#1

COMPLETE

Collector: Web Link (Web Link)
Started: Thursday, September 05, 2013 11:09:36 AM
Last Modified: Thursday, September 05, 2013 11:21:37 AM
Time Spent: 00:12:00

Page 2: Questions

Q1

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

First in human	**Never**
Multiple rising dose	**Never**
Drug-drug interaction	**Sometimes**
Special population	**Never**
Other clin pharm	**Never**
Proof of concept	**Never**
Dose ranging	**Never**
Pivotal	**Never**
Other	**Never**

Q2

Never

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

Q3

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

CYP1A2	**No**
CYP2A6	**No**
CYP2B6	**No**
CYP2C8	**No**
CYP2C9	**No**
CYP2C19	**No**
CYP2D6	**Yes**
CYP3A4	**No**
CYP3A5	**No**
Other phase I enzyme	**No**
UGT1A1	**No**
TPMT	**No**
Other phase II enzyme	**No**
OATP1B1	**Yes**
BCRP	**No**
MDR1	**No**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

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?

No,
If No suggest alternatives:
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

Q6

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

Never

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Sometimes**
Special population	**Never**
Other clin pharm	**Never**
Proof of concept	**Never**
Dose ranging	**Never**
Pivotal	**Never**
Other	**Never**

Q8

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

Inclusion criterion	**No**
Exclusion criterion	**No**
Dose Adjustment	**No**

Q9 **Respondent skipped this question**

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

Q10 **External Lab**

Where is your ADME PGx testing performed for clinical studies?

Q11

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

cost and lack of internal resources

Q12 **Respondent skipped this question**

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

Q13

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

Respondent skipped this question

Q14

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

PK Outlier	**Candidate gene approaches**
Drug-drug interaction	**Candidate gene approaches**
Known PK property	**Candidate gene approaches**
Unclear PK property	**Candidate gene approaches**

Q15

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

Yes

Q16

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

No

Q17

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

No

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)

Phase I	**No (Optional)**
Drug interaction studies	**No (Optional)**
Phase II	**No (Optional)**
Phase III	**No (Optional)**
PhaseIV	**No (Optional)**

Q19

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

No

Q20

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

Respondent skipped this question

Q21

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

Respondent skipped this question

Q22

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

Stayed the same

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**No**
CLIA (Clinical Laboratory Improvement Amendments)	**No**
CAP (College of American Pathologists)	**No**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**No**
ISO (International Organization of Standardization)	**No**
CLSI (Clinical and Laboratory Standards Institute)	**No**

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

Never

Q27

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

No

Q28

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

No

Q29

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

PharmGKB,

dbSNP,

1000genome,

Literature,

determined by platform,

Other (please specify):

Ensembl

Q30

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

Literature,

Platform specific (eg. DMET Chip)

Q31

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

No

Q32

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

no

Page 3: About your company

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.

630861

Q34

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

Less than 1 billion US dollars

#2

COMPLETE

Collector: Web Link (Web Link)
Started: Thursday, September 05, 2013 3:45:00 PM
Last Modified: Thursday, September 05, 2013 4:05:31 PM
Time Spent: 00:20:30

Page 2: Questions

Q1

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

First in human	**Sometimes**
Multiple rising dose	**Usually**
Drug-drug interaction	**Usually**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Never**
Dose ranging	**Sometimes**
Pivotal	**Never**

Q2

Sometimes

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

Q3

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

CYP1A2	**No**
CYP2A6	**No**
CYP2B6	**Yes**
CYP2C8	**No**
CYP2C9	**Yes**
CYP2C19	**Yes**
CYP2D6	**Yes**
CYP3A4	**Yes**
CYP3A5	**Yes**
Other phase I enzyme	**Yes**
UGT1A1	**Yes**
TPMT	**No**
Other phase II enzyme	**Yes**
OATP1B1	**Yes**
BCRP	**No**
MDR1	**No**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Retrospective, when high PK variability or PK outlier observed

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?

Yes

Q6

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

Sometimes

Q7

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

First in human	**Usually**
Multiple rising dose	**Usually**
Drug-drug interaction	**Always**
Special population	**Sometimes**
Other clin pharm	**Never**
Proof of concept	**Never**
Dose ranging	**Sometimes**
Pivotal	**Never**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**
Dose Adjustment	**No**

Q9

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

First in human,
Multiple rising dose,
Drug-drug interaction,
Special population,
Dose ranging

Q10

Where is your ADME PGx testing performed for clinical studies?

Both internal and external labs

Q11

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

Laboratory certification

Q12

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

Taqman ADME assay,
Sanger sequencing

Q13

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

through-put or number of markers

Q14

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

PK Outlier	**Candidate gene approaches**
Drug-drug interaction	**Candidate gene approaches**
Known PK property	**Candidate gene approaches**
Unclear PK property	**Hypothesis free approaches**

Which platforms were used?
taqman

Q15 **Yes**

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

Q16 **Yes**

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

Q17 **Yes**

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

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)

Phase I	**No (Optional)**
Drug interaction studies	**Yes (Mandatory)**
Phase II	**No (Optional)**
Phase III	**No (Optional)**
PhaseIV	**No (Optional)**

Q19

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

Yes

Q20

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

previously validated

Q21

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

An unreplicated result has been used for internal decision making but not in a regulatory submission

Q22

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

Stayed the same

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

GCLP (Good Clinical Laboratory Practice)	**No**
GLP (Good Laboratory Practice)	**Yes**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**
CAP (College of American Pathologists)	**Yes**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**No**
ISO (International Organization of Standardization)	**No**
CLSI (Clinical and Laboratory Standards Institute)	**No**

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	**Always**
Q27 Have regulatory authorities requested/suggested sample collections in you clinical development programs during review meetings?	**Yes**
Q28 Have regulatory authorities requested/suggested analysis in you clinical development programs during review meetings?	**No**
Q29 What sources are used to determine allele/SNP selection? all that apply	**PharmGKB,** **dbSNP,** **1000genome,** **Literature**
Q30 What sources are used to determine result interpretation? all that apply	**PharmGKB,** **Literature,** **Platform specific (eg. DMET Chip)**
Q31 Have recent FDA and EMA guidances impacted practice of PGx in your company?	**Yes**
Q32 Have NGS, GWAS or other technologies impacted practice of PGx at your company?	**no**

Page 3: About your company

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.

281307

Q34

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

More than 2 billion US dollars

#3

COMPLETE

Collector: Web Link (Web Link)
Started: Monday, September 16, 2013 3:53:48 PM
Last Modified: Monday, September 16, 2013 4:31:53 PM
Time Spent: 00:38:04

Page 2: Questions

Q1

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

First in human	**Always**
Multiple rising dose	**Always**
Drug-drug interaction	**Sometimes**
Special population	**Usually**
Other clin pharm	**Sometimes**
Proof of concept	**Always**
Dose ranging	**Sometimes**
Pivotal	**Usually**
Other	**Sometimes**

Q2

Sometimes

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

Q3

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

CYP1A2	**Yes**
CYP2A6	**Yes**
CYP2B6	**Yes**
CYP2C8	**Yes**
CYP2C9	**Yes**
CYP2C19	**Yes**
CYP2D6	**Yes**
CYP3A4	**Yes**
CYP3A5	**Yes**
Other phase I enzyme	**Yes**
UGT1A1	**Yes**
TPMT	**Yes**
Other phase II enzyme	**Yes**
OATP1B1	**Yes**
BCRP	**Yes**
MDR1	**Yes**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Standard practice to broadly genotype and collect data across program

,

Retrospective, when high PK variability or PK outlier observed

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?

Yes

Q6

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

Sometimes

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Sometimes**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**
Other	**Sometimes**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**
Dose Adjustment	**Yes**
If yes which genes CYP2D6, CYP2C9	

Q9

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

Multiple rising dose,

Special population,

Dose ranging

Q10

Where is your ADME PGx testing performed for clinical studies?

Both internal and external labs

Q11

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

Quality level requirement

Q12

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

Taqman ADME assay,

Affymetrix DMET chip,

Sanger sequencing

Q13

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

cost, throughput, # of SNPs, TAT

Q14

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

PK Outlier	**Candidate gene approaches, Hypothesis free approaches, Was it successful?**
Known PK property	**Candidate gene approaches, Was it successful?**
Unclear PK property	**Hypothesis free approaches, Was it successful?**

Which platforms were used?
Taqman, DMET

Q15

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

Yes

Q16

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

Yes

Q17

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

Yes

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)

Phase I	**Yes (Mandatory), No (Optional)**
Drug interaction studies	**No (Optional)**
Phase II	**No (Optional)**
Phase III	**No (Optional)**
PhaseIV	**Yes (Mandatory), No (Optional)**

Q19

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

Yes

Q20

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

Yes for a previously validated ADME marker

Q21

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

An unreplicated result has been used for internal decision making but not in a regulatory submission

Q22

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

Increased substantially (>50%)

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**No**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**
CAP (College of American Pathologists)	**Yes**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**Yes**
ISO (International Organization of Standardization)	**Yes**
CLSI (Clinical and Laboratory Standards Institute)	**No**

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

Always

Q27

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

No

Q28

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

Yes

Q29

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

PharmGKB,

dbSNP,

1000genome,

Literature

Q30

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

PharmGKB,

Literature

Q31

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

No

Q32

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

no

Page 3: About your company

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.

125375

Q34

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

More than 2 billion US dollars

#4

COMPLETE

Collector: Web Link (Web Link)
Started: Wednesday, September 11, 2013 6:34:07 AM
Last Modified: Wednesday, September 18, 2013 1:08:12 PM
Time Spent: Over a day

Page 2: Questions

Q1

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

First in human	**Usually**
Multiple rising dose	**Usually**
Drug-drug interaction	**Usually**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**
Other	**Sometimes**

Q2

usually

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

Q3

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

CYP1A2	**Yes**
CYP2A6	**Yes**
CYP2B6	**Yes**
CYP2C8	**Yes**
CYP2C9	**Yes**
CYP2C19	**Yes**
CYP2D6	**Yes**
CYP3A4	**Yes**
CYP3A5	**Yes**
Other phase I enzyme	**Yes**
UGT1A1	**Yes**
TPMT	**No**
Other phase II enzyme	**Yes**
OATP1B1	**Yes**
BCRP	**Yes**
MDR1	**Yes**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Standard practice to broadly genotype and collect data across program

,

Retrospective, when high PK variability or PK outlier observed

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?

Yes

Q6

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

Usually

Q7

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

First in human	**Usually**
Multiple rising dose	**Usually**
Drug-drug interaction	**Always**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**
Other	**Sometimes**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**
Dose Adjustment	**Yes**

Q9

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

First in human,
Multiple rising dose,
Drug-drug interaction,
Dose ranging,
Pivotal

Q10

Where is your ADME PGx testing performed for clinical studies?

Both internal and external labs

Q11

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

quality certificate + resources + technical capabilities + platforms

Q12

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

Taqman ADME assay,

Other (please specify):

pyrosequencing

Q13

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

quality + possibility of validation + cost + ease of use + sensitivity

Q14

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

PK Outlier	**Candidate gene approaches, Hypothesis free approaches, Was it successful?**
Drug-drug interaction	**Candidate gene approaches, Was it successful?**
Known PK property	**Candidate gene approaches, Hypothesis free approaches, Was it successful?**
Unclear PK property	**Was it successful?**

Q15

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

Yes

Q16

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

Yes

Q17

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

Yes

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)

Phase I	**Yes (Mandatory), No (Optional)**
Drug interaction studies	**Yes (Mandatory), No (Optional)**
Phase II	**Yes (Mandatory), No (Optional)**
Phase III	**Yes (Mandatory), No (Optional)**
PhaseIV	**No (Optional)**

Q19

Yes

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

Q20

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

previously validated

Q21

Respondent skipped this question

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

Q22

Increased substantially (>50%)

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

Q23

Yes

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

Q24

If yes to 23 specify diagnostic type

UGT1A1

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**No**
CLIA (Clinical Laboratory Improvement Amendments)	**No**
CAP (College of American Pathologists)	**No**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**No**
ISO (International Organization of Standardization)	**No**
CLSI (Clinical and Laboratory Standards Institute)	**No**

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

Always

Q27

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

Yes

Q28

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

Yes

Q29

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

PharmGKB,

dbSNP,

1000genome,

Literature,

determined by platform,

Other (please specify):

NGS

Q30

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

PharmGKB,

Literature,

Platform specific (eg. DMET Chip)

Q31

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

Yes

Q32

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

yes,

If yes, How?:

Identification of markers

Page 3: About your company

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.

857046

Q34

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

More than 2 billion US dollars

#5

COMPLETE

Collector: Web Link (Web Link)
Started: Wednesday, September 04, 2013 12:47:31 PM
Last Modified: Sunday, September 22, 2013 10:26:59 PM
Time Spent: Over a week

Page 2: Questions

Q1

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

First in human	**Sometimes**
Multiple rising dose	**Never**
Drug-drug interaction	**Always**
Special population	**Sometimes**
Other clin pharm	**Never**
Proof of concept	**Never**
Dose ranging	**Never**
Pivotal	**Sometimes**
Other	**Never**

Q2

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

Sometimes

Q3

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

CYP2C9	**Yes**
CYP2D6	**Yes**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

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?

Yes

Q6

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

Sometimes

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Never**
Drug-drug interaction	**Always**
Special population	**Sometimes**
Other clin pharm	**Never**
Proof of concept	**Never**
Dose ranging	**Never**
Pivotal	**Sometimes**
Other	**Never**

Q8

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

Inclusion criterion	**No**
Exclusion criterion	**No**
Dose Adjustment	**No**

Q9

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

Respondent skipped this question

Q10

Where is your ADME PGx testing performed for clinical studies?

Both internal and external labs

Q11

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

Lack of internal resources

Q12

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

Taqman ADME assay,

Sanger sequencing,

Other (please specify):

Illumina chip, Pyrosequencing, DDPCR

Q13

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

Cost, ease use,

Q14

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

PK Outlier	**Candidate gene approaches**
Drug-drug interaction	**Candidate gene approaches**
Known PK property	**Candidate gene approaches**
Unclear PK property	**Candidate gene approaches**

Q15

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

Yes

Q16

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

Yes

Q17

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

Yes

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)

Phase I	**No (Optional)**
Drug interaction studies	**No (Optional)**
Phase II	**No (Optional)**
Phase III	**No (Optional)**
PhaseIV	**No (Optional)**

Q19

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

No

Q20

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

Respondent skipped this question

Q21

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

Respondent skipped this question

Q22

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

Increased substantially (>50%)

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**Yes**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**
CAP (College of American Pathologists)	**Yes**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**No**
ISO (International Organization of Standardization)	**Yes**
CLSI (Clinical and Laboratory Standards Institute)	**No**

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

Never

Q27

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

Respondent skipped this question

Q28

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

Respondent skipped this question

Q29

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

PharmGKB,

dbSNP,

1000genome,

Literature

Q30

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

PharmGKB,

Literature

Q31

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

No

Q32

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

Respondent skipped this question

Page 3: About your company

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.

429931

Q34

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

Less than 1 billion US dollars

#6

COMPLETE

Collector: Web Link (Web Link)
Started: Monday, September 23, 2013 12:42:06 PM
Last Modified: Monday, September 23, 2013 1:09:32 PM
Time Spent: 00:27:25

Page 2: Questions

Q1

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

First in human	**Usually**
Multiple rising dose	**Usually**
Drug-drug interaction	**Sometimes**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**

Q2

Sometimes

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

Q3

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

CYP1A2	**No**
CYP2A6	**No**
CYP2B6	**No**
CYP2C8	**No**
CYP2C9	**Yes**
CYP2C19	**Yes**
CYP2D6	**Yes**
CYP3A4	**Yes**
CYP3A5	**Yes**
Other phase I enzyme	**Yes**
UGT1A1	**Yes**
TPMT	**No**
Other phase II enzyme	**Yes**
OATP1B1	**Yes**
BCRP	**Yes**
MDR1	**Yes**
Other (please specify)	**GSTP1, GSTM1, UGT1A9, UGT1B15**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Retrospective, when high PK variability or PK outlier observed

,

Other (please specify):

concomitant meds that are polymorphicly metabolized

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?

No,

If No suggest alternatives:

in vivo clearance >50% is our trigger point

Q6

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

Sometimes

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Sometimes**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**
Dose Adjustment	**No**
If yes which genes CYP2D6, CYP2C19	

Q9

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

First in human

Q10

Where is your ADME PGx testing performed for clinical studies?

Both internal and external labs

Q11

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

China

Q12

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

Taqman ADME assay

Q13

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

cost, ease of use, quality (CLIA certified)

Q14

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

PK Outlier	**Candidate gene approaches**
Drug-drug interaction	**Candidate gene approaches**
Known PK property	**Candidate gene approaches, Was it successful?**
Which platforms were used? quantitive PCR	

Q15

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

Yes

Q16

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

Yes

Q17

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

Yes

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)

Phase I	**Yes (Mandatory)**
Drug interaction studies	**Yes (Mandatory)**
Phase II	**No (Optional)**
Phase III	**No (Optional)**
PhaseIV	**No (Optional)**

Q19

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

No

Q20

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

Respondent skipped this question

Q21

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

Respondent skipped this question

Q22

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

Stayed the same

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**No**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**
CAP (College of American Pathologists)	**No**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**No**
ISO (International Organization of Standardization)	**No**
CLSI (Clinical and Laboratory Standards Institute)	**Yes**

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

Always

Q27

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

No

Q28

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

No

Q29

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

dbSNP,

Literature

Q30

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

PharmGKB,

Literature

Q31

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

No

Q32

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

no

Page 3: About your company

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.

989785

Q34

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

More than 2 billion US dollars

#7

COMPLETE

Collector: Web Link (Web Link)
Started: Tuesday, September 24, 2013 4:58:42 PM
Last Modified: Tuesday, September 24, 2013 5:19:45 PM
Time Spent: 00:21:03

Page 2: Questions

Q1

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

First in human	**Always**
Multiple rising dose	**Usually**
Drug-drug interaction	**Sometimes**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Always**
Dose ranging	**Always**
Pivotal	**Always**

Q2

Sometimes

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

Q3

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

CYP1A2	**Yes**
CYP2A6	**Yes**
CYP2B6	**Yes**
CYP2C8	**Yes**
CYP2C9	**Yes**
CYP2C19	**Yes**
CYP2D6	**Yes**
CYP3A4	**Yes**
CYP3A5	**Yes**
Other phase I enzyme	**Yes**
UGT1A1	**Yes**
TPMT	**Yes**
Other phase II enzyme	**Yes**
OATP1B1	**Yes**
BCRP	**Yes**
MDR1	**Yes**
Other (please specify)	**We use multi-gene platforms (eg DMET chip) So we capture data on all**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Retrospective, when high PK variability or PK outlier observed

,

Other (please specify):

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)

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?

No,
If No suggest alternatives:
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

Q6

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

Always

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Sometimes**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**
Other	**Sometimes**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**

If yes which genes
CYP2D6 and UGT1A1. While not specifically trial design we have included specific genotyping in pivotal studies based on phase 2 exploratory data

Q9

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

Other clin pharm

Q10

Where is your ADME PGx testing performed for clinical studies?

External Lab

Q11

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

Laboratory certifcationa and lack of internal resources

Q12

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

Respondent skipped this question

Q13

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

Respondent skipped this question

Q14

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

PK Outlier	**Candidate gene approaches, Hypothesis free approaches, Was it successful?**
Drug-drug interaction	**Candidate gene approaches, Hypothesis free approaches**
Known PK property	**Candidate gene approaches, Hypothesis free approaches, Was it successful?**
Unclear PK property	**Candidate gene approaches, Hypothesis free approaches**

Which platforms were used?

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

Q15

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

Yes

Q16

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

Yes

Q17

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

Yes

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)

Phase I	**Yes (Mandatory), No (Optional)**
Drug interaction studies	**Yes (Mandatory), No (Optional)**
Phase II	**Yes (Mandatory), No (Optional)**
Phase III	**Yes (Mandatory), No (Optional)**
PhaseIV	**No (Optional)**

Q19

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

Yes

Q20

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

BOTH Validated and novel

Q21

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

An unreplicated result has been used for internal decision making but not in a regulatory submission

,

An unreplicated result based on a known valid biomarker has been used in a regulatory submission

Q22

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

Increased substantially (>50%)

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**
CAP (College of American Pathologists)	**Yes**
ISO (International Organization of Standardization)	**Yes**

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

Always,
Comments:
CLIA

Q27

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

Yes

Q28

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

Yes

Q29

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

PharmGKB,

dbSNP,

1000genome,

Literature

Q30

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

PharmGKB,

Literature,

Platform specific (eg. DMET Chip)

Q31

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

Yes,
If Yes, How?:
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

Q32

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

yes,
If yes, How?:
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

Page 3: About your company

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.

534921

Q34

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

More than 2 billion US dollars

#8

COMPLETE

Collector: Web Link (Web Link)
Started: Tuesday, September 24, 2013 7:15:41 PM
Last Modified: Tuesday, September 24, 2013 7:34:05 PM
Time Spent: 00:18:23

Page 2: Questions

Q1

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

First in human	**Usually**
Multiple rising dose	**Usually**
Drug-drug interaction	**Usually**
Special population	**Usually**
Proof of concept	**Usually**
Dose ranging	**Usually**
Pivotal	**Usually**

Q2

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

usually

Q3

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

Other (please specify)	**We have not done yet. Hoping to perform in the future.**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Standard practice to broadly genotype and collect data across program

,

Retrospective, when high PK variability or PK outlier observed

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?

Yes

Q6

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

Never

Q7

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

Other	**Never**

Q8

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

Inclusion criterion	**No**
Exclusion criterion	**No**
Dose Adjustment	**No**

Q9

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

Respondent skipped this question

Q10

Where is your ADME PGx testing performed for clinical studies?

External Lab

Q11

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

Genotyping expertise, lab certification, battery of testings

Q12

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

Taqman ADME assay,

Affymetrix DMET chip

Q13

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

Cost and ease of use etc..

Q14

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

PK Outlier	**Was it successful?**
Drug-drug interaction	**Hypothesis free approaches**
Known PK property	**Hypothesis free approaches**
Unclear PK property	**Was it successful?**

Q15 **Yes**

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

Q16 **Yes**

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

Q17 **No**

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

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)

Phase I	**No (Optional)**
Drug interaction studies	**No (Optional)**
Phase II	**No (Optional)**
Phase III	**No (Optional)**

Q19 **No**

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

Q20

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

Respondent skipped this question

Q21

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

Respondent skipped this question

Q22

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

Stayed the same

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**Yes**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**
CAP (College of American Pathologists)	**Yes**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**No**
ISO (International Organization of Standardization)	**Yes**
CLSI (Clinical and Laboratory Standards Institute)	**Yes**

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

Sometimes

Q27

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

No

Q28

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

No

Q29

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

Literature

Q30

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

PharmGKB,

Literature,

Platform specific (eg. DMET Chip)

Q31

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

No

Q32

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

no

Page 3: About your company

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.

373538

Q34

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

Less than 1 billion US dollars

#9

COMPLETE

Collector: Web Link (Web Link)
Started: Thursday, August 15, 2013 1:48:37 PM
Last Modified: Wednesday, September 25, 2013 8:38:47 PM
Time Spent: Over a month
IP Address: 67.204.81.36

Page 2: Questions

Q1

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

First in human	**Always**
Multiple rising dose	**Always**
Drug-drug interaction	**Always**
Special population	**Always**
Other clin pharm	**Always**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**
Other	**Sometimes**

Q2

Sometimes

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

Q3

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

CYP1A2	**No**
CYP2A6	**No**
CYP2B6	**No**
CYP2C8	**No**
CYP2C9	**No**
CYP2C19	**No**
CYP2D6	**Yes**
CYP3A4	**Yes**
CYP3A5	**Yes**
Other phase I enzyme	**No**
UGT1A1	**No**
TPMT	**No**
Other phase II enzyme	**No**
OATP1B1	**No**
BCRP	**No**
MDR1	**No**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Retrospective, when high PK variability or PK outlier observed

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?

Yes

Q6

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

Sometimes

Q7

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

First in human	**Never**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Sometimes**
Special population	**Never**
Other clin pharm	**Never**
Proof of concept	**Never**
Dose ranging	**Never**
Pivotal	**Never**
Other	**Never**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**
Dose Adjustment	**Yes**

If yes which genes
CYP2D6

Q9 **Drug-drug interaction**

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

Q10 **Both internal and external labs**

Where is your ADME PGx testing performed for clinical studies?

Q11

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

Lack of internal resource, lab certification

Q12 **Taqman ADME assay,**

Affymetrix DMET chip,

Roche AmpliChip

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

Q13

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

cost, throughput, ease of use, number of markers (case by case)

Q14

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

PK Outlier	**Candidate gene approaches, Hypothesis free approaches**
Drug-drug interaction	**Candidate gene approaches**

Which platforms were used?
DMET, TaqMan, AmpliChip

Q15 **Yes**

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

Q16 **Yes**

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

Q17 **No**

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

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)

Phase I	**No (Optional)**
Drug interaction studies	**No (Optional)**
Phase II	**No (Optional)**
Phase III	**No (Optional)**
PhaseIV	**No (Optional)**

Q19 **No**

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

Q20

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

Respondent skipped this question

Q21

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

Respondent skipped this question

Q22

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

Stayed the same

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**Yes**
CLIA (Clinical Laboratory Improvement Amendments)	**No**
CAP (College of American Pathologists)	**No**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**No**
ISO (International Organization of Standardization)	**No**
CLSI (Clinical and Laboratory Standards Institute)	**No**

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

usually

Q27

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

Yes

Q28

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

No

Q29

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

dbSNP,

1000genome,

Literature

Q30

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

PharmGKB,

Literature

Q31

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

No

Q32

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

yes,
If yes, How?:
NGS implementation

Page 3: About your company

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.

963872

Q34

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

1-2 billion US dollars

#10

COMPLETE

Collector: Web Link (Web Link)
Started: Thursday, September 26, 2013 1:02:54 PM
Last Modified: Thursday, September 26, 2013 1:29:47 PM
Time Spent: 00:26:52

Page 2: Questions

Q1

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

First in human	**Usually**
Multiple rising dose	**Usually**
Special population	**Usually**
Proof of concept	**Usually**
Dose ranging	**Usually**
Pivotal	**Usually**

Q2

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

Sometimes

Q3

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

Other (please specify)	**targeted genes case by case**

Q4

What triggers genotyping? Check all that apply

Retrospective, when high PK variability or PK outlier observed

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?

No,
If No suggest alternatives:
It is not so straightforward depends on candidate enzymes, tranporters & current understanding of clinical relevance

Q6

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

Never

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Sometimes**
Proof of concept	**Sometimes**

Q8

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

Inclusion criterion	**No**
Exclusion criterion	**No**
Dose Adjustment	**No**

Q9

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

Respondent skipped this question

Q10

Where is your ADME PGx testing performed for clinical studies?

External Lab

Q11

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

Capabilities & quality

Q12

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

Respondent skipped this question

Q13

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

Respondent skipped this question

Q14

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

PK Outlier	**Candidate gene approaches, Hypothesis free approaches**
Unclear PK property	**Hypothesis free approaches**

Q15

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

Yes

Q16

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

Yes

Q17

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

No

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)

Phase I	**No (Optional)**
Phase II	**No (Optional)**

Q19

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

No

Q20

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

Respondent skipped this question

Q21

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

Respondent skipped this question

Q22

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

Respondent skipped this question

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

GLP (Good Laboratory Practice)	**Yes**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**
ISO (International Organization of Standardization)	**Yes**

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

Comments:
No experience in inclusion/exclusion ADME PGx

Q27

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

No

Q28

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

No

Q29

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

PharmGKB,

dbSNP,

1000genome,

Literature

Q30

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

Literature

Q31

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

Yes,
If Yes, How?:
Interna currently l processes under evaluation

Q32

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

yes,
If yes, How?:
NGS under evaluation

Page 3: About your company

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.

395509

Q34

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

Less than 1 billion US dollars

#11

COMPLETE

Collector: Web Link (Web Link)
Started: Thursday, September 26, 2013 2:02:33 PM
Last Modified: Thursday, September 26, 2013 2:11:10 PM
Time Spent: 00:08:36

Page 2: Questions

Q1

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

First in human	**Always**
Multiple rising dose	**Always**
Drug-drug interaction	**Always**
Special population	**Always**
Other clin pharm	**Always**
Proof of concept	**Always**
Dose ranging	**Always**
Pivotal	**Always**
Other	**Always**

Q2

Always

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

Q3

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

CYP1A2	**No**
CYP2A6	**No**
CYP2B6	**No**
CYP2C8	**Yes**
CYP2C9	**Yes**
CYP2C19	**Yes**
CYP2D6	**Yes**
CYP3A4	**No**
CYP3A5	**Yes**
UGT1A1	**Yes**
TPMT	**No**
OATP1B1	**Yes**
BCRP	**Yes**
MDR1	**No**
Other (please specify)	**other UGTs based on in vitro data**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Retrospective, when high PK variability or PK outlier observed

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?

Yes

Q6

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

Sometimes

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Sometimes**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**
Other	**Sometimes**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**
Dose Adjustment	**No**

If yes which genes
CYP2D6, CYP2C19, CYP2C9

Q9 **Respondent skipped this question**

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

Q10 **External Lab**

Where is your ADME PGx testing performed for clinical studies?

Q11

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

laboratory certification

Q12 **Respondent skipped this question**

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

Q13

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

Respondent skipped this question

Q14

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

PK Outlier	**Candidate gene approaches, Hypothesis free approaches, Was it successful?**
Drug-drug interaction	**Candidate gene approaches, Hypothesis free approaches**
Known PK property	**Candidate gene approaches, Was it successful?**
Unclear PK property	**Candidate gene approaches, Hypothesis free approaches, Was it successful?**

Q15

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

Yes

Q16

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

Yes

Q17

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

Yes

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)

Phase I	**No (Optional)**
Drug interaction studies	**No (Optional)**
Phase II	**No (Optional)**
Phase III	**No (Optional)**
PhaseIV	**No (Optional)**

Q19

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

Yes

Q20

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

validated marker

Q21

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

An independent replication has always been necessary

Q22

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

Decreased Substantially (>50%)

Q23

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

Yes

Q24

If yes to 23 specify diagnostic type

Amplichip

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**Yes**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**

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

Always

Q27

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

Respondent skipped this question

Q28

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

Respondent skipped this question

Q29

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

PharmGKB,

dbSNP,

1000genome

Q30

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

PharmGKB,

Literature

Q31

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

Yes,
If Yes, How?:
raise internal awareness of ADME genetics

Q32

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

no

Page 3: About your company

Q33

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610787

Q34

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

More than 2 billion US dollars

#12

COMPLETE

Collector: Web Link (Web Link)
Started: Friday, September 27, 2013 5:57:25 PM
Last Modified: Friday, September 27, 2013 6:11:48 PM
Time Spent: 00:14:23

Page 2: Questions

Q1

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

First in human	**Usually**
Multiple rising dose	**Usually**
Drug-drug interaction	**Usually**
Special population	**Sometimes**
Other clin pharm	**Usually**
Proof of concept	**Usually**
Dose ranging	**Usually**
Pivotal	**Usually**
Other	**Sometimes**

Q2

Sometimes

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

Q3

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

CYP1A2	**No**
CYP2A6	**Yes**
CYP2B6	**Yes**
CYP2C8	**No**
CYP2C9	**Yes**
CYP2C19	**Yes**
CYP2D6	**Yes**
CYP3A4	**Yes**
CYP3A5	**Yes**
Other phase I enzyme	**Yes**
UGT1A1	**Yes**
TPMT	**No**
Other phase II enzyme	**Yes**
OATP1B1	**Yes**
BCRP	**No**
MDR1	**Yes**
Other (please specify)	**EPHX1, EPHX2, GSTM1, GSTT1, GSTP1, NAT1, NAT2, UGT1A9, UGT2B4, UGT2B7, SLCO2B1, SLCO1B3, SLC10A1, ABCG2, ABCC2**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Retrospective, when high PK variability or PK outlier observed

,

Other (please specify):

Regulatory Requests

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?

No,

If No suggest alternatives:

Our organization generally has considered 30% as the appropriate cutoff for overall clearance

Q6

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

Sometimes

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Usually**
Special population	**Never**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**
Other	**Never**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**
Dose Adjustment	**Yes**

If yes which genes
CYP2D6, CYP2C9, CYP2C19 (ADME genes listed only)

Q9

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

Multiple rising dose,
Drug-drug interaction,
Other clin pharm,
Dose ranging

Q10

Where is your ADME PGx testing performed for clinical studies?

External Lab

Q11

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

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.

Q12

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

Other (please specify):

Not applicable

Q13

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

Not applicable

Q14

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

PK Outlier	**Candidate gene approaches, Was it successful?**
Drug-drug interaction	**Candidate gene approaches, Was it successful?**
Known PK property	**Candidate gene approaches, Was it successful?**
Unclear PK property	**Candidate gene approaches, Was it successful?**

Which platforms were used?

Small scale genotyping (e.g., Taqman, sanger sequencing)

Q15

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

Yes

Q16

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

Yes

Q17

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

Yes

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)

Phase I	**Yes (Mandatory), No (Optional)**
Drug interaction studies	**Yes (Mandatory), No (Optional)**
Phase II	**Yes (Mandatory), No (Optional)**
Phase III	**No (Optional)**
PhaseIV	**No (Optional)**

Q19

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

Yes

Q20

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

Previously validated

Q21

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

An unreplicated result has been used for internal decision making but not in a regulatory submission

Q22

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

Stayed the same

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Not applicable

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**Yes**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**
CAP (College of American Pathologists)	**No**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**No**
ISO (International Organization of Standardization)	**No**
CLSI (Clinical and Laboratory Standards Institute)	**No**

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

Always

Q27

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

Yes

Q28

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

Yes

Q29

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

PharmGKB,

dbSNP,

1000genome,

Literature,

Other (please specify):

Gene-specific nomenclature pages (e.g., Karolinska webpage for P450s, UGT allele tables); Pharmaaddme.org

Q30

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

PharmGKB,

Literature

Q31

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

Yes,
If Yes, How?:
Provided justification for collection and analysis of DNA samples

Q32

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

no,
If yes, How?:
No, not in the context of ADME-related PGx

Page 3: About your company

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.

178524

Q34

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

More than 2 billion US dollars

#13

COMPLETE

Collector: Web Link (Web Link)
Started: Thursday, October 03, 2013 9:55:33 AM
Last Modified: Thursday, October 03, 2013 10:31:14 AM
Time Spent: 00:35:40

Page 2: Questions

Q1

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

First in human	**Usually**
Multiple rising dose	**Usually**
Drug-drug interaction	**Usually**
Special population	**Sometimes**
Other clin pharm	**Usually**
Proof of concept	**Usually**
Dose ranging	**Usually**
Pivotal	**Usually**
Other	**Sometimes**

Q2

Sometimes

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

Q3

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

CYP1A2	**Yes**
CYP2A6	**No**
CYP2B6	**No**
CYP2C8	**No**
CYP2C9	**No**
CYP2C19	**No**
CYP2D6	**Yes**
CYP3A4	**No**
CYP3A5	**No**
Other phase I enzyme	**No**
UGT1A1	**No**
TPMT	**No**
Other phase II enzyme	**No**
OATP1B1	**No**
BCRP	**No**
MDR1	**No**
Other (please specify)	**NAT2**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Retrospective, when high PK variability or PK outlier observed

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?

Yes

Q6

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

Sometimes

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Sometimes**
Special population	**Never**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**
Other	**Sometimes**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**No**
Dose Adjustment	**No**

Q9 **Other clin pharm**

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

Q10 **External Lab**

Where is your ADME PGx testing performed for clinical studies?

Q11

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

Performance charateristics and experience

Q12 **Respondent skipped this question**

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

Q13

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

Respondent skipped this question

Q14

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

Known PK property	**Candidate gene approaches**

Q15

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

Yes

Q16

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

Yes

Q17

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

No

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)

Phase I	**Yes (Mandatory), No (Optional)**
Drug interaction studies	**No (Optional)**
Phase II	**Yes (Mandatory), No (Optional)**
Phase III	**No (Optional)**
PhaseIV	**No (Optional)**

Q19

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

No

Q20

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

Respondent skipped this question

Q21

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

Respondent skipped this question

Q22

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

Increased substantially (>50%)

Q23

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

Yes

Q24

If yes to 23 specify diagnostic type

COBAS, FISH

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**No**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**Yes**
ISO (International Organization of Standardization)	**Yes**

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

Always

Q27

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

No

Q28 Have regulatory authorities requested/suggested analysis in you clinical development programs during review meetings?	**No**
Q29 What sources are used to determine allele/SNP selection? all that apply	**PharmGKB,** **dbSNP,** **1000genome,** **Literature,** **determined by platform**
Q30 What sources are used to determine result interpretation? all that apply	**PharmGKB,** **Literature,** **Platform specific (eg. DMET Chip)**
Q31 Have recent FDA and EMA guidances impacted practice of PGx in your company?	**Yes**
Q32 Have NGS, GWAS or other technologies impacted practice of PGx at your company?	**yes**

Page 3: About your company

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.

659869

Q34 What were the pharmaceutical R&D expenses of your company in 2008?	**Less than 1 billion US dollars**

#14

INCOMPLETE

Collector: Web Link (Web Link)
Started: Thursday, August 15, 2013 2:41:00 PM
Last Modified: Thursday, October 03, 2013 5:06:44 PM
Time Spent: Over a month
IP Address: 152.51.56.1

Page 2: Questions

Q1

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

Respondent skipped this question

Q2

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

Respondent skipped this question

Q3

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

Respondent skipped this question

Q4

What triggers genotyping? Check all that apply

Respondent skipped this question

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?

Respondent skipped this question

Q6

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

Respondent skipped this question

Q7

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

Respondent skipped this question

Q8

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

Respondent skipped this question

Q9

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

Respondent skipped this question

Q10

Where is your ADME PGx testing performed for clinical studies?

Respondent skipped this question

Q11

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

Respondent skipped this question

Q12

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

NextGen sequencing

Q13

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

Respondent skipped this question

Q14

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

Respondent skipped this question

Q15

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

Respondent skipped this question

Q16

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

Yes

Q17

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

No

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)

Respondent skipped this question

Q19

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

Respondent skipped this question

Q20

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

Respondent skipped this question

Q21

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

PG-PK results have not been used

Q22

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

Respondent skipped this question

Q23

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

Respondent skipped this question

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

Respondent skipped this question

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

Respondent skipped this question

Q27

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

Respondent skipped this question

Q28

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

Respondent skipped this question

Q29

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

Respondent skipped this question

Q30

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

Respondent skipped this question

Q31

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

Respondent skipped this question

Q32

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

Respondent skipped this question

Page 3: About your company

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.

Respondent skipped this question

Q34

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

Respondent skipped this question

#15

COMPLETE

Collector: Web Link (Web Link)
Started: Thursday, October 03, 2013 9:39:05 PM
Last Modified: Thursday, October 03, 2013 10:11:56 PM
Time Spent: 00:32:50

Page 2: Questions

Q1

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

First in human	**Always**
Multiple rising dose	**Always**
Drug-drug interaction	**Sometimes**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Always**
Dose ranging	**Always**
Pivotal	**Sometimes**
Other	**Sometimes**

Q2

Sometimes

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

Q3

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

CYP2C9	**Yes**
CYP2D6	**Yes**
CYP3A4	**Yes**
CYP3A5	**Yes**
UGT1A1	**Yes**
Other (please specify)	**ABCB1, ABCG2**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Retrospective, when high PK variability or PK outlier observed

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?

Yes

Q6

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

Sometimes

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Sometimes**
Special population	**Never**
Other clin pharm	**Never**
Proof of concept	**Never**
Dose ranging	**Never**
Pivotal	**Never**
Other	**Never**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**
Dose Adjustment	**No**
If yes which genes	CYP2D6

Q9

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

Drug-drug interaction

Q10

Where is your ADME PGx testing performed for clinical studies?

External Lab

Q11

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

Expertise

Q12

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

Respondent skipped this question

Q13

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

Respondent skipped this question

Q14

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

PK Outlier	**Candidate gene approaches, Was it successful?**
Drug-drug interaction	**Candidate gene approaches, Was it successful?**
Known PK property	**Candidate gene approaches, Was it successful?**

Which platforms were used?
Please elaborate on "unclear PK property

Q15

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

Yes

Q16

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

Yes

Q17

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

No

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)

Phase I	**Yes (Mandatory)**
Drug interaction studies	**Yes (Mandatory)**

Q19

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

Yes

Q20

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

Yes

Q21

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

An unreplicated result based on a known valid biomarker has been used in a regulatory submission

Q22

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

Stayed the same

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

Other (please specify)	**GCP**

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

Always

Q27

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

No

Q28

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

No

Q29

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

Literature,

determined by platform

Q30

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

Literature,

Platform specific (eg. DMET Chip)

Q31

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

No

Q32

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

no

Page 3: About your company

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.

401763

Q34

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

More than 2 billion US dollars

#16

COMPLETE

Collector: Web Link (Web Link)
Started: Friday, October 04, 2013 7:42:50 PM
Last Modified: Friday, October 04, 2013 8:01:52 PM
Time Spent: 00:19:02

Page 2: Questions

Q1

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

First in human	**Always**
Multiple rising dose	**Always**
Drug-drug interaction	**Always**
Special population	**Always**
Other clin pharm	**Always**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**

Q2

Sometimes

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

Q3

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

CYP1A2	**Yes**
CYP2A6	**Yes**
CYP2B6	**Yes**
CYP2C8	**Yes**
CYP2C9	**Yes**
CYP2C19	**Yes**
CYP2D6	**Yes**
CYP3A4	**Yes**
CYP3A5	**Yes**
Other phase I enzyme	**Yes**
UGT1A1	**Yes**
TPMT	**No**
Other phase II enzyme	**Yes**
OATP1B1	**Yes**
BCRP	**Yes**
MDR1	**Yes**
Other (please specify)	**The Affymetrix DMET chip is used, although TMPT data are not collected.**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Standard practice to broadly genotype and collect data across program

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?

Yes

Q6

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

Always

Q7

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

First in human	**Always**
Multiple rising dose	**Always**
Drug-drug interaction	**Always**
Special population	**Always**
Other clin pharm	**Usually**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**
Dose Adjustment	**No**

If yes which genes
CYP2D6, CYP2C19, UGT1A1, OATP1B1

Q9

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

Drug-drug interaction,
Other clin pharm

Q10

Where is your ADME PGx testing performed for clinical studies?

External Lab

Q11

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

Overall R&D agreement for that to be done at a specific CRO.

Q12

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

Respondent skipped this question

Q13

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

Respondent skipped this question

Q14

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

PK Outlier	**Candidate gene approaches, Hypothesis free approaches, Was it successful?**
Drug-drug interaction	**Candidate gene approaches, Was it successful?**
Known PK property	**Candidate gene approaches, Was it successful?**
Unclear PK property	**Hypothesis free approaches**

Which platforms were used?
TaqMan, Illumina Beadchip, Affy DMET

Q15

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

Yes

Q16

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

Yes

Q17

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

Yes

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)

Phase I	**Yes (Mandatory), No (Optional)**
Drug interaction studies	**Yes (Mandatory)**
Phase II	**Yes (Mandatory)**
PhaseIV	**Yes (Mandatory)**

Q19

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

Yes

Q20

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

CYP2D6, CYP2C19

Q21

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

An unreplicated result has been used for internal decision making but not in a regulatory submission

,

An unreplicated result based on a known valid biomarker has been used in a regulatory submission

Q22

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

Increased substantially (>50%)

Q23

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

No

Q24

If yes to 23 specify diagnostic type

Respondent skipped this question

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?

GCLP (Good Clinical Laboratory Practice)	**No**
GLP (Good Laboratory Practice)	**Yes**
CLIA (Clinical Laboratory Improvement Amendments)	**No**
CAP (College of American Pathologists)	**No**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**No**
ISO (International Organization of Standardization)	**No**
CLSI (Clinical and Laboratory Standards Institute)	**No**

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	**Always,** Comments: GLP quality only
Q27 Have regulatory authorities requested/suggested sample collections in you clinical development programs during review meetings?	**Yes**
Q28 Have regulatory authorities requested/suggested analysis in you clinical development programs during review meetings?	**Yes**
Q29 What sources are used to determine allele/SNP selection? all that apply	**PharmGKB,** **dbSNP,** **1000genome,** **Literature,** **determined by platform**
Q30 What sources are used to determine result interpretation? all that apply	**PharmGKB,** **Literature,** **Platform specific (eg. DMET Chip)**
Q31 Have recent FDA and EMA guidances impacted practice of PGx in your company?	**No,** If Yes, How?: Practices were consistent with these guidances.
Q32 Have NGS, GWAS or other technologies impacted practice of PGx at your company?	**no,** If yes, How?: In discussion to move some work to NGS platforms to try to improve quality of results.

Page 3: About your company

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.

105355

Q34

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

More than 2 billion US dollars

#17

COMPLETE

Collector: Web Link (Web Link)
Started: Tuesday, October 08, 2013 8:11:10 PM
Last Modified: Tuesday, October 08, 2013 8:48:00 PM
Time Spent: 00:36:49

Page 2: Questions

Q1

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

First in human	**Always**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Sometimes**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**
Other	**Sometimes**

Q2

Sometimes

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

Q3

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

CYP1A2	**Yes**
CYP2A6	**Yes**
CYP2B6	**Yes**
CYP2C8	**Yes**
CYP2C9	**Yes**
CYP2C19	**Yes**
CYP2D6	**Yes**
CYP3A4	**Yes**
CYP3A5	**Yes**
Other phase I enzyme	**Yes**
UGT1A1	**Yes**
TPMT	**No**
Other phase II enzyme	**Yes**
OATP1B1	**Yes**
BCRP	**No**
MDR1	**Yes**
Other (please specify)	**DMET Chip, ABCB1**

Q4

What triggers genotyping? Check all that apply

When preclinical data indicate a role for a specific gene in a compound's PK

,

Other (please specify):

FDA requirement

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?

Yes

Q6

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

Sometimes

Q7

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

First in human	**Sometimes**
Multiple rising dose	**Sometimes**
Drug-drug interaction	**Sometimes**
Special population	**Sometimes**
Other clin pharm	**Sometimes**
Proof of concept	**Sometimes**
Dose ranging	**Sometimes**
Pivotal	**Sometimes**
Other	**Sometimes**

Q8

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

Inclusion criterion	**Yes**
Exclusion criterion	**Yes**
Dose Adjustment	**No**
If yes which genes CYP2C19	

Q9

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

Multiple rising dose,

Other

Q10

Where is your ADME PGx testing performed for clinical studies?

External Lab

Q11

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

Lack of internal resources

Q12

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

Respondent skipped this question

Q13

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

Respondent skipped this question

Q14

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

Respondent skipped this question

Q15

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

Yes

Q16

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

Yes

Q17

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

No

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)

Phase I	**Yes (Mandatory)**
Drug interaction studies	**Yes (Mandatory)**
Phase II	**No (Optional)**
Phase III	**No (Optional)**
PhaseIV	**No (Optional)**

Q19

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

No

Q20

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

Respondent skipped this question

Q21

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

Respondent skipped this question

Q22

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

Increased substantially (>50%)

Q23

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

Yes

Q24

If yes to 23 specify diagnostic type

DMET chip

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?

GCLP (Good Clinical Laboratory Practice)	**Yes**
GLP (Good Laboratory Practice)	**Yes**
CLIA (Clinical Laboratory Improvement Amendments)	**Yes**
CAP (College of American Pathologists)	**Yes**
IFCC (International Federation of Clinical Chemistry and Laboratory Medicine)	**No**
ISO (International Organization of Standardization)	**Yes**
CLSI (Clinical and Laboratory Standards Institute)	**Yes**

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

Sometimes

Q27

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

No

Q28

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

No

Q29

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

Other (please specify):

Other interpretation platform

Q30

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

Platform specific (eg. DMET Chip)

Q31

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

Yes,

If Yes, How?:

Implemented samples collection per FDA guidance

Q32

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

no

Page 3: About your company

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.

120970

Q34

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

1-2 billion US dollars