Q1 Q1 How often has your company collected DNA with consent for ADME-related genotyping in:

Answered: 16 Skipped: 1

	ALWAYS	USUALLY	SOMETIMES	NEVER	TOTAL
First in human	43.75% 7	37.50% 6	12.50% 2	6.25% 1	16
Multiple rising dose	31.25% 5	50.00% 8	6.25% 1	12.50% 2	16
Drug-drug interaction	26.67% 4	33.33% 5	40.00% 6	0.00% 0	15
Special population	18.75% 3	18.75% 3	56.25% 9	6.25% 1	16
Other clin pharm	21.43% 3	14.29% 2	50.00% 7	14.29% 2	14
Proof of concept	25.00% 4	25.00% 4	31.25% 5	18.75% 3	16
Dose ranging	18.75% 3	25.00% 4	43.75% 7	12.50% 2	16
Pivotal	12.50% 2	31.25% 5	43.75% 7	12.50% 2	16
Other	10.00% 1	0.00% 0	70.00% 7	20.00% 2	10

Q2 How often has your company specified ADME PGx analysis in study protocols?

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
Always	6.25%	1
usually	12.50%	2
Sometimes	75.00%	12
Never	6.25%	1
TOTAL		16

Q3 Breadth of genotyping. Please check whether your company currently genotypes each gene.

Answered: 14 Skipped: 3

	YES	NO	TOTAL
CYP1A2	50.00% 6	50.00% 6	12
CYP2A6	50.00% 6	50.00% 6	12
CYP2B6	58.33% 7	41.67% 5	12
CYP2C8	50.00% 6	50.00% 6	12
CYP2C9	78.57% 11	21.43% 3	14
CYP2C19	75.00% 9	25.00% 3	12
CYP2D6	100.00% 14	0.00% 0	14
CYP3A4	76.92% 10	23.08% 3	13
CYP3A5	84.62% 11	15.38% 2	13
Other phase I enzyme	72.73% 8	27.27% 3	11
UGT1A1	76.92% 10	23.08% 3	13
TPMT	16.67% 2	83.33% 10	12
Other phase II enzyme	72.73% 8	27.27% 3	11
OATP1B1	83.33% 10	16.67% 2	12
BCRP	50.00% 6	50.00% 6	12
MDR1	58.33% 7	41.67% 5	12

#	OTHER (PLEASE SPECIFY)	DATE
1	DMET Chip, ABCB1	10/8/2013 9:47 PM
2	The Affymetrix DMET chip is used, although TMPT data are not collected.	10/4/2013 9:02 PM
3	ABCB1, ABCG2	10/3/2013 11:12 PM
4	NAT2	10/3/2013 11:28 AM
5	EPHX1, EPHX2, GSTM1, GSTT1, GSTP1, NAT1, NAT2, UGT1A9, UGT2B4, UGT2B7,	9/27/2013 7:11 PM

	SLCO2B1, SLCO1B3, SLC10A1, ABCG2, ABCC2	
6	other UGTs based on in vitro data	9/26/2013 3:11 PM
7	targeted genes case by case	9/26/2013 2:30 PM
8	We have not done yet. Hoping to perform in the future.	9/24/2013 8:33 PM
9	We use multi-gene platforms (eg DMET chip) So we capture data on all	9/24/2013 6:19 PM
10	GSTP1, GSTM1, UGT1A9, UGT1B15	9/23/2013 2:09 PM

Q4 What triggers genotyping? Check all that apply

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
When preclinical data indicate a role for a specific gene in a compound's PK	93.75%	15
Standard practice to broadly genotype and collect data across program	25.00%	4
Retrospective, when high PK variability or PK outlier observed	75.00%	12
Total Respondents: 16		

#	OTHER (PLEASE SPECIFY)	DATE
1	FDA requirement	10/8/2013 9:47 PM
2	Regulatory Requests	9/27/2013 7:11 PM
3	If adverse events have emerged (even in absence of pk variability) that might be explained by genetic determinants of drug disposition (transporters, adduct formation, etc)	9/24/2013 6:19 PM
4	concomitant meds that are polymorphicly metabolized	9/23/2013 2:09 PM

Q5 During Ph1, the EMA Guidance states that genotyping should be conducted if a polymorphic enzyme constitutes >25% of the overall clearance, and >50% based on in vitro data. Are the EMA thresholds appropriate?

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
Yes	68.75%	11
No	31.25%	5
TOTAL		16

#	IF NO SUGGEST ALTERNATIVES	DATE
1	Our organization generally has considered 30% as the appropriate cutoff for overall clearance	9/27/2013 7:11 PM
2	It is not so straightforward depends on candidate enzymes, tranporters & current understanding of clinical relevance	9/26/2013 2:30 PM
3	Each program has multiple things to consider in the context of the drug clearance it is not a simple cut off that should trigger genotyping. e.g. the disease indication, PK variability, therapeutic window (clinical bounds), the frequency of the variant , the ethnic population being studied etc	9/24/2013 6:19 PM
4	in vivo clearance >50% is our trigger point	9/23/2013 2:09 PM
5	Criterion is a bit out of reality since ADME is usually not part of early Phase I and, therefore, contribution of partial clearances not yet known	9/5/2013 12:20 PM

Q6 How often does your company have a written plan or strategy for a compound in development that includes prospective ADME genotyping during Ph1?

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
Always	12.50%	2
Usually	6.25%	1
Sometimes	62.50%	10
Never	18.75%	3
TOTAL		16

Q7 How often has your company performed ADME-related genotyping in:

Answered: 16 Skipped: 1

	ALWAYS	USUALLY	SOMETIMES	NEVER	TOTAL RESPONDENTS
First in human	6.67% 1	13.33% 2	73.33% 11	6.67% 1	15
Multiple rising dose	6.67% 1	13.33% 2	73.33% 11	6.67% 1	15
Drug-drug interaction	28.57% 4	7.14% 1	64.29% 9	0.00% 0	14
Special population	7.14% 1	0.00% 0	57.14% 8	35.71% 5	14
Other clin pharm	0.00% 0	7.14% 1	57.14% 8	35.71% 5	14
Proof of concept	0.00% 0	0.00% 0	66.67% 10	33.33% 5	15
Dose ranging	0.00% 0	0.00% 0	71.43% 10	28.57% 4	14
Pivotal	0.00% 0	0.00% 0	71.43% 10	28.57% 4	14
Other	0.00% 0	0.00% 0	50.00% 6	50.00% 6	12

Q8 Has your company used ADME-related genotype(s) in study design?

Answered: 16 Skipped: 1

	YES	NO	TOTAL RESPONDENTS
Inclusion criterion	75.00% 12	25.00% 4	16
Exclusion criterion	68.75% 11	31.25% 5	16
Dose Adjustment	26.67% 4	73.33% 11	15

#	IF YES WHICH GENES	DATE
1	CYP2C19	10/8/2013 9:47 PM
2	CYP2D6, CYP2C19, UGT1A1, OATP1B1	10/4/2013 9:02 PM
3	CYP2D6	10/3/2013 11:12 PM
4	CYP2D6, CYP2C9, CYP2C19 (ADME genes listed only)	9/27/2013 7:11 PM
5	CYP2D6, CYP2C19, CYP2C9	9/26/2013 3:11 PM
6	CYP2D6	9/25/2013 9:37 PM
7	CYP2D6 and UGT1A1. While not specifically trial design we have included specific genotyping in pivotal studies based on phase 2 exploratory data	9/24/2013 6:19 PM
8	CYP2D6, CYP2C19	9/23/2013 2:09 PM
9	CYP2D6, CYP2C9	9/16/2013 5:29 PM

Q9 If Yes to Study design what types of study? All that apply

Answered: 11 Skipped: 6

ANSWER CHOICES	RESPONSES	
First in human	27.27%	3
Multiple rising dose	45.45%	5
Drug-drug interaction	54.55%	6
Special population	18.18%	2
Other clin pharm	36.36%	4
Proof of concept	0.00%	0
Dose ranging	36.36%	4
Pivotal	9.09%	1
Other	9.09%	1
Total Respondents: 11		

Q10 Where is your ADME PGx testing performed for clinical studies?

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
Internal Lab	0.00%	0
External Lab	62.50%	10
Both internal and external labs	37.50%	6
TOTAL		16

Q11 If you use an external vendor what drives the decision? (examples, Laboratory certification, lack of internal resources….)

Answered: 16 Skipped: 1

#	RESPONSES	DATE
1	Lack of internal resources	10/8/2013 9:47 PM
2	Overall R&D agreement for that to be done at a specific CRO.	10/4/2013 9:02 PM
3	Expertise	10/3/2013 11:12 PM
4	Performance charateristics and experience	10/3/2013 11:28 AM
5	Until recently, ADME genotyping was performed both internally and externally. Re-organization and prioritization of resources led to decision to use external lab exclusively for ADME genotyping.	9/27/2013 7:11 PM
6	laboratory certification	9/26/2013 3:11 PM
7	Capabilities & quality	9/26/2013 2:30 PM
8	Lack of internal resource, lab certification	9/25/2013 9:37 PM
9	Genotyping expertise, lab certification, battery of testings	9/24/2013 8:33 PM
10	Laboratory certifcationa and lack of internal resources	9/24/2013 6:19 PM
11	China	9/23/2013 2:09 PM
12	Lack of internal resources	9/22/2013 11:26 PM
13	quality certificate + resources + technical capabilities + platforms	9/18/2013 2:08 PM
14	Quality level requirement	9/16/2013 5:29 PM
15	Laboratory certification	9/5/2013 5:04 PM
16	cost and lack of internal resources	9/5/2013 12:20 PM

Q12 If genotyping is done in-house, what genotyping platform is used?

Answered: 8 Skipped: 9

ANSWER CHOICES	RESPONSES	
Taqman ADME assay	87.50%	7
Affymetrix DMET chip	37.50%	3
Roche AmpliChip	12.50%	1
Sanger sequencing	37.50%	3
NextGen sequencing	12.50%	1
Total Respondents: 8		

#	OTHER (PLEASE SPECIFY)	DATE
1	Not applicable	9/27/2013 7:11 PM
2	Illumina chip, Pyrosequencing, DDPCR	9/22/2013 11:26 PM
3	pyrosequencing	9/18/2013 2:08 PM

Q13 Please state reasons for the choice of your in-house genotyping platform(s) (cost, through-put, ease of use, number of markers…)

Answered: 8 Skipped: 9

#	RESPONSES	DATE
1	Not applicable	9/27/2013 7:11 PM
2	cost, throughput, ease of use, number of markers (case by case)	9/25/2013 9:37 PM
3	Cost and ease of use etc..	9/24/2013 8:33 PM
4	cost, ease of use, quality (CLIA certified)	9/23/2013 2:09 PM
5	Cost, ease use,	9/22/2013 11:26 PM
6	quality + possibility of validation + cost + ease of use + sensitivity	9/18/2013 2:08 PM
7	cost, throughput, # of SNPs, TAT	9/16/2013 5:29 PM
8	through-put or number of markers	9/5/2013 5:04 PM

Q14 If ADME PGx is planned to evaluate PK variability, will any specific approach / platform your company be considered for the following situation:

Answered: 15 Skipped: 2

	CANDIDATE GENE APPROACHES	HYPOTHESIS FREE APPROACHES	WAS IT SUCCESSFUL?	TOTAL RESPONDENTS
PK Outlier	92.86% 13	50.00% 7	57.14% 8	14
Drug-drug interaction	91.67% 11	25.00% 3	33.33% 4	12
Known PK property	92.31% 12	23.08% 3	61.54% 8	13
Unclear PK property	45.45% 5	54.55% 6	45.45% 5	11

#	WHICH PLATFORMS WERE USED?	DATE
1	TaqMan, Illumina Beadchip, Affy DMET	10/4/2013 9:02 PM
2	Please elaborate on "unclear PK property	10/3/2013 11:12 PM
3	Small scale genotyping (e.g., Taqman, sanger sequencing)	9/27/2013 7:11 PM
4	DMET, TaqMan, AmpliChip	9/25/2013 9:37 PM
5	Depends on the knowledge available on likely candidate gene and cost for individual assays and cost to design and validate an assay. Once you go over a threshold of genotyping assays larger platforms can be used and analyses are pre-specified in the statistical analysis plan. There is interest in moving toward NGS platforms	9/24/2013 6:19 PM
6	quantitive PCR	9/23/2013 2:09 PM
7	Taqman, DMET	9/16/2013 5:29 PM
8	taqman	9/5/2013 5:04 PM

Q15 Has your company kept/banked DNA beyond the initialperiod of the clinical trial?

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
Yes	100.00%	16
No	0.00%	0
TOTAL		16

Q16 Have stored samples been used to address emerging issues during and/or after clinical trial?

Answered: 17 Skipped: 0

ANSWER CHOICES	RESPONSES	
Yes	94.12%	16
No	5.88%	1
TOTAL		17

Q17 Have regulatory authorities requested/suggested additional analysis on stored samples?

Answered: 17 Skipped: 0

ANSWER CHOICES	RESPONSES	
Yes	52.94%	9
No	47.06%	8
TOTAL		17

Q18 When ADME PGx research has been included in a trial, has it been required for subject enrollment or optional for each subject? (OK to check both boxes in a row)

Answered: 16 Skipped: 1

	YES (MANDATORY)	NO (OPTIONAL)	TOTAL RESPONDENTS
Phase I	56.25% 9	81.25% 13	16
Drug interaction studies	53.33% 8	66.67% 10	15
Phase II	33.33% 5	93.33% 14	15
Phase III	15.38% 2	100.00% 13	13
PhaseIV	15.38% 2	92.31% 12	13

Q19 . Has ADME PGx information been used for decision making at your company

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
Yes	50.00%	8
No	50.00%	8
TOTAL		16

Q20 If yes to 19, was it for a previously validated ADME marker (eg CYP2D6) or novel marker

Answered: 8 Skipped: 9

#	RESPONSES	DATE
1	CYP2D6, CYP2C19	10/4/2013 9:02 PM
2	Yes	10/3/2013 11:12 PM
3	Previously validated	9/27/2013 7:11 PM
4	validated marker	9/26/2013 3:11 PM
5	BOTH Validated and novel	9/24/2013 6:19 PM
6	previously validated	9/18/2013 2:08 PM
7	Yes for a previously validated ADME marker	9/16/2013 5:29 PM
8	previously validated	9/5/2013 5:04 PM

Q21 If yes to 19, what level of validation of the finding was required? Answer all that apply

Answered: 8 Skipped: 9

ANSWER CHOICES	RESPONSES	
An independent replication has always been necessary	12.50%	1
An unreplicated result has been used for internal decision making but not in a regulatory submission	62.50%	5
An unreplicated result based on a known valid biomarker has been used in a regulatory submission	37.50%	3
An unreplicated result based on another biomarker has been used in a regulatory submission	0.00%	0
PG-PK results have not been used	12.50%	1
Total Respondents: 8		

Q22 How has your company’s use of high-throughput genotyping platforms changed in the last five years?

Answered: 15 Skipped: 2

ANSWER CHOICES	RESPONSES	
Increased substantially (>50%)	46.67%	7
Decreased Substantially (>50%)	6.67%	1
Stayed the same	46.67%	7
TOTAL		15

Q23 Has your company used an FDA-approved in vitro diagnostic (UGT1A1 kit or CYP2D6/2C19 chip ….) in the last five years?

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
Yes	25.00%	4
No	75.00%	12
TOTAL		16

Q24 If yes to 23 specify diagnostic type

Answered: 5 Skipped: 12

#	RESPONSES	DATE
1	DMET chip	10/8/2013 9:47 PM
2	COBAS, FISH	10/3/2013 11:28 AM
3	Not applicable	9/27/2013 7:11 PM
4	Amplichip	9/26/2013 3:11 PM
5	UGT1A1	9/18/2013 2:08 PM

Q25 Does your company apply the following standards for human DNA sample collection and generation of human genotype data that might be used in regulatory submissions?

Answered: 15 Skipped: 2

	YES	NO	TOTAL
GCLP (Good Clinical Laboratory Practice)	85.71% 12	14.29% 2	14
GLP (Good Laboratory Practice)	64.29% 9	35.71% 5	14
CLIA (Clinical Laboratory Improvement Amendments)	73.33% 11	26.67% 4	15
CAP (College of American Pathologists)	50.00% 6	50.00% 6	12
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	16.67% 2	83.33% 10	12
ISO (International Organization of Standardization)	50.00% 7	50.00% 7	14
CLSI (Clinical and Laboratory Standards Institute)	27.27% 3	72.73% 8	11

#	OTHER (PLEASE SPECIFY)	DATE
1	GCP	10/3/2013 11:12 PM

Q26 If ADME PGx is used for inclusion/exclusion criteria does your company use a regulated (certified by one of the above agencies) PGx lab to analyze and report ADME genotypes/phenotypes

Answered: 15 Skipped: 2

ANSWER CHOICES	RESPONSES	
Always	66.67%	10
usually	6.67%	1
Sometimes	13.33%	2
Never	13.33%	2
TOTAL		15

#	COMMENTS	DATE
1	GLP quality only	10/4/2013 9:02 PM
2	No experience in inclusion/exclusion ADME PGx	9/26/2013 2:30 PM
3	CLIA	9/24/2013 6:19 PM

Q27 Have regulatory authorities requested/suggested sample collections in you clinical development programs during review meetings?

Answered: 14 Skipped: 3

ANSWER CHOICES	RESPONSES	
Yes	42.86%	6
No	57.14%	8
TOTAL		14

Q28 Have regulatory authorities requested/suggested analysis in you clinical development programs during review meetings?

Answered: 14 Skipped: 3

ANSWER CHOICES	RESPONSES	
Yes	35.71%	5
No	64.29%	9
TOTAL		14

Q29 What sources are used to determine allele/SNP selection? all that apply

Answered: 15 Skipped: 2

ANSWER CHOICES	RESPONSES	
PharmGKB	73.33%	11
dbSNP	86.67%	13
1000genome	80.00%	12
Literature	93.33%	14
determined by platform	33.33%	5
Total Respondents: 15		

#	OTHER (PLEASE SPECIFY)	DATE
1	Other interpretation platform	10/8/2013 9:47 PM
2	Gene-specific nomenclature pages (e.g., Karolinska webpage for P450s, UGT allele tables); Pharmaaddme.org	9/27/2013 7:11 PM
3	NGS	9/18/2013 2:08 PM
4	Ensembl	9/5/2013 12:20 PM

Q30 What sources are used to determine result interpretation? all that apply

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
PharmGKB	75.00%	12
Literature	93.75%	15
Platform specific (eg. DMET Chip)	56.25%	9
Total Respondents: 16		

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

Q31 Have recent FDA and EMA guidances impacted practice of PGx in your company?

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
Yes	50.00%	8
No	50.00%	8
TOTAL		16

#	IF YES, HOW?	DATE
1	Implemented samples collection per FDA guidance	10/8/2013 9:47 PM
2	Practices were consistent with these guidances.	10/4/2013 9:02 PM
3	Provided justification for collection and analysis of DNA samples	9/27/2013 7:11 PM
4	raise internal awareness of ADME genetics	9/26/2013 3:11 PM
5	Interna currently l processes under evaluation	9/26/2013 2:30 PM
6	Guidances are always taken into consideration when considering internal practices around PGx. Guidances have helped drive PGx hypotheses into our development programs, increased collection, and increased implementation of genotyping to answer ADME PGx questions	9/24/2013 6:19 PM

Q32 Have NGS, GWAS or other technologies impacted practice of PGx at your company?

Answered: 15 Skipped: 2

ANSWER CHOICES	RESPONSES	
yes	33.33%	5
no	66.67%	10
TOTAL		15

#	IF YES, HOW?	DATE
1	In discussion to move some work to NGS platforms to try to improve quality of results.	10/4/2013 9:02 PM
2	No, not in the context of ADME-related PGx	9/27/2013 7:11 PM
3	NGS under evaluation	9/26/2013 2:30 PM
4	NGS implementation	9/25/2013 9:37 PM
5	Yes can be applied to understand if there are large signals for response for new Mechanisms. We are considering NGS platform for all genotyping moving forward but not yet implemented for ADME genotyping	9/24/2013 6:19 PM
6	Identification of markers	9/18/2013 2:08 PM

Q33 Please insert the survey code you were given by Covington & Burling (Jenny Green) This code will be used only to assure that each company submits only one response, and to remind companies about submitting the survey. The code key will be maintained only by Covington and Burling (Legal Monitor) and will not be shared with members of the I-PWG.

Answered: 16 Skipped: 1

#	RESPONSES	DATE
1	120970	10/8/2013 9:48 PM
2	105355	10/4/2013 9:02 PM
3	401763	10/3/2013 11:12 PM
4	659869	10/3/2013 11:31 AM
5	178524	9/27/2013 7:12 PM
6	610787	9/26/2013 3:11 PM
7	395509	9/26/2013 2:30 PM
8	963872	9/25/2013 9:39 PM
9	373538	9/24/2013 8:34 PM
10	534921	9/24/2013 6:20 PM
11	989785	9/23/2013 2:10 PM
12	429931	9/22/2013 11:27 PM
13	857046	9/18/2013 2:08 PM
14	125375	9/16/2013 5:32 PM
15	281307	9/5/2013 5:06 PM
16	630861	9/5/2013 12:22 PM

Q34 What were the pharmaceutical R&D expenses of your company in 2008?

Answered: 16 Skipped: 1

ANSWER CHOICES	RESPONSES	
Less than 1 billion US dollars	31.25%	5
1-2 billion US dollars	12.50%	2
More than 2 billion US dollars	56.25%	9
TOTAL		16