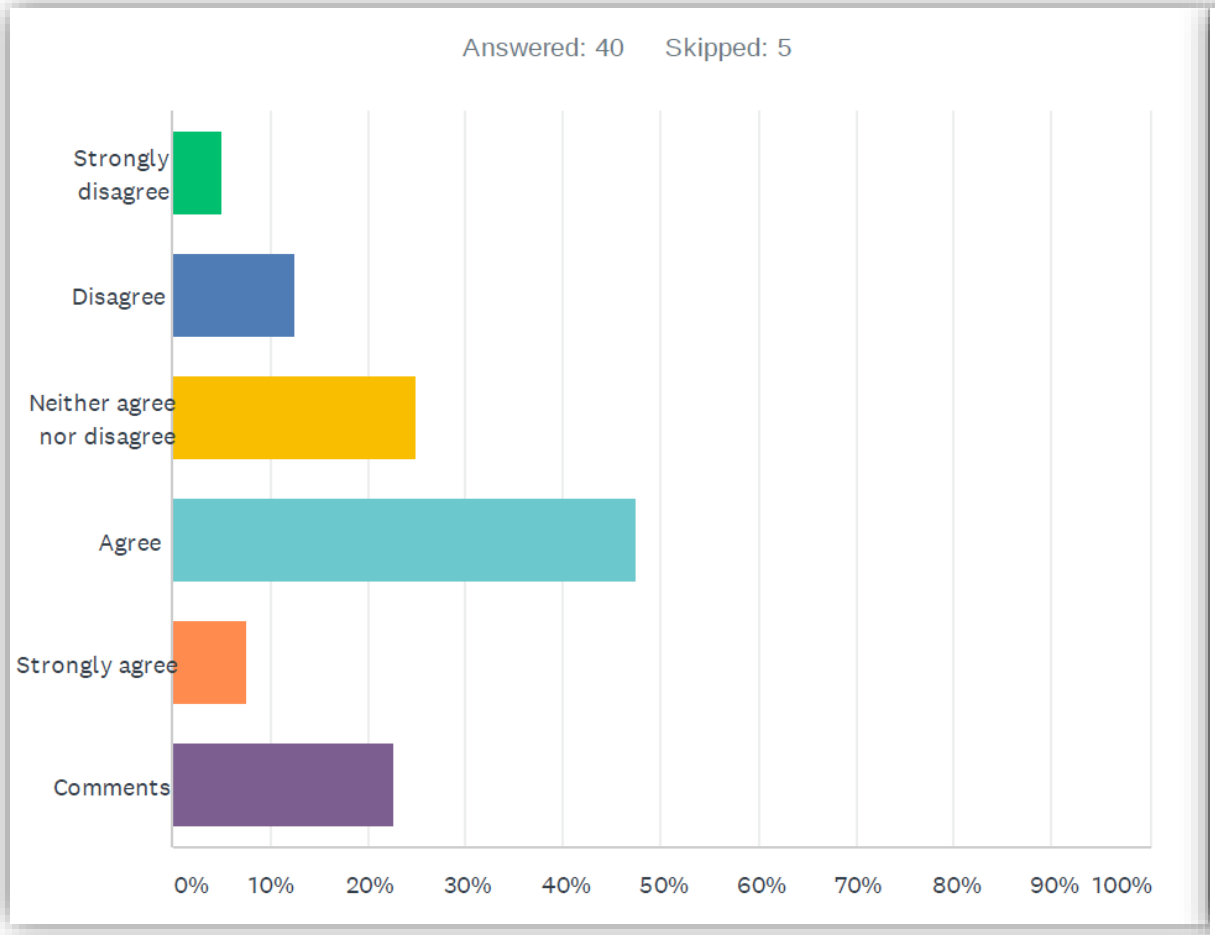
- Pace of Change
- Technical Rejection Criteria
- DART preparedness
- Ease of Use
- Non-submission uses for SEND

Pace of Change

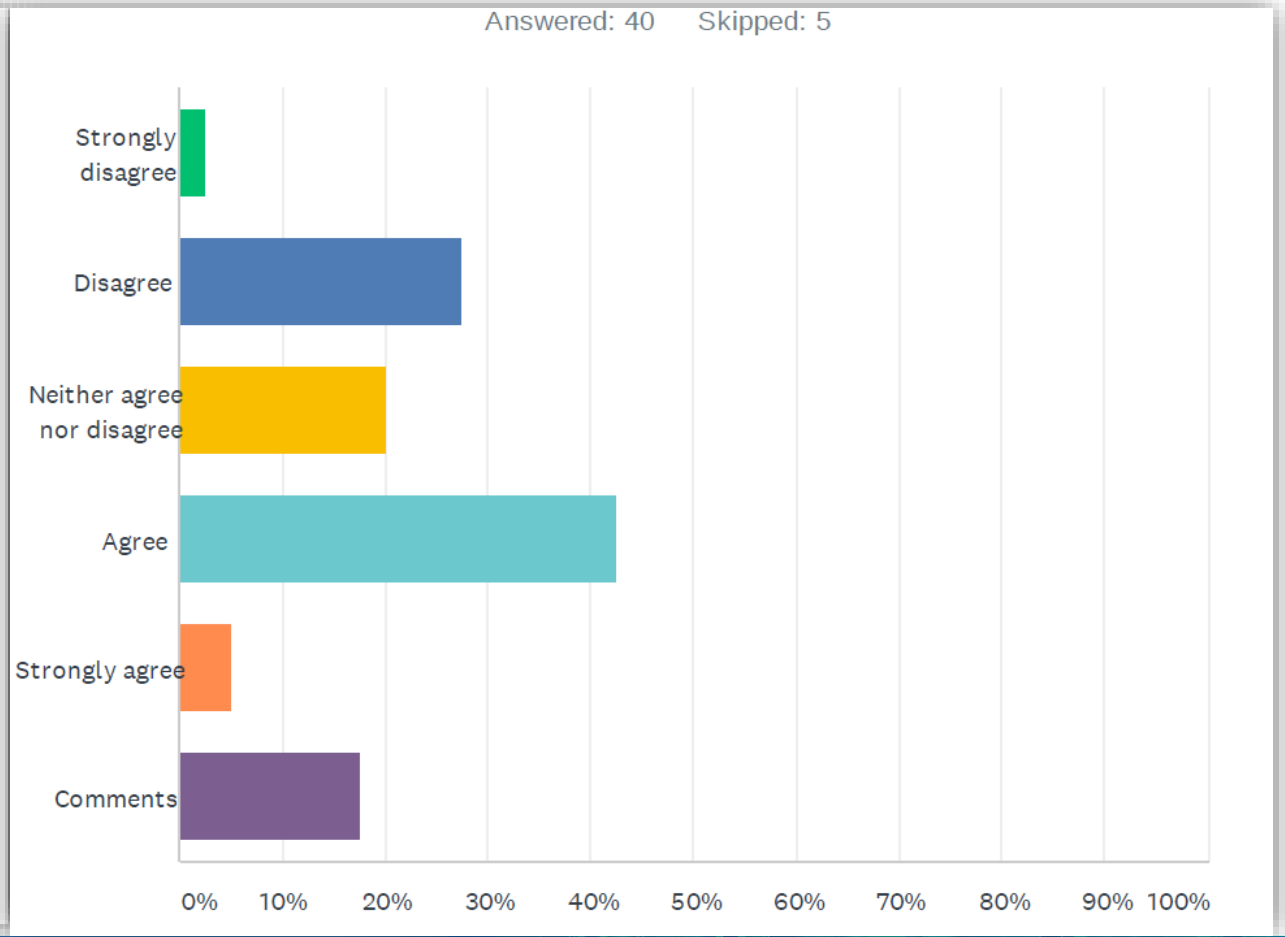
Pace of Change Summary

- 55% of respondents thought the pace of SEND standard changes worked well for their organization. 17% disagreed.
- 47% respondents thought that the pace of TCG changes worked well for their organization. 30% disagreed.

Q15 CDISC releases new versions of the SEND standard every two years. This pace works well for my organization.



Q16 FDA releases new versions of the TCG every quarter (error). This pace works well for my organization.



Comments summary:
CDISC doesn't release new SEND versions every year
Each new release creates additional work to implement.

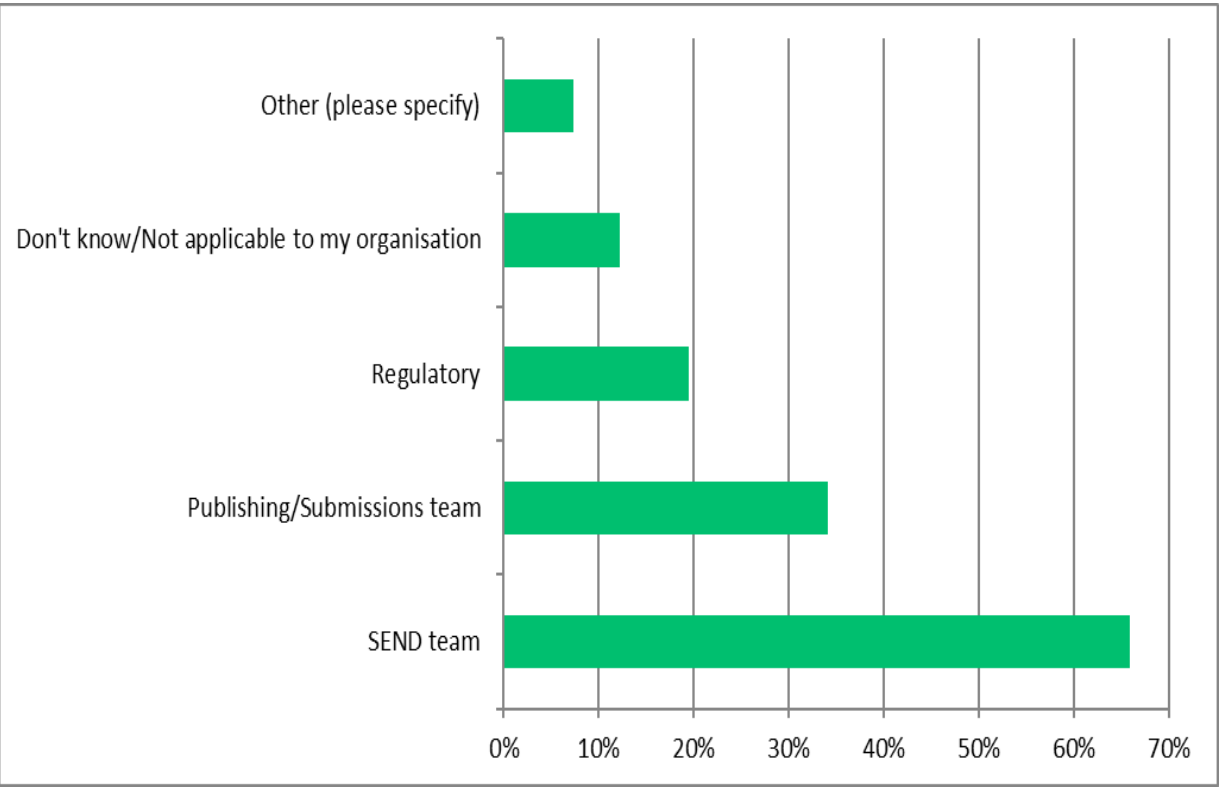
Technical Rejection Criteria

TRC - summary

- The creation of TRC-compliant datasets is mainly the responsibility of the SEND Team or a publishing/submissions team.
- Compliance with TRC is the responsibility of a SEND team or a cross-functional team.
- A small number of organizations indicated the use of the TRC-self check tool as their means of ensuring compliance.
  - Some of the other respondents' teams may also do this
- 44% respondents were not concerned with the TRC enforcement whilst another 40% were slightly concerned.
- Respondents' primary concerns were the potential for delays in submission timelines and the additional work needed to check for compliance.

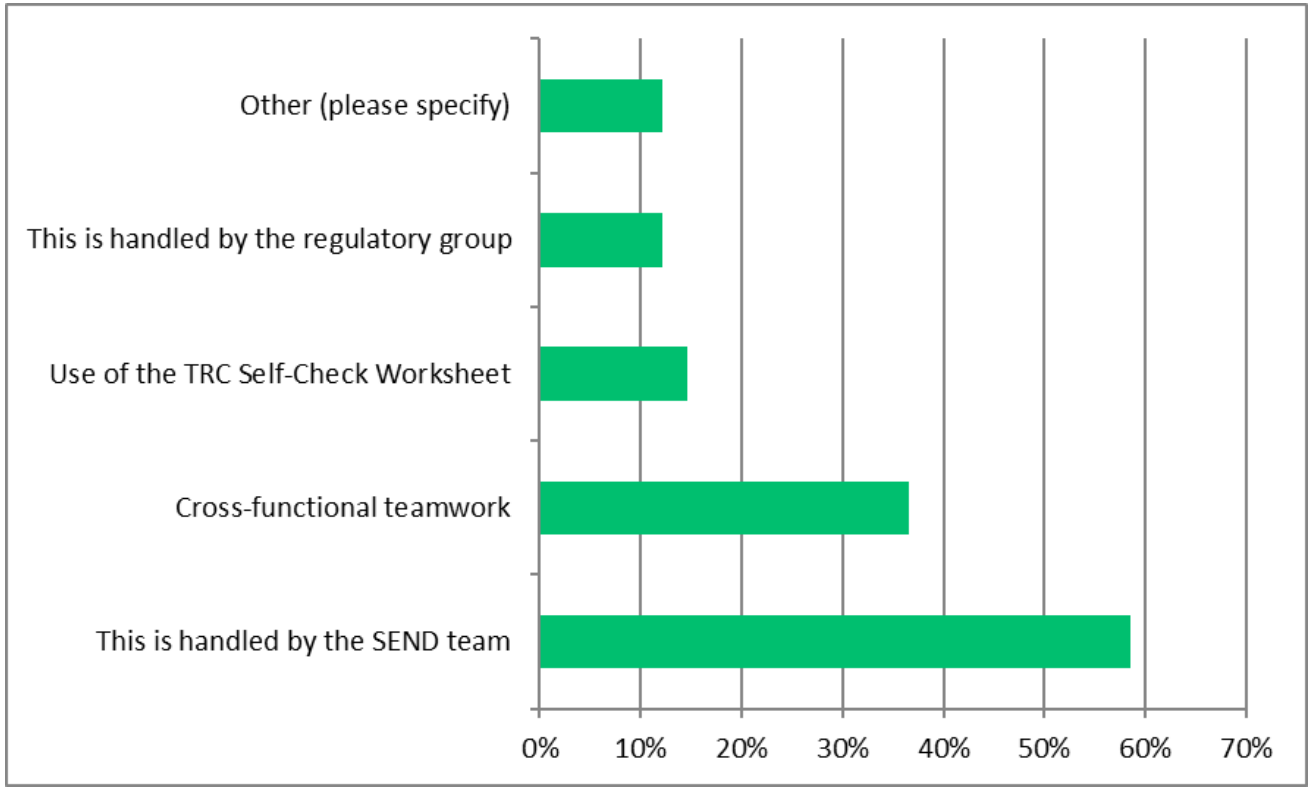
Q11 Which group in your organization is responsible for submitting/preparing the TRC-compliant files?

Answered: 41. Skipped: 4.



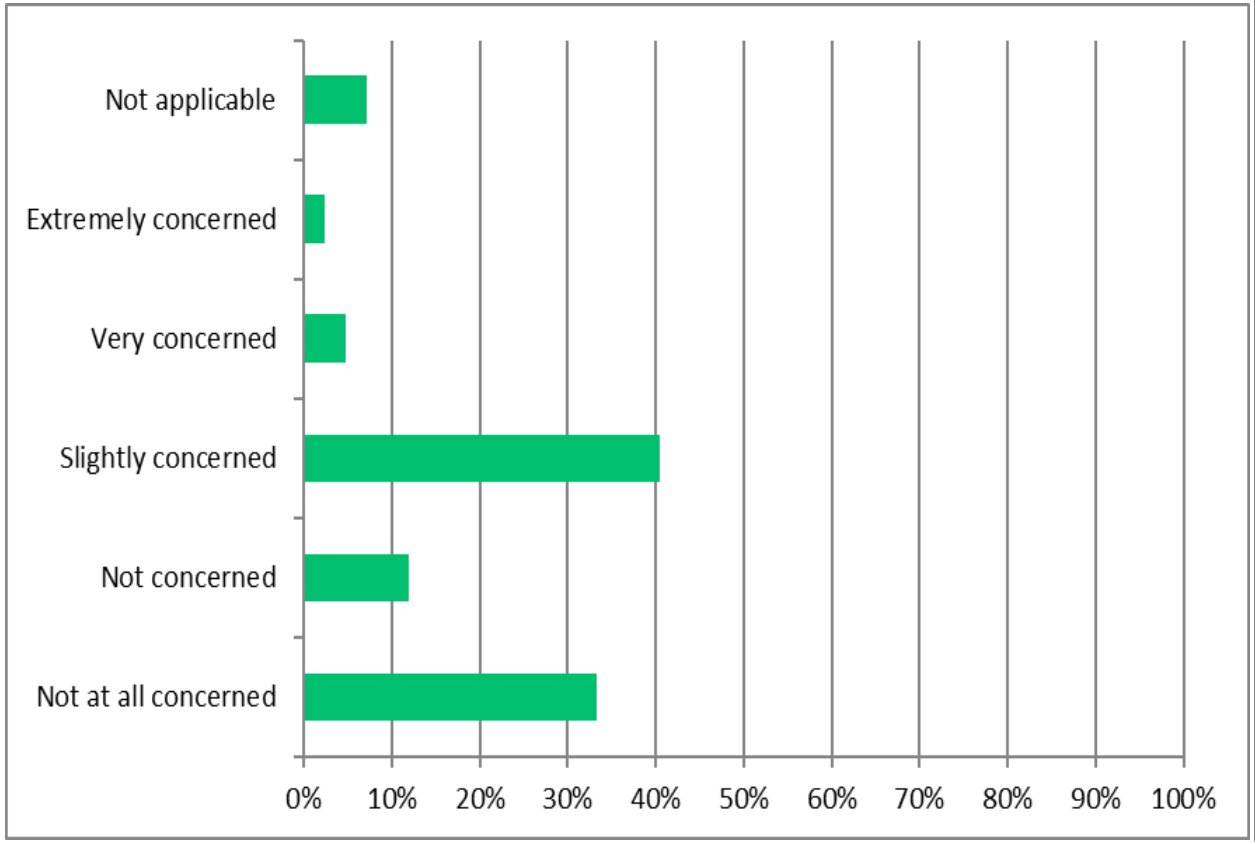
Q14 How will you ensure your deliverables are TRC-compliant? (Select all that apply)

Answered: 41. Skipped: 4.



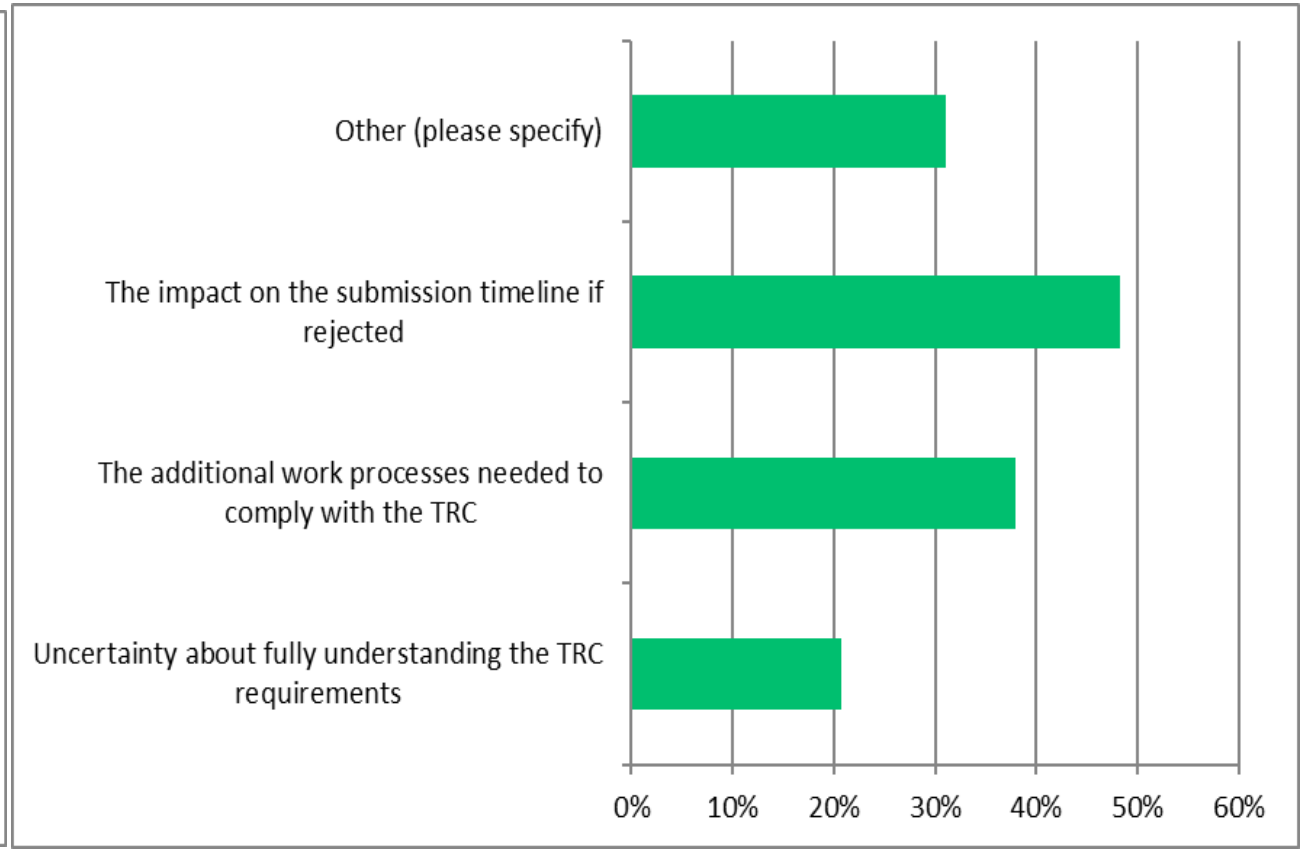
Q12 How concerned are you about the implementation of TRC on 15th Sep 2021?

Answered: 42. Skipped: 3.



Q13 My concerns about TRC implementation are due to. (select all that apply):

Answered: 29. Skipped: 16.



Summary of textual concerns:

Sponsor ID is not provided to the SEND preparer, leaving the sponsor to expend additional effort to modify the SEND dataset.

The simplified TS required by the FDA does not have the same structure as a regular TS domain.

Some uncertainty within organizations about the requirement.

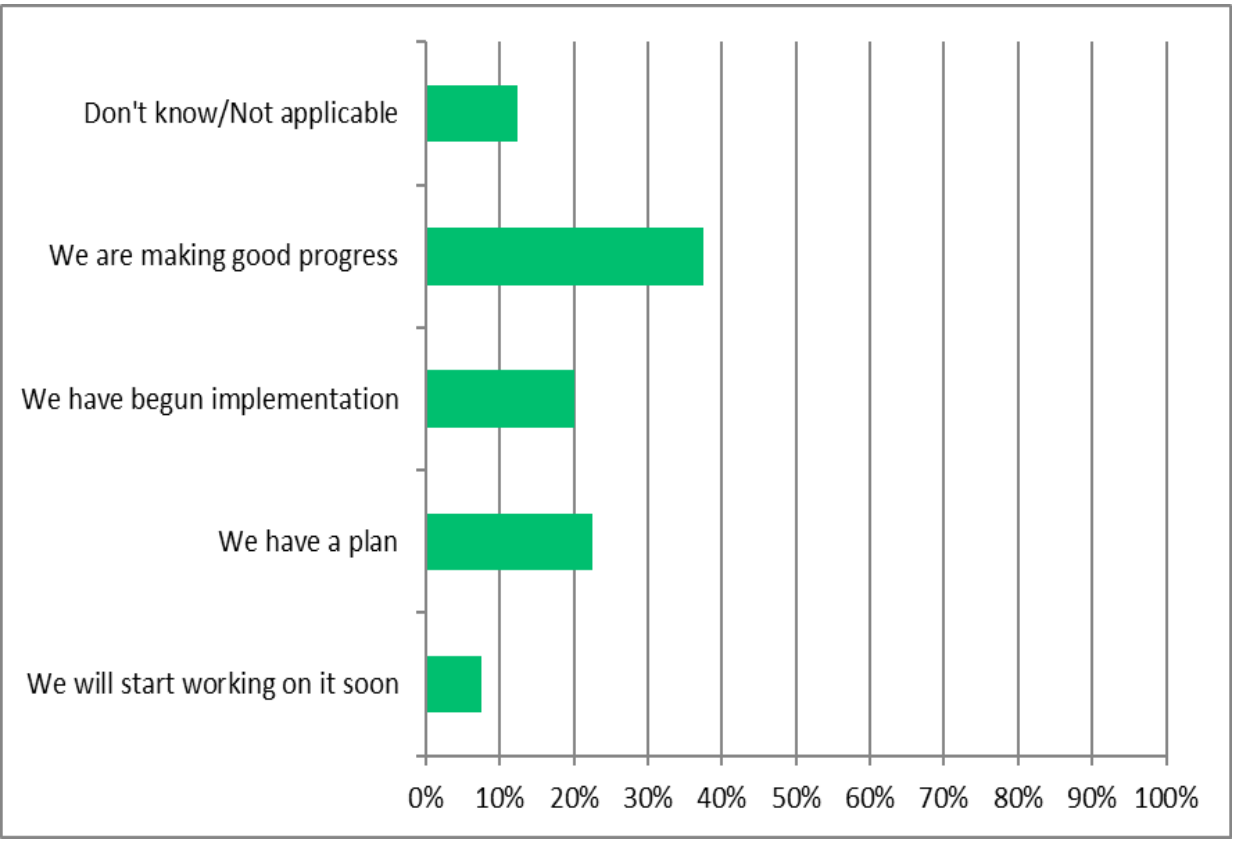
SENDIG DART preparedness

SENDIG DART Summary

- 57% of respondents are underway with implementing SENDIG DART.
- 87% respondents to whom this applied expect to be ready in the next 12 months with the rest in the following 12 months.

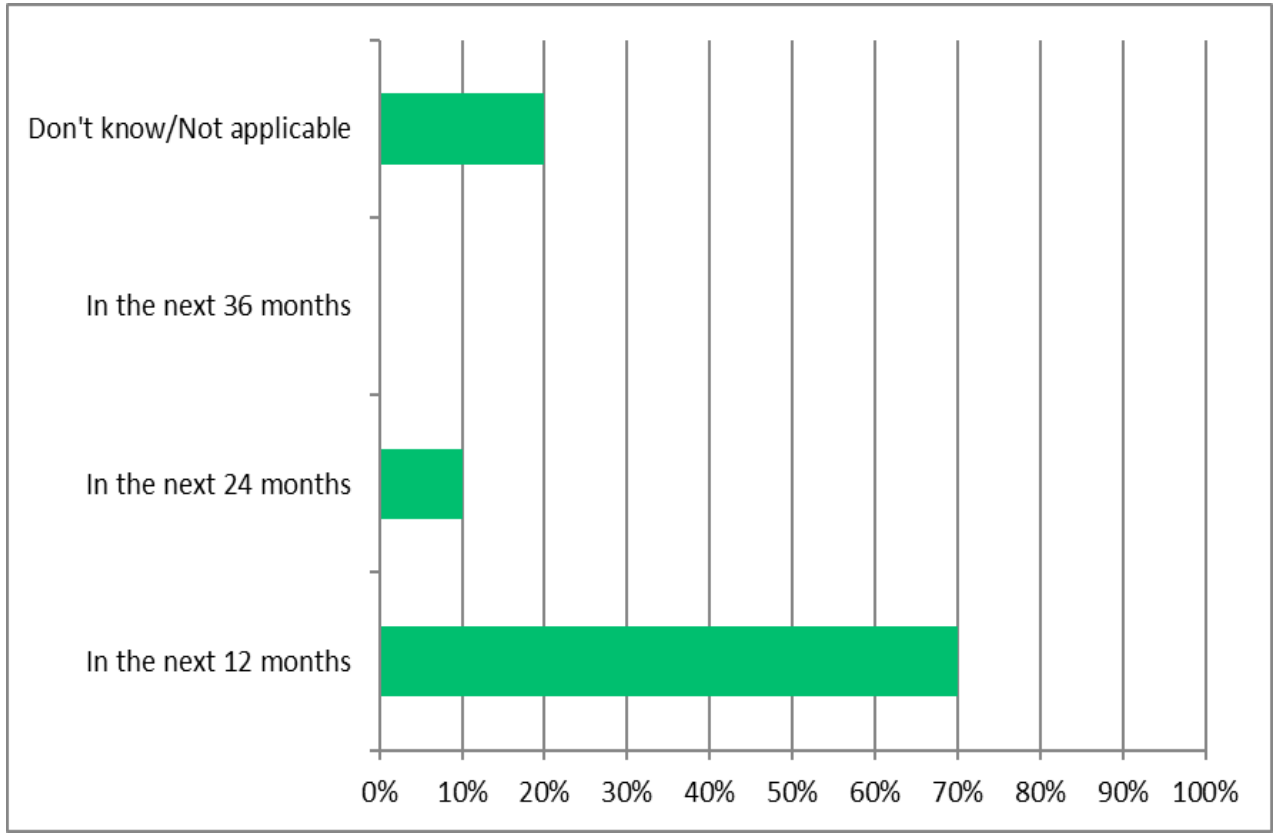
Q17 How prepared is your organization for implementing the EFD standard?

Answered: 40. Skipped: 5.



Q18 When do you expect to be ready to produce SENDIG DART-compliant datasets for EFD studies?

Answered: 40. Skipped: 5.

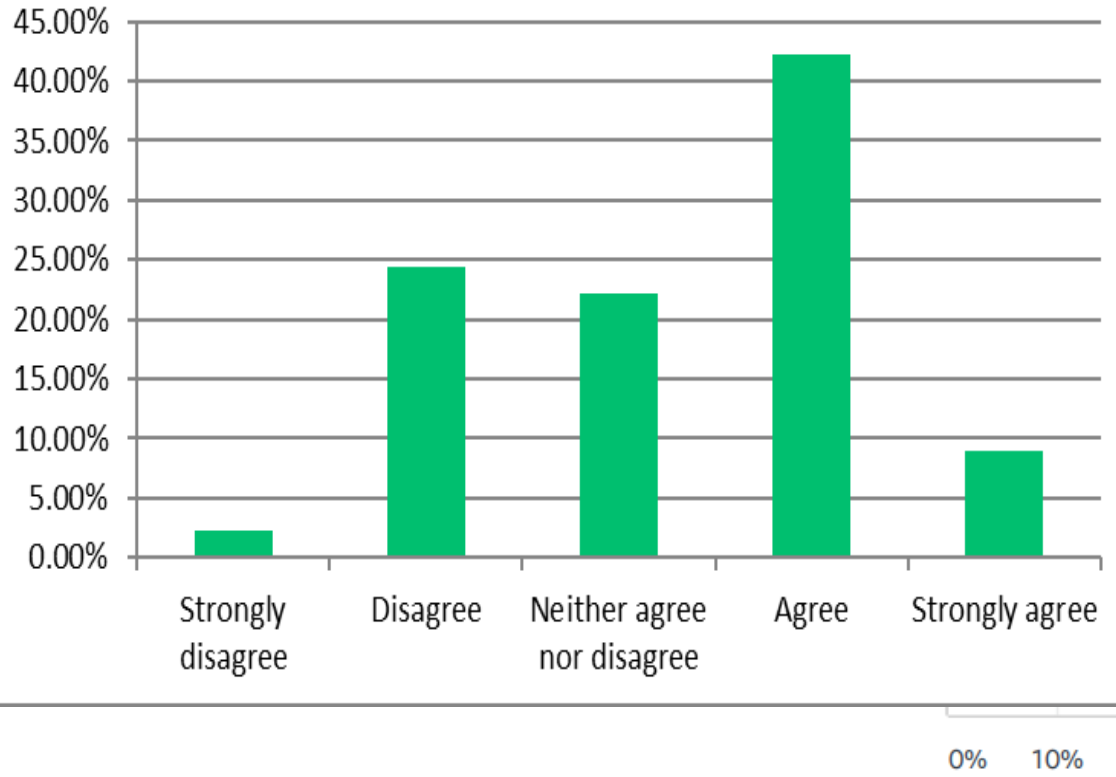


SEND – Ease of Use

SEND Ease of Use - summary

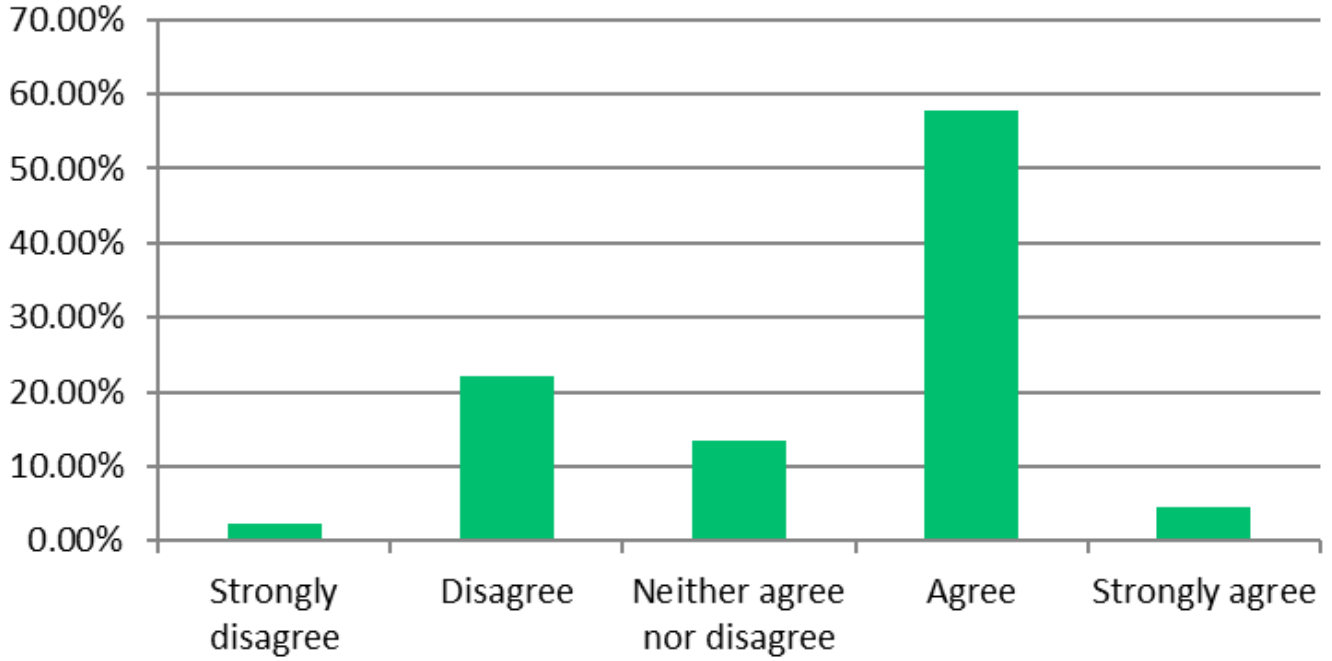
- Most people believe that SEND is easy to use for regulatory submissions.
- There's a general feeling that the SENDIG would benefit from more examples.
  - More complex examples with multi-domain scenarios
  - Modelling of Latin Square and ADME studies mentioned
- There is general support for nSDRG in its current form, although some desire for rationalization with DEFINE
- Almost 30% of respondents are not clear what studies are in scope for SEND.
- FDA SBIA webinars seen as good source of information.

For the purpose of compiling data for regulatory submission, the SEND standard is easy to use.



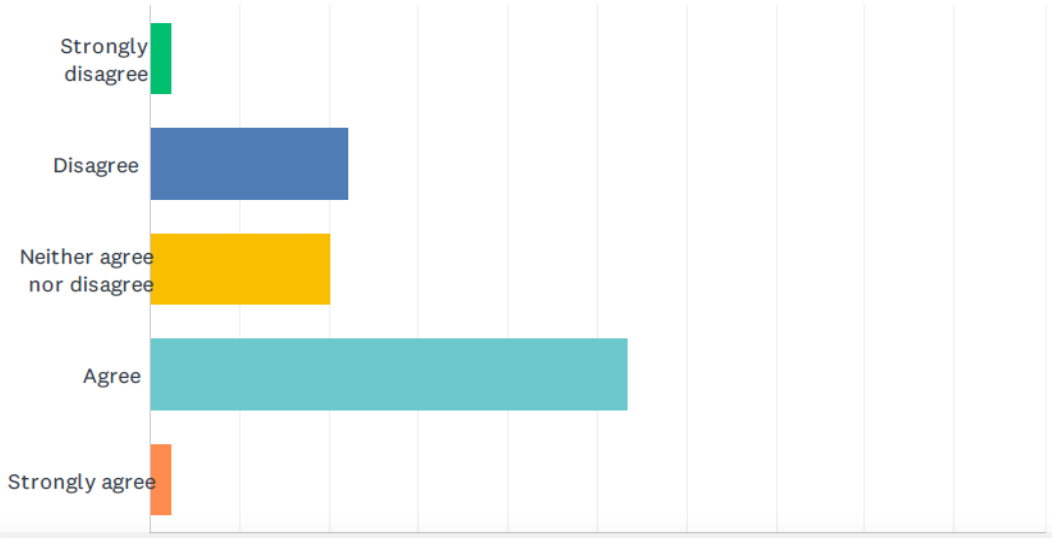
0% 10%

The SENDIG adequately supports the creation of SEND files for the study designs currently in scope.



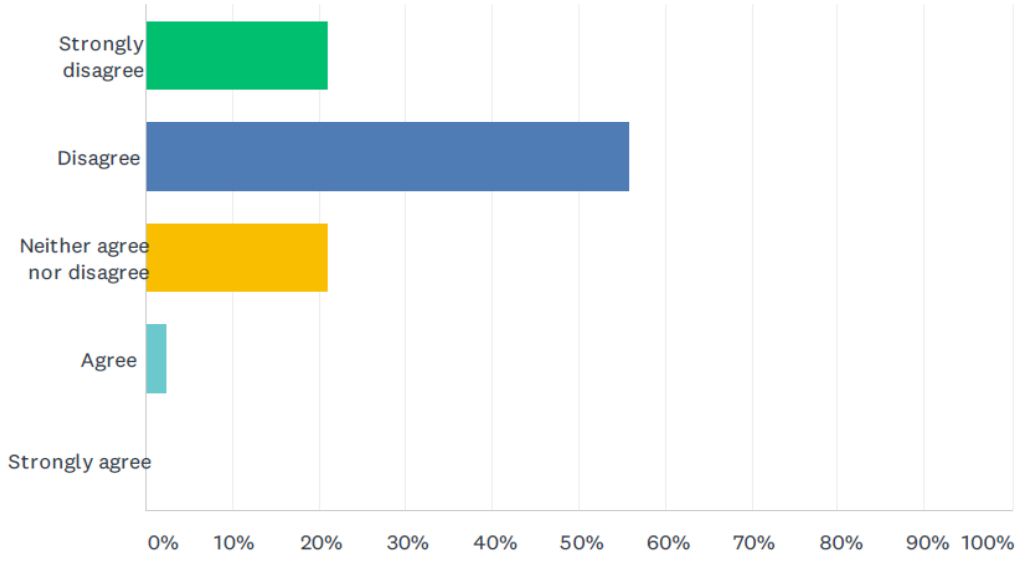
Q3 There are too few examples in the SENDIG.

Answered: 45 Skipped: 0



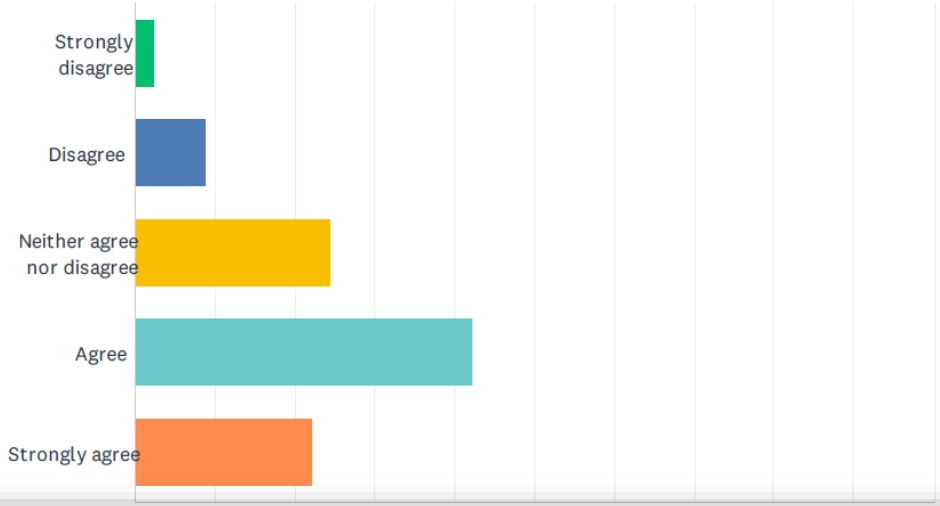
Q4 There are too many examples in the SENDIG.

Answered: 43 Skipped: 2



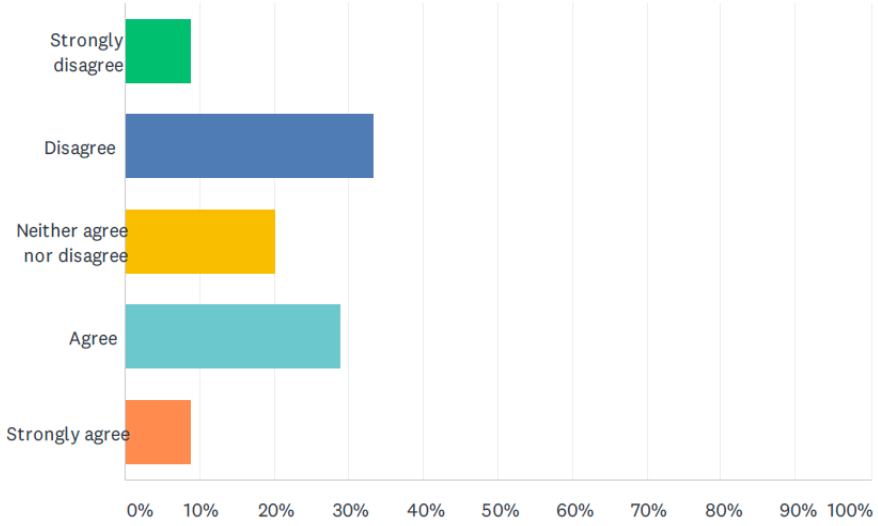
Q5 I support modelling more complex use cases involving multiple domains in the SENDIG.

Answered: 45 Skipped: 0



Q6 It would be an improvement if the SENDIG examples were compiled in an appendix or separate supporting document.

Answered: 45 Skipped: 0



Q7. Please provide specific enhancements or examples you would like to see in the SENDIG. N=21

Topic	Count
Study designs	4
Variables - GRPID, CL, tissue conc.	4
Examples – whole study	3
Cross study analysis	2
Define	2
domains & custom domains	2
Define	2
Balancing submission vs other uses	1
Codex	1
Formatting of IG	1
Protocol amendments	1
Scope	1
SENDIG vs STDMIG	1
Tools	1
TS, reconcile IG vs sdTCG	1

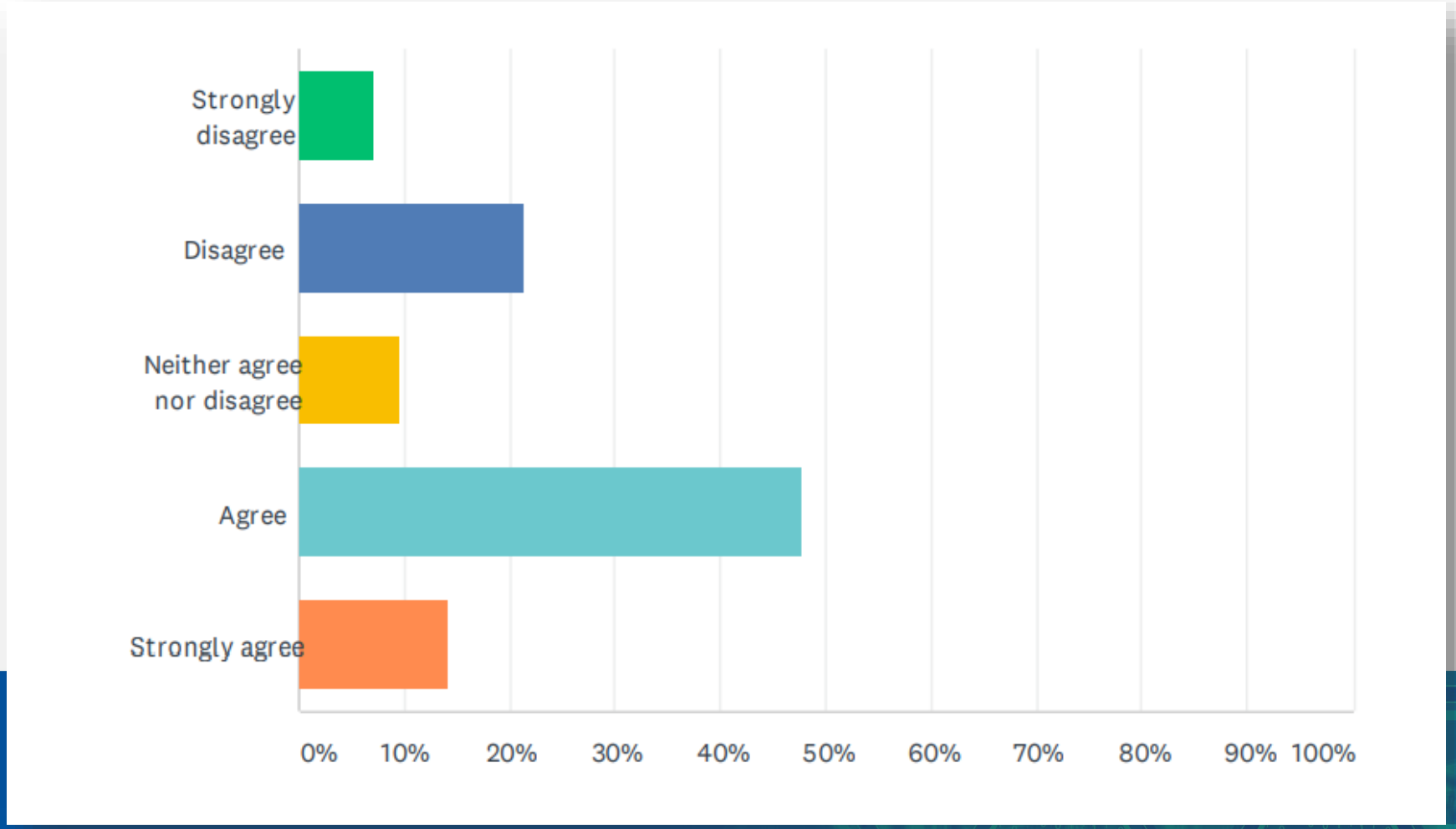
Theme	Q7. Please provide specific enhancements or examples you would like to see in the SENDIG.
balancing submission vs other uses	just caution on complicating the compilation of variables in domains that are not needed for agency visualizations
codex	A separate list of what exactly is in scope vs out of scope
cross study analysis	It would be nice if the SENDIG could be enhanced to address the cross-study analysis issues that BioCelerate has raised.
cross study analysis	Huge need for further standardisation of MI and CL findings in order to facilitate cross-study analysis.
custom domains	Not much clarity either in current SENDIG v3.1 or sdTCG on custom domains. For example, when we see CNS data reported, should this be included in SEND as custom domain (NS)? or not? It would be helpful if we have some assumption on this regard in either of the above specified documents.
Define	All references to the Define separated into own section, tabulation in some way of the assumptions for each domain - highlight/provide use cases where applicable
Define	Define file requirements/expectations to support consistency amongst industry (e.g. use of codelists, value level meta data, clearer definition of Origins - with real examples)
domains	Modelling of antidrug antibodies. New domains for data for CBER submissions which are not covered by the current SENDIG.
Examples	Examples should be realistic; suggest using real data from current study designs.
Examples	I think SENDIG is appropriately showing the examples, since they are very compact, but easy to understand. Personally, separate SEND datasets examples via xpt format with define.xml and nSDRG for further understanding the more complex case uses.
Examples - whole study	In addition to examples, have a set of exemplar studies with study report, nSDRG, define.xml and SEND dataset as an appendix. For example, parallel, parallel with protocol amendment, complex repeat dose with CV, RE, etc., repeat dose study with biomarkers, ADA, and immunophenotyping, crossover, Latin square, Latin square with protocol amendment and so on.
formatting of IG	In the CDISC notes sections, please stop using dark grey highlighter. Either eliminate color altogether or use light colors, e.g. red for Required, yellow for Expected, green for Permitted. We frequently use screen shots of IG sections as communication and training tools.
protocol amendments	The SENDIG needs to explicitly state how protocol amendments should be modeled in trial design.

Theme	Q7 continued. Please provide specific enhancements or examples you would like to see in the SENDIG.
Scope	I would like to see ADME studies included
SENDIG vs STDMIG	Ambiguous descriptions in SENDIG and unnecessary discrepancies between SENDIG and SDTMIG should be removed from SENDIG. (e.g., There are, by definition, no time gaps between Elements; therefore, the value of SEENDTC for one Element will always be immediately before or the same as the value of SESTDTC for the next Element.) These descriptions confuse IG users.
study designs	Latin square study designs addressed
study designs	More complex trial design examples.
study designs	Studies with multiple negative control types. More complex trial design setups.
study designs	The SENDIG should explain how multi-phase studies can be modelled, e.g., Single study with multiple phases (escalating dose and repeat dose phases).
tools	List of parameters for TS and TX domain should be compiled in a separate document so the reaction time to new required parameters by the TCG could be decreased.
TS, reconcile IG vs sdTCG	It would be nice to improve the current situation where it is not possible to create a TS domain (at a level acceptable to the FDA) simply by following the SENDIG; the contents in the latest version of sdTCG issued by the FDA must be reflected.
variable -GRPID	GRPID needs more detailed explanation for correct understanding.
Variables	For grouping purposes, some already existing variables could be introduced in specific domains: In postmortem domains MA and MI, nominal study day variables (--NOMDY/--NOMLBL) are missing. In DS domain, which typically has the same USUBJID's then DM, SETCD&SET could increase the readability. In TX, SETLBL could be used to group Trial Sets, therefore this parameter should be raised to 'Should include'.
variables - CL	Upgrade CL with controlled terminology for CLTEST and CLSTRESC.
variables - tissue concentration results	PC with tissue analysis results, especially if tissues analyzed were sectioned and CT does not provide enough specificity to indicate directionality or laterality - e.g., cervical spinal cord, dorsal and cervical spinal cord, ventral would be mapped to spinal cord, cervical and the dorsal and ventral are lost in the current model.

Theme	Q8. Are there any enhancements to the nSDRG that would make creating SEND submissions more efficient?
Clarify	Typical examples of data not included in the study report and what is in the report but not in the SEND data
Clarify	Clarity around the level of detail the FDA expects when citing differences between the report and datasets.
Clarify	Include a section about the tumor.xpt and it's correlation to the SEND datasets.
Clarify	I hope that the roles of nSDRG and Define-XML will be more clarified. The nSDRG should included only descriptions which Define-XMLs doesn't have, thereby saving time for creation and confirmation of nSDRGs and Define-XML and also efficiently keeping quality of them.
Clarify	Many variables/parameters are redundant or vague in their explanations. There are also situations where some study types do not fit cleanly into the SEND paradigm and more clear guidance on what to do in these instances would be helpful.
Clarify, simplify	More clarity on what is expected in validation section. Help to avoid including more detail than necessary in SDRG.
Keep FDA happy	I think it important for nSDRG to include FDA's request in order to assist efficient review; so, nSDRG is needed to timely revise according to their additional requests, such as those for describing in nSDRG the terms list for categorical and severity data and/or cautions of uses of --SUPP qualifiers especially of --CALCN. I think the current draft of nSDRG is quite well. I look forward to the release of the final version.
Keep FDA happy, simplify	Rather making it too complex, we must keep it as simple as is just providing domain level details in Sec.4 and the differences in Sec.6.1 for FDA reviewers. First of all, the FDA requirements and expectations i.e. what level of details the FDA reviewers wanted to see it in nSDRG is could to be determined. Thus, the data managers can easily understand the "purpose" of the nSDRG document and would prepare it accordingly and would also help maintaining the data consistence across the globe.
make nSDRG unneccesary	move the info to a machine readable space.
make nSDRG unneccesary	no additional enhancements to the nSDRG would be necessary, if the SENDIG was perfect and could covered every case. But if the intent is just to show and explain validation, this information may be added to define.xml. Addition of a reverse lookup index would be helpful.

Theme	Q8 continued. Are there any enhancements to the nSDRG that would make creating SEND submissions more efficient?
make nSDRG unneccesary	The nsdrg should not be the focus for enhancements for submissions...it is created after the dataset is done as an explanatory tool. Improving the dataset packages so that there needs to be less in the nsdrg would be far more effective and efficient. Improving the information surrounding what is needed in the define file (and why) would provide a better mechanism for electronic access to relevant, explanatory data. Getting agreement that the nsdrg does not need to repeat things that are already in the report or should be in the define file would be better than adding unnecessary "enhancements" to the nsdrg that make creation more manual and time consuming than it already is.
make nSDRG unneccesary	If the SENDIG was perfect and covered every case it would be unnecessary. But if the intent is just to show and explain validation, this information may be added to define.xml. Addition of a reverse lookup index would be helpful.
Organize the structure	Include tables to be filled for: Full scale for categorical results for lab tests (e.g. urinalysis), including codes used in study report. Lab tests without units MA and MI severities Standard texts / examples for dataset explanations, e.g. whether EX contains nominal doses or actual doses including references to the body weight used for the dose setting. Guidance for how much explanation is needed for mapping of LBTESTs to the study report. E.g. is it necessary to state that LBTEST Erythrocytes are named Red Blood Cell Count in the study report. Isn't this well known to the FDA reviewers already? Table to map the PK parameters in the study report to the PPTESTs in the PP domain. Table to map the compound name in the report to the compound name in the different domains, e.g. TS, EX, PC.
Remove duplicates	Remove trial design replication - feels like a duplication of work when the SEND domains relate these, removal of validation results/explanations section?
Remove duplicates	Replace the sections that can be extracted from the SEND datasets, like the table of domains, the relationship between sponsor defined group codes and the SEND's study structure, the version of SEND, the CT version, etc.
Simplify	Develop standard texts explaining that there are discrepancies between the number of decimals used in the study report and the datasets - or a guidance text stating that this is self explanatory and hence not needed.
	No ;)
	Nothing in particular.
	No
	No

Q9 I am confident in my understanding of which studies are in scope of SEND.



Q10 If not confident, which resource do you use for help?

resource	Oustanding need?	If not confident, which resource do you use for help?
CoDEX		CDISC CoDEX (Confirmed Data End Points)
CoDEX	yes	CODEX is somewhat helpful at the endpoint level.
CoDEX	yes	SENDIG, CoDEx, FDA publications, guess. Some studies are clearly in-scope, some are clearly out-of-scope, others are not clear.
CoDEX	yes	The CoDex associated with each SENDIG is what I used until I heard FDA state something different than what was in the that document.
CoDEX	yes	The codex, but this document could be significantly more clear about what is in scope and what is not.
Consultant		SEND software company
eDATA		eData Peers
eDATA		We would consider contacting the FDA/eDATA in the relevant cases (as necessary).
FDA SBIA		FDA SBIA Webinars and sessions at F2F, FDA study data standards
online sources		e.g. PhUSE and/or CDISC wiki
online sources	yes	Usually try without success looking through FDA, Phuse, and CDISC websites.
sdTCG		sdTCG
sdTCG		The TCG now has some examples, which is good. Otherwise, it would be the SBIA webinars or asking the CDER eData team by email.
	yes	I hope for a decision tree to decide whether a study is in scope of SEND or not.
	yes	None now available due to the statement made without any further clarification, previously TCG/TRC used

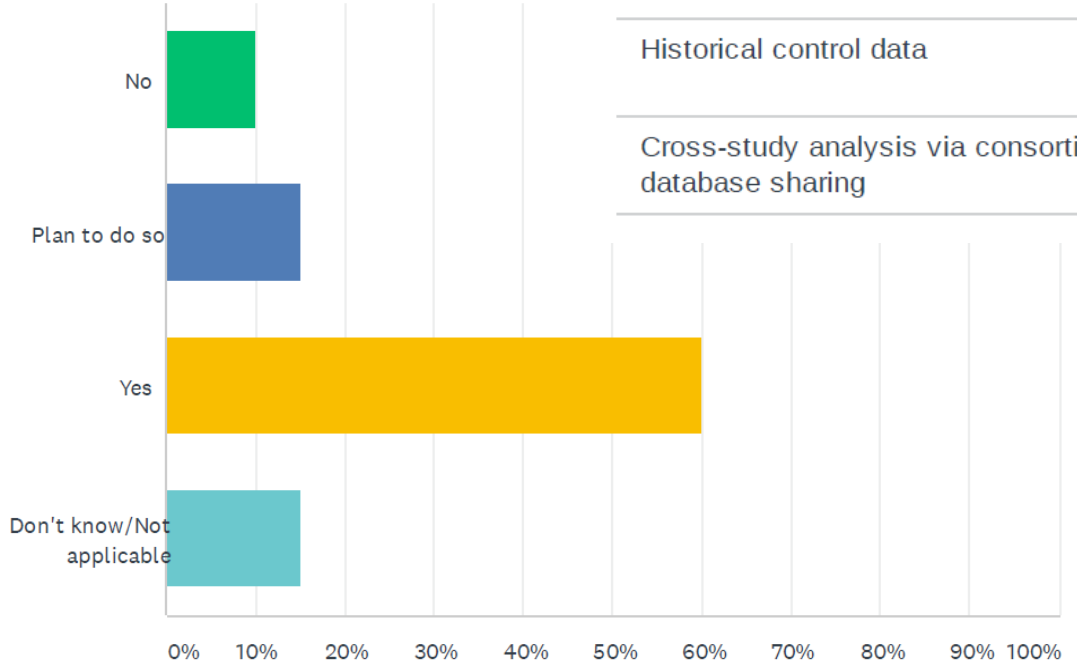
Non-submission uses of SEND

Non-submission uses of SEND Summary

- 60% respondents use SEND for non-submission purposes and another 15% plan to.
- The top 3 current uses for the data are:
  - Data analysis and/or cross-study analysis
  - Cross-study analysis via consortia database sharing
  - Project team use for study results review, discussions
- The use of SEND for historical control data looks like an upcoming area
- Almost 25% respondents use the data for translational analysis with Clinical data
- 5% thought SEND supported these uses poorly, whilst the rest were divided equally between supporting it well and being neutral
- Respondents thought that more standardization and better separation of some variables would be helpful for analysis.
- There was strong support for: increased machine readability, incorporation of nSDRG content into the DEFINE files and a standardized machine-readable study protocol/study plan template.

Q19 Beyond compiling SEND packages for FDA submissions, is your company currently using SEND datasets for other purposes, e.g. data analysis, data warehousing?

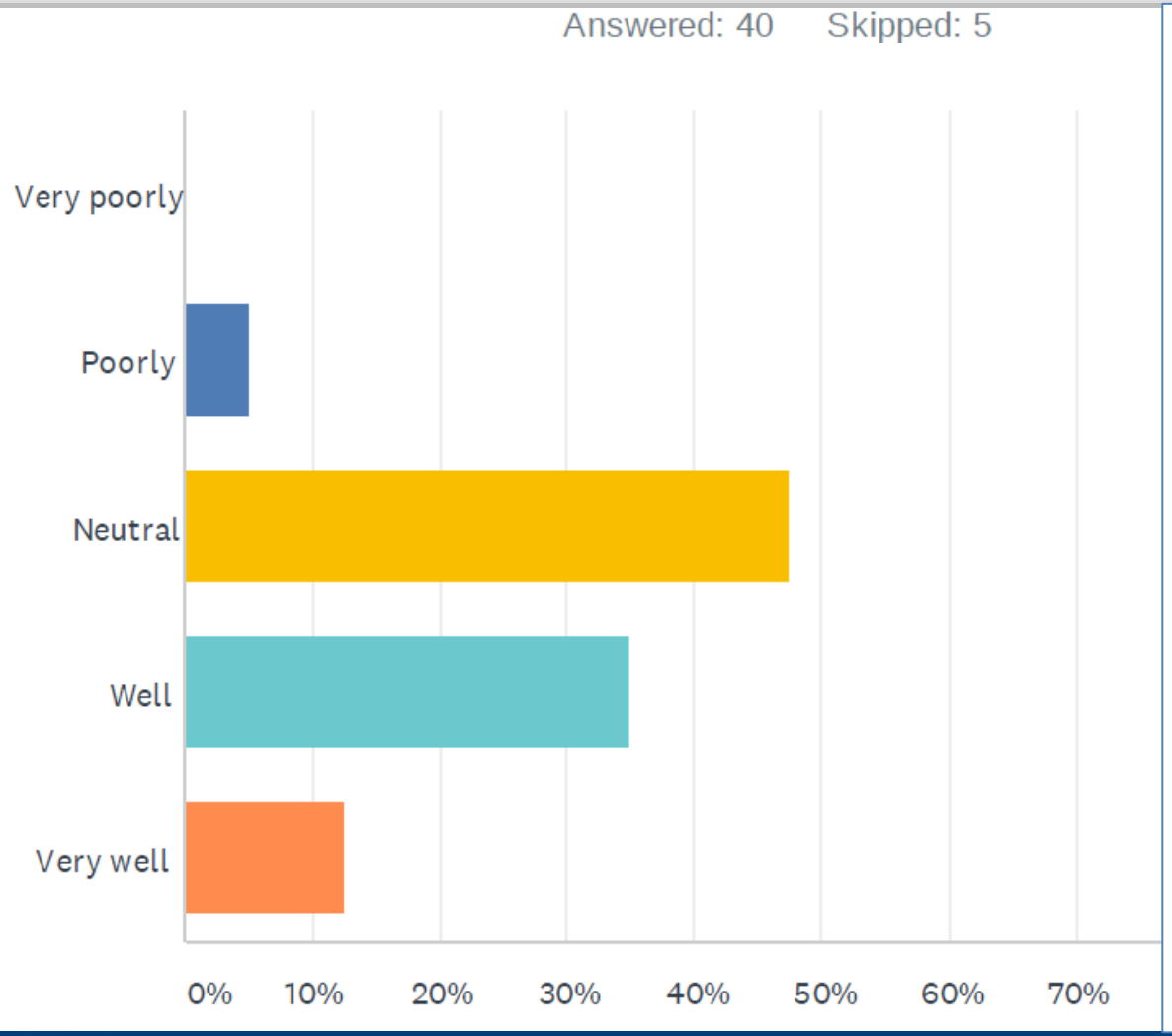
Answered: 40



Q20 Does your organization use SEND data for:

	NO	PLAN TO DO SO	YES	DON'T KNOW/NOT APPLICABLE	TOTAL	WEIGHTED AVERAGE
Data analysis and/or cross-study analysis	12.50% 5	22.50% 9	50.00% 20	15.00% 6	40	2.67
Project team use for study results review, discussions	12.82% 5	25.64% 10	41.03% 16	20.51% 8	39	2.69
Translational analysis of clinical data	30.00% 12	15.00% 6	22.50% 9	32.50% 13	40	2.58
Historical control data	23.08% 9	25.64% 10	30.77% 12	20.51% 8	39	2.49
Cross-study analysis via consortia database sharing	20.51% 8	10.26% 4	43.59% 17	25.64% 10	39	2.74

Q21 How well does the standard support these uses?

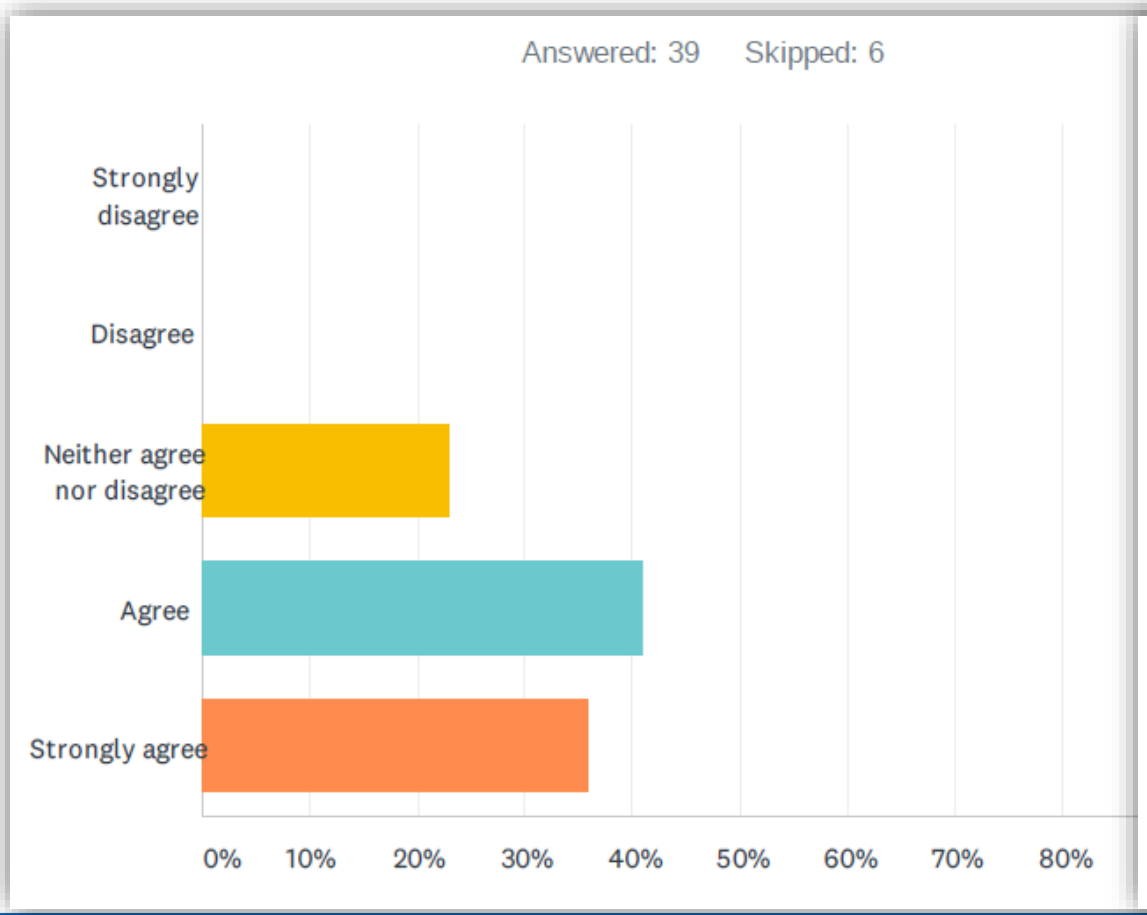


Q22 Explain why you chose this option.

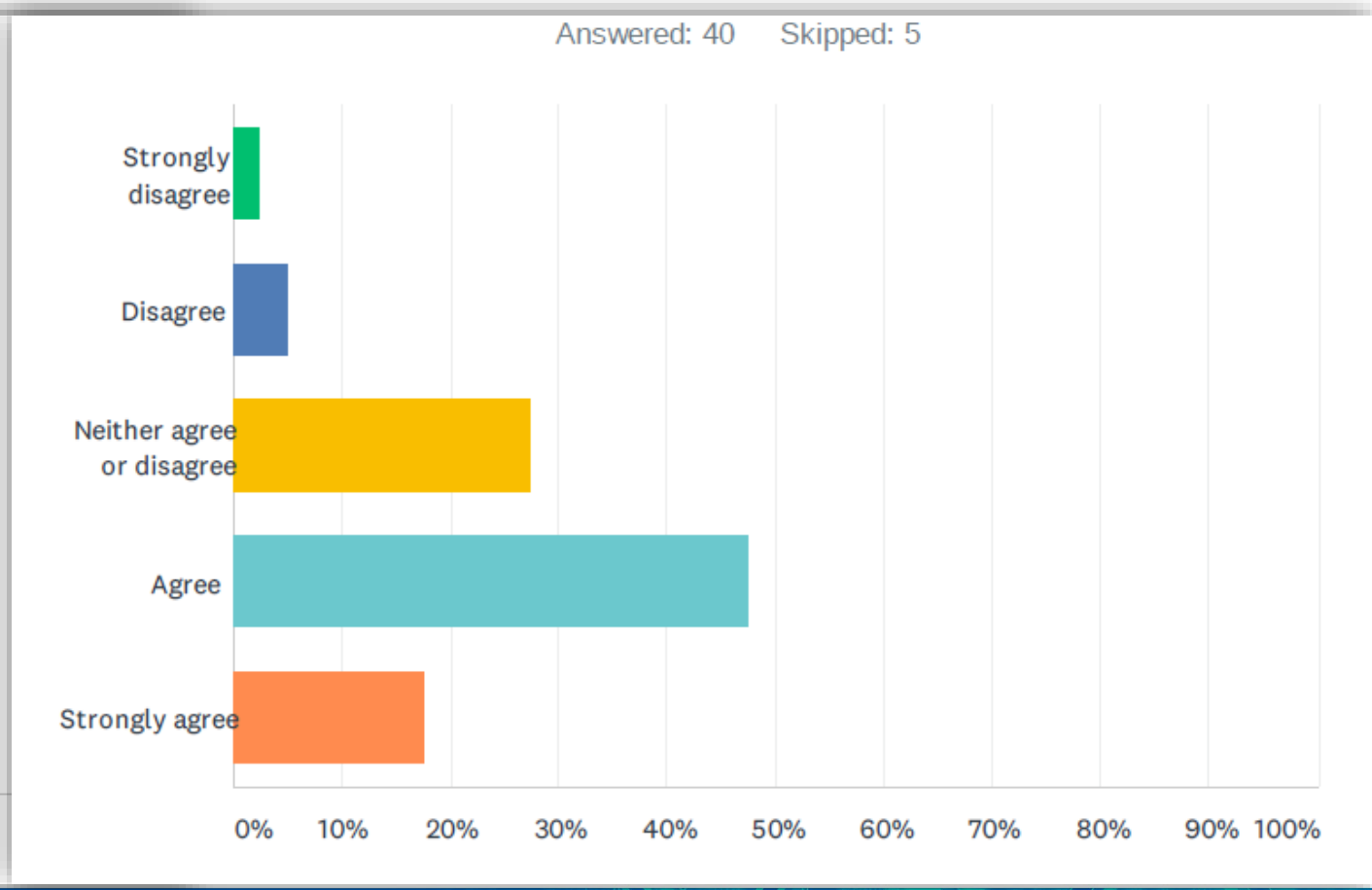
Summary of comments:

- SEND is helpful to many respondents as a vehicle for cross study analysis and information exchange.
- Respondents seem to be using a modified version of SEND for these purposes.
- Some respondents wanted to see further standardization applied to areas of the standard.

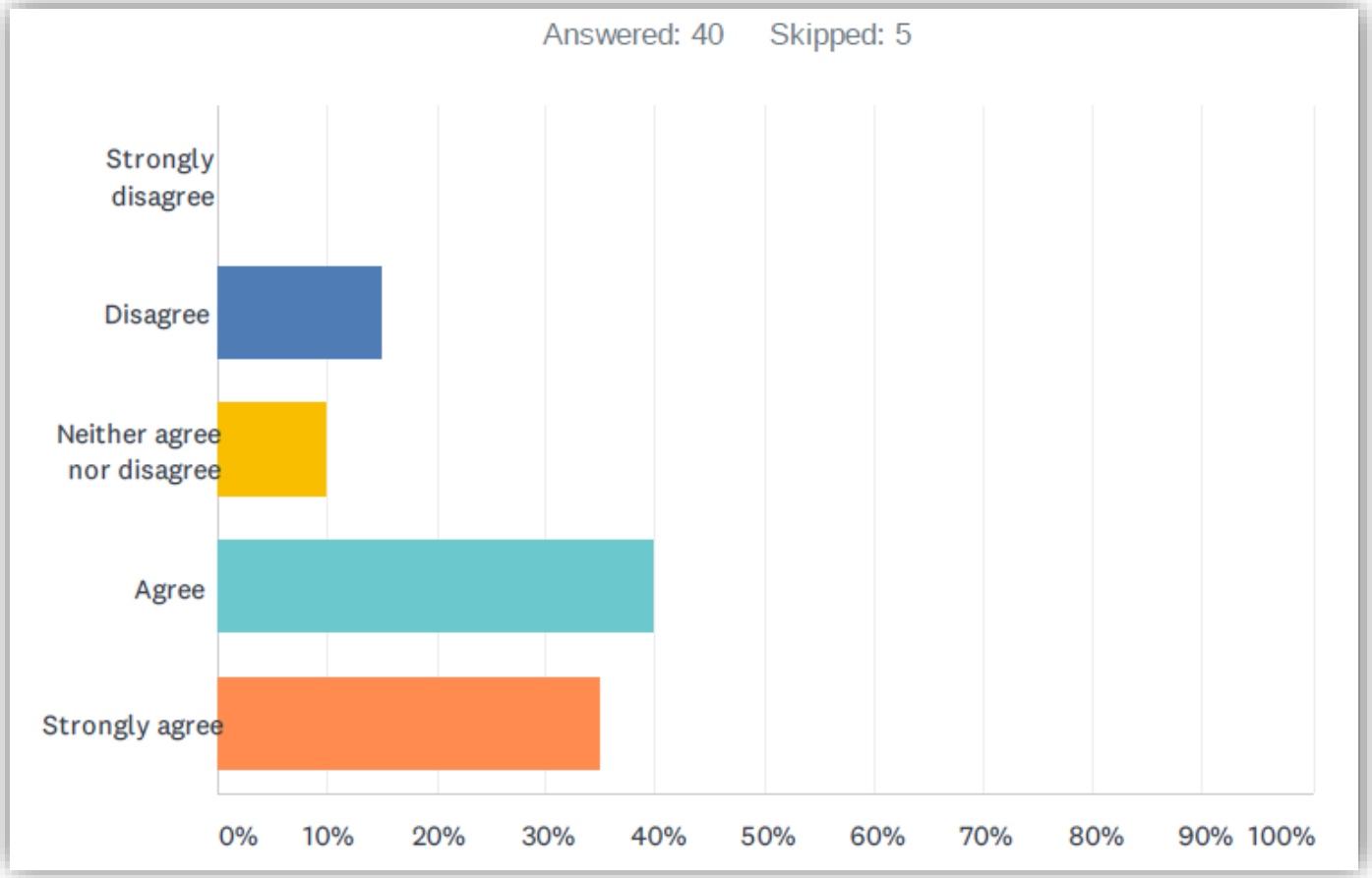
Q23 I support increased machine readability of SEND data in principle.



Q24 I support moving some elements of the nSDRG into the Define file to increase machine readability of SEND data.



Q25. I support the concept of a standardized machine-readable study protocol/study plan template.



Conclusion

- Generally, in good shape
- Pace of change is acceptable/accommodated
- Many suggestions on enhancements of IG and nSDRG
- Uncertainty remains on scope of SEND
- Significant use of SEND beyond submission and increasing
- Support of increased machine readability in principle, hints of differences in approach

Discussion

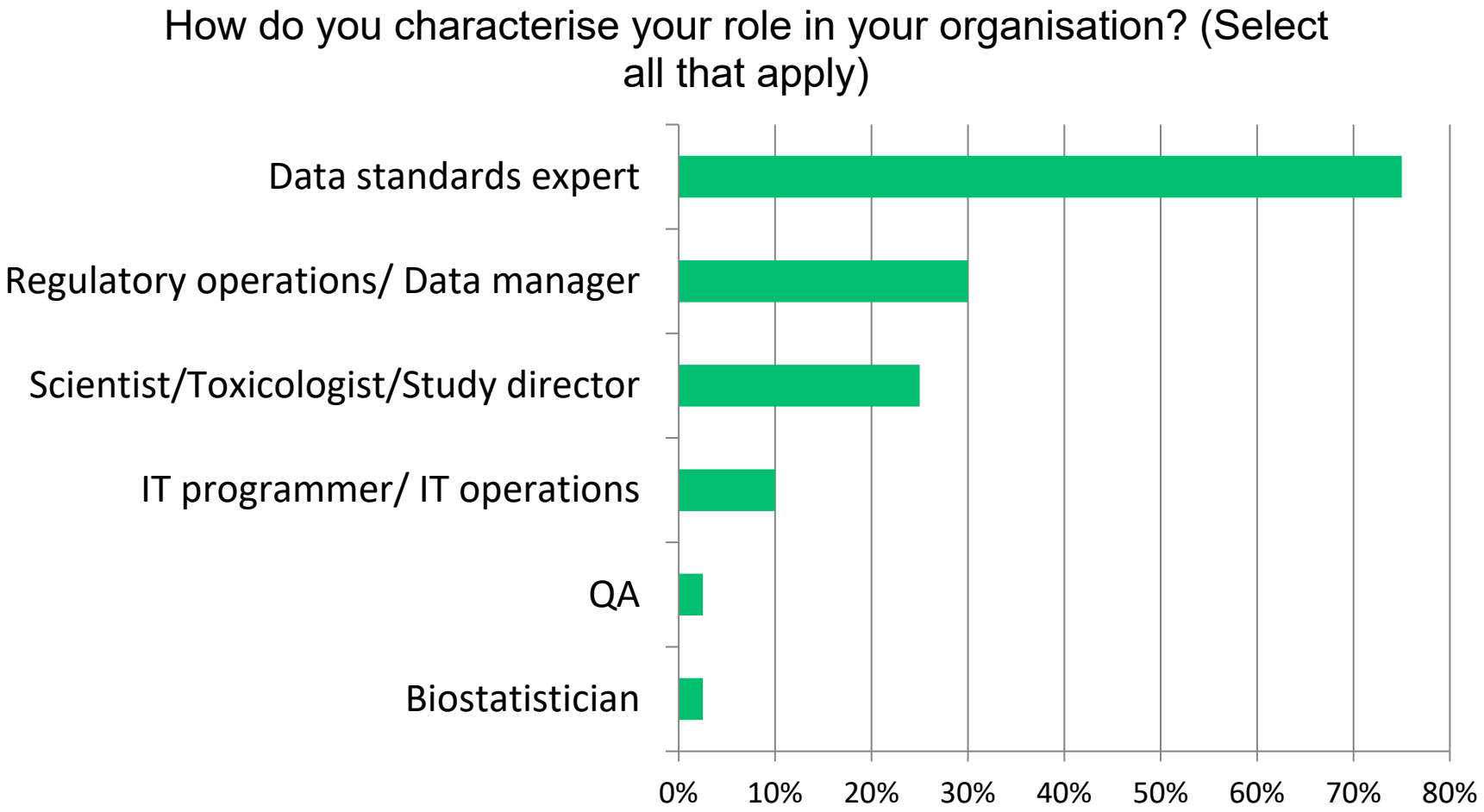
Rank these three ideas in order of priority

- Increased automation, e.g., nSDRG to define
- Increased standardization/harmonization, e.g., protocol, MI?
- Creation of Study design user guides, complete data set example? E.g. latin square

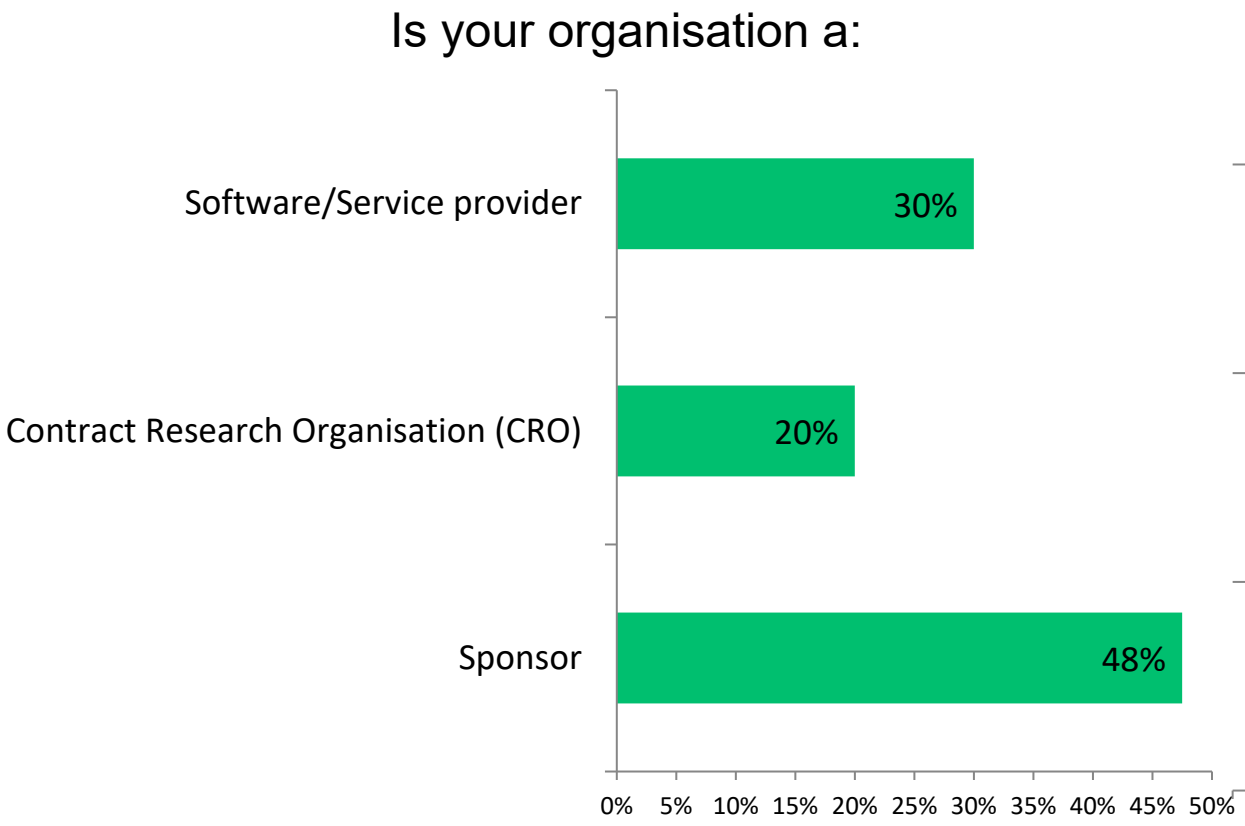
Feedback

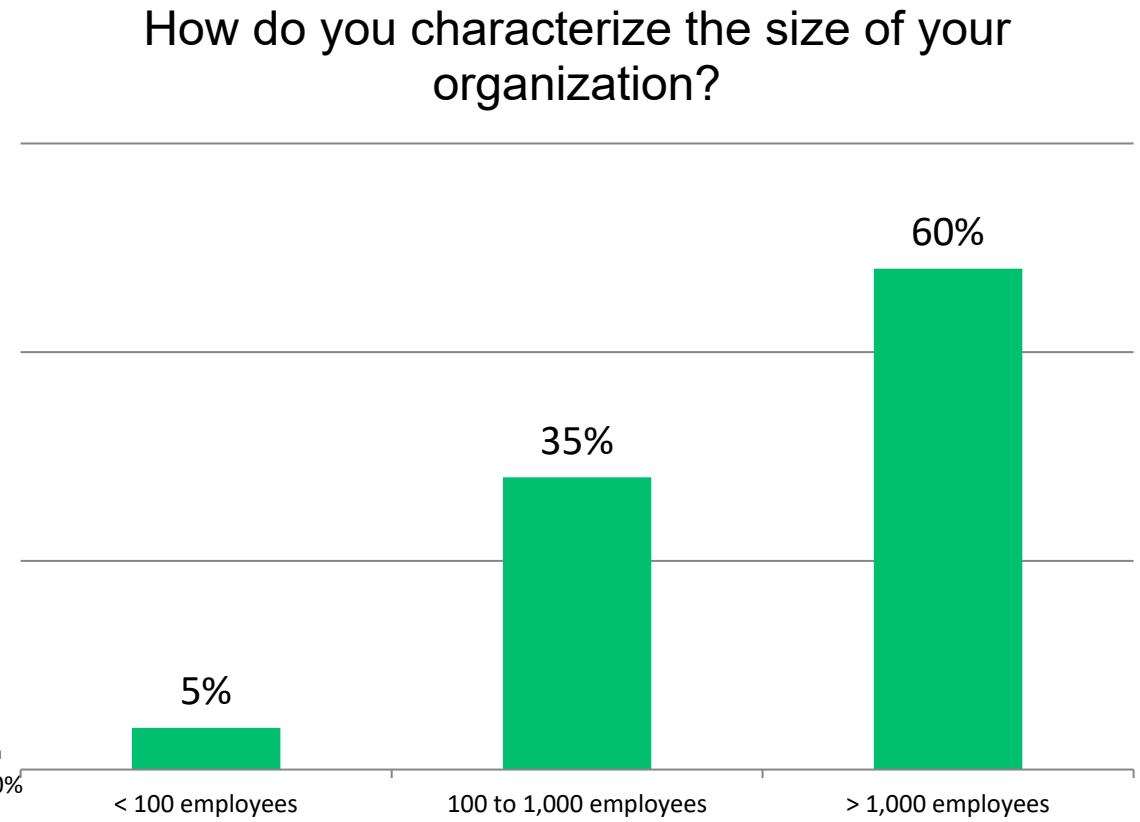
- Did you like the new survey topics?
- What do you want to talk about?
- Email –workinggroups@phuse.global

Role of Respondents, n=45



Demographics





Demographics

Belgium
Denmark
France
Germany
Japan
Switzerland
The Netherlands
UK
USA