

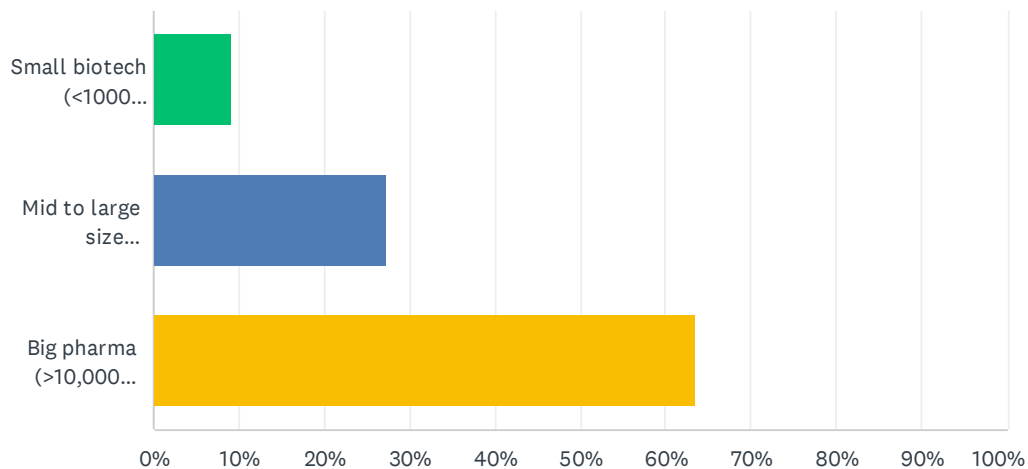
## Q1 Please provide your company identifying code provided to you by Julian Arbuckle:

Answered: 10   Skipped: 1

#	RESPONSES	DATE
1	2276	6/14/2022 10:07 PM
2	8871	6/13/2022 3:16 AM
3	2999	6/10/2022 5:13 PM
4	2772	6/10/2022 4:31 PM
5	7755	6/10/2022 6:13 AM
6	8008	6/7/2022 5:12 PM
7	7333	6/7/2022 12:57 PM
8	4099	6/7/2022 12:22 PM
9	2299	6/2/2022 8:06 PM
10	3444	5/20/2022 2:03 PM

## Q2 What type of company are you representing? [Multiple choice, one answer]:

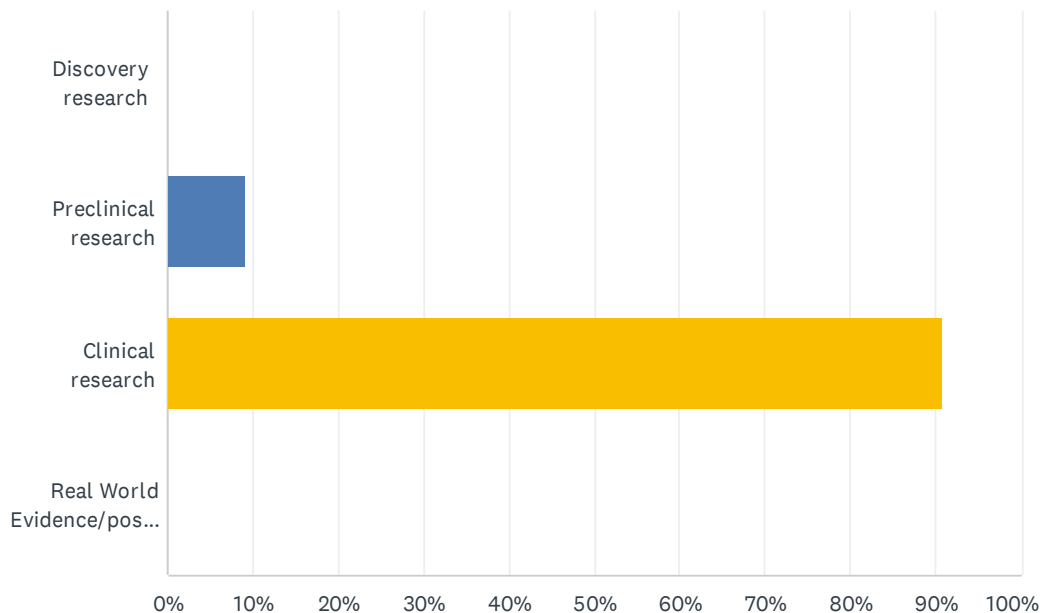
Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
Small biotech (<1000 employees)	9.09%	1
Mid to large size biotechnology (>1000 - ≤10,000 employees)	27.27%	3
Big pharma (>10,000 employees)	63.64%	7
TOTAL		11

### Q3 What is your most common stage of data that you work on within the company? [multiple choice, one answer]

Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
Discovery research	0.00%	0
Preclinical research	9.09%	1
Clinical research	90.91%	10
Real World Evidence/post-approval	0.00%	0
TOTAL		11

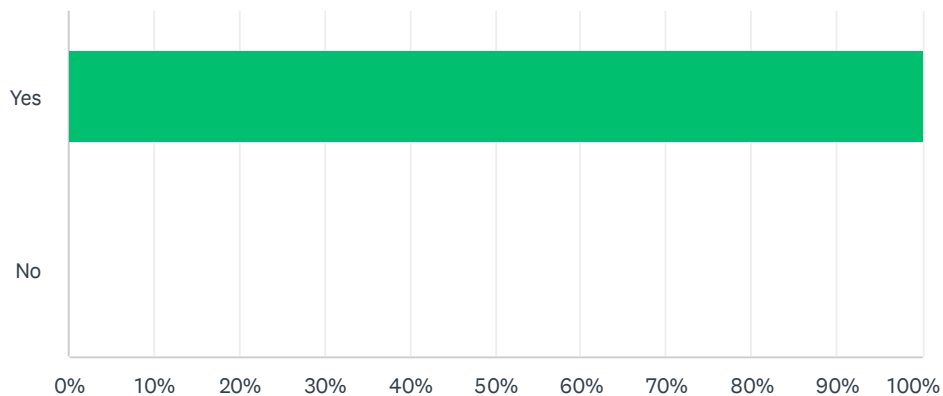
## Q4 In broad terms, what role best describes your position at the company (e.g. statistical geneticist?) [open text]

Answered: 11 Skipped: 0

#	RESPONSES	DATE
1	Bridging discovery and preclinical work to ensure clinical readiness of preclinical assets	6/14/2022 10:07 PM
2	Specimen Management/Informed Consent/Bioinformatics Research	6/13/2022 3:16 AM
3	supporting inclusion of broad PGx analysis in clinical studies	6/10/2022 5:13 PM
4	Genetics lab scientist; biomarker lead; biospecimen oversight head; bioinformaticist	6/10/2022 4:31 PM
5	Biomarker specialist	6/10/2022 6:13 AM
6	Pharmacogenomics head	6/7/2022 5:12 PM
7	Biomarker/PGx SME	6/7/2022 12:57 PM
8	Analysis of clinical trial genomic data	6/7/2022 12:22 PM
9	Clinical geneticist	6/2/2022 8:06 PM
10	Consent management expert, with a focus on consent for genetic analysis	5/20/2022 2:03 PM
11	genomic Operational Expert	5/20/2022 8:34 AM

## Q5 Is your company currently using (internally or externally sourced) Next Generation Sequencing (NGS) technologies for clinical PGx studies?

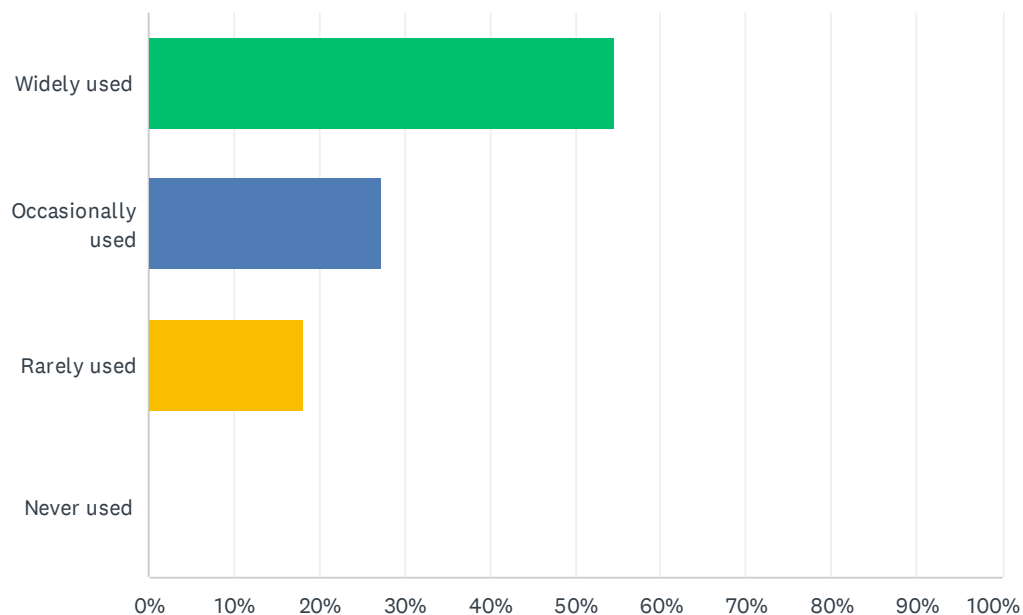
Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
Yes	100.00%	11
No	0.00%	0
TOTAL		11

## Q6 How often does your company currently use NGS technologies for clinical PGx studies? [Multiple choice, choose one answer]

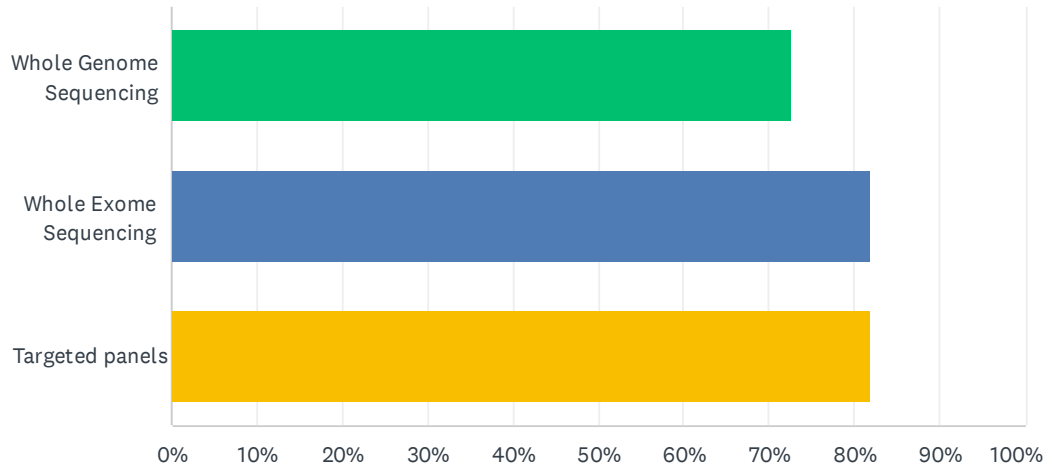
Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
Widely used	54.55%	6
Occasionally used	27.27%	3
Rarely used	18.18%	2
Never used	0.00%	0
TOTAL		11

## Q7 For DNA sequencing, what approaches are being used? [Check all that apply]

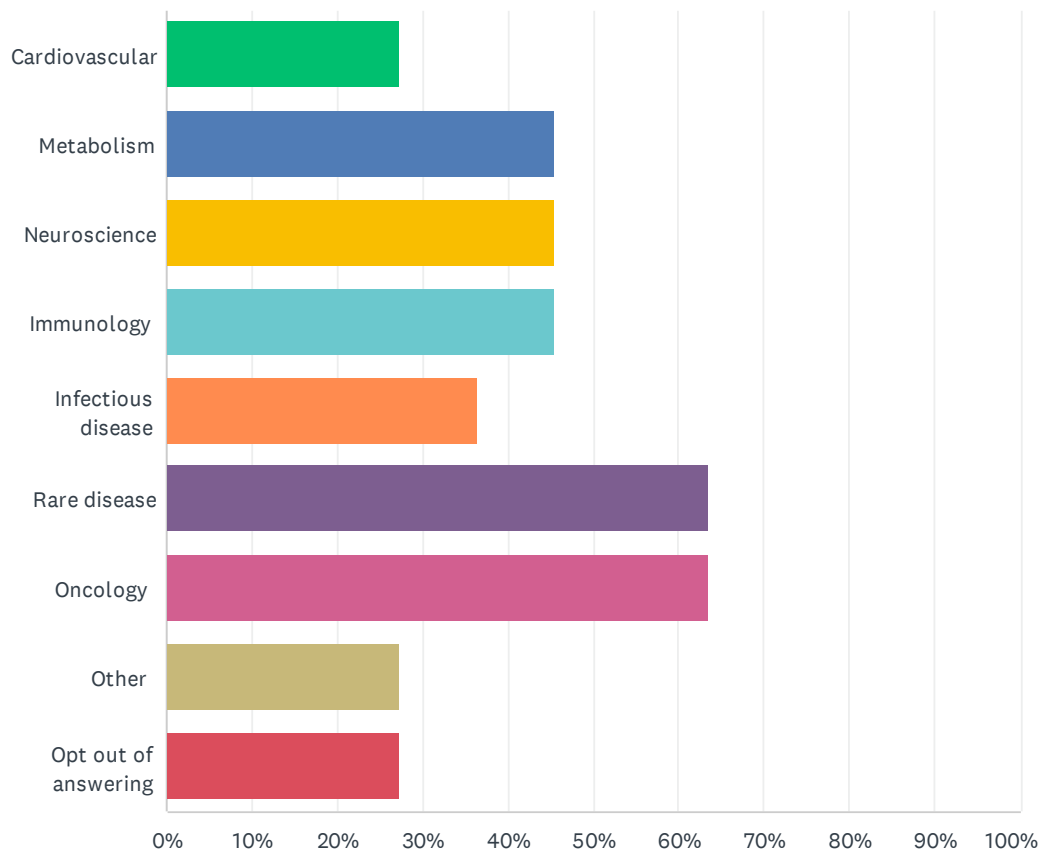
Answered: 11   Skipped: 0



ANSWER CHOICES	RESPONSES	
Whole Genome Sequencing	72.73%	8
Whole Exome Sequencing	81.82%	9
Targeted panels	81.82%	9
Total Respondents: 11		

## Q8 Which indications are using NGS for clinical PGx studies at your company? [Check all that apply]

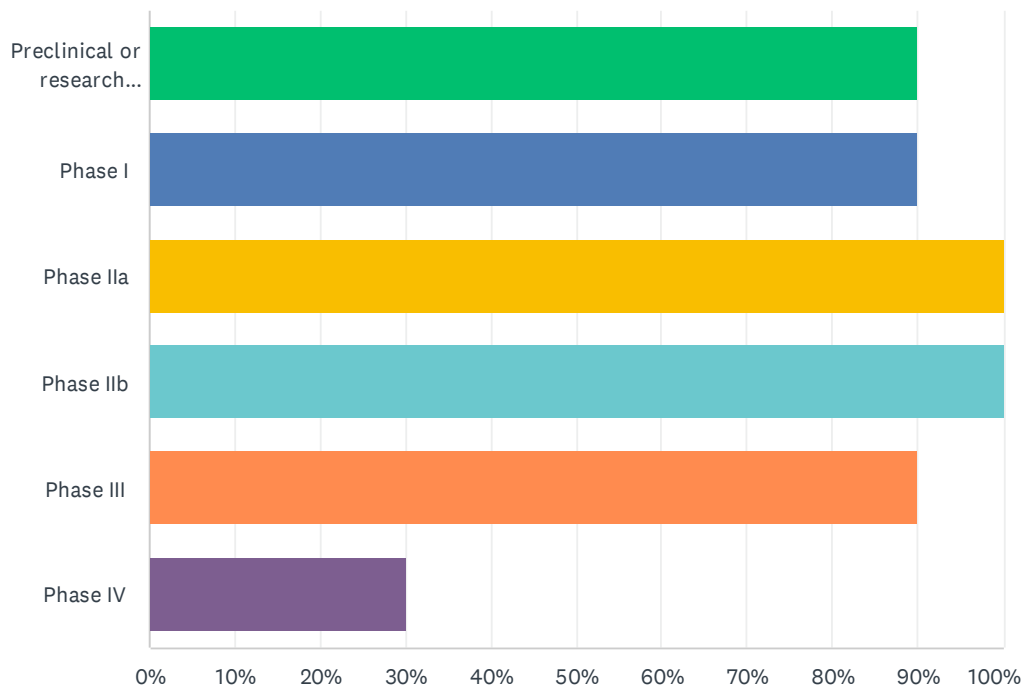
Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
Cardiovascular	27.27%	3
Metabolism	45.45%	5
Neuroscience	45.45%	5
Immunology	45.45%	5
Infectious disease	36.36%	4
Rare disease	63.64%	7
Oncology	63.64%	7
Other	27.27%	3
Opt out of answering	27.27%	3
Total Respondents: 11		

## Q9 Which phases of clinical development have utilized NGS technologies at your company? [Check all that apply]

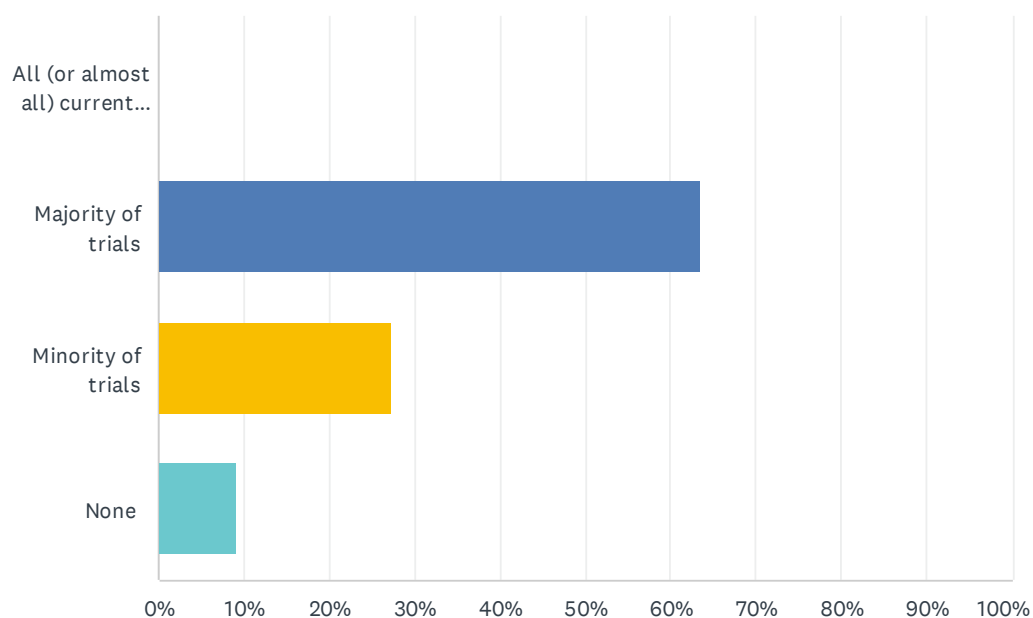
Answered: 10 Skipped: 1



ANSWER CHOICES	RESPONSES	
Preclinical or research focused	90.00%	9
Phase I	90.00%	9
Phase IIa	100.00%	10
Phase IIb	100.00%	10
Phase III	90.00%	9
Phase IV	30.00%	3
Total Respondents: 10		

## Q10 To what extent are you using WES/WGS in your trials? [Choose one]

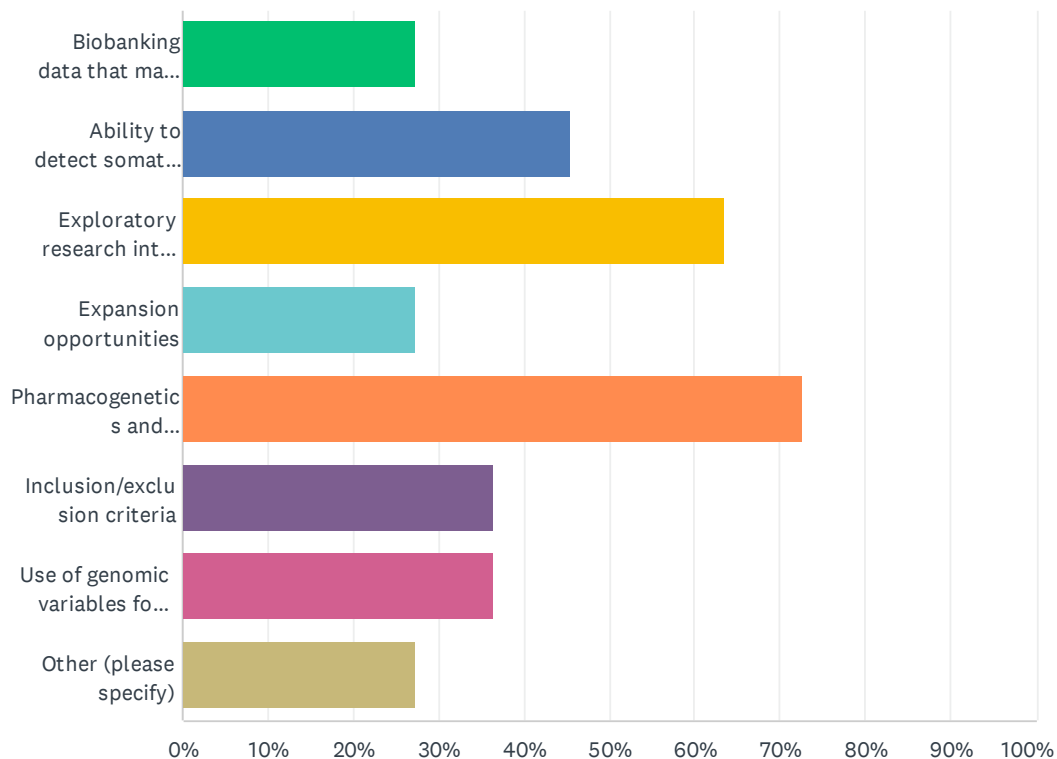
Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
All (or almost all) current trials	0.00%	0
Majority of trials	63.64%	7
Minority of trials	27.27%	3
None	9.09%	1
TOTAL		11

## Q11 What are your main motivations for generating WES/WGS in trials? [Select all that apply]

Answered: 11 Skipped: 0

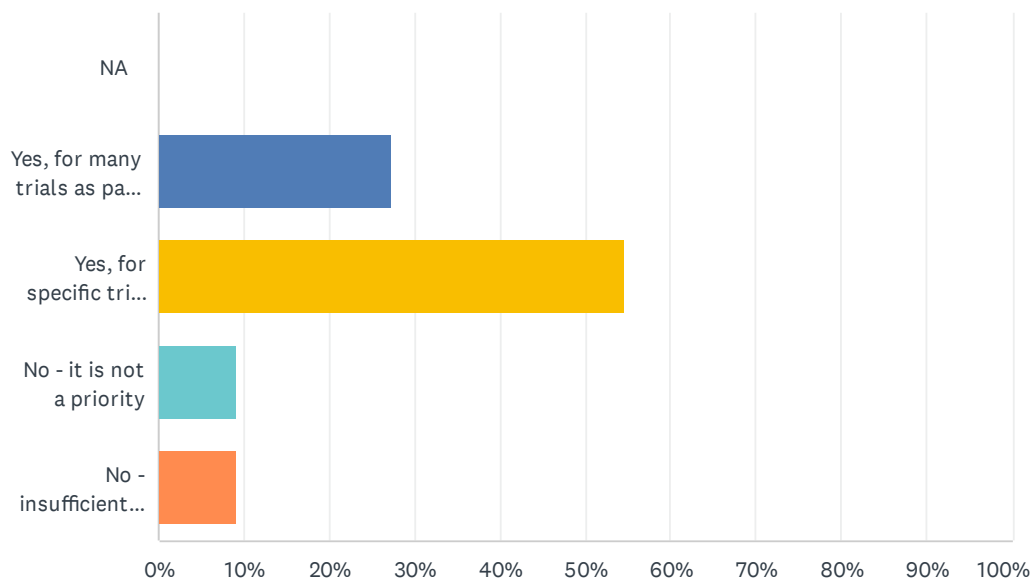


ANSWER CHOICES	RESPONSES	
Biobanking data that may be hard to retrieve later	27.27%	3
Ability to detect somatic mutations	45.45%	5
Exploratory research into disease/new targets	63.64%	7
Expansion opportunities	27.27%	3
Pharmacogenetics and predicting response	72.73%	8
Inclusion/exclusion criteria	36.36%	4
Use of genomic variables for stratification/covariates in trial	36.36%	4
Other (please specify)	27.27%	3
Total Respondents: 11		

#	OTHER (PLEASE SPECIFY)	DATE
1	Monitoring pharmacodynamic response	6/10/2022 4:31 PM
2	NA	6/10/2022 6:13 AM
3	investigation with multiple scope from the above	5/20/2022 8:34 AM

## Q12 Is WES/WGS data being generated retrospectively in older completed studies? [Choose one]

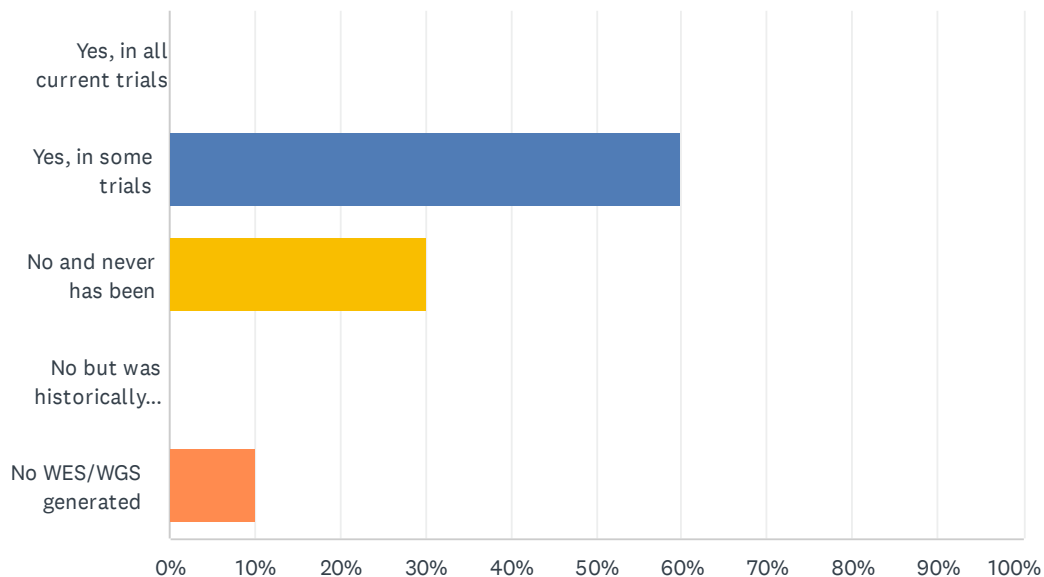
Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
NA	0.00%	0
Yes, for many trials as part of broader company wide effort	27.27%	3
Yes, for specific trials when a specific question arises	54.55%	6
No - it is not a priority	9.09%	1
No - insufficient samples/consent etc.	9.09%	1
TOTAL		11

## Q13 Is taking part in WES/WGS ever mandatory for participant inclusion into a trial? [Choose one]

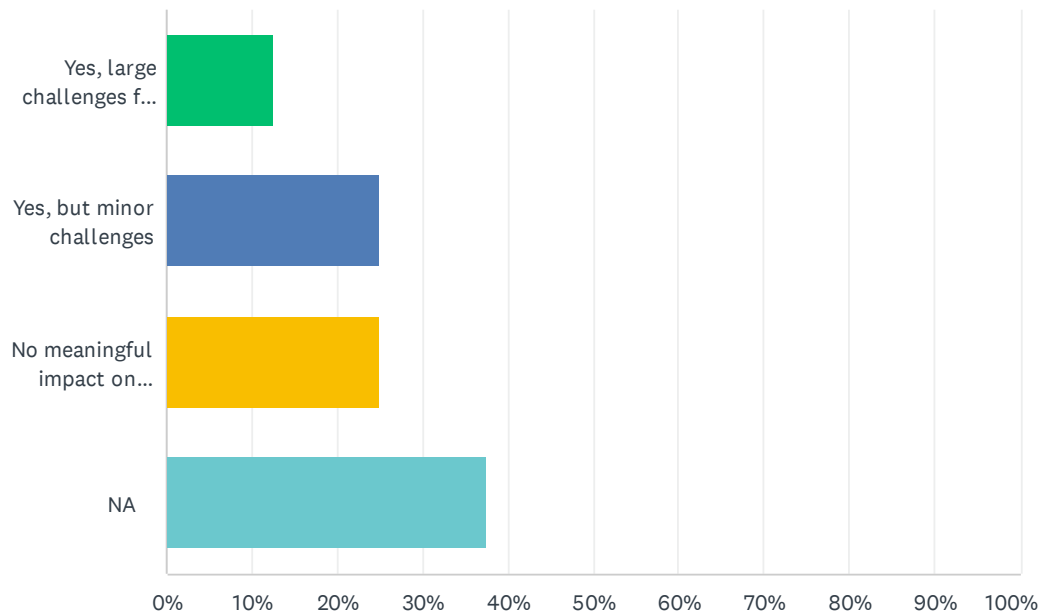
Answered: 10   Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes, in all current trials	0.00%	0
Yes, in some trials	60.00%	6
No and never has been	30.00%	3
No but was historically the case	0.00%	0
No WES/WGS generated	10.00%	1
TOTAL		10

**Q14 If you answered "Yes" to Q13, did mandatory WES/WGS cause a significant challenge to recruitment into trials? (more than any other form of genetic data collection) [Select one option]**

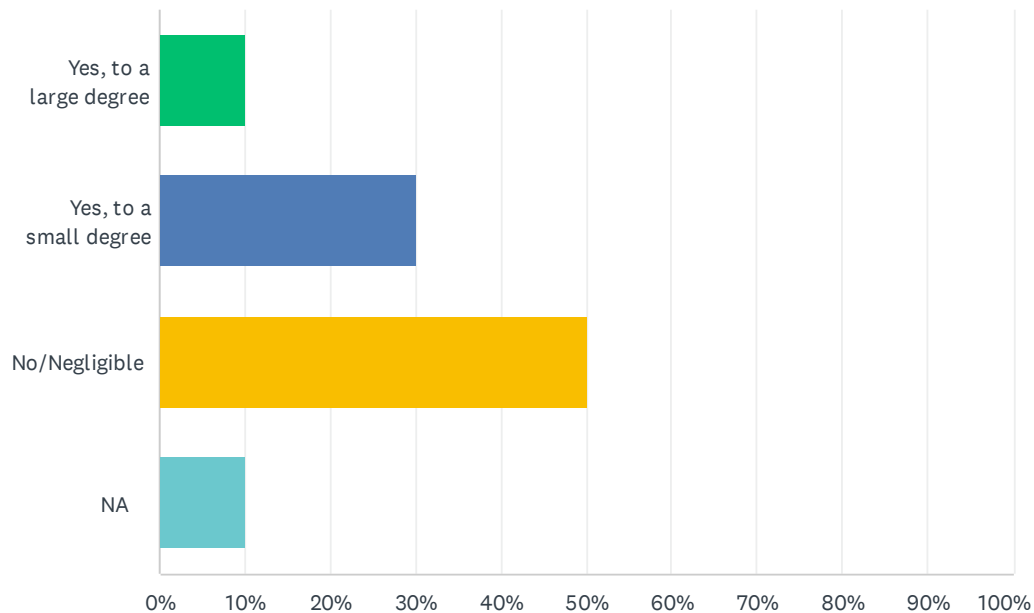
Answered: 8   Skipped: 3



ANSWER CHOICES	RESPONSES	
Yes, large challenges for recruitment	12.50%	1
Yes, but minor challenges	25.00%	2
No meaningful impact on recruitment	25.00%	2
NA	37.50%	3
TOTAL		8

**Q15 In general, when requesting WES/WGS in trials does it lead to reduced uptake of enrolment in the trial, or other logistical challenges?**  
[Select one option]

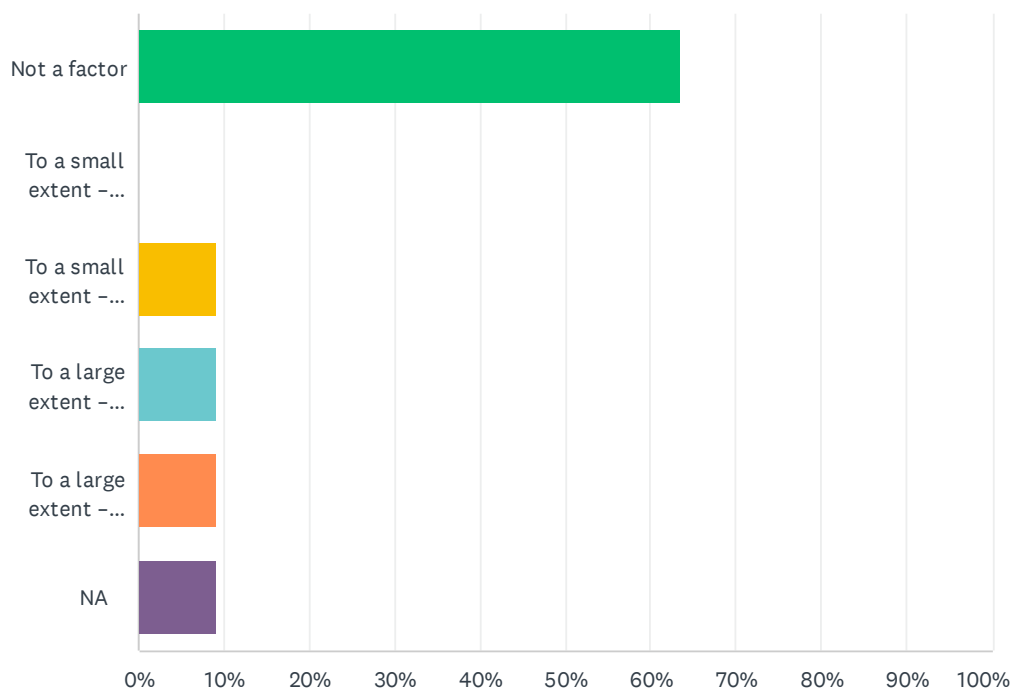
Answered: 10 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes, to a large degree	10.00%	1
Yes, to a small degree	30.00%	3
No/Negligible	50.00%	5
NA	10.00%	1
Total Respondents: 10		

# Q16 To what extent have the American College of Medical Genetics' guidelines for returning genomic results to participants influenced your decision to include WES/WGS in trials? [Select one option]

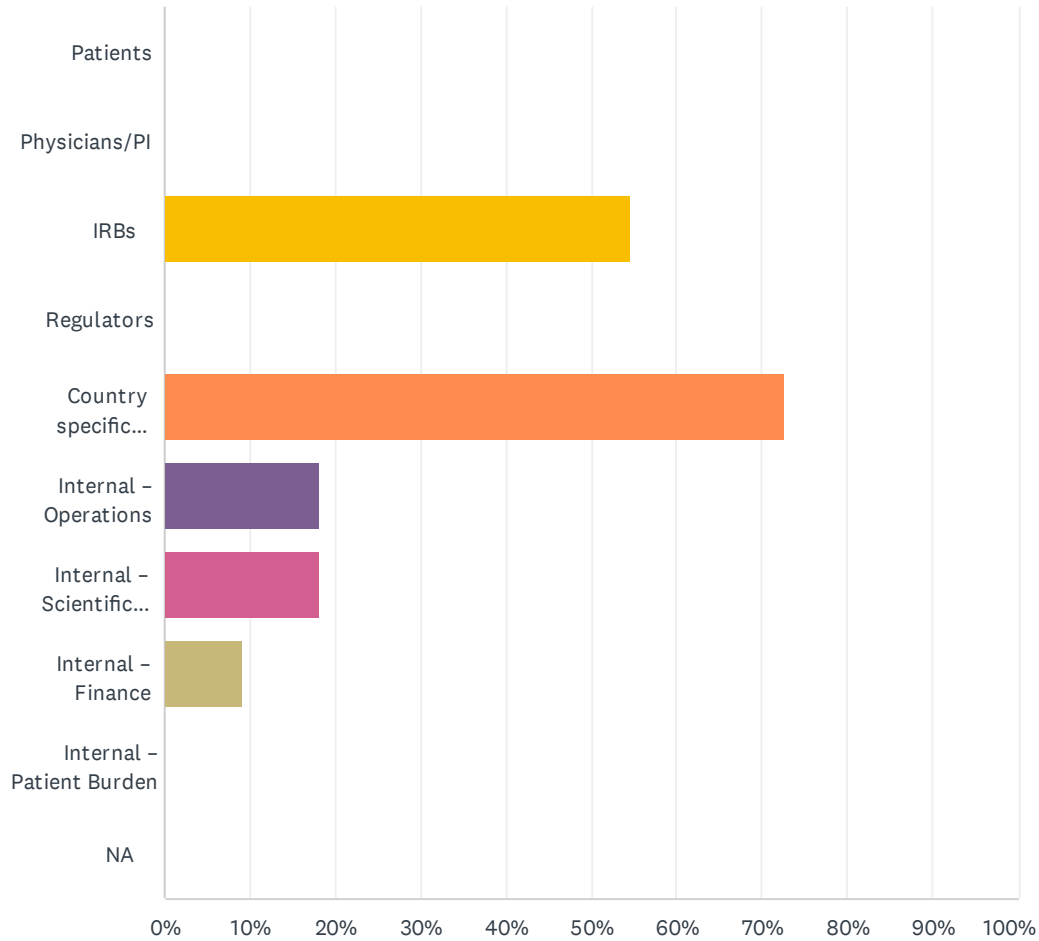
Answered: 11 Skipped: 0



ANSWER CHOICES	RESPONSES	
Not a factor	63.64%	7
To a small extent – increasing likelihood of WES/WGS use	0.00%	0
To a small extent – decreasing likelihood of WES/WGS use	9.09%	1
To a large extent – increasing likelihood of WES/WGS use	9.09%	1
To a large extent – decreasing likelihood of WES/WGS use	9.09%	1
NA	9.09%	1
Total Respondents: 11		

## Q17 Where do you receive the most pushback around inclusion of WES/WGS in trials? [One choice]

Answered: 11 Skipped: 0



## WGS in Clinical Trials - BioMarin Company Survey

ANSWER CHOICES	RESPONSES	
Patients	0.00%	0
Physicians/PI	0.00%	0
IRBs	54.55%	6
Regulators	0.00%	0
Country specific laws/guidelines	72.73%	8
Internal – Operations	18.18%	2
Internal – Scientific rationale	18.18%	2
Internal – Finance	9.09%	1
Internal – Patient Burden	0.00%	0
NA	0.00%	0
Total Respondents: 11		

## Q18 Are there any common pushbacks from patients around WES/WGS?

[Free text]

Answered: 6   Skipped: 5

#	RESPONSES	DATE
1	Not aware of any	6/14/2022 10:07 PM
2	None directly from patients	6/13/2022 3:16 AM
3	No	6/10/2022 4:31 PM
4	NA	6/10/2022 6:13 AM
5	Not of which I am aware	6/7/2022 12:57 PM
6	Concerns about local IRBs/rules making it difficult - and that impacting clinical operations.	6/7/2022 12:22 PM

## Q19 Are there any common pushbacks from sites/IRBs around WES/WGS? [Free text]

Answered: 8   Skipped: 3

#	RESPONSES	DATE
1	Not so far	6/14/2022 10:07 PM
2	when considering optional WES/WGS, there are requests to return results of clinical significance	6/10/2022 5:13 PM
3	Yes. Pushback due to sensitivity of genetic information.	6/10/2022 4:31 PM
4	NA	6/10/2022 6:13 AM
5	Scope of use, patient privacy protection, access to data and how incidental findings would be managed	6/7/2022 12:57 PM
6	Restrictions on use of samples for WGS, whether it is scientifically justified, return of results.	6/7/2022 12:22 PM
7	- some countries require that this is optional for study participants. Others require that the scope of use of generated data is restricted to research on the disease under investigation in the trial. Countries in EU ask that study participants be informed of incidental findings.	5/20/2022 2:03 PM
8	Ethic Committees	5/20/2022 8:34 AM

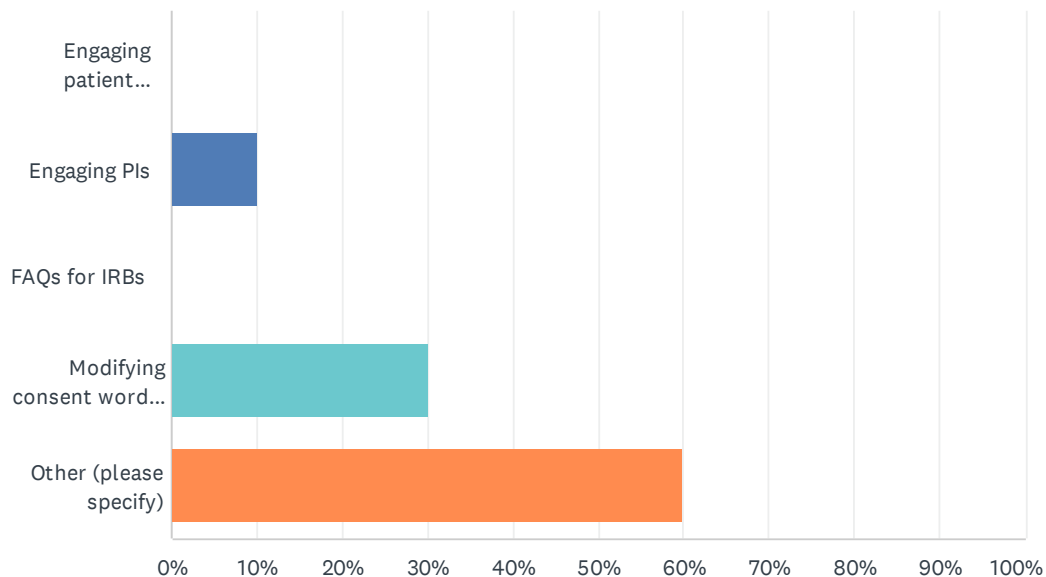
## Q20 Are there any particular countries where you have difficulty implementing WES/WGS? [Free text]

Answered: 10    Skipped: 1

#	RESPONSES	DATE
1	In the process of expanding into Europe i.e. at present no experience outside of North America	6/14/2022 10:07 PM
2	Yes, China, Turkey, Japan, Denmark, Israel.	6/13/2022 3:16 AM
3	Excluding countries which require return of results - Taiwan also requires lists of the genes which will be analysed	6/10/2022 5:13 PM
4	Turkey; China	6/10/2022 4:31 PM
5	NA	6/10/2022 6:13 AM
6	Turkey and Canada have both pushed back regarding potential WES/WGS even when optional	6/7/2022 12:57 PM
7	South Africa, Brazil, Taiwan	6/7/2022 12:22 PM
8	China, mostly.	6/2/2022 8:06 PM
9	Difficulties if WGS is mandatory for broad scope of research - very much challenged in Spain and other EU countries	5/20/2022 2:03 PM
10	yes	5/20/2022 8:34 AM

## Q21 Have you identified any particularly successful strategies for increasing patient uptake of WES/WGS? [Multiple choice]

Answered: 10 Skipped: 1

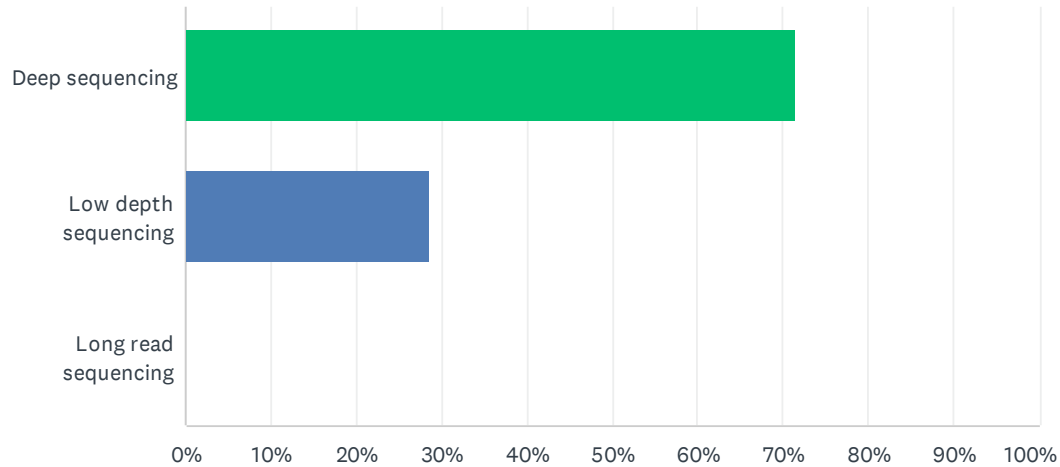


ANSWER CHOICES	RESPONSES	
Engaging patient advocacy groups	0.00%	0
Engaging PIs	10.00%	1
FAQs for IRBs	0.00%	0
Modifying consent wording to clarify risks/reason for research	30.00%	3
Other (please specify)	60.00%	6
<b>TOTAL</b>		<b>10</b>

#	OTHER (PLEASE SPECIFY)	DATE
1	Too early to tell	6/14/2022 10:07 PM
2	Both FAQs for IRBs and modifying consent wording	6/13/2022 3:16 AM
3	Multiple choice function not working - Engaging PI, FAQ for IRB and Modifying consent wording	6/10/2022 5:13 PM
4	No; patient uptake has not been a big issue for us	6/10/2022 4:31 PM
5	NA	6/10/2022 6:13 AM
6	Engaging PIs, FAQs for IRBs [multiple choice did not work]	6/7/2022 12:22 PM

## Q22 Which methods do you use for WES/WGS in clinical trials? [Select all that apply]

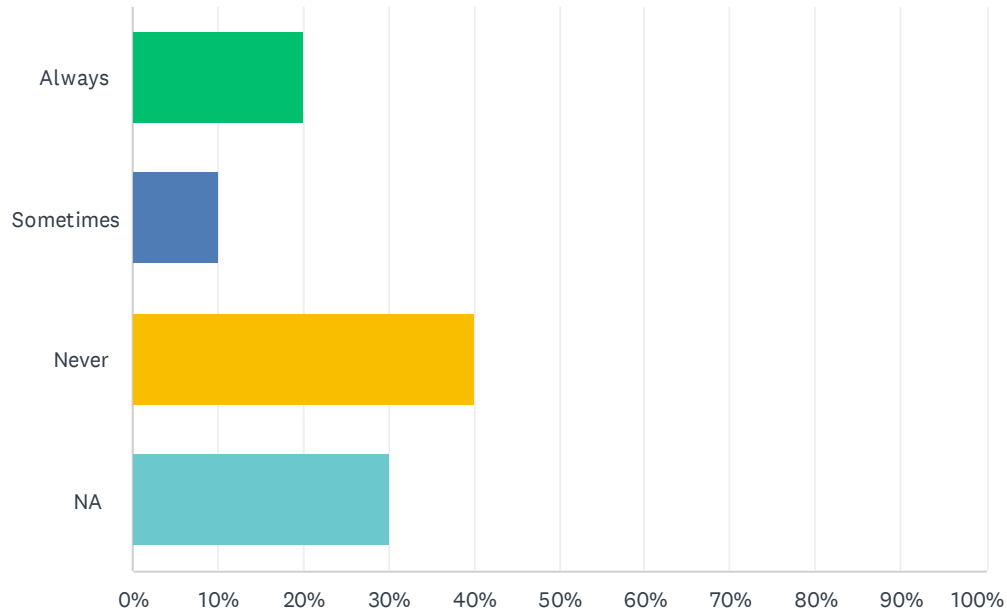
Answered: 7   Skipped: 4



ANSWER CHOICES	RESPONSES	
Deep sequencing	71.43%	5
Low depth sequencing	28.57%	2
Long read sequencing	0.00%	0
TOTAL		7

## Q23 Do you generate WES/WGS to a CLIA standard or equivalent? [Select one]

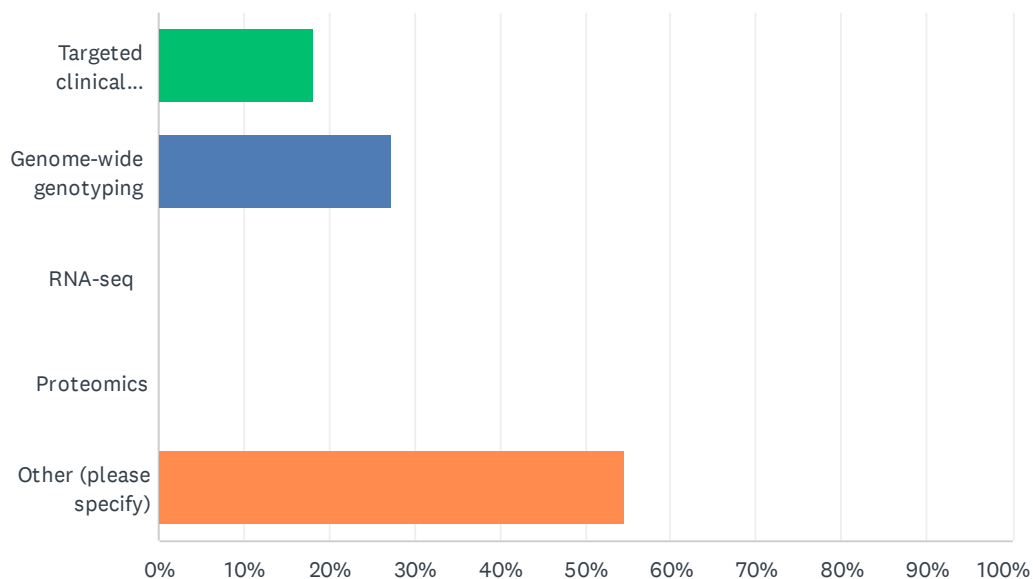
Answered: 10 Skipped: 1



ANSWER CHOICES	RESPONSES	
Always	20.00%	2
Sometimes	10.00%	1
Never	40.00%	4
NA	30.00%	3
TOTAL		10

## Q24 Do you generate WES/WGS alongside other data? [select all that apply]

Answered: 11 Skipped: 0

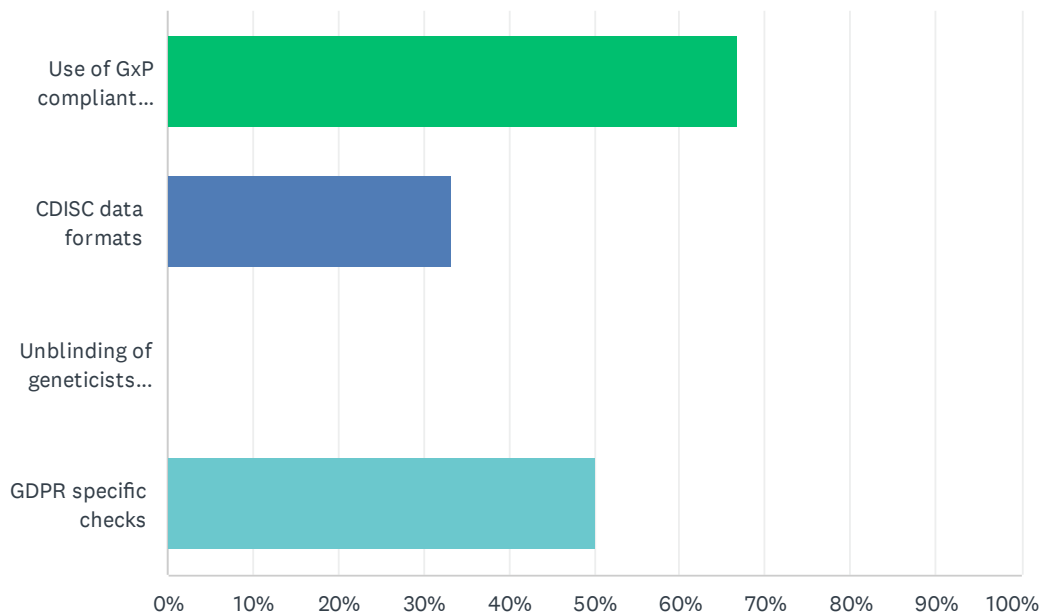


ANSWER CHOICES	RESPONSES	
Targeted clinical genotyping/gene panels	18.18%	2
Genome-wide genotyping	27.27%	3
RNA-seq	0.00%	0
Proteomics	0.00%	0
Other (please specify)	54.55%	6
TOTAL		11

#	OTHER (PLEASE SPECIFY)	DATE
1	All of the above	6/13/2022 3:16 AM
2	Multiple choice not working - Targeted panel, RNA-seq and proteomics	6/10/2022 5:13 PM
3	Question will not allow multiple choice. Answer is: Targeted panels + RNAseq + Proteomics + Metabolomics	6/10/2022 4:31 PM
4	NA	6/10/2022 6:13 AM
5	RNA-seq and proteomics (survey wouldn't let me check the 2 boxes)	6/7/2022 12:57 PM
6	All of the above	6/7/2022 12:22 PM

## Q25 Which data management processes do you include for WES/WGS data from clinical trials? [Select all that apply]

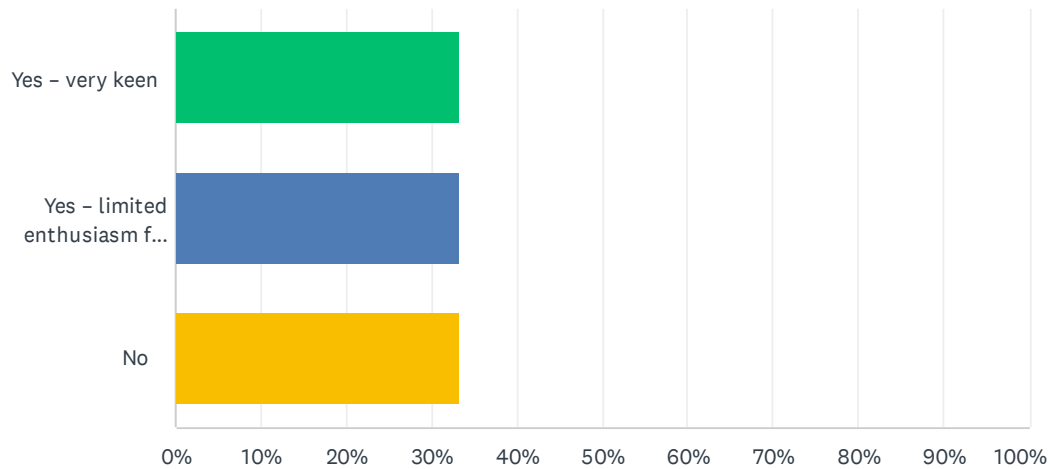
Answered: 6 Skipped: 5



ANSWER CHOICES	RESPONSES	
Use of GxP compliant platforms	66.67%	4
CDISC data formats	33.33%	2
Unblinding of geneticists prior to end of trial	0.00%	0
GDPR specific checks	50.00%	3
Total Respondents: 6		

## Q26 Is there appetite to share genomic data from clinical trials as part of cross-industry collaborations? [Select one]

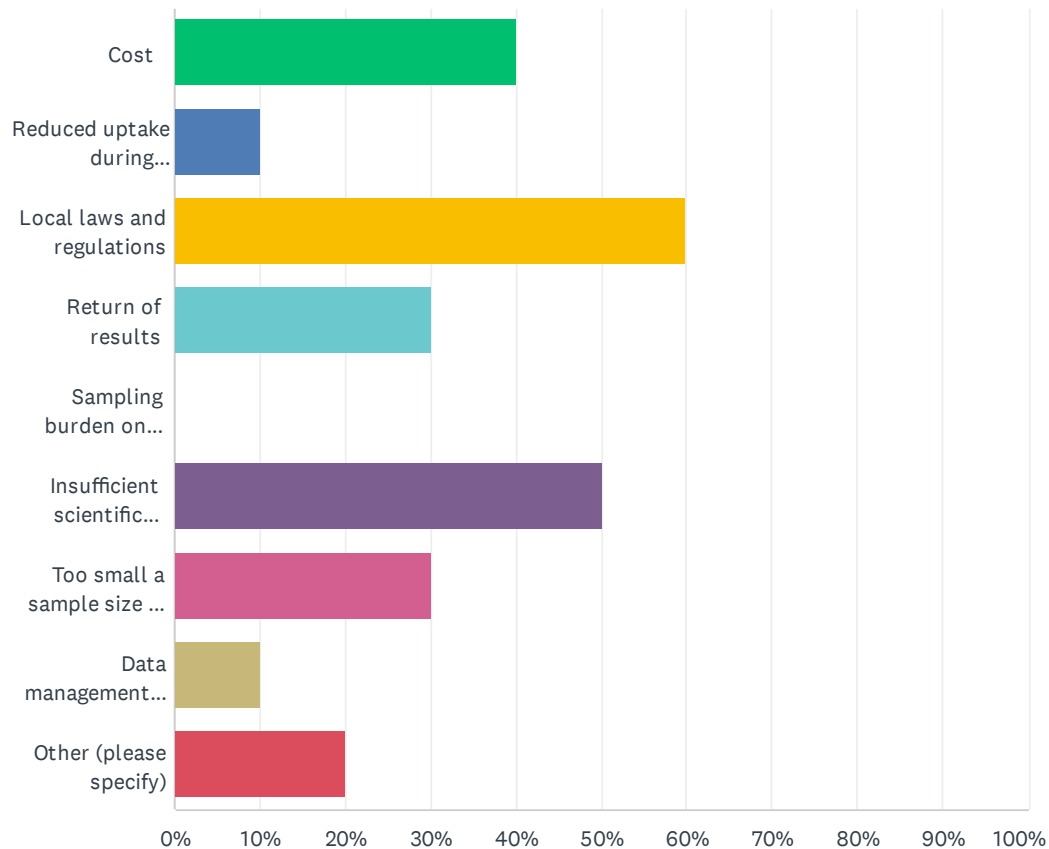
Answered: 9 Skipped: 2



ANSWER CHOICES	RESPONSES	
Yes – very keen	33.33%	3
Yes – limited enthusiasm for selected projects	33.33%	3
No	33.33%	3
TOTAL		9

## Q27 What are your main hesitations/bottlenecks for doing WES/WGS? [Select all that apply]

Answered: 10 Skipped: 1



ANSWER CHOICES	RESPONSES	
Cost	40.00%	4
Reduced uptake during recruitment	10.00%	1
Local laws and regulations	60.00%	6
Return of results	30.00%	3
Sampling burden on subjects	0.00%	0
Insufficient scientific justification	50.00%	5
Too small a sample size in trials	30.00%	3
Data management requirements	10.00%	1
Other (please specify)	20.00%	2
Total Respondents: 10		

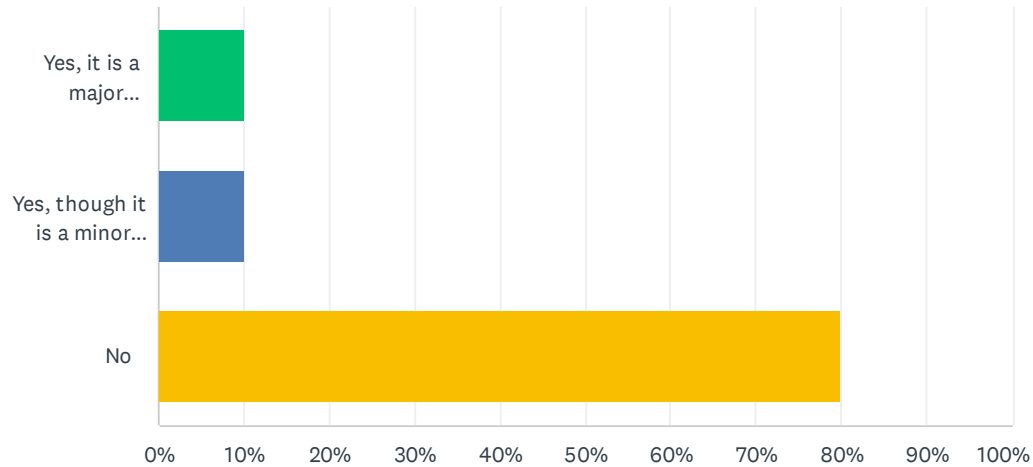
#	OTHER (PLEASE SPECIFY)	DATE
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## WGS in Clinical Trials - BioMarin Company Survey

1	WES is currently conducted in many trials, but where it is not, a mix of cost, sample size, and scientific justification main considerations	6/13/2022 3:16 AM
2	No hesitation.	6/7/2022 5:12 PM

## Q28 Does the ability to collect WES/WGS data influence the selection of trial sites? [Choose one]

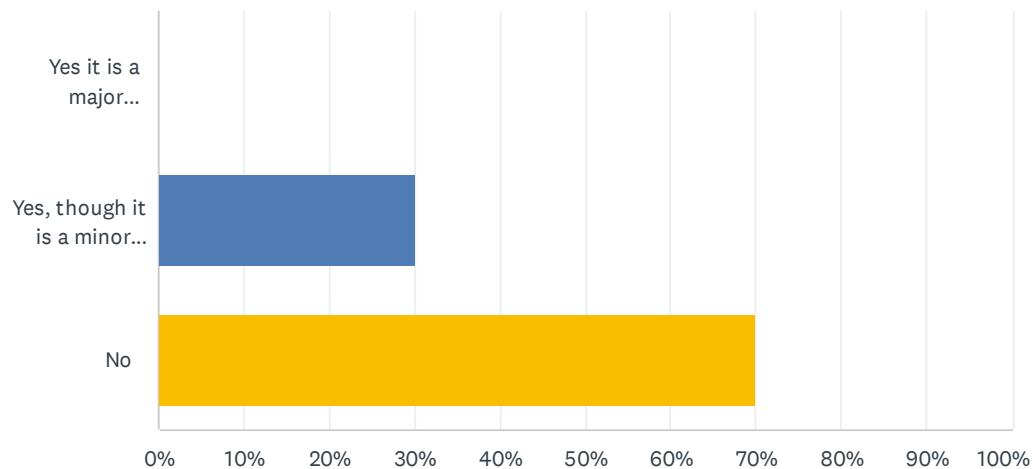
Answered: 10 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes, it is a major consideration	10.00%	1
Yes, though it is a minor consideration	10.00%	1
No	80.00%	8
TOTAL		10

## Q29 Does the ability to collect WGS data prevent basing trial sites within specific counties? [Choose one]

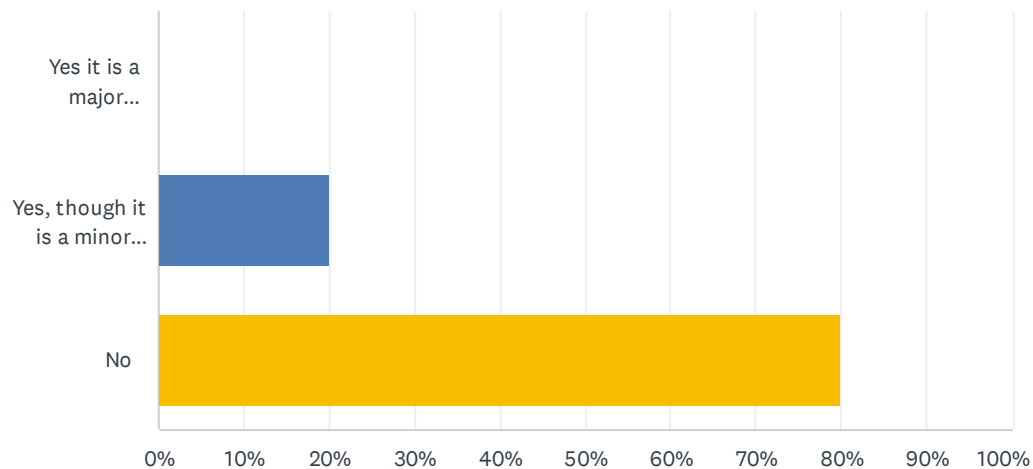
Answered: 10 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes it is a major consideration	0.00%	0
Yes, though it is a minor consideration	30.00%	3
No	70.00%	7
TOTAL		10

### Q30 Do the rules around the return of results around WES/WGS specifically influence the selection of trial sites/countries?

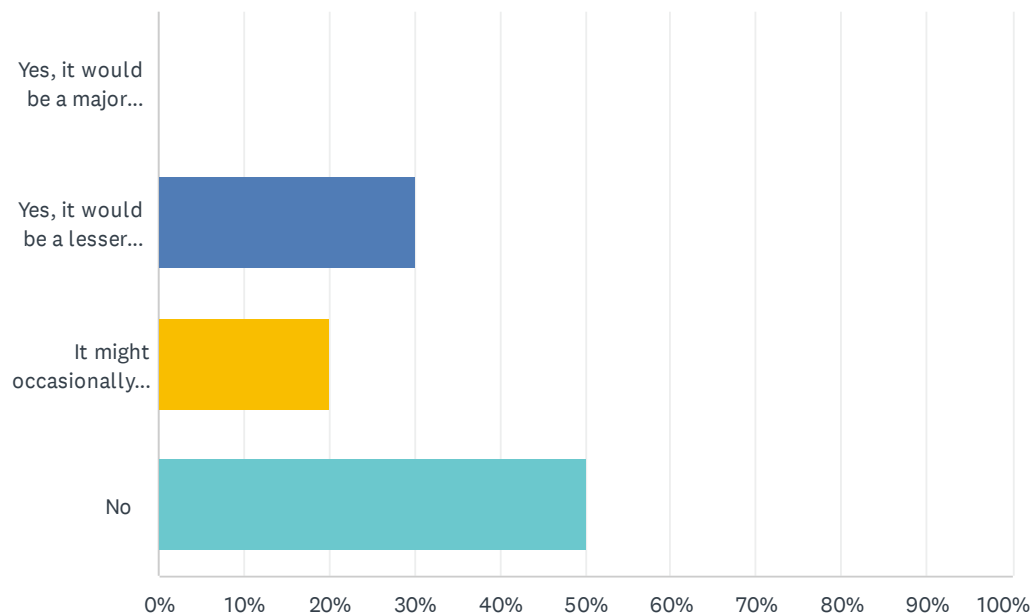
Answered: 10 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes it is a major consideration	0.00%	0
Yes, though it is a minor consideration	20.00%	2
No	80.00%	8
TOTAL		10

### Q31 Would easier/clearer rules around WES/WGS data collection in trials in a given country/site/jurisdiction increase the likelihood of your company basing a trial there?

Answered: 10 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes, it would be a major factor	0.00%	0
Yes, it would be a lesser factor	30.00%	3
It might occasionally be a factor	20.00%	2
No	50.00%	5
TOTAL		10

## Q32 Would your answers have changed if we had asked only about WES or WGS, rather than both? [Free text]

Answered: 10 Skipped: 1

#	RESPONSES	DATE
1	No	6/14/2022 10:07 PM
2	Yes, WES used far more widely than WGS in clinical trials	6/13/2022 3:16 AM
3	No	6/10/2022 5:13 PM
4	No	6/10/2022 4:31 PM
5	No	6/10/2022 6:13 AM
6	no	6/7/2022 5:12 PM
7	No, except for perhaps cost, WES and WGS have the same issues for us	6/7/2022 12:57 PM
8	No - though we prefer WGS given limited increase in cost and importance of non-genic regions	6/7/2022 12:22 PM
9	no	6/2/2022 8:06 PM
10	No	5/20/2022 2:03 PM

### Q33 Are there any other comments or clarifications you would like to make? [Free text]

Answered: 5   Skipped: 6

#	RESPONSES	DATE
1	The use of WGS in clinical trials is a very recent development and therefore only very limited experience exists to date	6/14/2022 10:07 PM
2	Answers to many questions somewhat indication-specific, and would vary if asked for a specific indication. For #22, assume "deep sequencing" means standard depth sequencing	6/13/2022 3:16 AM
3	-	6/10/2022 6:13 AM
4	WGS has not been used, WES is occasionally used, but rarely and in a research or post-trial research use. Most common use is NGS for targeted applications and we still get pushback from ECs/IRBs lumping "NGS" together regardless if targeted or broad. For question 15, we don't have mandatory inclusion of WES/WGS, but we do have this included as optional testing and so have had no issues impacting enrollment.	6/7/2022 12:57 PM
5	Feeling a trend for WGS/WES in US still an option, whereas in Europe (and other countries such as Israel) seems to become more complicated with stringent push-backs from ECs/IRBs when no very precise justification is given.	5/20/2022 8:34 AM