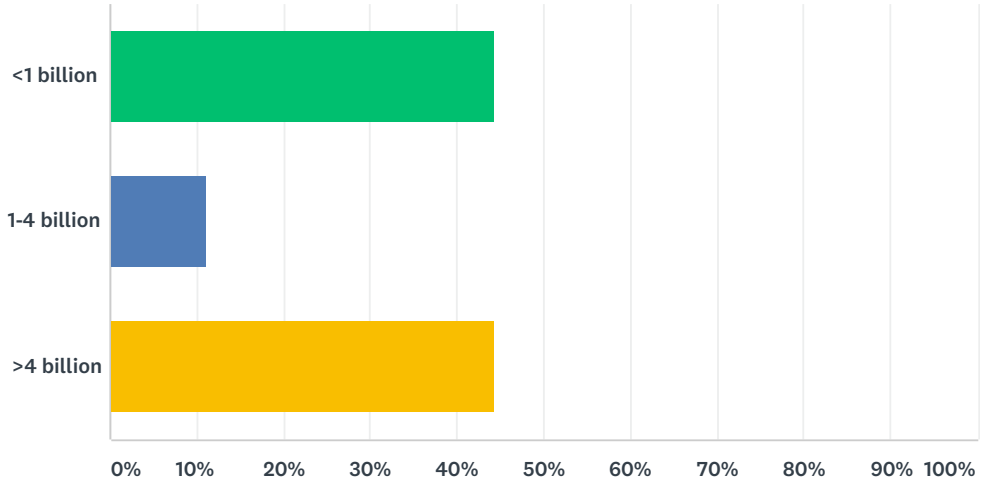
Q1 What were the pharmaceutical R&D expenses of your company in 2018?

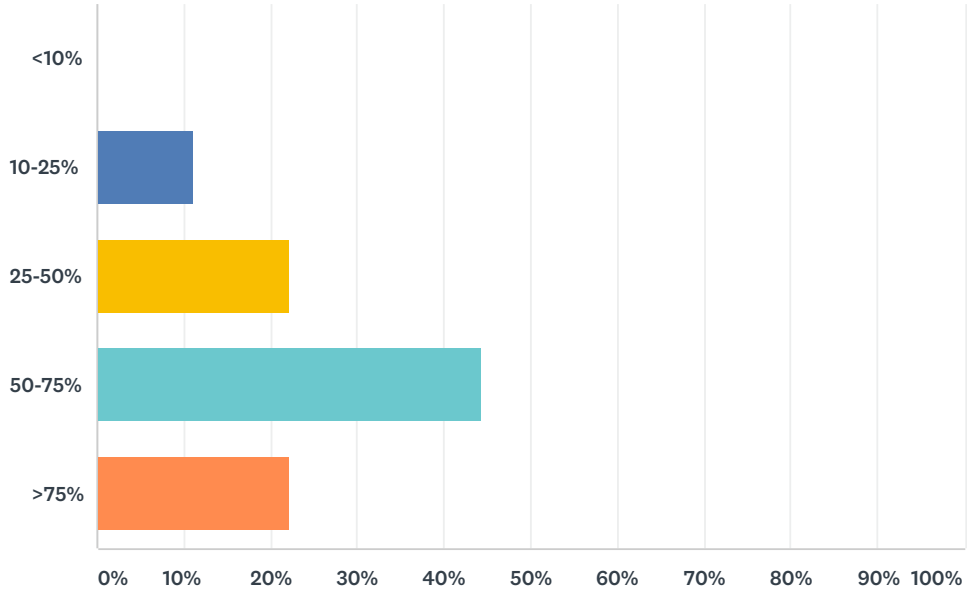
Answered: 9 Skipped: 0



ANSWER CHOICES	RESPONSES	
<1 billion	44.44%	4
1-4 billion	11.11%	1
>4 billion	44.44%	4
TOTAL		9

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

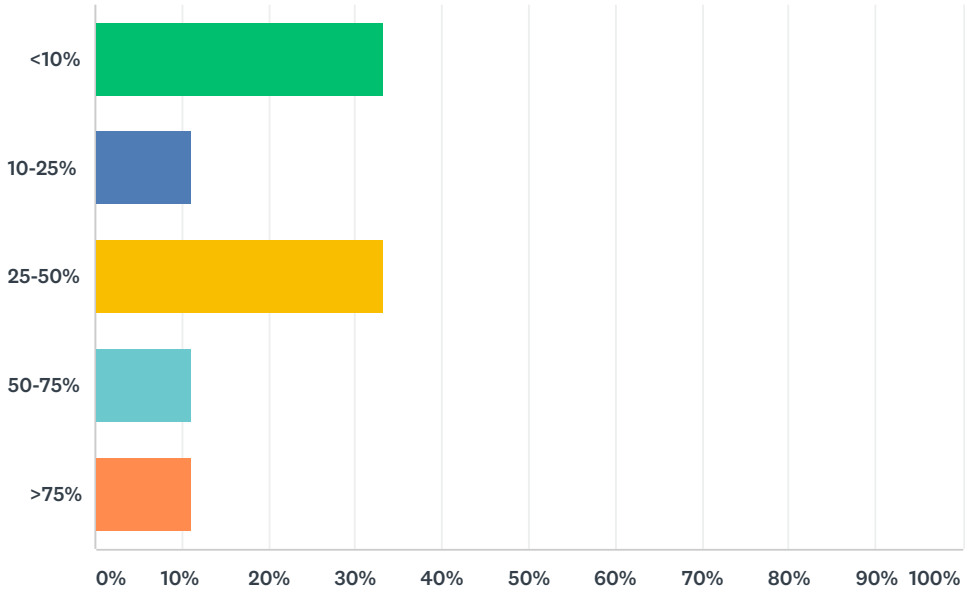
Answered: 9 Skipped: 0



ANSWER CHOICES	RESPONSES	
<10%	0.00%	0
10-25%	11.11%	1
25-50%	22.22%	2
50-75%	44.44%	4
>75%	22.22%	2
TOTAL		9

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

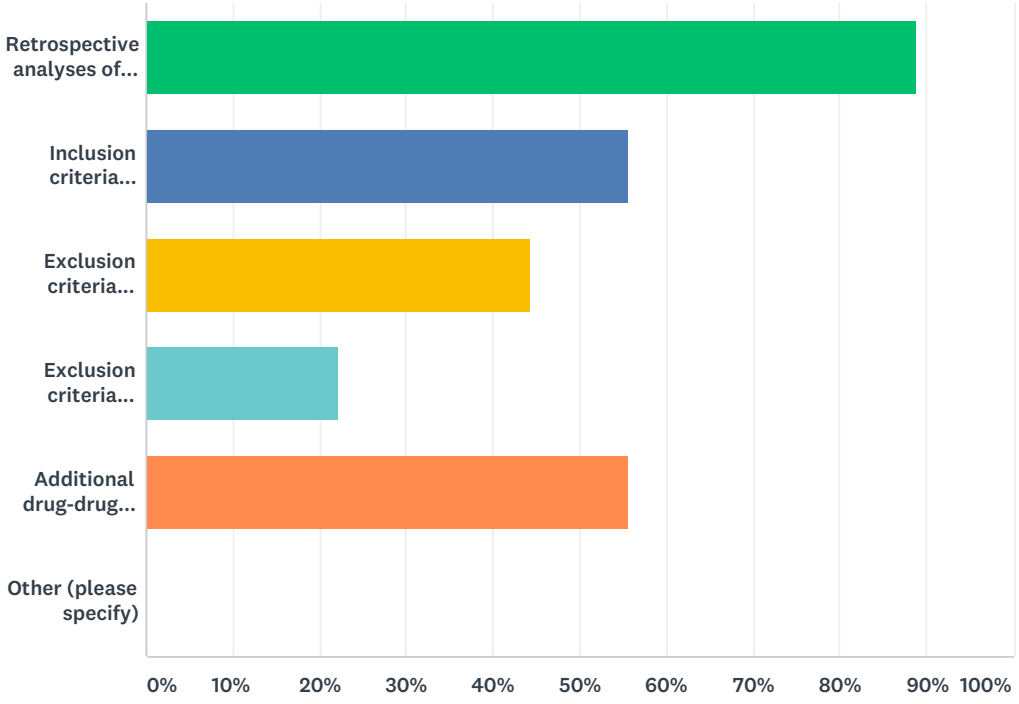
Answered: 9 Skipped: 0



ANSWER CHOICES	RESPONSES	
<10%	33.33%	3
10-25%	11.11%	1
25-50%	33.33%	3
50-75%	11.11%	1
>75%	11.11%	1
TOTAL		9

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: 9 Skipped: 0

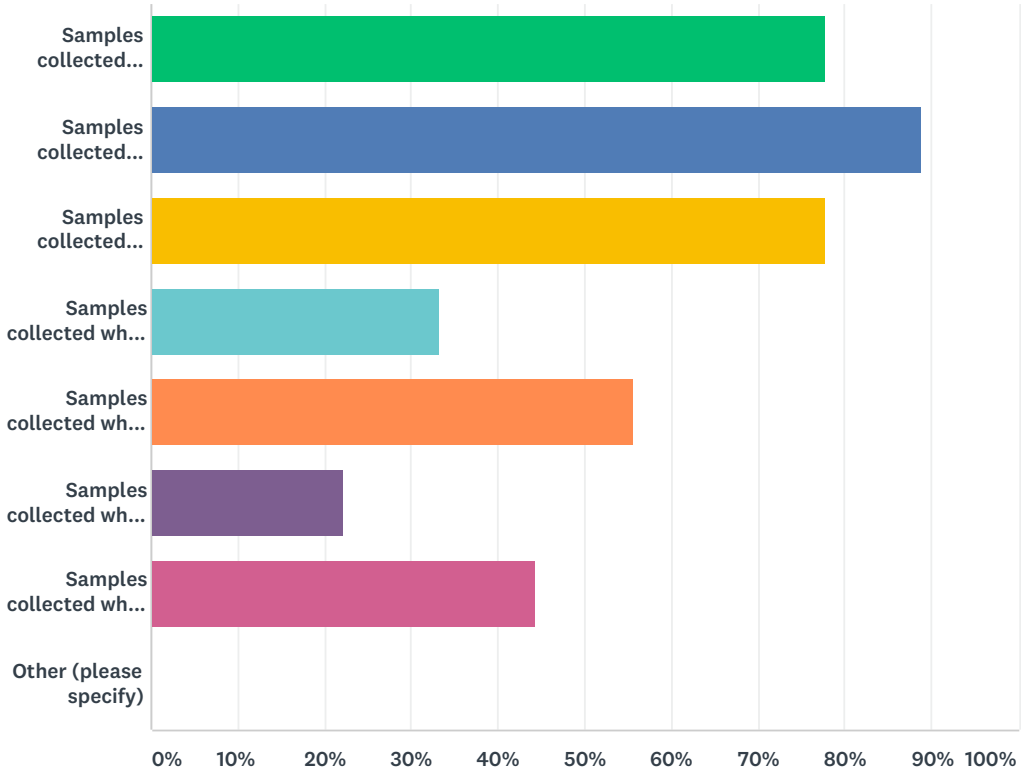


ANSWER CHOICES	RESPONSES	
Retrospective analyses of relevant polymorphisms with endpoints studied in trial subjects	88.89%	8
Inclusion criteria specified or separate trials conducted to asses genetic effects in an enriched patient population	55.56%	5
Exclusion criteria applied to restrict patients with genotypes predicted to result in significantly higher exposure to compound	44.44%	4
Exclusion criteria applied to restrict patients with genotypes predicted to result in significantly lower plasma exposure to compound	22.22%	2
Additional drug-drug interaction studies or modified design of planned drug-drug interaction studies	55.56%	5
Other (please specify)	0.00%	0
Total Respondents: 9		

#	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: 9 Skipped: 0

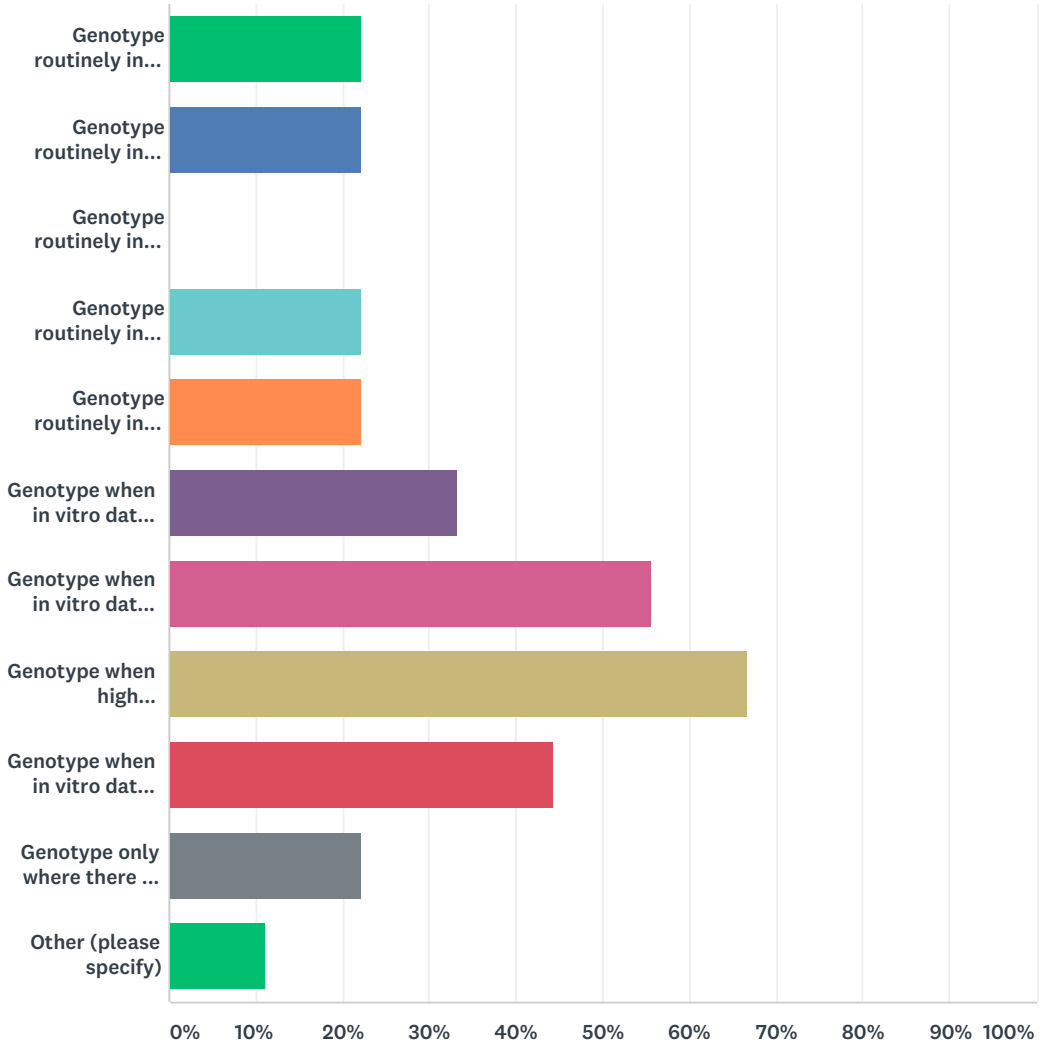


ANSWER CHOICES	RESPONSES	
Samples collected routinely in Phase I	77.78%	7
Samples collected routinely in Phase II	88.89%	8
Samples collected routinely in Phase III	77.78%	7
Samples collected when in vitro data suggests any involvement of a polymorphic enzyme or transporter	33.33%	3
Samples collected when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition	55.56%	5
Samples collected when high pharmacokinetic variability is observed in phase 1 clinical trials	22.22%	2
Samples collected when in vitro data suggests any enzyme or transporter is a major contributor to disposition	44.44%	4
Other (please specify)	0.00%	0
Total Respondents: 9		

#	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: 9 Skipped: 0



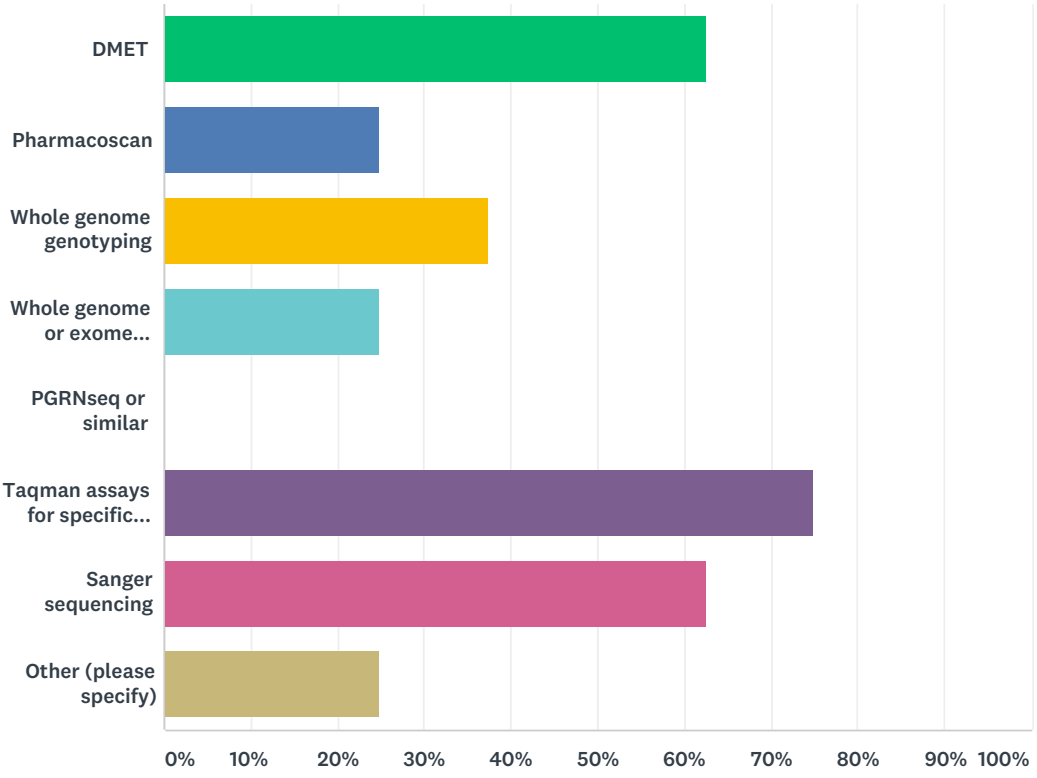
ANSWER CHOICES	RESPONSES	
Genotype routinely in all phase I studies	22.22%	2
Genotype routinely in DDI studies	22.22%	2
Genotype routinely in ascending dose studies	0.00%	0
Genotype routinely in phase II studies	22.22%	2
Genotype routinely in all phase III studies	22.22%	2
Genotype when in vitro data suggests any involvement of a polymorphic enzyme or transporter	33.33%	3
Genotype when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition	55.56%	5
Genotype when high pharmacokinetic variability is observed in phase 1 clinical trials	66.67%	6
Genotype when in vitro data suggests any enzyme or transporter is a major contributor to disposition	44.44%	4

Genotype only where there is expected to be sufficient power to conduct an analysis for specific genes/alleles of interest	22.22%	2
Other (please specify)	11.11%	1
Total Respondents: 9		

#	OTHER (PLEASE SPECIFY)	DATE
1	genotype when PK is variable AND a polymorphic enzyme/tranpsporter is a contributor	9/13/2019 5:20 PM

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

Answered: 8 Skipped: 1



ANSWER CHOICES	RESPONSES	
DMET	62.50%	5
Pharmacoscan	25.00%	2
Whole genome genotyping	37.50%	3
Whole genome or exome sequencing	25.00%	2
PGRNseq or similar	0.00%	0
Taqman assays for specific variants	75.00%	6
Sanger sequencing	62.50%	5
Other (please specify)	25.00%	2
Total Respondents: 8		

#	OTHER (PLEASE SPECIFY)	DATE
1	array - PMRA	10/11/2019 2:04 PM
2	Open Array (Taqman), Fragment Analysis, Ion Torrent S5 PGx Panel	9/13/2019 5:20 PM

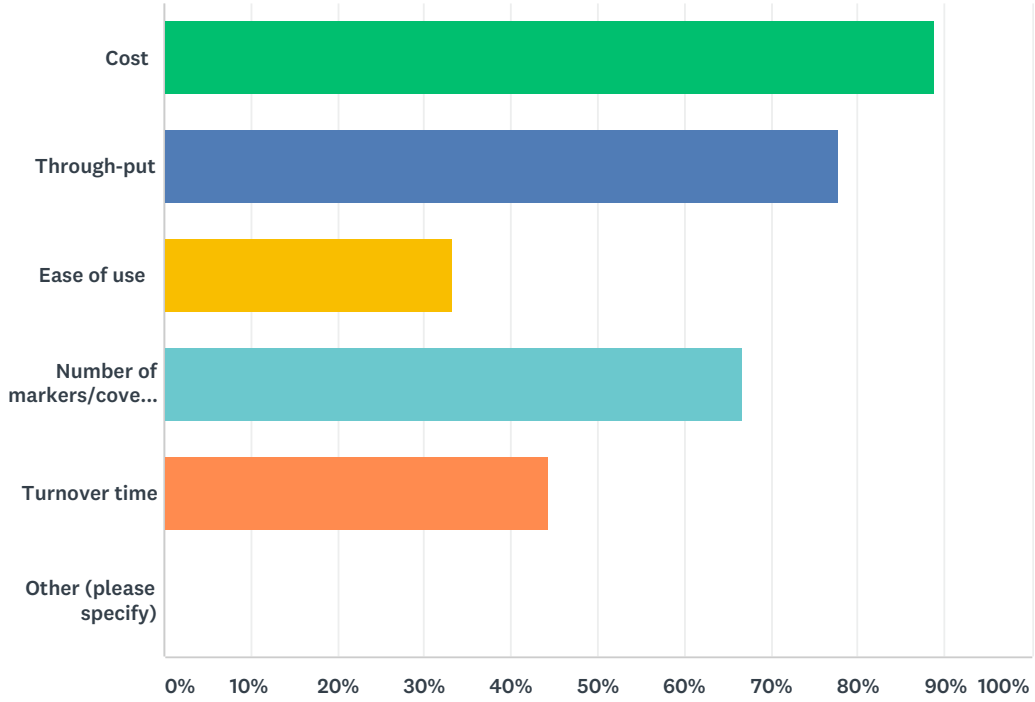
Q8 If you answered "Other" to Question 7 or if different genotyping technologies are used in different scenarios (eg. routine genotyping, PK outlier, phase of development, etc.) please describe further.

Answered: 3 Skipped: 6

#	RESPONSES	DATE
1	na	10/25/2019 1:19 PM
2	array for all supplemented with bespoke assays	10/11/2019 2:04 PM
3	Taqman Open Array, Fragment Analysis, Ion Torrent S5 PGx Panel: based on need of panel size and throughput	9/13/2019 5:20 PM

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

Answered: 9 Skipped: 0

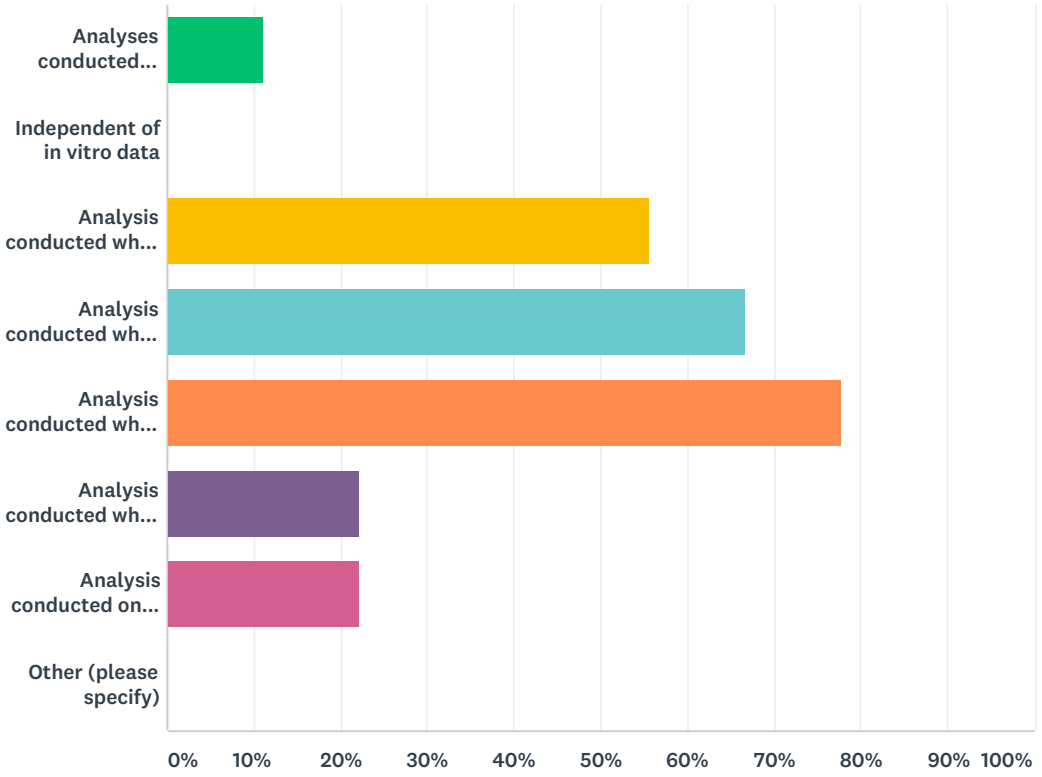


ANSWER CHOICES	RESPONSES	
Cost	88.89%	8
Through-put	77.78%	7
Ease of use	33.33%	3
Number of markers/coverage	66.67%	6
Turnover time	44.44%	4
Other (please specify)	0.00%	0
Total Respondents: 9		

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

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: 9 Skipped: 0

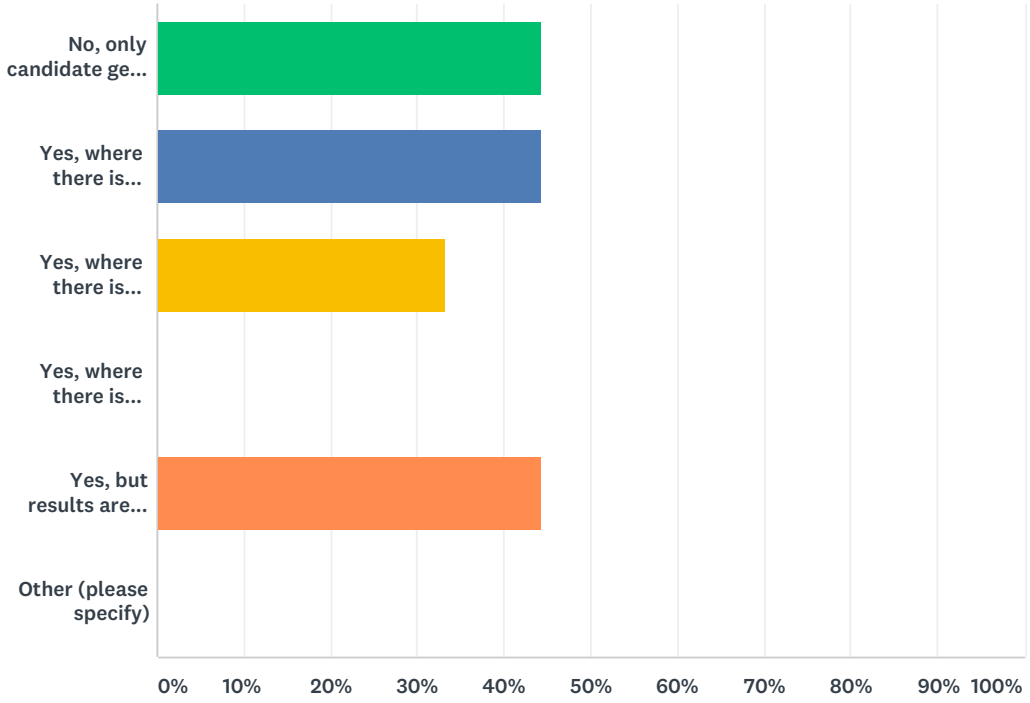


ANSWER CHOICES	RESPONSES	
Analyses conducted routinely	11.11%	1
Independent of in vitro data	0.00%	0
Analysis conducted when in vitro data suggests any involvement of a certain enzymes or transporters	55.56%	5
Analysis conducted when in vitro data suggests certain enzymes or transporters are a major contributor to disposition	66.67%	6
Analysis conducted when high pharmacokinetic variability is observed in phase 1 clinical trials	77.78%	7
Analysis conducted when in vitro data suggests any enzyme or transporter is a major contributor to disposition	22.22%	2
Analysis conducted only where there is expected to be sufficient statistical power to conduct an analysis for specific genes/alleles of interest	22.22%	2
Other (please specify)	0.00%	0
Total Respondents: 9		

#	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: 9 Skipped: 0



ANSWER CHOICES	RESPONSES	
No, only candidate genes based on preclinical or early clinical work are explored	44.44%	4
Yes, where there is unexplained PK variability	44.44%	4
Yes, where there is uncertainty around genes involved in disposition	33.33%	3
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	44.44%	4
Other (please specify)	0.00%	0
Total Respondents: 9		

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

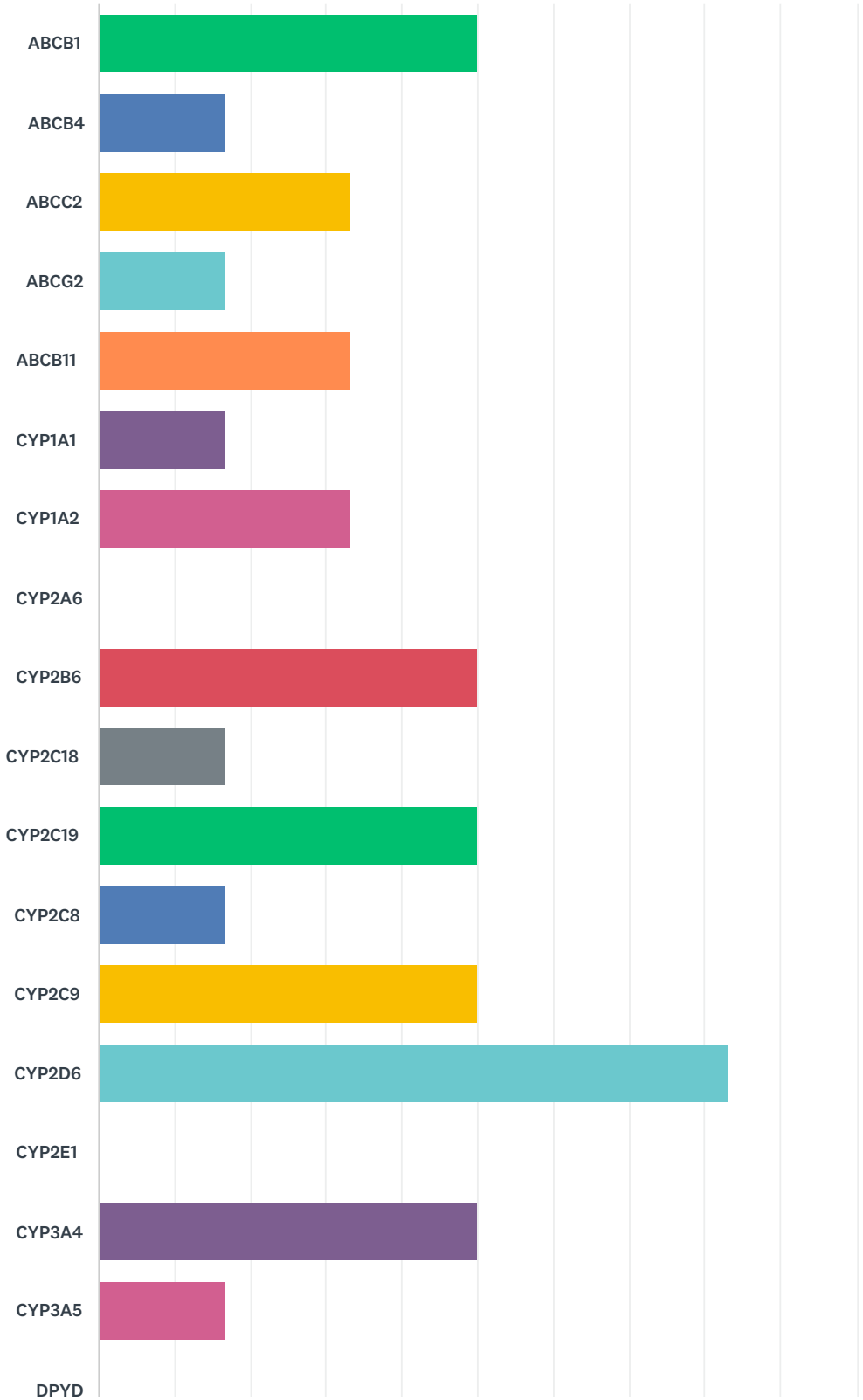
Q12 If you answered "No" to Question 11 please describe the main reasons why your company does not conduct such analyses (eg lack of scientific justification, cost of analyses, lack of resources, etc.).

Answered: 5 Skipped: 4

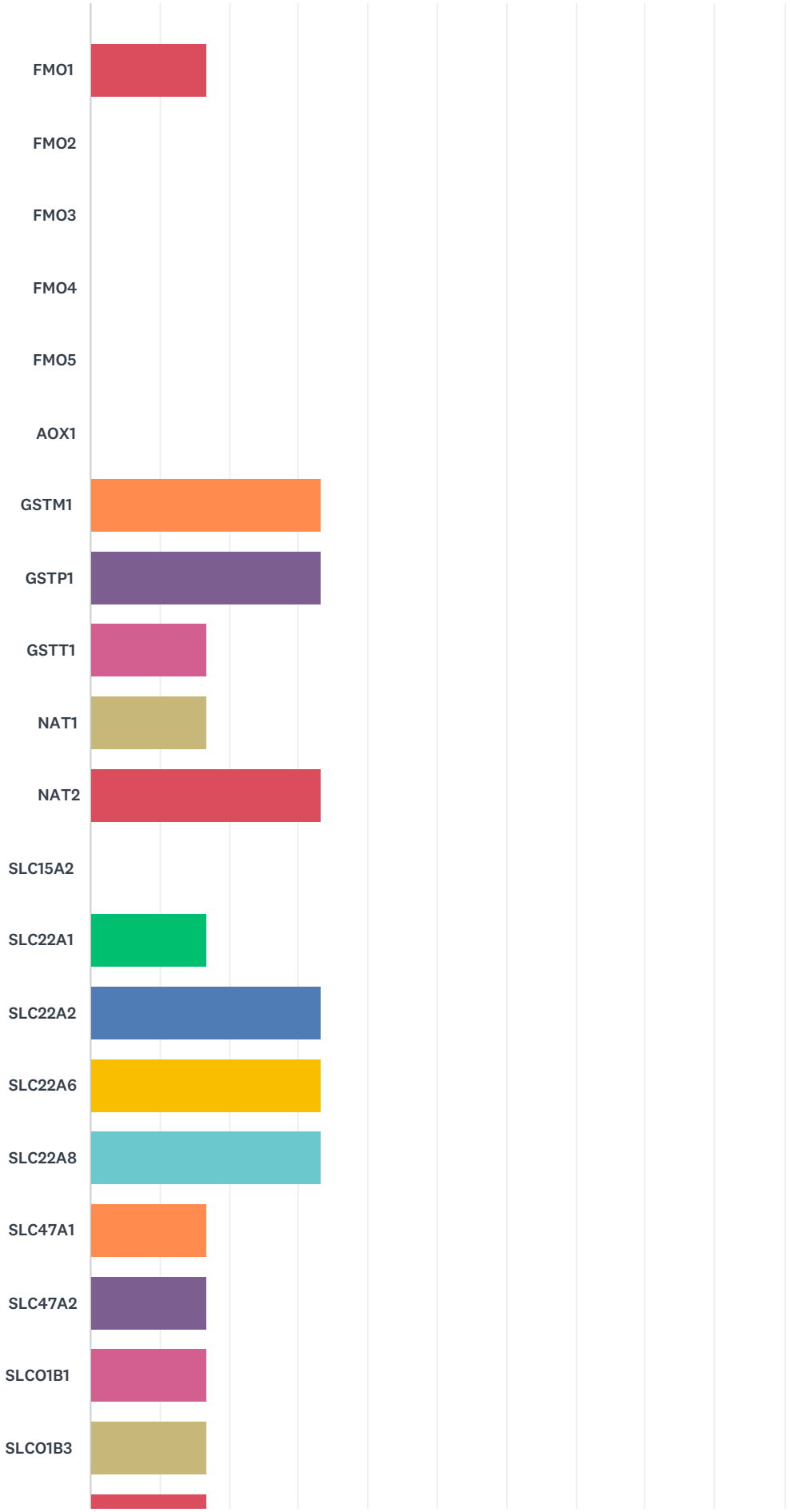
#	RESPONSES	DATE
1	na	10/25/2019 1:19 PM
2	cost of analyses and lack of resources	10/11/2019 8:40 PM
3	low chance of success	10/11/2019 2:04 PM
4	Cost, lack of novel genotype to phenotype clinical understanding, guidance documents, power concerns	9/13/2019 5:20 PM
5	Lack of scientific justification and resources	9/12/2019 2:42 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?

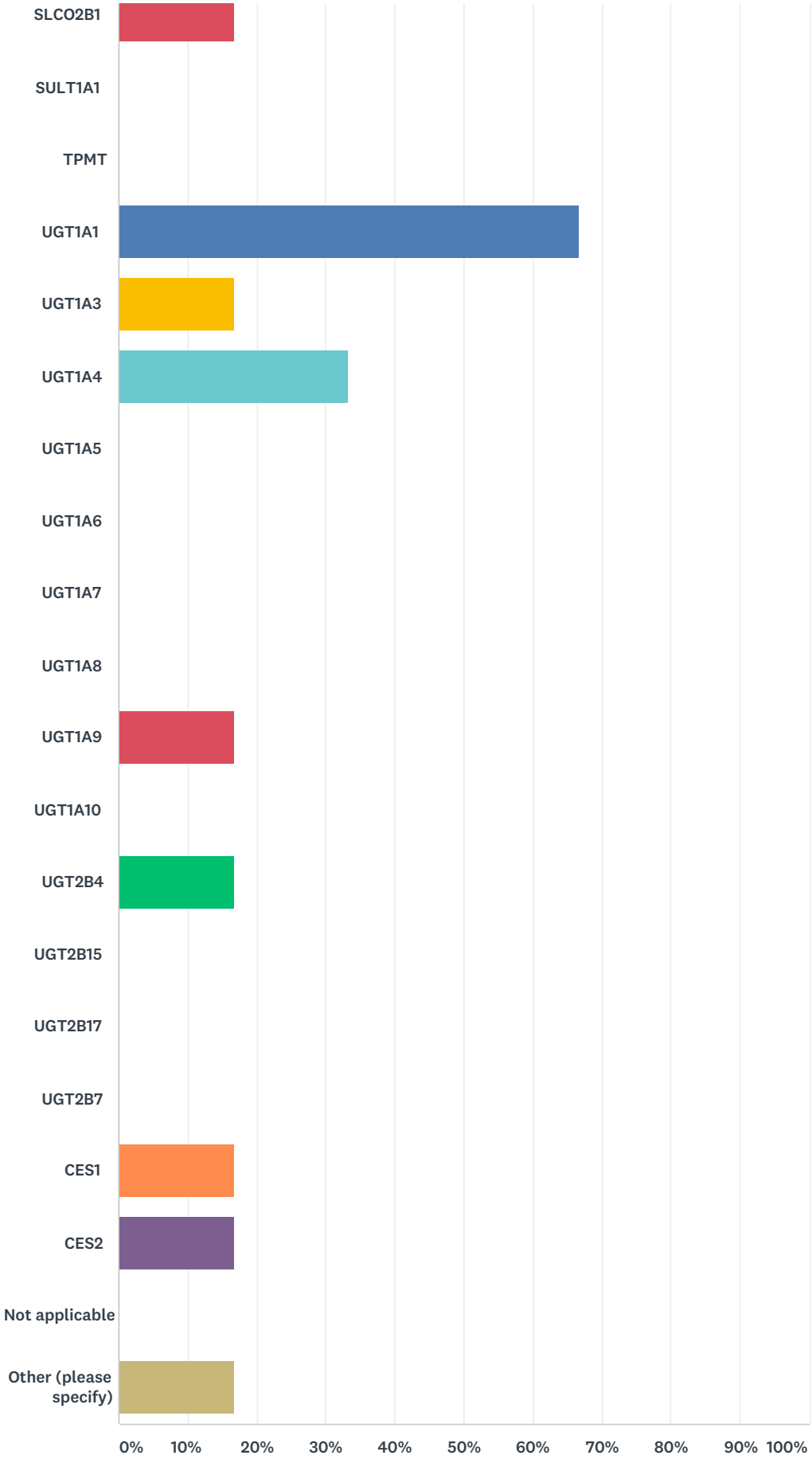
Answered: 6 Skipped: 3



Current ADME PGx Clinical Strategy/Implementation



Current ADME PGx Clinical Strategy/Implementation



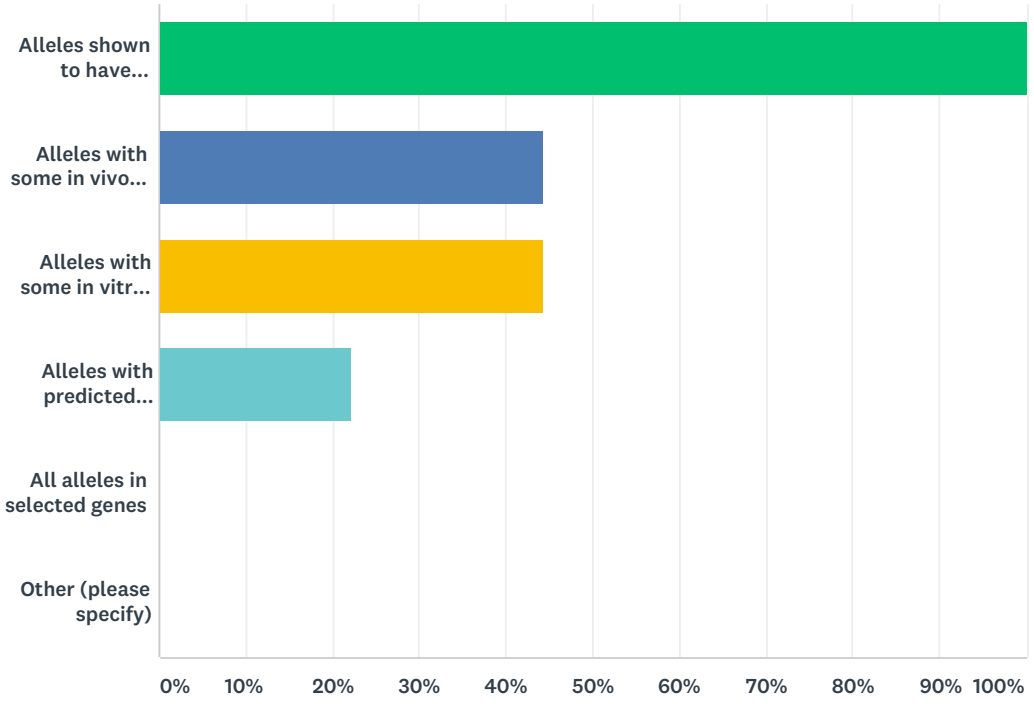
ANSWER CHOICES	RESPONSES	
ABCB1	50.00%	3
ABCB4	16.67%	1
ABCC2	33.33%	2
ABCG2	16.67%	1
ABCB11	33.33%	2
CYP1A1	16.67%	1
CYP1A2	33.33%	2
CYP2A6	0.00%	0
CYP2B6	50.00%	3
CYP2C18	16.67%	1
CYP2C19	50.00%	3
CYP2C8	16.67%	1
CYP2C9	50.00%	3
CYP2D6	83.33%	5
CYP2E1	0.00%	0
CYP3A4	50.00%	3
CYP3A5	16.67%	1
DPYD	0.00%	0
FMO1	16.67%	1
FMO2	0.00%	0
FMO3	0.00%	0
FMO4	0.00%	0
FMO5	0.00%	0
AOX1	0.00%	0
GSTM1	33.33%	2
GSTP1	33.33%	2
GSTT1	16.67%	1
NAT1	16.67%	1
NAT2	33.33%	2
SLC15A2	0.00%	0
SLC22A1	16.67%	1
SLC22A2	33.33%	2
SLC22A6	33.33%	2
SLC22A8	33.33%	2

SLC47A1	16.67%	1
SLC47A2	16.67%	1
SLCO1B1	16.67%	1
SLCO1B3	16.67%	1
SLCO2B1	16.67%	1
SULT1A1	0.00%	0
TPMT	0.00%	0
UGT1A1	66.67%	4
UGT1A3	16.67%	1
UGT1A4	33.33%	2
UGT1A5	0.00%	0
UGT1A6	0.00%	0
UGT1A7	0.00%	0
UGT1A8	0.00%	0
UGT1A9	16.67%	1
UGT1A10	0.00%	0
UGT2B4	16.67%	1
UGT2B15	0.00%	0
UGT2B17	0.00%	0
UGT2B7	0.00%	0
CES1	16.67%	1
CES2	16.67%	1
Not applicable	0.00%	0
Other (please specify)	16.67%	1
Total Respondents: 6		

#	OTHER (PLEASE SPECIFY)	DATE
1	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 10:11 PM

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

Answered: 9 Skipped: 0

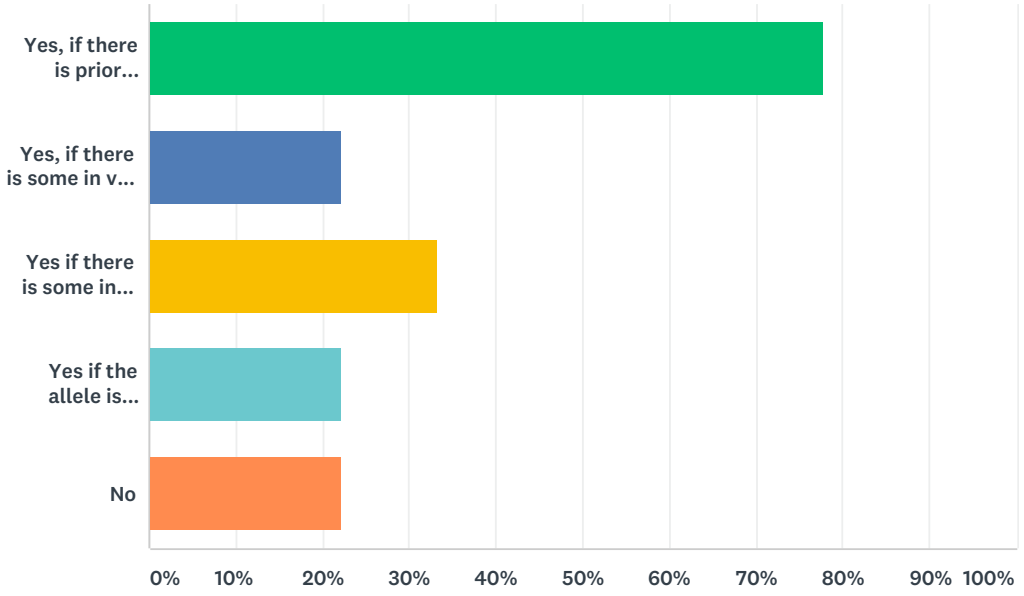


ANSWER CHOICES	RESPONSES	
Alleles shown to have clinically meaningful impact on PK of other substrates	100.00%	9
Alleles with some in vivo evidence of change in activity or expression	44.44%	4
Alleles with some in vitro evidence of change in activity or expression	44.44%	4
Alleles with predicted impact on protein function or expression based on in silico algorithms	22.22%	2
All alleles in selected genes	0.00%	0
Other (please specify)	0.00%	0
Total Respondents: 9		

#	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.

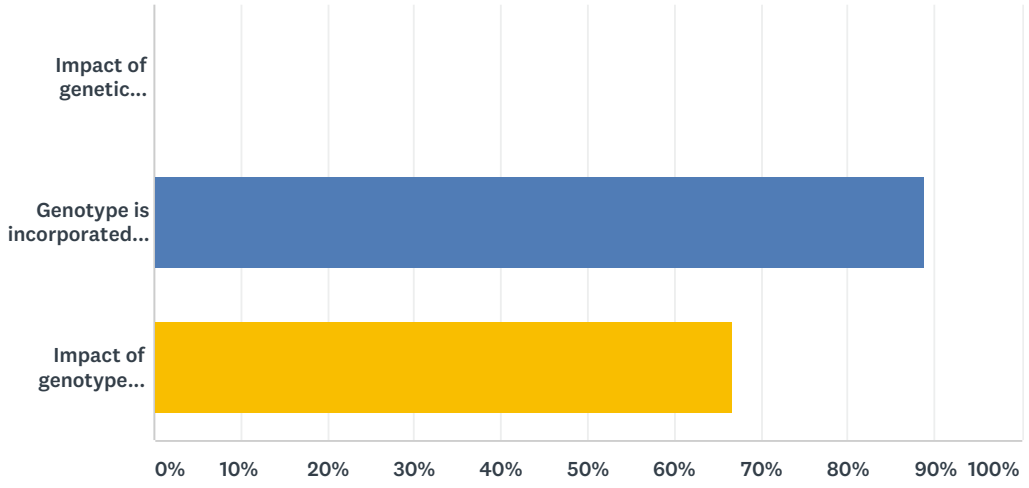
Answered: 9 Skipped: 0



ANSWER CHOICES	RESPONSES	
Yes, if there is prior evidence that the allele has a clinical meaningful impact on PK of other substrates	77.78%	7
Yes, if there is some in vivo evidence of functional impact of the allele	22.22%	2
Yes if there is some in vitro evidence of functional impact of the allele	33.33%	3
Yes if the allele is predicted to alter protein function or expression by in silico algorithms	22.22%	2
No	22.22%	2
Total Respondents: 9		

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: 9 Skipped: 0



ANSWER CHOICES	RESPONSES	
Impact of genetic variation is not analyzed in such studies	0.00%	0
Genotype is incorporated as a covariate in population PK models	88.89%	8
Impact of genotype assessed using PK parameter estimated using population PK models or other approaches from the data available	66.67%	6
Total Respondents: 9		

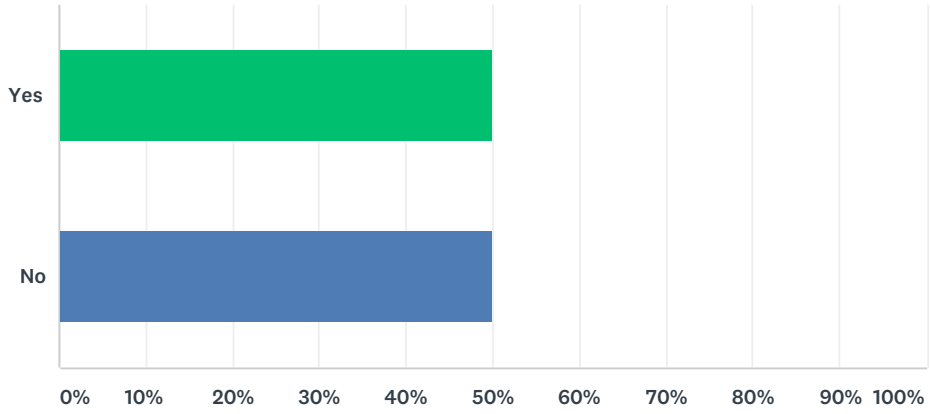
Q17 As a follow-up to Question 16 if multiple approaches have been used, please describe the factors that inform on choice of approach:

Answered: 6 Skipped: 3

#	RESPONSES	DATE
1	reproducibility	10/25/2019 1:19 PM
2	Data availability and quality.	10/14/2019 9:39 PM
3	Ideally would use both approaches in such scenarios.	10/11/2019 10:11 PM
4	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 8:40 PM
5	The level of evidence that is available	10/9/2019 1:58 PM
6	Depends on the clinical trial size (single vs. combinatorial), popPK vs thorough PK assessment.	9/13/2019 5:20 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: 8 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes	50.00%	4
No	50.00%	4
TOTAL		8

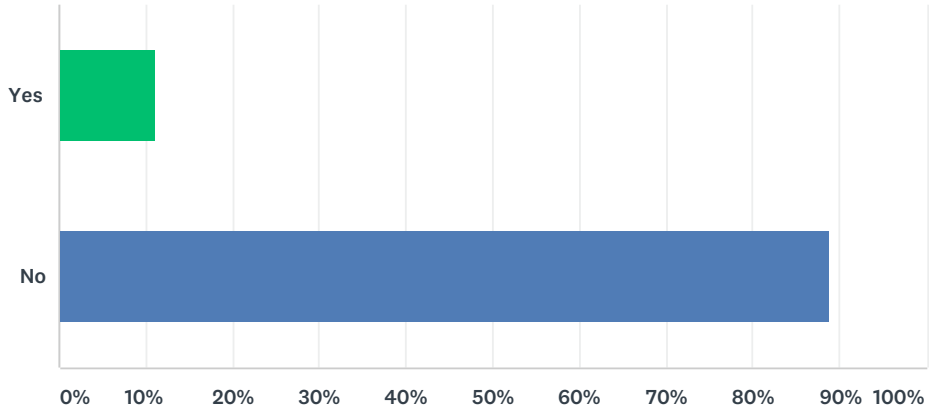
Q19 If you answered "Yes" to Question 19 please describe:

Answered: 3 Skipped: 6

#	RESPONSES	DATE
1	na	10/25/2019 1:19 PM
2	Yes if TMDD was a consideration for the program.	10/11/2019 10:11 PM
3	In vitro studies are done to inform the potential impact.	10/9/2019 1:58 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: 9 Skipped: 0



ANSWER CHOICES	RESPONSES	
Yes	11.11%	1
No	88.89%	8
TOTAL		9

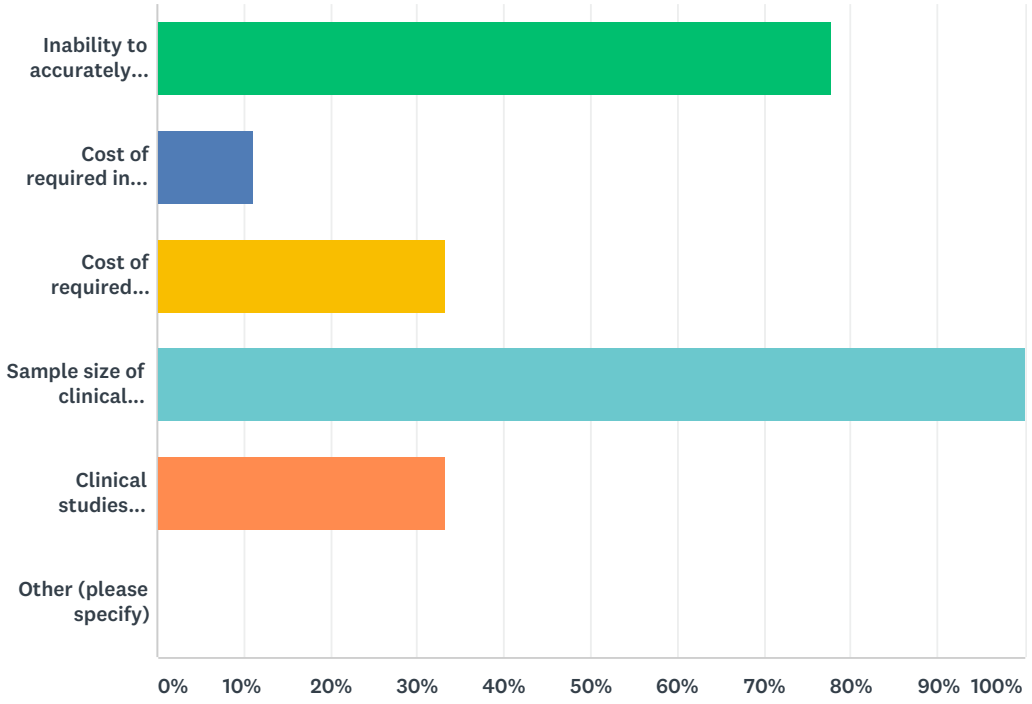
Q21 If you answered "Yes" to Question 21 please describe:

Answered: 2 Skipped: 7

#	RESPONSES	DATE
1	na	10/25/2019 1:19 PM
2	If tremendous variability in PK is observed, genotyping studies may be undertaken.	10/9/2019 1:58 PM

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

Answered: 9 Skipped: 0

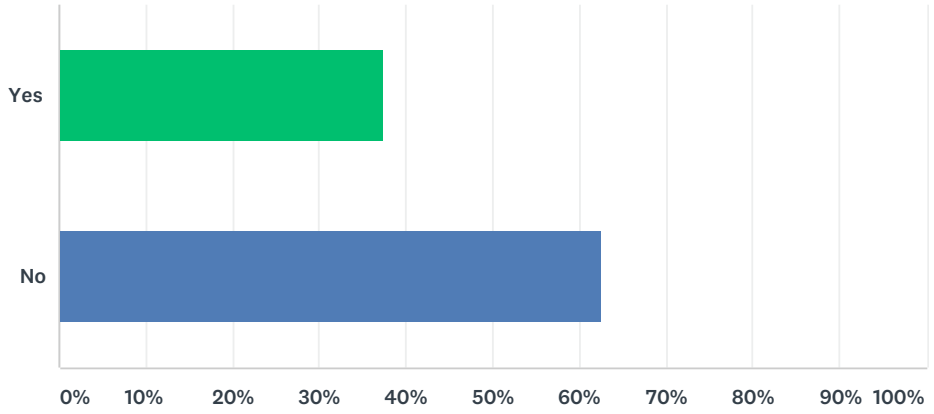


ANSWER CHOICES	RESPONSES	
Inability to accurately determine contribution of enzymes/transporters,	77.78%	7
Cost of required in vitro experiments	11.11%	1
Cost of required clinical studies	33.33%	3
Sample size of clinical studies limits ability to conduct genetic analyzes	100.00%	9
Clinical studies typically limited to certain populations	33.33%	3
Other (please specify)	0.00%	0
Total Respondents: 9		

#	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: 8 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes	37.50%	3
No	62.50%	5
TOTAL		8

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

Answered: 4 Skipped: 5

#	RESPONSES	DATE
1	na	10/25/2019 1:19 PM
2	HLA and ADME	10/11/2019 10:11 PM
3	genome wide and known genes	10/11/2019 2:04 PM
4	CYP2D6	9/12/2019 2:42 PM