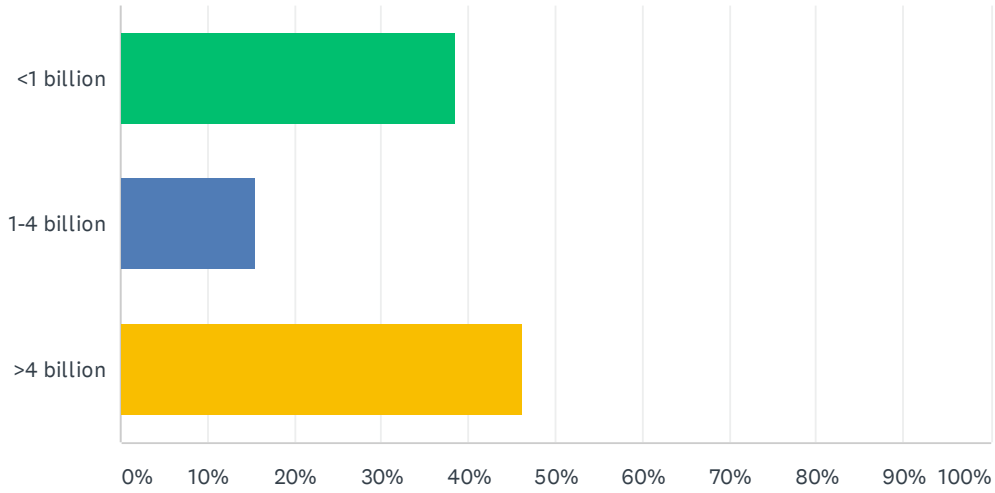
Q1 What were the pharmaceutical R&D expenses of your company in 2018?

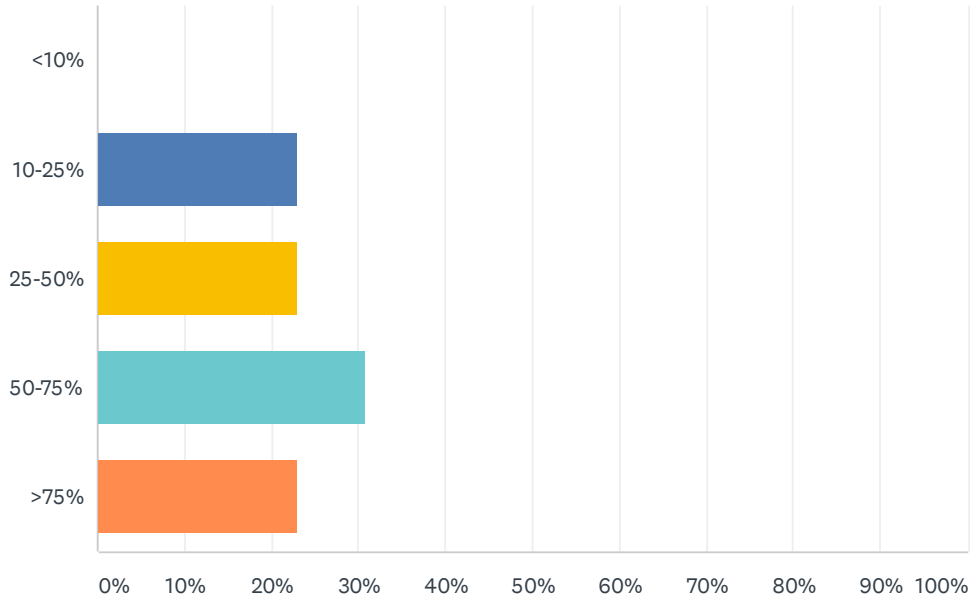
Answered: 13 Skipped: 0



ANSWER CHOICES	RESPONSES	
<1 billion	38.46%	5
1-4 billion	15.38%	2
>4 billion	46.15%	6
TOTAL		13

Q2 What percentage of your pipeline is represented by small molecules: <10%

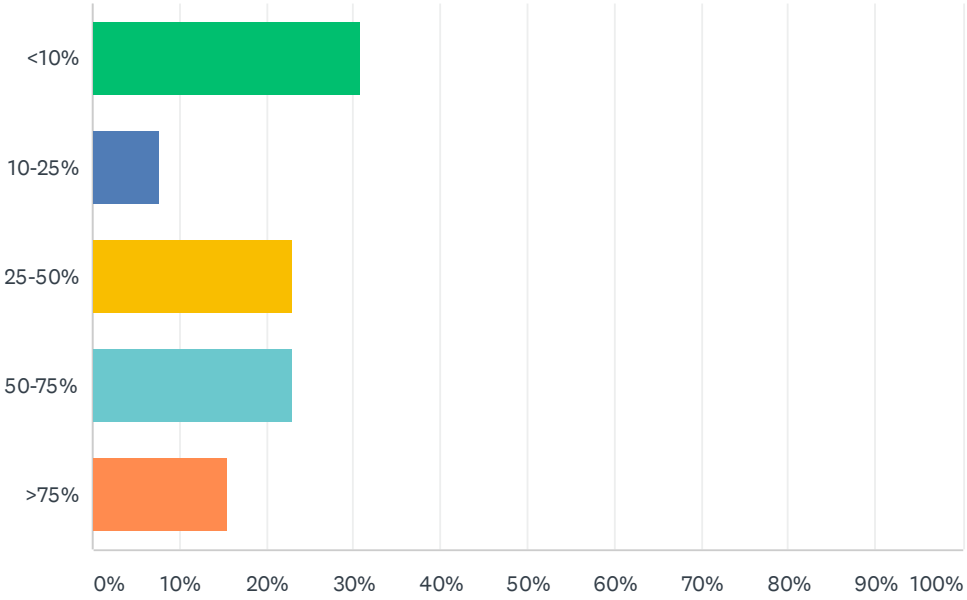
Answered: 13 Skipped: 0



ANSWER CHOICES	RESPONSES	
<10%	0.00%	0
10-25%	23.08%	3
25-50%	23.08%	3
50-75%	30.77%	4
>75%	23.08%	3
TOTAL		13

Q3 What percentage of your pipeline is represented by therapeutic proteins, vaccines, or other types of compounds (not small molecule): <10%,

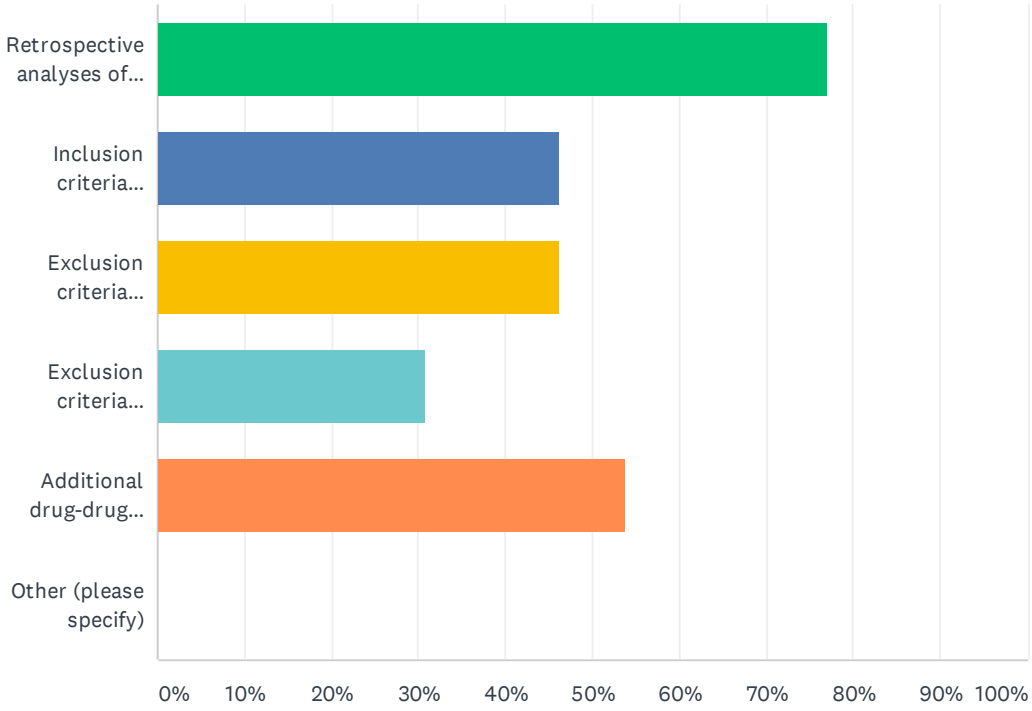
Answered: 13 Skipped: 0



ANSWER CHOICES	RESPONSES	
<10%	30.77%	4
10-25%	7.69%	1
25-50%	23.08%	3
50-75%	23.08%	3
>75%	15.38%	2
TOTAL		13

Q4 If your company advances drug candidates metabolized or transported by enzymes/transporters with genetic variation that might result in clinically meaningful differences in compound disposition, what additional steps have been taken in the clinical development program of this compound? Select all that apply.

Answered: 13 Skipped: 0

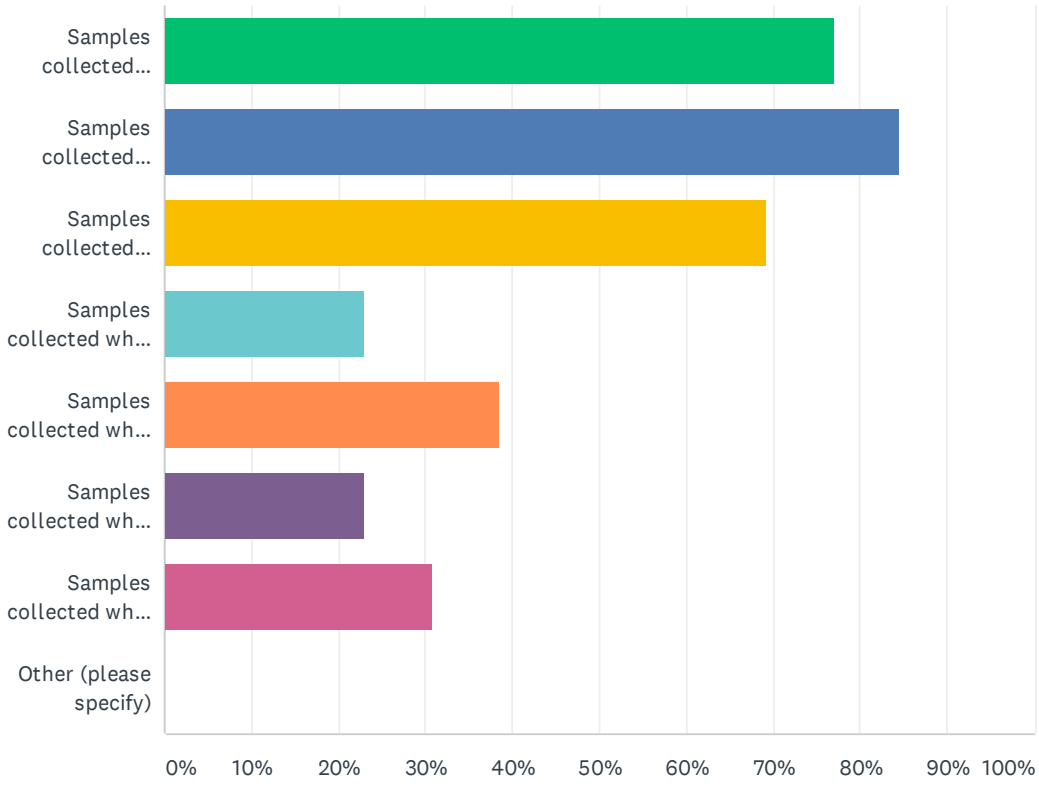


ANSWER CHOICES	RESPONSES	
Retrospective analyses of relevant polymorphisms with endpoints studied in trial subjects	76.92%	10
Inclusion criteria specified or separate trials conducted to asses genetic effects in an enriched patient population	46.15%	6
Exclusion criteria applied to restrict patients with genotypes predicted to result in significantly higher exposure to compound	46.15%	6
Exclusion criteria applied to restrict patients with genotypes predicted to result in significantly lower plasma exposure to compound	30.77%	4
Additional drug-drug interaction studies or modified design of planned drug-drug interaction studies	53.85%	7
Other (please specify)	0.00%	0
Total Respondents: 13		

#	OTHER (PLEASE SPECIFY)	DATE
	There are no responses.	

Q5 Under what circumstances does your company collected DNA with consent for ADME-related genotyping? Select all that apply.

Answered: 13 Skipped: 0

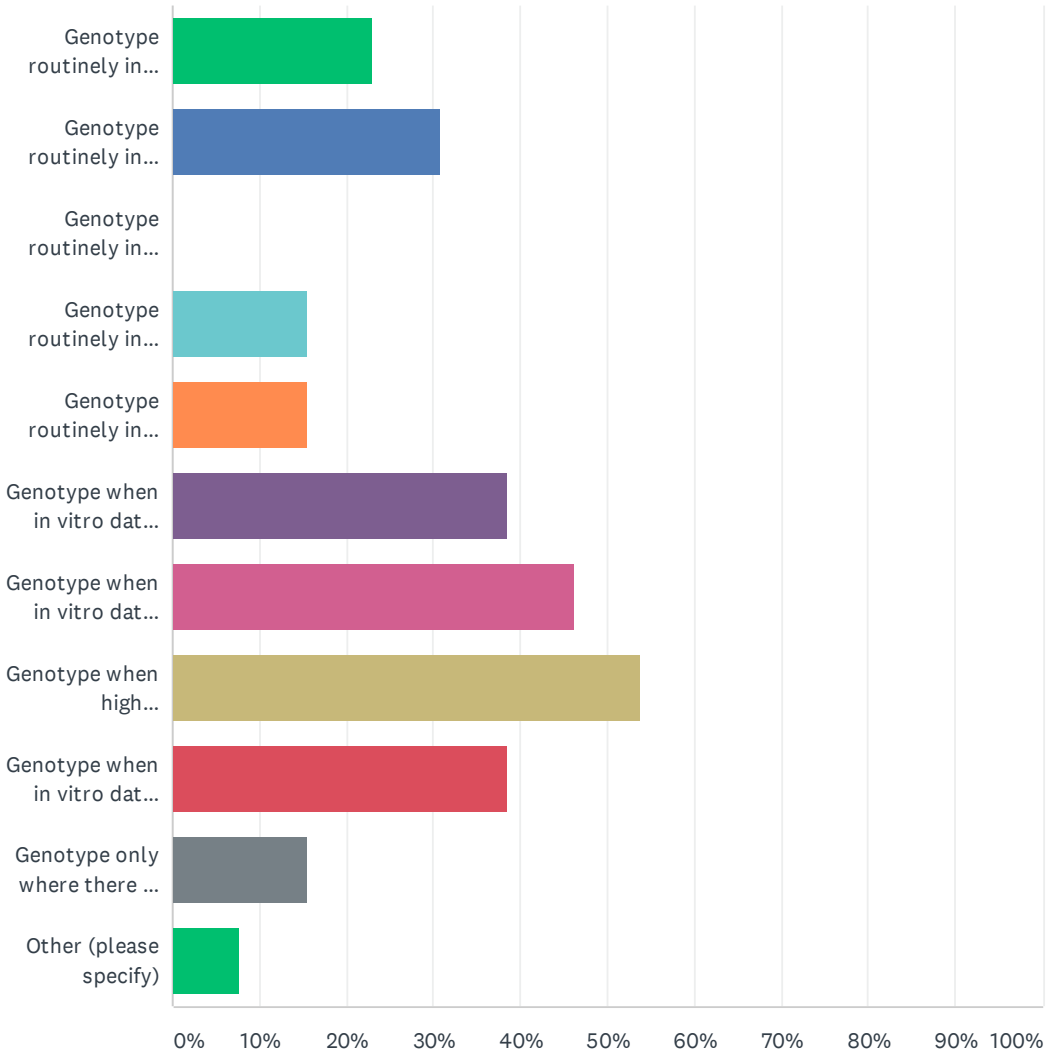


ANSWER CHOICES	RESPONSES	
Samples collected routinely in Phase I	76.92%	10
Samples collected routinely in Phase II	84.62%	11
Samples collected routinely in Phase III	69.23%	9
Samples collected when in vitro data suggests any involvement of a polymorphic enzyme or transporter	23.08%	3
Samples collected when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition	38.46%	5
Samples collected when high pharmacokinetic variability is observed in phase 1 clinical trials	23.08%	3
Samples collected when in vitro data suggests any enzyme or transporter is a major contributor to disposition	30.77%	4
Other (please specify)	0.00%	0
Total Respondents: 13		

#	OTHER (PLEASE SPECIFY)	DATE
	There are no responses.	

Q6 Under what circumstances does your company genotype drug metabolism enzymes and transporters? Select all that apply.

Answered: 13 Skipped: 0

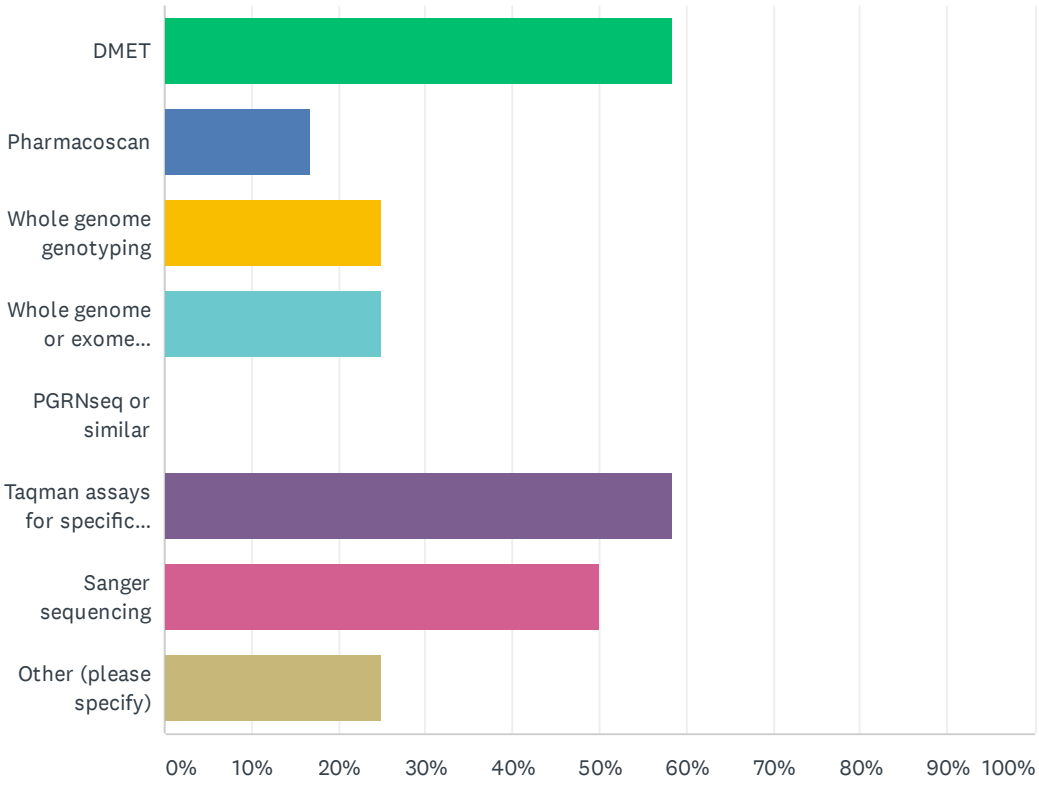


ANSWER CHOICES	RESPONSES	
Genotype routinely in all phase I studies	23.08%	3
Genotype routinely in DDI studies	30.77%	4
Genotype routinely in ascending dose studies	0.00%	0
Genotype routinely in phase II studies	15.38%	2
Genotype routinely in all phase III studies	15.38%	2
Genotype when in vitro data suggests any involvement of a polymorphic enzyme or transporter	38.46%	5
Genotype when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition	46.15%	6
Genotype when high pharmacokinetic variability is observed in phase 1 clinical trials	53.85%	7
Genotype when in vitro data suggests any enzyme or transporter is a major contributor to disposition	38.46%	5
Genotype only where there is expected to be sufficient power to conduct an analysis for specific genes/alleles of interest	15.38%	2
Other (please specify)	7.69%	1
Total Respondents: 13		

#	OTHER (PLEASE SPECIFY)	DATE
1	genotype when PK is variable AND a polymorphic enzyme/tranpsporter is a contributor	9/13/2019 6:20 PM

Q7 What technologies do you/would you use to genotype variants/genes of interest? Select all that apply.

Answered: 12 Skipped: 1



ANSWER CHOICES	RESPONSES	
DMET	58.33%	7
Pharmacoscan	16.67%	2
Whole genome genotyping	25.00%	3
Whole genome or exome sequencing	25.00%	3
PGRNseq or similar	0.00%	0
Taqman assays for specific variants	58.33%	7
Sanger sequencing	50.00%	6
Other (please specify)	25.00%	3
Total Respondents: 12		

#	OTHER (PLEASE SPECIFY)	DATE
1	pyrosequencing	2/11/2020 10:51 PM
2	array - PMRA	10/11/2019 3:04 PM
3	Open Array (Taqman), Fragment Analysis, Ion Torrent S5 PGx Panel	9/13/2019 6:20 PM

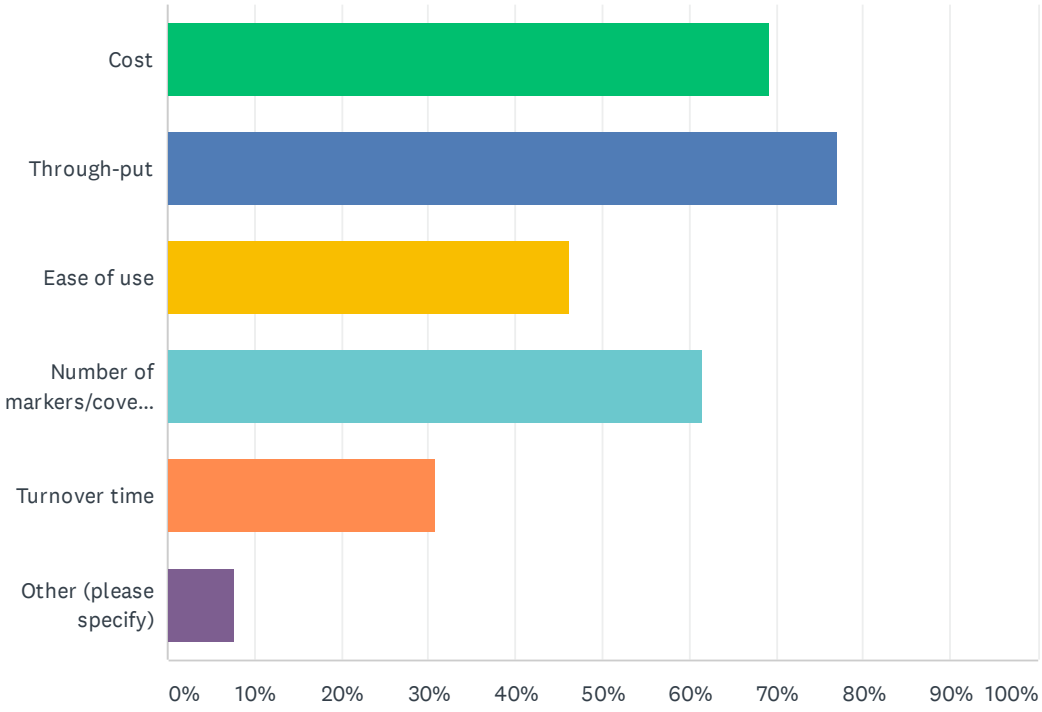
Q8 If you answered "Other" to Question 7 or if different genotyping technologies are used in different scenarios (eg. routine genotyping, PK outlier, phase of development, etc.) please describe further.

Answered: 4 Skipped: 9

#	RESPONSES	DATE
1	If single gene is of interest, pyrosequencing is used. If more genes are of interest, DMET is used.	2/11/2020 10:51 PM
2	na	10/25/2019 2:19 PM
3	array for all supplemented with bespoke assays	10/11/2019 3:04 PM
4	Taqman Open Array, Fragment Analysis, Ion Torrent S5 PGx Panel: based on need of panel size and throughput	9/13/2019 6:20 PM

Q9 Please state reasons for the choice of your genotyping platform(s):

Answered: 13 Skipped: 0

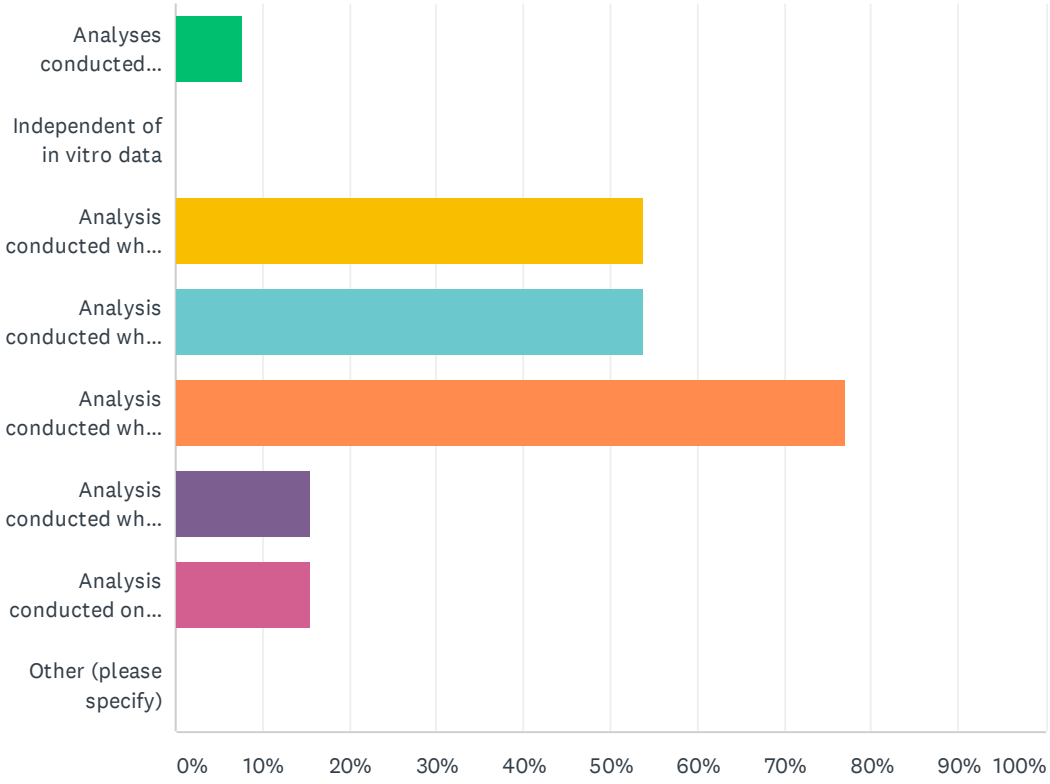


ANSWER CHOICES	RESPONSES	
Cost	69.23%	9
Through-put	76.92%	10
Ease of use	46.15%	6
Number of markers/coverage	61.54%	8
Turnover time	30.77%	4
Other (please specify)	7.69%	1
Total Respondents: 13		

#	OTHER (PLEASE SPECIFY)	DATE
1	Established, high confidence.	2/27/2020 1:32 PM

Q10 Under what circumstances does your company conduct an ADME PGx analysis? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:

Answered: 13 Skipped: 0

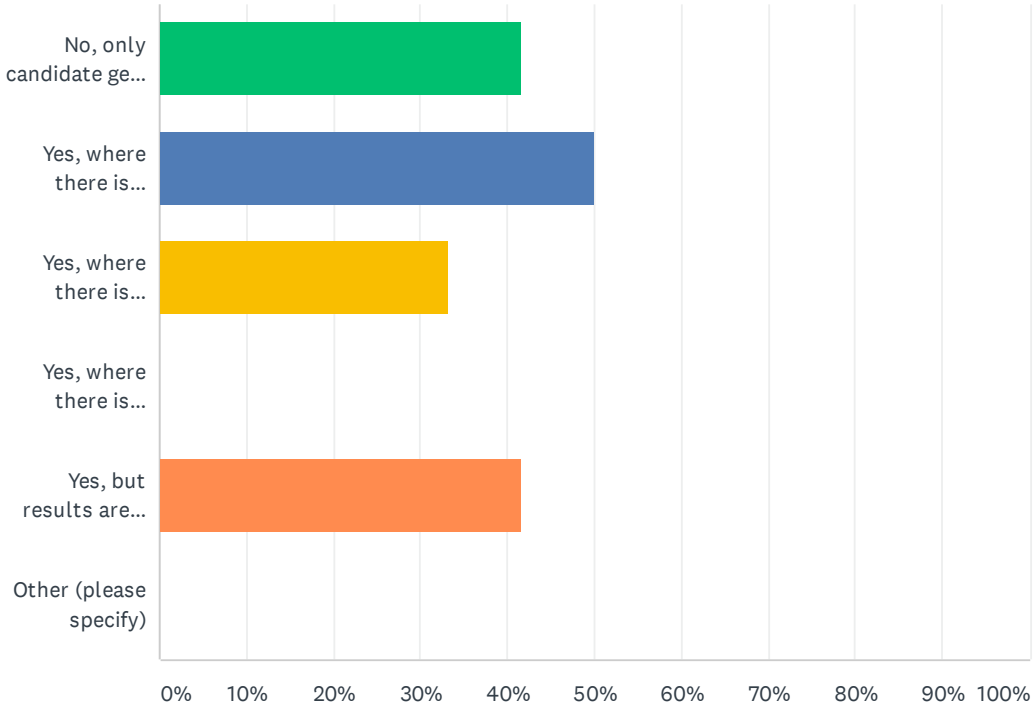


ANSWER CHOICES	RESPONSES	
Analyses conducted routinely	7.69%	1
Independent of in vitro data	0.00%	0
Analysis conducted when in vitro data suggests any involvement of a certain enzymes or transporters	53.85%	7
Analysis conducted when in vitro data suggests certain enzymes or transporters are a major contributor to disposition	53.85%	7
Analysis conducted when high pharmacokinetic variability is observed in phase 1 clinical trials	76.92%	10
Analysis conducted when in vitro data suggests any enzyme or transporter is a major contributor to disposition	15.38%	2
Analysis conducted only where there is expected to be sufficient statistical power to conduct an analysis for specific genes/alleles of interest	15.38%	2
Other (please specify)	0.00%	0
Total Respondents: 13		

#	OTHER (PLEASE SPECIFY)	DATE
	There are no responses.	

Q11 Are there scenarios in which a hypothesis-free approach is used in ADME PGx analyses – where a larger number of genes and alleles are tested than those suspected to be involved in clearance based on pre-clinical work and knowledge about the compound's disposition? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:

Answered: 12 Skipped: 1



ANSWER CHOICES	RESPONSES	
No, only candidate genes based on preclinical or early clinical work are explored	41.67%	5
Yes, where there is unexplained PK variability	50.00%	6
Yes, where there is uncertainty around genes involved in disposition	33.33%	4
Yes, where there is adequate statistical power for such approaches Yes, in all analyses	0.00%	0
Yes, but results are used only for hypothesis generation	41.67%	5
Other (please specify)	0.00%	0
Total Respondents: 12		

#	OTHER (PLEASE SPECIFY)	DATE
	There are no responses.	

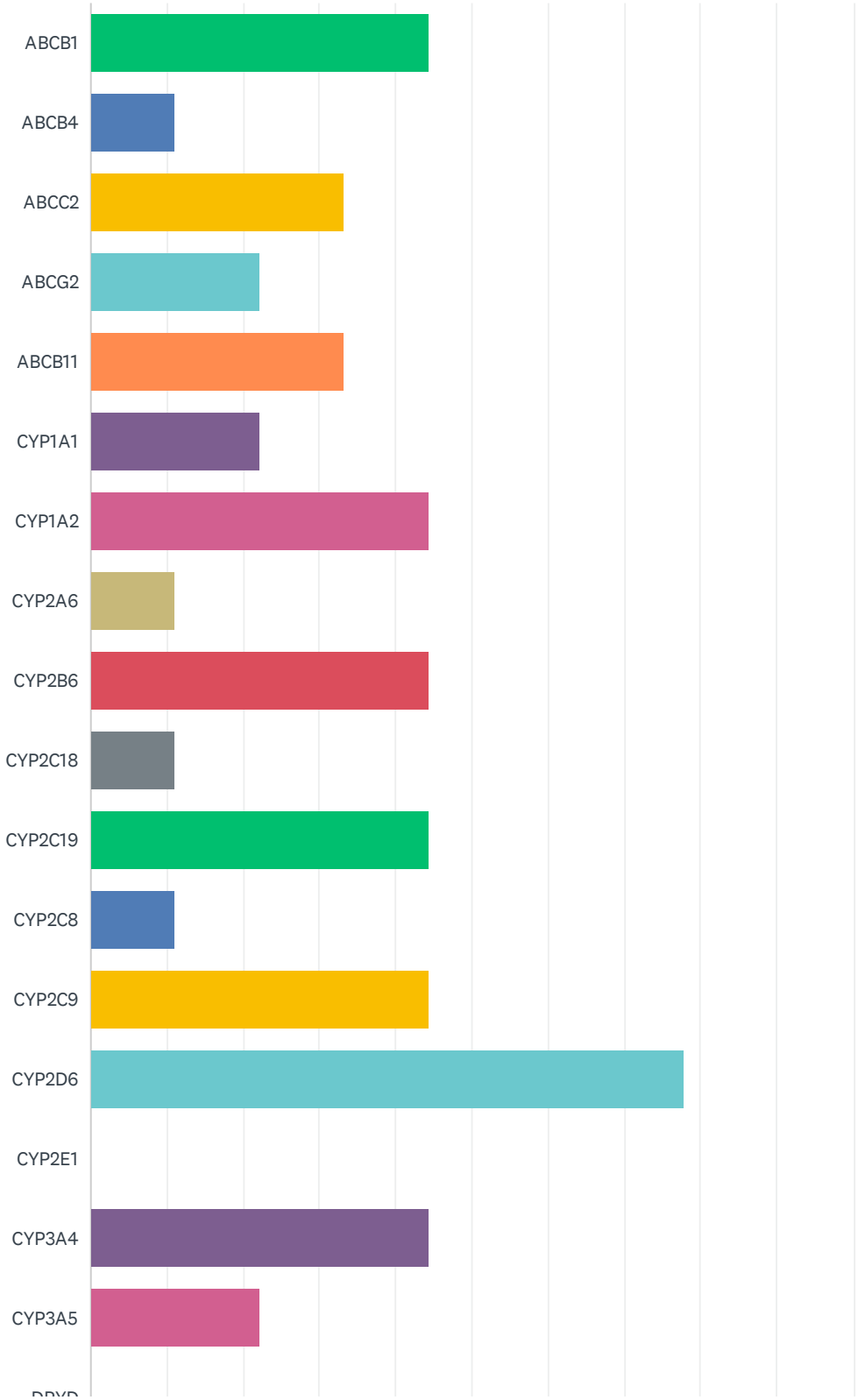
Q12 If you answered "No" to Question 11 please describe the main reasons why your company does not conduct such analyses (eg lack of scientific justification, cost of analyses, lack of resources, etc.).

Answered: 6 Skipped: 7

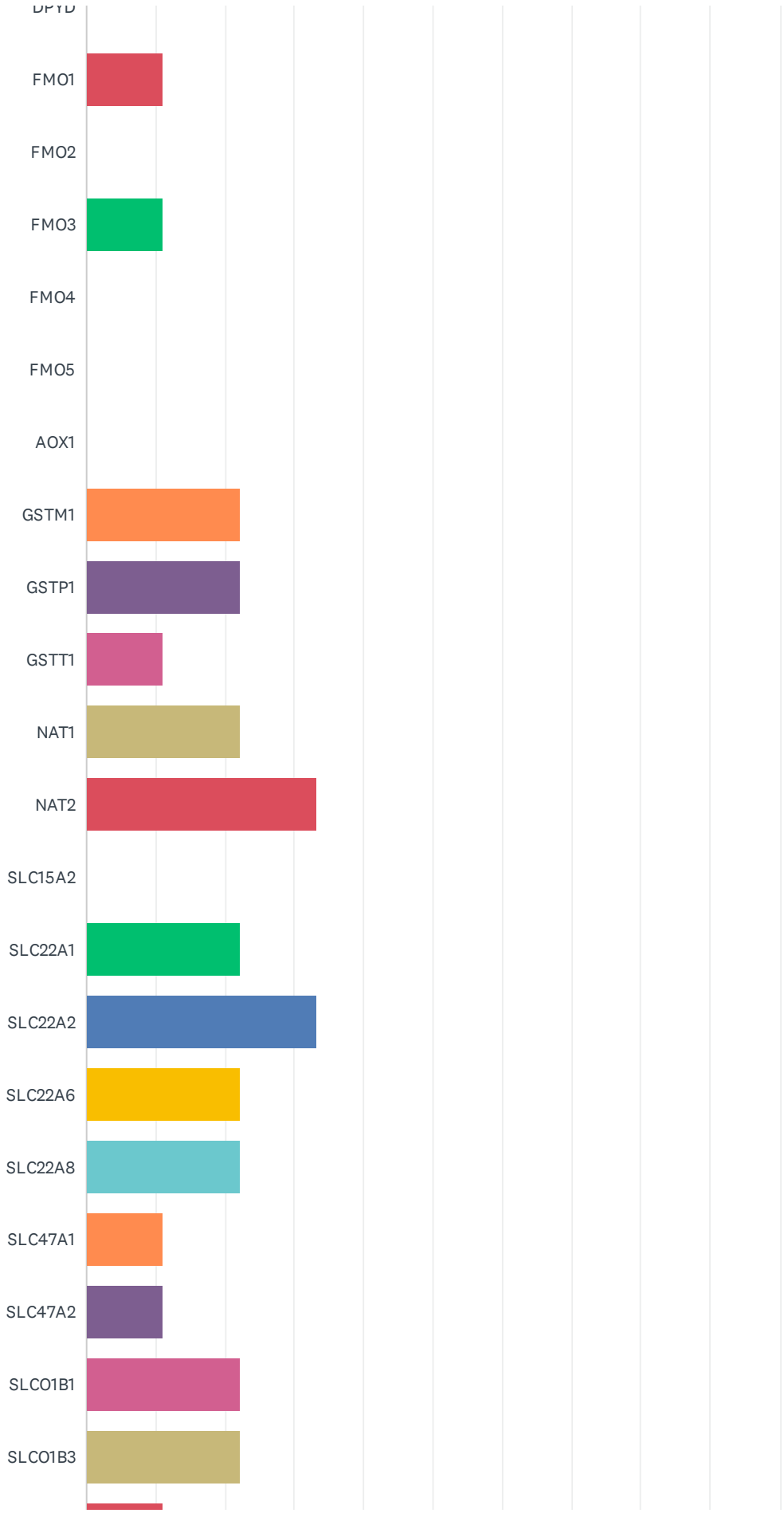
#	RESPONSES	DATE
1	lack of scientific justification	2/11/2020 10:51 PM
2	na	10/25/2019 2:19 PM
3	cost of analyses and lack of resources	10/11/2019 9:40 PM
4	low chance of success	10/11/2019 3:04 PM
5	Cost, lack of novel genotype to phenotype clinical understanding, guidance documents, power concerns	9/13/2019 6:20 PM
6	Lack of scientific justification and resources	9/12/2019 3:42 PM

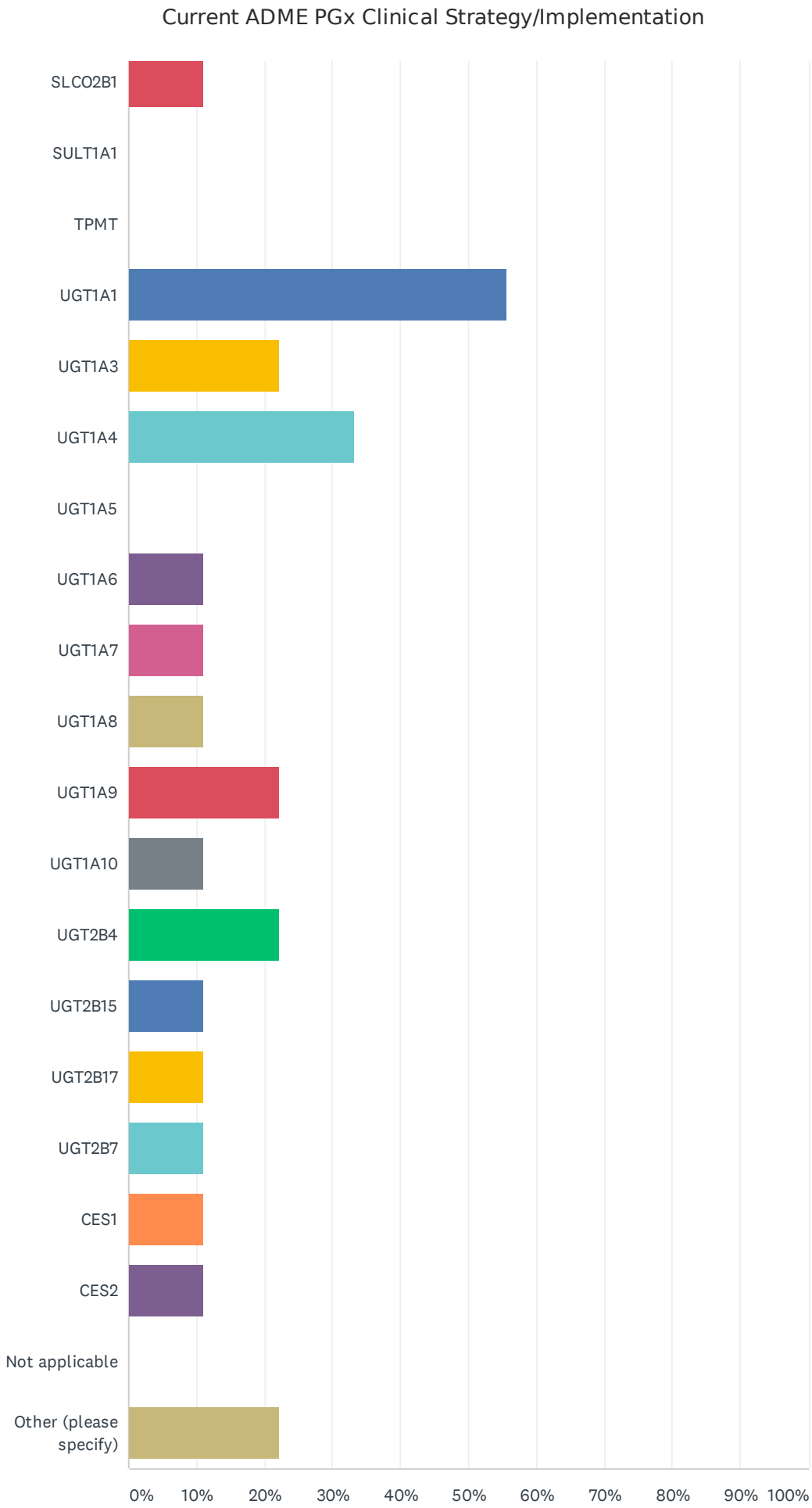
Q13 If genotyping and/or statistical analysis is triggered only when there is evidence of involvement of certain enzymes or transporters, which genes would trigger genotyping/analysis?

Answered: 9 Skipped: 4



Current ADME PGx Clinical Strategy/Implementation




Current ADME PGx Clinical Strategy/Implementation
SLCO2B1
SULT1A1
TPMT
UGT1A1
UGT1A3
UGT1A4
UGT1A5
UGT1A6
UGT1A7
UGT1A8
UGT1A9
UGT1A10
UGT2B4
UGT2B15
UGT2B17
UGT2B7
CES1
CES2
Not applicable
Other (please specify)
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%

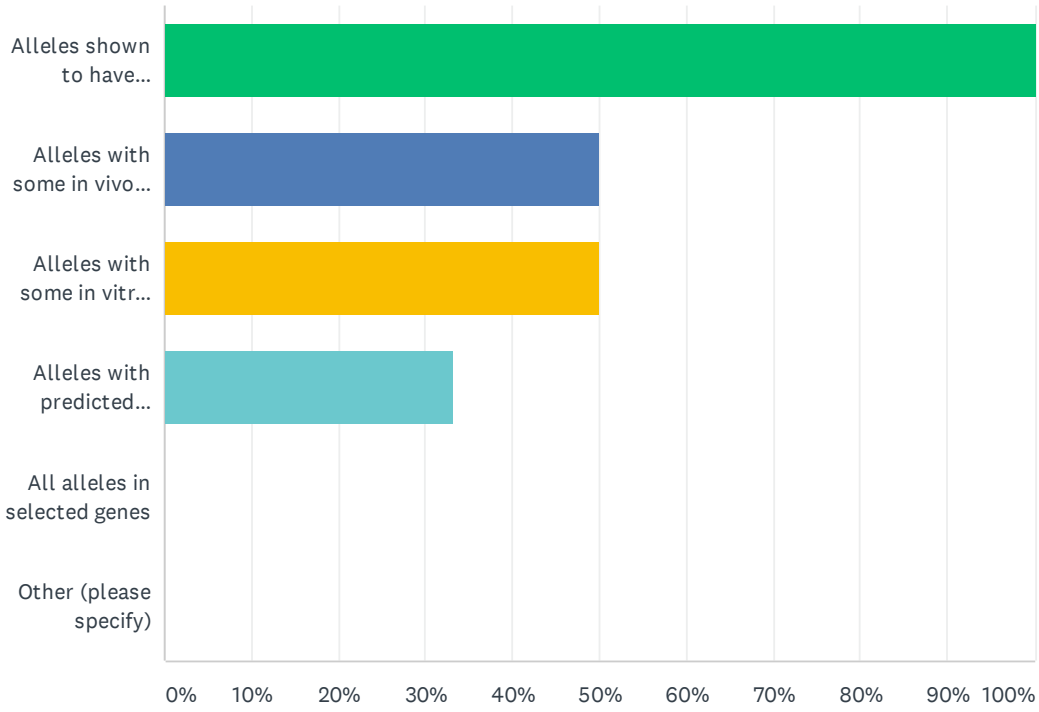
ANSWER CHOICES	RESPONSES	
ABCB1	44.44%	4
ABCB4	11.11%	1
ABCC2	33.33%	3
ABCG2	22.22%	2
ABCB11	33.33%	3
CYP1A1	22.22%	2
CYP1A2	44.44%	4
CYP2A6	11.11%	1
CYP2B6	44.44%	4
CYP2C18	11.11%	1
CYP2C19	44.44%	4
CYP2C8	11.11%	1
CYP2C9	44.44%	4
CYP2D6	77.78%	7
CYP2E1	0.00%	0
CYP3A4	44.44%	4
CYP3A5	22.22%	2
DPYD	0.00%	0
FMO1	11.11%	1
FMO2	0.00%	0
FMO3	11.11%	1
FMO4	0.00%	0
FMO5	0.00%	0
AOX1	0.00%	0
GSTM1	22.22%	2
GSTP1	22.22%	2
GSTT1	11.11%	1
NAT1	22.22%	2
NAT2	33.33%	3
SLC15A2	0.00%	0
SLC22A1	22.22%	2
SLC22A2	33.33%	3
SLC22A6	22.22%	2

[illegible]	[illegible]	[illegible]
SLC22A8	22.22%	2
SLC47A1	11.11%	1
SLC47A2	11.11%	1
SLCO1B1	22.22%	2
SLCO1B3	22.22%	2
SLCO2B1	11.11%	1
SULT1A1	0.00%	0
TPMT	0.00%	0
UGT1A1	55.56%	5
UGT1A3	22.22%	2
UGT1A4	33.33%	3
UGT1A5	0.00%	0
UGT1A6	11.11%	1
UGT1A7	11.11%	1
UGT1A8	11.11%	1
UGT1A9	22.22%	2
UGT1A10	11.11%	1
UGT2B4	22.22%	2
UGT2B15	11.11%	1
UGT2B17	11.11%	1
UGT2B7	11.11%	1
CES1	11.11%	1
CES2	11.11%	1
Not applicable	0.00%	0
Other (please specify)	22.22%	2
Total Respondents: 9		

#	OTHER (PLEASE SPECIFY)	DATE
1	Any gene is considered, usually prioritize based on in vitro/ preclinical experiments	2/25/2020 3:38 PM
2	Any enzyme/transporter with known functional polymorphisms and significant contribution to disposition; decision and specific genes made on a program by program basis	10/11/2019 11:11 PM

Q14 When ADME PGx analyses are conducted, what alleles are included in analyses? Select all that apply.

Answered: 12 Skipped: 1

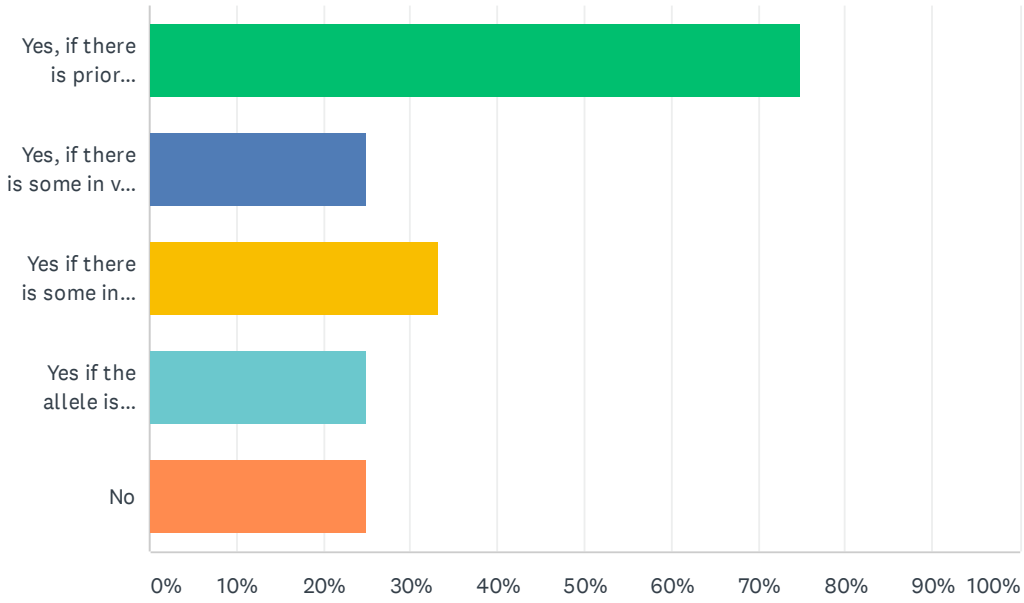


ANSWER CHOICES	RESPONSES	
Alleles shown to have clinically meaningful impact on PK of other substrates	100.00%	12
Alleles with some in vivo evidence of change in activity or expression	50.00%	6
Alleles with some in vitro evidence of change in activity or expression	50.00%	6
Alleles with predicted impact on protein function or expression based on in silico algorithms	33.33%	4
All alleles in selected genes	0.00%	0
Other (please specify)	0.00%	0
Total Respondents: 12		

#	OTHER (PLEASE SPECIFY)	DATE
	There are no responses.	

Q15 Do you include rare alleles (population frequency <1% in all populations) in ADME PGx analyses? Select all that apply.

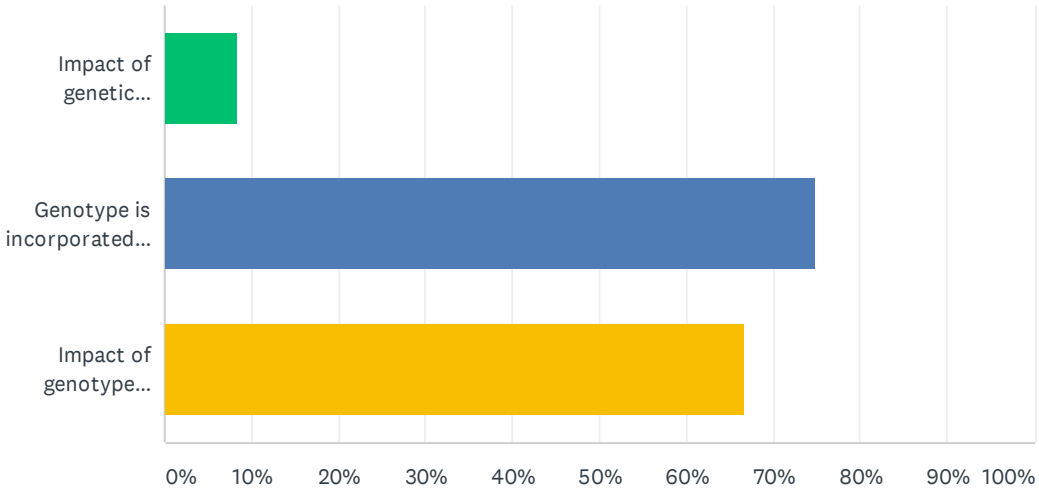
Answered: 12 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes, if there is prior evidence that the allele has a clinical meaningful impact on PK of other substrates	75.00%	9
Yes, if there is some in vivo evidence of functional impact of the allele	25.00%	3
Yes if there is some in vitro evidence of functional impact of the allele	33.33%	4
Yes if the allele is predicted to alter protein function or expression by in silico algorithms	25.00%	3
No	25.00%	3
Total Respondents: 12		

Q16 How Is is the impact of genetic variation on compound disposition assessed using population PK models in Phase II and beyondin studies with sparse pharmacokinetic sampling?

Answered: 12 Skipped: 1



ANSWER CHOICES	RESPONSES	
Impact of genetic variation is not analyzed in such studies	8.33%	1
Genotype is incorporated as a covariate in population PK models	75.00%	9
Impact of genotype assessed using PK parameter estimated using population PK models or other approaches from the data available	66.67%	8
Total Respondents: 12		

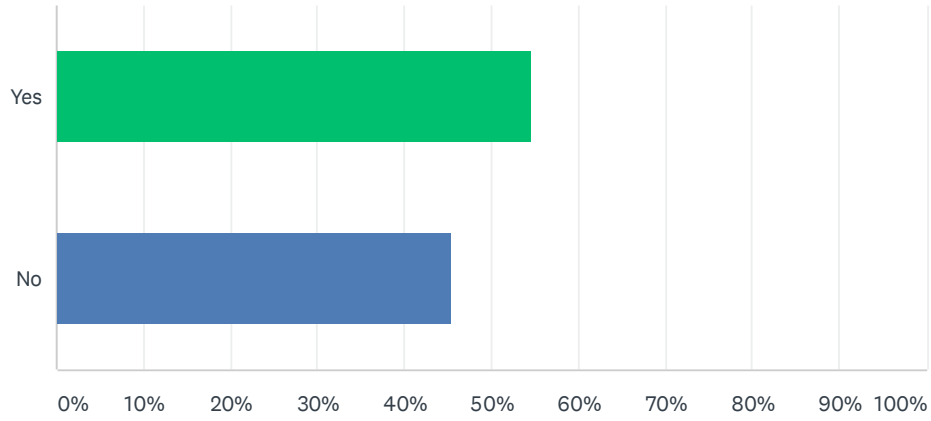
Q17 As a follow-up to Question 16 if multiple approaches have been used, please describe the factors that inform on choice of approach:

Answered: 7 Skipped: 6

#	RESPONSES	DATE
1	Situation-dependent.	2/27/2020 1:32 PM
2	reproducibility	10/25/2019 2:19 PM
3	Data availability and quality.	10/14/2019 10:39 PM
4	Ideally would use both approaches in such scenarios.	10/11/2019 11:11 PM
5	Approach is chosen based on how much data is available and purpose of analysis. For qualitative assessment, correlation analysis is sufficient. To quantitatively estimate the effect, incorporating into population PK analysis is needed.	10/11/2019 9:40 PM
6	The level of evidence that is available	10/9/2019 2:58 PM
7	Depends on the clinical trial size (single vs. combinatorial), popPK vs thorough PK assessment.	9/13/2019 6:20 PM

Q18 Does your organization typically consider potential impact of genetic variants on PK of therapeutic proteins, including the drug target in cases where target mediated drug disposition is relevant?

Answered: 11 Skipped: 2



ANSWER CHOICES	RESPONSES	
Yes	54.55%	6
No	45.45%	5
TOTAL		11

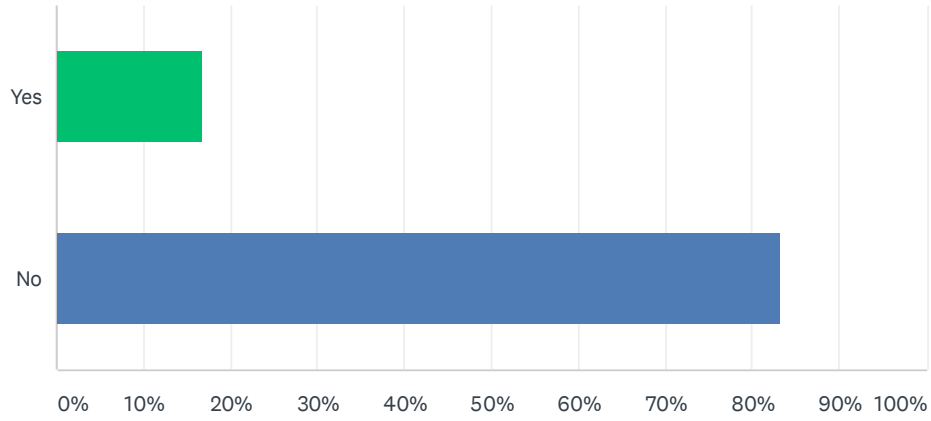
Q19 If you answered "Yes" to Question 19 please describe:

Answered: 5 Skipped: 8

#	RESPONSES	DATE
1	Situation-dependent.	2/27/2020 1:32 PM
2	If TMDD is suspected, target levels are measured in patient samples to access the variability, as well as utilizing available mRNA data from human body mapping. In vitro experiments on target turn-over and internalization may also be performed to inform the TMDD model	2/25/2020 3:38 PM
3	na	10/25/2019 2:19 PM
4	Yes if TMDD was a consideration for the program.	10/11/2019 11:11 PM
5	In vitro studies are done to inform the potential impact.	10/9/2019 2:58 PM

Q20 Does your organization assess the impact of genomic variation (e.g. impact of microRNAs, epigenetic changes, changes in expression) on PK of your compounds?

Answered: 12 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes	16.67%	2
No	83.33%	10
TOTAL		12

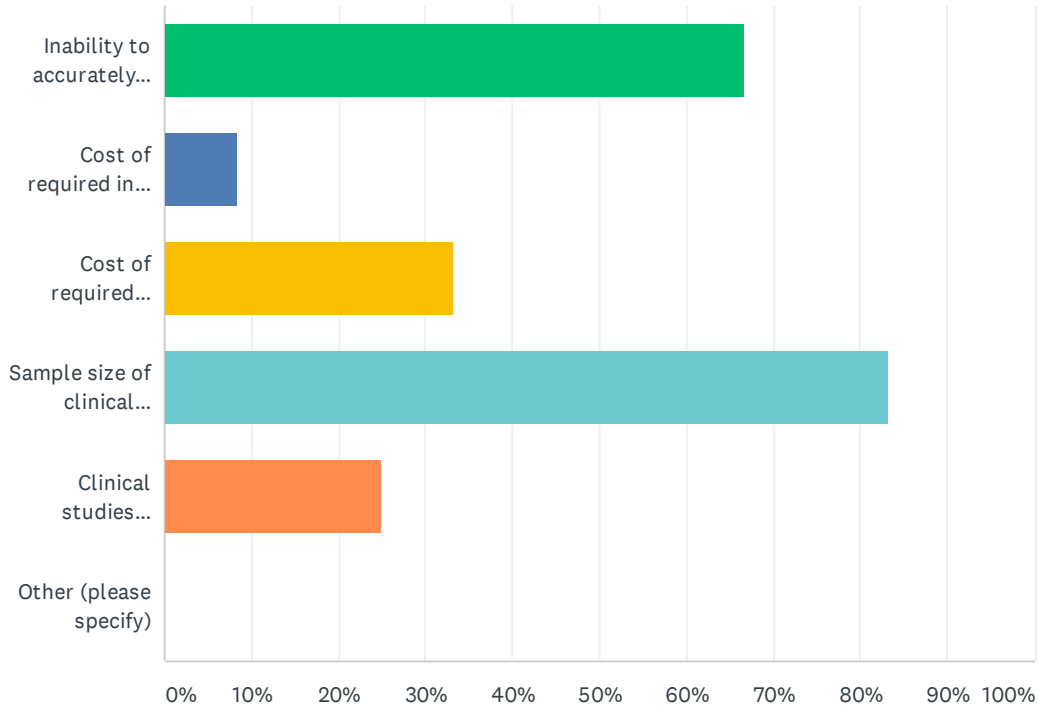
Q21 If you answered "Yes" to Question 21 please describe:

Answered: 3 Skipped: 10

#	RESPONSES	DATE
1	This is not routine, and focusing in the oncology space	2/25/2020 3:38 PM
2	na	10/25/2019 2:19 PM
3	If tremendous variability in PK is observed, genotyping studies may be undertaken.	10/9/2019 2:58 PM

Q22 What are the major limitations to accurately assess impact of genetic variation on compound disposition? Select all that apply.

Answered: 12 Skipped: 1

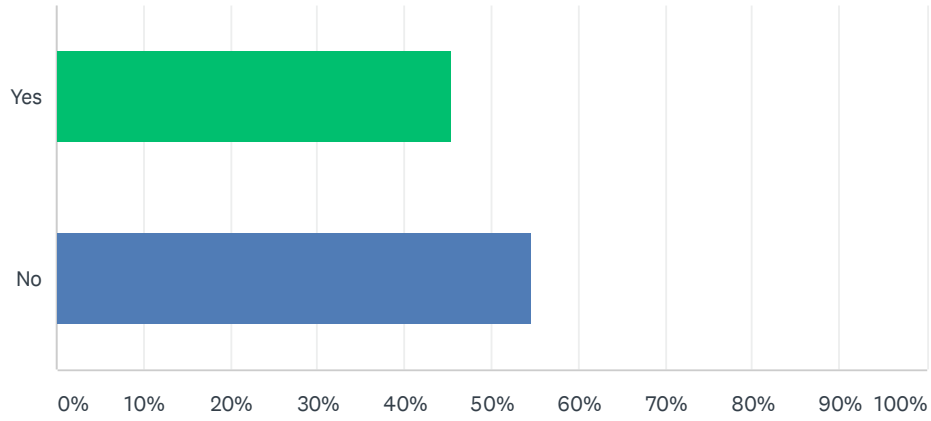


ANSWER CHOICES	RESPONSES	
Inability to accurately determine contribution of enzymes/transporters,	66.67%	8
Cost of required in vitro experiments	8.33%	1
Cost of required clinical studies	33.33%	4
Sample size of clinical studies limits ability to conduct genetic analyzes	83.33%	10
Clinical studies typically limited to certain populations	25.00%	3
Other (please specify)	0.00%	0
Total Respondents: 12		

#	OTHER (PLEASE SPECIFY)	DATE
	There are no responses.	

Q23 For compounds expected to have higher risk of drug-induced liver injury (DILI), are analyses conducted to look for genetic variants associated with higher risk of DILI?

Answered: 11 Skipped: 2



ANSWER CHOICES	RESPONSES	
Yes	45.45%	5
No	54.55%	6
TOTAL		11

Q24 If you answered "Yes" to Question 24 please describe what genes are targeted for such analyses:

Answered: 5 Skipped: 8

#	RESPONSES	DATE
1	Situation-dependent.	2/27/2020 1:32 PM
2	na	10/25/2019 2:19 PM
3	HLA and ADME	10/11/2019 11:11 PM
4	genome wide and known genes	10/11/2019 3:04 PM
5	CYP2D6	9/12/2019 3:42 PM