Industry Pharmacogenomics Working Group (I-PWG) - Overview

ASHG/PGRN

Dr. Jean-Claude Marshall (I-PWG Co-Chair)
Overview

• I-PWG – Who we are, Mission & goals
• I-PWG Member Companies
• Overview of I-PWG Activities
• Overview of I-PWG Task Force/Working Group Activities
• I-PWG Membership Surveys and Examples
• I-PWG External Meeting Engagement

Conflicts of Interest

• I am an employee of Pfizer
• I own Pfizer stock
I-PWG Overview

Who we are:

- The Industry Pharmacogenomics Working Group (I-PWG) was established in 2000 and is comprised of functionally diverse members from pharmaceutical and biotechnology companies.
- Our diverse membership is made up of those engaging in regulatory, statistical, technological, genomic and biological research as well as operations.
- We engage pre-competitively to address emerging issues related to pharmacogenomics.
I-PWG Overview

Revised in 2017

Mission:
• To improve patient care through the integration of pharmacogenomics in drug development

Goals:
• Impact the integration of pharmacogenomic research into global drug development and regulatory policy through sharing and promoting best practices
• Facilitate the use of genomic data to inform drug labels and clinical decision making
• Promote education of pharmacogenomic science
I-PWG Activity

I-PWG Membership Monthly Meetings:

• Invited guest speakers from Academia, Regulatory, Industry, Patient Advocacy, Legal etc.. invited to speak to the membership

• Topics in 2018 included: Feedback on the NAS Genomics Roundtable in Precision Medicine Initiative, Advances in Pharmacogenomics of Adverse Drug Reactions, Genomics England – Realising the potential of population data

• Invited speakers provided regulatory guidance on PGx research in Israel, Denmark & China

• Meetings focus on knowledge/best-practice sharing of information across the member companies
I-PWG Activity

I-PWG core activity conducted via various Working Groups/Task Forces:

• Current Task Forces: ADME, DNA Collection, Education & Communication, Regulatory

• Previous Task Forces include: Emerging Technologies, Sample & Data Coding, PGx Study Design, Global Sample Harmonization & VXDS
ADME Task Force 2018 Plans

• Creation of a list of variants, develop a database and their functional relevance based on clinical data
• Interest in joining International Transporter Consortium
• Standardize genotypes/haplotypes that could be considered a standard assay based on clinical data and experience
  – Would welcome input on this from PGRN
• Protein metabolizing DMEs
• Invite speakers from Academia, Industry and Agencies/Regulators
DNA Collection Task Force 2018 Plans

Plans to facilitate a PRIMR Advancing Ethical Research Conference Workshop titled “Pharmacogenomics and Precision Medicine: Partnering to enable DNA research in global clinical trials” with a focus on:

• Improving the understanding by industry of the difficulties faced by various IRB and ethics professionals in reviewing this research

• Addressing how industry is responding to evolving regulatory landscape with regard to sample collection practices (e.g. GDPR)

• What is the impact of technology on DNA Collection and management (e.g. e-consent, natural language processing of consents for permissions, use of meta-data or controlled vocabulary for managing permissions)? Are there options for I-PWG to influence these technologies?

• Are there challenges with collecting other samples for nucleic acid future research beyond germline genetics (e.g. RNA, DNA for epigenetics, pathogen or somatic)?
Education & Communication Task Force 2018 Plans

- Increase awareness of I-PWG to external stakeholders
- Identification of other organizations that have similar approaches to education for collaboration opportunities in education
- Potentially develop additional education materials covering the following topics: Whole Genome Sequencing, Companion/Complimentary Diagnostics, Prospective & Retrospective analysis
## Education Taskforce Video

6 Minute, animated with voice description video  
Recently finalized, and will be posted for all to use

Here is where you can go for more information:

| **Industry Pharmacogenomics Working Group (I-PWG)**  
**www.i-pwg.org** | The I-PWG has a number of educational resources including web-based courses, audiovisual resources, podcasts and textbook recommendations |
| European Patients’ Academy (EUPATI)  
**www.eupati.eu** | This site provides a wealth of patient education and training to increase the capacity and capability of patients to understand and contribute to medicines research and development |
| Genetics Home Reference  
**ghr.nlm.nih.gov** | This site provides helpful information about the effects of genetic variations on human health |
| Human Genome Project Information  
**http://web.ornl.gov/sci/techresources/Human_Genome/education/index.shtml** | This site provides a wealth of genetics information in various formats (publications, teaching aids, videos, webcasts, etc.). This includes a quick “Genetics 101” lesson |
| Personalized Medicine Coalition  
**http://www.personalizedmedicinecoalition.org** | This site provides info on various biomarkers and also introduces readers to the movers and shakers in this field |
Regulatory Task Force 2018

• Speakers: Identify and coordinate regulatory related speakers for I-PWG monthly meetings

• I-PWG Regulatory Repository: Develop page on I-PWG website containing links to regulatory resources (including HHS global regulatory library)

• Review PGx Related Regulations & Guidelines

• Follow-up on status of EMA Guideline on Good Pharmacogenomic Practice (submitted comments Sep 2016, final guideline in effect as of Sept 1 2018)

• Review and comment, when possible, on regulations that could impact PGx research.
EMA Guideline on Good PGx Practice

• Comments submitted by I-PWG and individual member companies to the EMA
• Almost every member company provided direct feedback to the I-PWG to be compiled.
• All member companies agreed to the feedback that was then sent on to the EMA
• A total of 32 combined comments, totaling 15 pages of text, were sent to the EMA
• Several issues still remain with the final guidance as it was released
  – “In cases where the inter-individual differences in PK or PD are high and not explained by known genetic variants, it is recommended that genomic DNA sequencing is carried out using broader approaches such as whole exome sequencing (WES) or whole genome sequencing (WGS) with subsequent bioinformatic analyses of sequences in appropriate genomic regions.”
EMA Guideline on Good PGx Practice – Pfizer Perspective

- Pharmacogenomic genotyping only carried out in cases where the majority of a compound’s Fm is through a polymorphic enzyme (or transporter) that has polymorphisms of known clinical significance

- The majority of early clinical trials have PK and PD differences, many of which are not explained without substantial investigation at the site
  - Missed doses
  - Double dosing
  - Sample labeling errors
  - Unknown

PGx Practice – Pfizer Perspective

![Pie chart showing stage distribution with 96.3% Clinical and 3.7% Other categories.]

![Bar chart showing distribution by study type with Clinical, Discovery, Preclinical, etc. categories.]

ADME Genotyping Support by RU/BU:
- Clinical: 28.4%
- Discovery: 18.7%
- Preclinical: 12.1%
- Empty: 6.6%
- Other: 6.0%
- Unknown: 6.0%

![Bar chart showing study type distribution with Custom Extraction, Gene Expression, Genotyping, etc. categories.]

Color by:
- Study
- RU/BU
- Other categories:
  - Academic
  - ADME CoE
  - GEP
  - MI
  - RURU
  - ORU
  - PGx
  - RORU
I-PWG regularly surveys its membership on a range of topics

Company specific surveys addressed the following queries:

• Has your company implemented (or do you plan to) the exclusion of clinical trial Patient IDs in sample manifests sent to external biomarker assay labs as a specific measure to address Global Data Privacy Regulation (GDPR) compliance?
  
• Feedback: It was observed that a majority of member companies had limited experience in this area. There were however some specific insights learnt by some companies that will be potentially useful for the membership planning to take this approach

• Has your company had any previous experience in depositing whole exome or whole genome sequencing data that was generated as part of a global clinical trial onto external databases?

• Feedback: Useful insights provided by companies on how to modify ICFs to enable this approach

Findings from all surveys are shared with each member company
Survey Feedback

Regulatory Task Force:

• Specific insights learnt about the collection and shipment of PGx samples in Denmark, Germany & Israel. It was observed that member companies had similar experiences regarding the collection of samples and were able to share these learnings with those companies who do not routinely collect samples in these countries.

• Additional survey conducted focusing on the collection & storage of PGx samples in China. The outcome of this survey has led to the Task Force to pursue plans to meet with the Chinese Regulatory Agencies in late 4Q18/1Q19 in the context of information sharing/informal dialogue basis.

Education & Communication Task Force:

• Feedback from the survey has enabled the Task Force to begin developing more targeted & relevant education material for clinical trial patients (videos, brochures etc..)
Q14 Is DNA collection a requirement in all phase II-III protocols?

Answered: 14    Skipped: 0

- Yes: 35.71%
- No: 64.29%
Q16 Does your company have a policy for returning NGS generated results to patients participating in exploratory PGx studies in clinical trials? (Check all that apply)

Answer Choices

<table>
<thead>
<tr>
<th>Policy Description</th>
<th>Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Will not return results under any circumstances</td>
<td>30.00%</td>
</tr>
<tr>
<td>Only returned if NGS or follow-up assays performed under CLIA regulations</td>
<td>40.00%</td>
</tr>
<tr>
<td>Only returned in countries where it is required by law</td>
<td>60.00%</td>
</tr>
<tr>
<td>Only returned for incidental findings</td>
<td>0.00%</td>
</tr>
<tr>
<td>In some circumstances exploratory results can be returned</td>
<td>20.00%</td>
</tr>
</tbody>
</table>

Total Respondents: 10
I-PWG External Meeting Engagement

FDA/I-PWG Workshop Meeting (1Q17) - Sample Collection Roundtable discussion included the following topics:

- Can companies work together with regulatory agencies, to increase global sample collection?
- Bias and statistical issues with incomplete sample collection?
- How to collaborate & work with global health authorities?
- How to partner with FDA and others to increase use of PGx in drug development?
- How best to utilize NGS technology and data?
- Address the issue of the return of data to clinical trial participants?
I-PWG External Meeting Engagement

FDA/I-PWG Workshop Meeting (1Q17) - NGS Roundtable discussion included the following topics:

• Status and use of VXDS and Safe Harbor?
• FDA capability with NGS data?
• Work with FDA on NGS data standardization?
• Aggregate NGS data across industry to investigate disease?
• Precompetitive vs drug response?
• Companion and Complimentary Diagnostics?
I-PWG External Meeting Engagement

FDA Workshop Meeting (1Q17) - ADME Roundtable discussion included the following topics:

• How do the member company approaches to ADME vary?
• How to develop a “standardized” ADME gene panel and model (including ethnic variants)?
• Standardize genotype to phenotype calls?
• Experience with CYP vs non-CYP and transporter genes?
I-PWG 2018 Focus

- Continued/initiate external engagement with various regulatory agencies (EMA, FDA & HGRAC)
- Explore challenges and identify best practices that optimize collecting DNA samples from clinical trial patients in global clinical trials
- Interest in developing a standardized panel of ADME genes (CYPs, Transporters, UGTs, additional Phase 2 enzymes)
- Rollout of PGx patient video, develop educational webinars, identification of other organizations that have similar approaches to education for collaboration opportunities in education
Summary

• I-PWG – Who we are, Mission & goals
• I-PWG Member Companies – Who Participates
• Overview of I-PWG Activities – Current Focus for 2018
• Overview of I-PWG Task Force/Working Group Activities
• I-PWG External Meeting Engagement – Overview of previous workshop held with the FDA

Thank you!