#1

COMPLETE

Collector:	Email Invitation 1 (Email)
Started:	Thursday, September 12, 2019 2:13:54 PM
Last Modified:	Thursday, September 12, 2019 2:41:32 PM
Time Spent:	00:27:38
Email:	
IP Address:	

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Q1 What were the pharmaceutical R&D expenses of your company in 2018?	**<1 billion**
Q2 What percentage of your pipeline is represented by small molecules: <10%	**>75%**
Q3 What percentage of your pipeline is represented by therapeutic proteins, vaccines, or other types of compounds (not small molecule): <10%,	**<10%**
Q4 If your company advances drug candidates metabolized or transported by enzymes/transporters with genetic variation that might result in clinically meaningful differences in compound disposition, what additional steps have been taken in the clinical development program of this compound? Select all that apply.	**Retrospective analyses of relevant polymorphisms with endpoints studied in trial subjects** **,** **Inclusion criteria specified or separate trials conducted to asses genetic effects in an enriched patient population** **,** **Exclusion criteria applied to restrict patients with genotypes predicted to result in significantly higher exposure to compound** **,** **Exclusion criteria applied to restrict patients with genotypes predicted to result in significantly lower plasma exposure to compound**

Q5 Under what circumstances does your company collected DNA with consent for ADME-related genotyping? Select all that apply.	**Samples collected routinely in Phase I,** **Samples collected routinely in Phase II,** **Samples collected routinely in Phase III,** **Samples collected when in vitro data suggests any involvement of a polymorphic enzyme or transporter,** **Samples collected when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition,** **Samples collected when in vitro data suggests any enzyme or transporter is a major contributor to disposition**
Q6 Under what circumstances does your company genotype drug metabolism enzymes and transporters? Select all that apply.	**Genotype routinely in DDI studies,** **Genotype when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition**
Q7 What technologies do you/would you use to genotype variants/genes of interest? Select all that apply.	**DMET**
Q8 If you answered "Other" to Question 7 or if different genotyping technologies are used in different scenarios (eg. routine genotyping, PK outlier, phase of development, etc.) please describe further.	**Respondent skipped this question**
Q9 Please state reasons for the choice of your genotyping platform(s):	**Cost,** **Through-put,** **Ease of use**
Q10 Under what circumstances does your company conduct an ADME PGx analysis? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**Analysis conducted when in vitro data suggests any involvement of a certain enzymes or transporters,** **Analysis conducted when in vitro data suggests certain enzymes or transporters are a major contributor to disposition**

Q11 Are there scenarios in which a hypothesis-free approach is used in ADME PGx analyses – where a larger number of genes and alleles are tested than those suspected to be involved in clearance based on pre-clinical work and knowledge about the compound's disposition? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**No, only candidate genes based on preclinical or early clinical work are explored**

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

Lack of scientific justification and resources

Q13 If genotyping and/or statistical analysis is triggered only when there is evidence of involvement of certain enzymes or transporters, which genes would trigger genotyping/analysis?	**CYP1A2,** **CYP2B6,** **CYP2D6**
Q14 When ADME PGx analyses are conducted, what alleles are included in analyses? Select all that apply.	**Alleles shown to have clinically meaningful impact on PK of other substrates**
Q15 Do you include rare alleles (population frequency <1% in all populations) in ADME PGx analyses? Select all that apply.	**Yes, if there is prior evidence that the allele has a clinical meaningful impact on PK of other substrates**
Q16 How Is is the impact of genetic variation on compound disposition assessed using population PK models in Phase II and beyondin studies with sparse pharmacokinetic sampling?	**Impact of genotype assessed using PK parameter estimated using population PK models or other approaches from the data available**
Q17 As a follow-up to Question 16 if multiple approaches have been used, please describe the factors that inform on choice of approach:	**Respondent skipped this question**
Q18 Does your organization typically consider potential impact of genetic variants on PK of therapeutic proteins, including the drug target in cases where target mediated drug disposition is relevant?	**Yes**
Q19 If you answered "Yes" to Question 19 please describe:	**Respondent skipped this question**

Q20 Does your organization assess the impact of genomic variation (e.g. impact of microRNAs, epigenetic changes, changes in expression) on PK of your compounds?	**No**
Q21 If you answered "Yes" to Question 21 please describe:	**Respondent skipped this question**
Q22 What are the major limitations to accurately assess impact of genetic variation on compound disposition? Select all that apply.	**Sample size of clinical studies limits ability to conduct genetic analyzes**
Q23 For compounds expected to have higher risk of drug-induced liver injury (DILI), are analyses conducted to look for genetic variants associated with higher risk of DILI?	**Yes**

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

CYP2D6

#2

COMPLETE

Collector:	Email Invitation 1 (Email)
Started:	Friday, September 13, 2019 5:01:41 PM
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Q1 What were the pharmaceutical R&D expenses of your company in 2018?	**>4 billion**
Q2 What percentage of your pipeline is represented by small molecules: <10%	**50-75%**
Q3 What percentage of your pipeline is represented by therapeutic proteins, vaccines, or other types of compounds (not small molecule): <10%,	**25-50%**
Q4 If your company advances drug candidates metabolized or transported by enzymes/transporters with genetic variation that might result in clinically meaningful differences in compound disposition, what additional steps have been taken in the clinical development program of this compound? Select all that apply.	**Retrospective analyses of relevant polymorphisms with endpoints studied in trial subjects** **,** **Inclusion criteria specified or separate trials conducted to asses genetic effects in an enriched patient population** **,** **Exclusion criteria applied to restrict patients with genotypes predicted to result in significantly lower plasma exposure to compound** **,** **Additional drug-drug interaction studies or modified design of planned drug-drug interaction studies**

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

Samples collected routinely in Phase I,

Samples collected routinely in Phase II,

Samples collected routinely in Phase III,

Samples collected when in vitro data suggests any involvement of a polymorphic enzyme or transporter,

Samples collected when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition,

Samples collected when in vitro data suggests any enzyme or transporter is a major contributor to disposition

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

Genotype when in vitro data suggests any involvement of a polymorphic enzyme or transporter,

Genotype when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition,

Genotype when in vitro data suggests any enzyme or transporter is a major contributor to disposition,

Other (please specify):

genotype when PK is variable AND a polymorphic enzyme/tranpsporter is a contributor

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

Taqman assays for specific variants,

Sanger sequencing,

Other (please specify):

Open Array (Taqman), Fragment Analysis, Ion Torrent S5 PGx Panel

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

Taqman Open Array, Fragment Analysis, Ion Torrent S5 PGx Panel: based on need of panel size and throughput

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

Cost,

Through-put,

Ease of use ,

Number of markers/coverage ,

Turnover time

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

Analysis conducted when in vitro data suggests any involvement of a certain enzymes or transporters ,

Analysis conducted when in vitro data suggests certain enzymes or transporters are a major contributor to disposition ,

Analysis conducted when in vitro data suggests any enzyme or transporter is a major contributor to disposition

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

No, only candidate genes based on preclinical or early clinical work are explored

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

Cost, lack of novel genotype to phenotype clinical understanding, guidance documents, power concerns

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

ABCB1,

ABCC2,

ABCG2,

ABCB11,

CYP1A2,

CYP2B6,

CYP2C19,

CYP2C8,

CYP2C9,

CYP2D6,

CYP3A4,

CYP3A5,

GSTM1,

GSTP1,

GSTT1,

NAT1,

NAT2,

SLC22A1,

SLC22A2,

SLC22A6,

SLC22A8,

SLC47A1,

SLC47A2,

SLCO1B1,

SLCO1B3,

SLCO2B1,

UGT1A1,

UGT1A4,

UGT1A9,

CES1,

CES2

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

Alleles shown to have clinically meaningful impact on PK of other substrates

,

Alleles with some in vivo evidence of change in activity or expression

,

Alleles with some in vitro evidence of change in activity or expression

,

Alleles with predicted impact on protein function or expression based on in silico algorithms

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

Yes, if there is prior evidence that the allele has a clinical meaningful impact on PK of other substrates

,

Yes, if there is some in vivo evidence of functional impact of the allele

,

Yes if there is some in vitro evidence of functional impact of the allele

,

Yes if the allele is predicted to alter protein function or expression by in silico algorithms

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

Genotype is incorporated as a covariate in population PK models

,

Impact of genotype assessed using PK parameter estimated using population PK models or other approaches from the data available

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

Depends on the clinical trial size (single vs. combinatorial), popPK vs thorough PK assessment.

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

No

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

Respondent skipped this question

Q20 Does your organization assess the impact of genomic variation (e.g. impact of microRNAs, epigenetic changes, changes in expression) on PK of your compounds?	**No**
Q21 If you answered "Yes" to Question 21 please describe:	**Respondent skipped this question**
Q22 What are the major limitations to accurately assess impact of genetic variation on compound disposition? Select all that apply.	**Inability to accurately determine contribution of enzymes/transporters,** **,** **Cost of required clinical studies ,** **Sample size of clinical studies limits ability to conduct genetic analyzes** **,** **Clinical studies typically limited to certain populations**
Q23 For compounds expected to have higher risk of drug-induced liver injury (DILI), are analyses conducted to look for genetic variants associated with higher risk of DILI?	**No**
Q24 If you answered "Yes" to Question 24 please describe what genes are targeted for such analyses:	**Respondent skipped this question**

#3

COMPLETE

Collector:	Email Invitation 1 (Email)
Started:	Wednesday, October 09, 2019 1:50:18 PM
Last Modified:	Wednesday, October 09, 2019 1:58:08 PM
Time Spent:	00:07:50
Email:	
IP Address:	

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Q1 What were the pharmaceutical R&D expenses of your company in 2018?	**<1 billion**
Q2 What percentage of your pipeline is represented by small molecules: <10%	**50-75%**
Q3 What percentage of your pipeline is represented by therapeutic proteins, vaccines, or other types of compounds (not small molecule): <10%,	**10-25%**
Q4 If your company advances drug candidates metabolized or transported by enzymes/transporters with genetic variation that might result in clinically meaningful differences in compound disposition, what additional steps have been taken in the clinical development program of this compound? Select all that apply.	**Retrospective analyses of relevant polymorphisms with endpoints studied in trial subjects** , **Additional drug-drug interaction studies or modified design of planned drug-drug interaction studies**
Q5 Under what circumstances does your company collected DNA with consent for ADME-related genotyping? Select all that apply.	**Samples collected routinely in Phase I** , **Samples collected routinely in Phase II** , **Samples collected routinely in Phase III**
Q6 Under what circumstances does your company genotype drug metabolism enzymes and transporters? Select all that apply.	**Genotype when high pharmacokinetic variability is observed in phase 1 clinical trials** , **Genotype when in vitro data suggests any enzyme or transporter is a major contributor to disposition**

Q7 What technologies do you/would you use to genotype variants/genes of interest? Select all that apply.	**DMET,** **Whole genome genotyping,** **Whole genome or exome sequencing**
Q8 If you answered "Other" to Question 7 or if different genotyping technologies are used in different scenarios (eg. routine genotyping, PK outlier, phase of development, etc.) please describe further.	**Respondent skipped this question**
Q9 Please state reasons for the choice of your genotyping platform(s):	**Through-put,** **Number of markers/coverage**
Q10 Under what circumstances does your company conduct an ADME PGx analysis? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**Analysis conducted when in vitro data suggests certain enzymes or transporters are a major contributor to disposition** **,** **Analysis conducted when high pharmacokinetic variability is observed in phase 1 clinical trials**
Q11 Are there scenarios in which a hypothesis-free approach is used in ADME PGx analyses – where a larger number of genes and alleles are tested than those suspected to be involved in clearance based on pre-clinical work and knowledge about the compound's disposition? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**Yes, but results are used only for hypothesis generation**
Q12 If you answered "No" to Question 11 please describe the main reasons why your company does not conduct such analyses (eg lack of scientific justification, cost of analyses, lack of resources, etc.).	**Respondent skipped this question**

Q13 If genotyping and/or statistical analysis is triggered only when there is evidence of involvement of certain enzymes or transporters, which genes would trigger genotyping/analysis?	**ABCB1,** **ABCB4,** **ABCC2,** **CYP2C9,** **CYP2D6,** **CYP3A4,** **UGT1A1,** **UGT1A3,** **UGT1A4**
Q14 When ADME PGx analyses are conducted, what alleles are included in analyses? Select all that apply.	**Alleles shown to have clinically meaningful impact on PK of other substrates** **,** **Alleles with some in vivo evidence of change in activity or expression**
Q15 Do you include rare alleles (population frequency <1% in all populations) in ADME PGx analyses? Select all that apply.	**Yes, if there is prior evidence that the allele has a clinical meaningful impact on PK of other substrates**
Q16 How Is is the impact of genetic variation on compound disposition assessed using population PK models in Phase II and beyondin studies with sparse pharmacokinetic sampling?	**Genotype is incorporated as a covariate in population PK models** **,** **Impact of genotype assessed using PK parameter estimated using population PK models or other approaches from the data available**

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

The level of evidence that is available

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

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

In vitro studies are done to inform the potential impact.

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

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

If tremendous variability in PK is observed, genotyping studies may be undertaken.

Q22 What are the major limitations to accurately assess impact of genetic variation on compound disposition? Select all that apply.	**Inability to accurately determine contribution of enzymes/transporters,** **,** **Sample size of clinical studies limits ability to conduct genetic analyzes**
Q23 For compounds expected to have higher risk of drug-induced liver injury (DILI), are analyses conducted to look for genetic variants associated with higher risk of DILI?	**No**
Q24 If you answered "Yes" to Question 24 please describe what genes are targeted for such analyses:	**Respondent skipped this question**

#4

COMPLETE

Collector:	Email Invitation 2 (Email)
Started:	Friday, October 11, 2019 8:16:40 AM
Last Modified:	Friday, October 11, 2019 9:05:56 AM
Time Spent:	00:49:16
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Q1 What were the pharmaceutical R&D expenses of your company in 2018?	**<1 billion**
Q2 What percentage of your pipeline is represented by small molecules: <10%	**>75%**
Q3 What percentage of your pipeline is represented by therapeutic proteins, vaccines, or other types of compounds (not small molecule): <10%,	**<10%**
Q4 If your company advances drug candidates metabolized or transported by enzymes/transporters with genetic variation that might result in clinically meaningful differences in compound disposition, what additional steps have been taken in the clinical development program of this compound? Select all that apply.	**Retrospective analyses of relevant polymorphisms with endpoints studied in trial subjects**
Q5 Under what circumstances does your company collected DNA with consent for ADME-related genotyping? Select all that apply.	**Samples collected routinely in Phase I** **Samples collected routinely in Phase II** **Samples collected routinely in Phase III**

Q6 Under what circumstances does your company genotype drug metabolism enzymes and transporters? Select all that apply.	**Genotype when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition** , **Genotype when high pharmacokinetic variability is observed in phase 1 clinical trials** , **Genotype when in vitro data suggests any enzyme or transporter is a major contributor to disposition**
Q7 What technologies do you/would you use to genotype variants/genes of interest? Select all that apply.	**DMET,** **Taqman assays for specific variants,** **Sanger sequencing**
Q8 If you answered "Other" to Question 7 or if different genotyping technologies are used in different scenarios (eg. routine genotyping, PK outlier, phase of development, etc.) please describe further.	**Respondent skipped this question**
Q9 Please state reasons for the choice of your genotyping platform(s):	**Cost,** **Number of markers/coverage**
Q10 Under what circumstances does your company conduct an ADME PGx analysis? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**Analysis conducted when high pharmacokinetic variability is observed in phase 1 clinical trials**
Q11 Are there scenarios in which a hypothesis-free approach is used in ADME PGx analyses – where a larger number of genes and alleles are tested than those suspected to be involved in clearance based on pre-clinical work and knowledge about the compound's disposition? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**Yes, where there is unexplained PK variability** , **Yes, where there is uncertainty around genes involved in disposition** , **Yes, but results are used only for hypothesis generation**
Q12 If you answered "No" to Question 11 please describe the main reasons why your company does not conduct such analyses (eg lack of scientific justification, cost of analyses, lack of resources, etc.).	**Respondent skipped this question**

Q13 If genotyping and/or statistical analysis is triggered only when there is evidence of involvement of certain enzymes or transporters, which genes would trigger genotyping/analysis?	**CYP2C19,** **CYP2C9,** **CYP2D6,** **NAT2,** **UGT1A1**
Q14 When ADME PGx analyses are conducted, what alleles are included in analyses? Select all that apply.	**Alleles shown to have clinically meaningful impact on PK of other substrates**
Q15 Do you include rare alleles (population frequency <1% in all populations) in ADME PGx analyses? Select all that apply.	**Yes, if there is prior evidence that the allele has a clinical meaningful impact on PK of other substrates**
Q16 How Is is the impact of genetic variation on compound disposition assessed using population PK models in Phase II and beyondin studies with sparse pharmacokinetic sampling?	**Genotype is incorporated as a covariate in population PK models**
Q17 As a follow-up to Question 16 if multiple approaches have been used, please describe the factors that inform on choice of approach:	**Respondent skipped this question**
Q18 Does your organization typically consider potential impact of genetic variants on PK of therapeutic proteins, including the drug target in cases where target mediated drug disposition is relevant?	**Respondent skipped this question**
Q19 If you answered "Yes" to Question 19 please describe:	**Respondent skipped this question**
Q20 Does your organization assess the impact of genomic variation (e.g. impact of microRNAs, epigenetic changes, changes in expression) on PK of your compounds?	**No**
Q21 If you answered "Yes" to Question 21 please describe:	**Respondent skipped this question**

Q22 What are the major limitations to accurately assess impact of genetic variation on compound disposition? Select all that apply.	**Inability to accurately determine contribution of enzymes/transporters,** **,** **Sample size of clinical studies limits ability to conduct genetic analyzes**
Q23 For compounds expected to have higher risk of drug-induced liver injury (DILI), are analyses conducted to look for genetic variants associated with higher risk of DILI?	**Respondent skipped this question**
Q24 If you answered "Yes" to Question 24 please describe what genes are targeted for such analyses:	**Respondent skipped this question**

#5

COMPLETE

Collector:	Email Invitation 1 (Email)
Started:	Friday, October 11, 2019 1:59:39 PM
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Q1 What were the pharmaceutical R&D expenses of your company in 2018?	**>4 billion**
Q2 What percentage of your pipeline is represented by small molecules: <10%	**50-75%**
Q3 What percentage of your pipeline is represented by therapeutic proteins, vaccines, or other types of compounds (not small molecule): <10%,	**25-50%**
Q4 If your company advances drug candidates metabolized or transported by enzymes/transporters with genetic variation that might result in clinically meaningful differences in compound disposition, what additional steps have been taken in the clinical development program of this compound? Select all that apply.	**Retrospective analyses of relevant polymorphisms with endpoints studied in trial subjects** **,** **Inclusion criteria specified or separate trials conducted to asses genetic effects in an enriched patient population** **,** **Additional drug-drug interaction studies or modified design of planned drug-drug interaction studies**

Q5 Under what circumstances does your company collected DNA with consent for ADME-related genotyping? Select all that apply.	**Samples collected routinely in Phase II ,** **Samples collected routinely in Phase III ,** **Samples collected when in vitro data suggests any involvement of a polymorphic enzyme or transporter ,** **Samples collected when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition ,** **Samples collected when high pharmacokinetic variability is observed in phase 1 clinical trials ,** **Samples collected when in vitro data suggests any enzyme or transporter is a major contributor to disposition**
Q6 Under what circumstances does your company genotype drug metabolism enzymes and transporters? Select all that apply.	**Genotype routinely in phase II studies,** **Genotype routinely in all phase III studies ,** **Genotype when in vitro data suggests any involvement of a polymorphic enzyme or transporter ,** **Genotype when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition ,** **Genotype when high pharmacokinetic variability is observed in phase 1 clinical trials ,** **Genotype when in vitro data suggests any enzyme or transporter is a major contributor to disposition**
Q7 What technologies do you/would you use to genotype variants/genes of interest? Select all that apply.	**Taqman assays for specific variants,** **Sanger sequencing,** Other (please specify): array - PMRA

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

array for all supplemented with bespoke assays

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

Cost,

Through-put,

Ease of use ,

Number of markers/coverage ,

Turnover time

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

Analyses conducted routinely,

Analysis conducted when in vitro data suggests any involvement of a certain enzymes or transporters ,

Analysis conducted when in vitro data suggests certain enzymes or transporters are a major contributor to disposition ,

Analysis conducted when high pharmacokinetic variability is observed in phase 1 clinical trials ,

Analysis conducted when in vitro data suggests any enzyme or transporter is a major contributor to disposition

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

No, only candidate genes based on preclinical or early clinical work are explored

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

low chance of success

Q13 If genotyping and/or statistical analysis is triggered only when there is evidence of involvement of certain enzymes or transporters, which genes would trigger genotyping/analysis?	**Respondent skipped this question**
Q14 When ADME PGx analyses are conducted, what alleles are included in analyses? Select all that apply.	**Alleles shown to have clinically meaningful impact on PK of other substrates**
Q15 Do you include rare alleles (population frequency <1% in all populations) in ADME PGx analyses? Select all that apply.	**No**
Q16 How Is is the impact of genetic variation on compound disposition assessed using population PK models in Phase II and beyondin studies with sparse pharmacokinetic sampling?	**Genotype is incorporated as a covariate in population PK models**
Q17 As a follow-up to Question 16 if multiple approaches have been used, please describe the factors that inform on choice of approach:	**Respondent skipped this question**
Q18 Does your organization typically consider potential impact of genetic variants on PK of therapeutic proteins, including the drug target in cases where target mediated drug disposition is relevant?	**Yes**
Q19 If you answered "Yes" to Question 19 please describe:	**Respondent skipped this question**
Q20 Does your organization assess the impact of genomic variation (e.g. impact of microRNAs, epigenetic changes, changes in expression) on PK of your compounds?	**No**
Q21 If you answered "Yes" to Question 21 please describe:	**Respondent skipped this question**
Q22 What are the major limitations to accurately assess impact of genetic variation on compound disposition? Select all that apply.	**Sample size of clinical studies limits ability to conduct genetic analyzes**
Q23 For compounds expected to have higher risk of drug-induced liver injury (DILI), are analyses conducted to look for genetic variants associated with higher risk of DILI?	**Yes**

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

genome wide and known genes

#6

COMPLETE

Collector:	Email Invitation 1 (Email)
Started:	Friday, October 11, 2019 8:08:45 PM
Last Modified:	Friday, October 11, 2019 8:40:13 PM
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Q1 What were the pharmaceutical R&D expenses of your company in 2018?	**<1 billion**
Q2 What percentage of your pipeline is represented by small molecules: <10%	**10-25%**
Q3 What percentage of your pipeline is represented by therapeutic proteins, vaccines, or other types of compounds (not small molecule): <10%,	**>75%**
Q4 If your company advances drug candidates metabolized or transported by enzymes/transporters with genetic variation that might result in clinically meaningful differences in compound disposition, what additional steps have been taken in the clinical development program of this compound? Select all that apply.	**Retrospective analyses of relevant polymorphisms with endpoints studied in trial subjects**
Q5 Under what circumstances does your company collected DNA with consent for ADME-related genotyping? Select all that apply.	**Samples collected when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition** **,** **Samples collected when high pharmacokinetic variability is observed in phase 1 clinical trials**
Q6 Under what circumstances does your company genotype drug metabolism enzymes and transporters? Select all that apply.	**Genotype when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition** **,** **Genotype when high pharmacokinetic variability is observed in phase 1 clinical trials**

Q7 What technologies do you/would you use to genotype variants/genes of interest? Select all that apply.	**Respondent skipped this question**
Q8 If you answered "Other" to Question 7 or if different genotyping technologies are used in different scenarios (eg. routine genotyping, PK outlier, phase of development, etc.) please describe further.	**Respondent skipped this question**
Q9 Please state reasons for the choice of your genotyping platform(s):	**Cost,** **Turnover time**
Q10 Under what circumstances does your company conduct an ADME PGx analysis? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**Analysis conducted when in vitro data suggests certain enzymes or transporters are a major contributor to disposition** **,** **Analysis conducted when high pharmacokinetic variability is observed in phase 1 clinical trials**
Q11 Are there scenarios in which a hypothesis-free approach is used in ADME PGx analyses – where a larger number of genes and alleles are tested than those suspected to be involved in clearance based on pre-clinical work and knowledge about the compound's disposition? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**No, only candidate genes based on preclinical or early clinical work are explored**

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

cost of analyses and lack of resources

Q13 If genotyping and/or statistical analysis is triggered only when there is evidence of involvement of certain enzymes or transporters, which genes would trigger genotyping/analysis?	**Respondent skipped this question**
Q14 When ADME PGx analyses are conducted, what alleles are included in analyses? Select all that apply.	**Alleles shown to have clinically meaningful impact on PK of other substrates**
Q15 Do you include rare alleles (population frequency <1% in all populations) in ADME PGx analyses? Select all that apply.	**Yes, if there is prior evidence that the allele has a clinical meaningful impact on PK of other substrates**

Q16 How Is is the impact of genetic variation on compound disposition assessed using population PK models in Phase II and beyondin studies with sparse pharmacokinetic sampling?	**Genotype is incorporated as a covariate in population PK models** , **Impact of genotype assessed using PK parameter estimated using population PK models or other approaches from the data available**

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

Approach is chosen based on how much data is available and purpose of analysis. For qualitative assessment, correlation analysis is sufficient. To quantitatively estimate the effect, incorporating into population PK analysis is needed.

Q18 Does your organization typically consider potential impact of genetic variants on PK of therapeutic proteins, including the drug target in cases where target mediated drug disposition is relevant?	**No**
Q19 If you answered "Yes" to Question 19 please describe:	**Respondent skipped this question**
Q20 Does your organization assess the impact of genomic variation (e.g. impact of microRNAs, epigenetic changes, changes in expression) on PK of your compounds?	**No**
Q21 If you answered "Yes" to Question 21 please describe:	**Respondent skipped this question**
Q22 What are the major limitations to accurately assess impact of genetic variation on compound disposition? Select all that apply.	**Inability to accurately determine contribution of enzymes/transporters,** , **Sample size of clinical studies limits ability to conduct genetic analyzes**
Q23 For compounds expected to have higher risk of drug-induced liver injury (DILI), are analyses conducted to look for genetic variants associated with higher risk of DILI?	**No**
Q24 If you answered "Yes" to Question 24 please describe what genes are targeted for such analyses:	**Respondent skipped this question**

#7

COMPLETE

Collector:	Email Invitation 1 (Email)
Started:	Friday, October 11, 2019 10:02:23 PM
Last Modified:	Friday, October 11, 2019 10:11:27 PM
Time Spent:	00:09:03
Email:	
IP Address:	

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Q1 What were the pharmaceutical R&D expenses of your company in 2018?	**>4 billion**
Q2 What percentage of your pipeline is represented by small molecules: <10%	**50-75%**
Q3 What percentage of your pipeline is represented by therapeutic proteins, vaccines, or other types of compounds (not small molecule): <10%,	**25-50%**
Q4 If your company advances drug candidates metabolized or transported by enzymes/transporters with genetic variation that might result in clinically meaningful differences in compound disposition, what additional steps have been taken in the clinical development program of this compound? Select all that apply.	**Retrospective analyses of relevant polymorphisms with endpoints studied in trial subjects** **,** **Inclusion criteria specified or separate trials conducted to asses genetic effects in an enriched patient population** **,** **Exclusion criteria applied to restrict patients with genotypes predicted to result in significantly higher exposure to compound**
Q5 Under what circumstances does your company collected DNA with consent for ADME-related genotyping? Select all that apply.	**Samples collected routinely in Phase I** **,** **Samples collected routinely in Phase II** **,** **Samples collected routinely in Phase III**

Q6 Under what circumstances does your company genotype drug metabolism enzymes and transporters? Select all that apply.	**Genotype routinely in all phase I studies** , **Genotype routinely in phase II studies,** **Genotype routinely in all phase III studies**
Q7 What technologies do you/would you use to genotype variants/genes of interest? Select all that apply.	**Whole genome genotyping,** **Whole genome or exome sequencing,** **Taqman assays for specific variants,** **Sanger sequencing,** **Pharmacoscan**
Q8 If you answered "Other" to Question 7 or if different genotyping technologies are used in different scenarios (eg. routine genotyping, PK outlier, phase of development, etc.) please describe further.	**Respondent skipped this question**
Q9 Please state reasons for the choice of your genotyping platform(s):	**Cost,** **Through-put,** **Number of markers/coverage**
Q10 Under what circumstances does your company conduct an ADME PGx analysis? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**Analysis conducted when in vitro data suggests any involvement of a certain enzymes or transporters** , **Analysis conducted when in vitro data suggests certain enzymes or transporters are a major contributor to disposition** , **Analysis conducted when high pharmacokinetic variability is observed in phase 1 clinical trials**
Q11 Are there scenarios in which a hypothesis-free approach is used in ADME PGx analyses – where a larger number of genes and alleles are tested than those suspected to be involved in clearance based on pre-clinical work and knowledge about the compound's disposition? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**Yes, where there is unexplained PK variability**

Q12 If you answered "No" to Question 11 please describe the main reasons why your company does not conduct such analyses (eg lack of scientific justification, cost of analyses, lack of resources, etc.).	**Respondent skipped this question**
Q13 If genotyping and/or statistical analysis is triggered only when there is evidence of involvement of certain enzymes or transporters, which genes would trigger genotyping/analysis?	Other (please specify): Any enzyme/transporter with known functional polymorphisms and significant contribution to disposition; decision and specific genes made on a program by program basis
Q14 When ADME PGx analyses are conducted, what alleles are included in analyses? Select all that apply.	**Alleles shown to have clinically meaningful impact on PK of other substrates** , **Alleles with some in vivo evidence of change in activity or expression** , **Alleles with some in vitro evidence of change in activity or expression** , **Alleles with predicted impact on protein function or expression based on in silico algorithms**
Q15 Do you include rare alleles (population frequency <1% in all populations) in ADME PGx analyses? Select all that apply.	**Yes, if there is prior evidence that the allele has a clinical meaningful impact on PK of other substrates** , **Yes, if there is some in vivo evidence of functional impact of the allele** , **Yes if there is some in vitro evidence of functional impact of the allele** , **Yes if the allele is predicted to alter protein function or expression by in silico algorithms**
Q16 How Is is the impact of genetic variation on compound disposition assessed using population PK models in Phase II and beyondin studies with sparse pharmacokinetic sampling?	**Genotype is incorporated as a covariate in population PK models** , **Impact of genotype assessed using PK parameter estimated using population PK models or other approaches from the data available**

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

Ideally would use both approaches in such scenarios.

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

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

Yes if TMDD was a consideration for the program.

Q20 Does your organization assess the impact of genomic variation (e.g. impact of microRNAs, epigenetic changes, changes in expression) on PK of your compounds?	**No**
Q21 If you answered "Yes" to Question 21 please describe:	**Respondent skipped this question**
Q22 What are the major limitations to accurately assess impact of genetic variation on compound disposition? Select all that apply.	**Inability to accurately determine contribution of enzymes/transporters,** **,** **Cost of required clinical studies ,** **Sample size of clinical studies limits ability to conduct genetic analyzes** **,** **Clinical studies typically limited to certain populations**
Q23 For compounds expected to have higher risk of drug-induced liver injury (DILI), are analyses conducted to look for genetic variants associated with higher risk of DILI?	**Yes**

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

HLA and ADME

#8

COMPLETE

Collector:	Email Invitation 3 (Email)
Started:	Monday, October 14, 2019 9:21:53 PM
Last Modified:	Monday, October 14, 2019 9:38:44 PM
Time Spent:	00:16:51
Email:	
IP Address:	

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Q1 What were the pharmaceutical R&D expenses of your company in 2018?	**>4 billion**
Q2 What percentage of your pipeline is represented by small molecules: <10%	**25-50%**
Q3 What percentage of your pipeline is represented by therapeutic proteins, vaccines, or other types of compounds (not small molecule): <10%,	**50-75%**
Q4 If your company advances drug candidates metabolized or transported by enzymes/transporters with genetic variation that might result in clinically meaningful differences in compound disposition, what additional steps have been taken in the clinical development program of this compound? Select all that apply.	**Retrospective analyses of relevant polymorphisms with endpoints studied in trial subjects** , **Inclusion criteria specified or separate trials conducted to asses genetic effects in an enriched patient population** , **Exclusion criteria applied to restrict patients with genotypes predicted to result in significantly higher exposure to compound** , **Additional drug-drug interaction studies or modified design of planned drug-drug interaction studies**
Q5 Under what circumstances does your company collected DNA with consent for ADME-related genotyping? Select all that apply.	**Samples collected routinely in Phase I** , **Samples collected routinely in Phase II** , **Samples collected routinely in Phase III**

Q6 Under what circumstances does your company genotype drug metabolism enzymes and transporters? Select all that apply.	**Genotype when high pharmacokinetic variability is observed in phase 1 clinical trials** **,** **Genotype only where there is expected to be sufficient power to conduct an analysis for specific genes/alleles of interest**
Q7 What technologies do you/would you use to genotype variants/genes of interest? Select all that apply.	**DMET,** **Taqman assays for specific variants,** **Sanger sequencing,** **Pharmacoscan**
Q8 If you answered "Other" to Question 7 or if different genotyping technologies are used in different scenarios (eg. routine genotyping, PK outlier, phase of development, etc.) please describe further.	**Respondent skipped this question**
Q9 Please state reasons for the choice of your genotyping platform(s):	**Cost,** **Through-put,** **Turnover time**
Q10 Under what circumstances does your company conduct an ADME PGx analysis? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**Analysis conducted when high pharmacokinetic variability is observed in phase 1 clinical trials** **,** **Analysis conducted only where there is expected to be sufficient statistical power to conduct an analysis for specific genes/alleles of interest**
Q11 Are there scenarios in which a hypothesis-free approach is used in ADME PGx analyses – where a larger number of genes and alleles are tested than those suspected to be involved in clearance based on pre-clinical work and knowledge about the compound's disposition? "Analysis" refers to statistical/computational exploration of collected data, after genotyping. Select all that apply:	**Yes, where there is unexplained PK variability** **,** **Yes, where there is uncertainty around genes involved in disposition** **,** **Yes, but results are used only for hypothesis generation**
Q12 If you answered "No" to Question 11 please describe the main reasons why your company does not conduct such analyses (eg lack of scientific justification, cost of analyses, lack of resources, etc.).	**Respondent skipped this question**

Q13 If genotyping and/or statistical analysis is triggered only when there is evidence of involvement of certain enzymes or transporters, which genes would trigger genotyping/analysis?	**Respondent skipped this question**
Q14 When ADME PGx analyses are conducted, what alleles are included in analyses? Select all that apply.	**Alleles shown to have clinically meaningful impact on PK of other substrates** , **Alleles with some in vivo evidence of change in activity or expression** , **Alleles with some in vitro evidence of change in activity or expression**
Q15 Do you include rare alleles (population frequency <1% in all populations) in ADME PGx analyses? Select all that apply.	**No**
Q16 How Is is the impact of genetic variation on compound disposition assessed using population PK models in Phase II and beyondin studies with sparse pharmacokinetic sampling?	**Genotype is incorporated as a covariate in population PK models** , **Impact of genotype assessed using PK parameter estimated using population PK models or other approaches from the data available**

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

Data availability and quality.

Q18 Does your organization typically consider potential impact of genetic variants on PK of therapeutic proteins, including the drug target in cases where target mediated drug disposition is relevant?	**No**
Q19 If you answered "Yes" to Question 19 please describe:	**Respondent skipped this question**
Q20 Does your organization assess the impact of genomic variation (e.g. impact of microRNAs, epigenetic changes, changes in expression) on PK of your compounds?	**No**

Q21 If you answered "Yes" to Question 21 please describe:	**Respondent skipped this question**
Q22 What are the major limitations to accurately assess impact of genetic variation on compound disposition? Select all that apply.	**Inability to accurately determine contribution of enzymes/transporters,** **,** **Sample size of clinical studies limits ability to conduct genetic analyzes**
Q23 For compounds expected to have higher risk of drug-induced liver injury (DILI), are analyses conducted to look for genetic variants associated with higher risk of DILI?	**No**
Q24 If you answered "Yes" to Question 24 please describe what genes are targeted for such analyses:	**Respondent skipped this question**

#9

COMPLETE

Collector:	Email Invitation 1 (Email)
Started:	Friday, October 25, 2019 1:08:31 PM
Last Modified:	Friday, October 25, 2019 1:18:57 PM
Time Spent:	00:10:25
Email:	
IP Address:	

Page 1: I-PWG ADME Task Force Survey

Q1 What were the pharmaceutical R&D expenses of your company in 2018?	**1-4 billion**
Q2 What percentage of your pipeline is represented by small molecules: <10%	**25-50%**
Q3 What percentage of your pipeline is represented by therapeutic proteins, vaccines, or other types of compounds (not small molecule): <10%,	**<10%**
Q4 If your company advances drug candidates metabolized or transported by enzymes/transporters with genetic variation that might result in clinically meaningful differences in compound disposition, what additional steps have been taken in the clinical development program of this compound? Select all that apply.	**Exclusion criteria applied to restrict patients with genotypes predicted to result in significantly higher exposure to compound** , **Additional drug-drug interaction studies or modified design of planned drug-drug interaction studies**
Q5 Under what circumstances does your company collected DNA with consent for ADME-related genotyping? Select all that apply.	**Samples collected routinely in Phase I** , **Samples collected routinely in Phase II** , **Samples collected when in vitro data suggests a polymorphic enzyme or transporter is a major contributor to disposition** , **Samples collected when in vitro data suggests any enzyme or transporter is a major contributor to disposition**

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

Genotype routinely in all phase I studies

,

Genotype routinely in DDI studies,

Genotype when in vitro data suggests any involvement of a polymorphic enzyme or transporter

,

Genotype when high pharmacokinetic variability is observed in phase 1 clinical trials

,

Genotype only where there is expected to be sufficient power to conduct an analysis for specific genes/alleles of interest

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

DMET,

Whole genome genotyping,

Taqman assays for specific variants

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

na

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

Cost,

Through-put,

Number of markers/coverage

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

Analysis conducted when in vitro data suggests any involvement of a certain enzymes or transporters

,

Analysis conducted when high pharmacokinetic variability is observed in phase 1 clinical trials

,

Analysis conducted only where there is expected to be sufficient statistical power to conduct an analysis for specific genes/alleles of interest

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

Yes, where there is unexplained PK variability

Yes, where there is uncertainty around genes involved in disposition

Yes, but results are used only for hypothesis generation

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

na

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

ABCB1,

ABCB11,

CYP1A1,

CYP2B6,

CYP2C18,

CYP2C19,

CYP2D6,

CYP3A4,

FMO1,

GSTM1,

GSTP1,

SLC22A2,

SLC22A6,

SLC22A8,

UGT1A1,

UGT2B4

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

Alleles shown to have clinically meaningful impact on PK of other substrates

Alleles with some in vitro evidence of change in activity or expression

Q15 Do you include rare alleles (population frequency <1% in all populations) in ADME PGx analyses? Select all that apply.	**Yes, if there is prior evidence that the allele has a clinical meaningful impact on PK of other substrates** **,** **Yes if there is some in vitro evidence of functional impact of the allele**
Q16 How Is is the impact of genetic variation on compound disposition assessed using population PK models in Phase II and beyondin studies with sparse pharmacokinetic sampling?	**Genotype is incorporated as a covariate in population PK models**

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

reproducibility

Q18 Does your organization typically consider potential impact of genetic variants on PK of therapeutic proteins, including the drug target in cases where target mediated drug disposition is relevant?	**No**

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

na

Q20 Does your organization assess the impact of genomic variation (e.g. impact of microRNAs, epigenetic changes, changes in expression) on PK of your compounds?	**No**

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

na

Q22 What are the major limitations to accurately assess impact of genetic variation on compound disposition? Select all that apply.	**Inability to accurately determine contribution of enzymes/transporters,** **,** **Cost of required in vitro experiments ,** **Cost of required clinical studies ,** **Sample size of clinical studies limits ability to conduct genetic analyzes** **,** **Clinical studies typically limited to certain populations**
Q23 For compounds expected to have higher risk of drug-induced liver injury (DILI), are analyses conducted to look for genetic variants associated with higher risk of DILI?	**No**

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

na