Patient Centric Sampling: How the COVID-19 Pandemic is Shifting the Landscape

Melanie Anderson
IQ CPLG/TALG PCS Working Group
IQ CPLG/TALG Patient Centric Sampling (PCS) Working Group Members

<table>
<thead>
<tr>
<th>Member Company</th>
<th>PCS Member</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbvie</td>
<td>Rizzo, David</td>
</tr>
<tr>
<td></td>
<td>Zha, Jiuhong</td>
</tr>
<tr>
<td></td>
<td>Kamradt, Kent</td>
</tr>
<tr>
<td>Amgen</td>
<td>James, Christopher</td>
</tr>
<tr>
<td>Astellas</td>
<td>Ito, Mototsugu</td>
</tr>
<tr>
<td>Blueprint Medicines</td>
<td>Perez, Nisha</td>
</tr>
<tr>
<td>BMS</td>
<td>Ji, Qin</td>
</tr>
<tr>
<td></td>
<td>Kozinn, Marc</td>
</tr>
<tr>
<td></td>
<td>Vakkalagadda, Blisse</td>
</tr>
<tr>
<td>Daiichi Sankyo</td>
<td>He, Ling</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>Williams, Tracy (Sponsor)</td>
</tr>
<tr>
<td></td>
<td>Zhang, Xin (Co-Chair)</td>
</tr>
<tr>
<td>Genentech</td>
<td>Maass, Katie</td>
</tr>
<tr>
<td>J&amp;J</td>
<td>Patel, Sehefali</td>
</tr>
<tr>
<td>MSD</td>
<td>Anderson, Melanie (Co-Chair)</td>
</tr>
<tr>
<td></td>
<td>Rudd, Deanne</td>
</tr>
<tr>
<td>Mitsubishi</td>
<td>Nakayama, Satoshi</td>
</tr>
<tr>
<td>Novartis</td>
<td>Leuthold, Luc Alexis</td>
</tr>
<tr>
<td></td>
<td>Li, Wenkui</td>
</tr>
<tr>
<td></td>
<td>Mikhailov, Dmitri</td>
</tr>
<tr>
<td>Otsuka</td>
<td>Kumar, Parag</td>
</tr>
<tr>
<td></td>
<td>Westcott-Baker, Lucas</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Kavetska, Olga</td>
</tr>
<tr>
<td>Sunovion</td>
<td>Lepak, Maureen</td>
</tr>
<tr>
<td>Roche</td>
<td>Matthew Barfield</td>
</tr>
<tr>
<td>Takeda</td>
<td>Jain, Gagan</td>
</tr>
<tr>
<td></td>
<td>Qian, Mark</td>
</tr>
<tr>
<td>Faegre Drinker Biddle &amp; Reath</td>
<td>Lyapustina, Sevtlana (IQ Secretariat)</td>
</tr>
</tbody>
</table>

Acknowledgement

This presentation was developed with the support of the International Consortium for Innovation and Quality in Pharmaceutical Development (IQ, www.iqconsortium.org). IQ is a not-for-profit organization of pharmaceutical and biotechnology companies with a mission of advancing science and technology to augment the capability of member companies to develop transformational solutions that benefit patients, regulators and the broader research and development community. The Consortium includes members that may be competitors as well as suppliers and customers. It is the intention of the Consortium to operate in strict compliance with antitrust laws. In particular, nothing discussed at this meeting is intended to result in an agreement on price, exclude suppliers from any market, or otherwise restrain competition. Those participating in this meeting are instructed to avoid discussion of competitively sensitive subjects, including costs, prices, sales, product marketing, and other confidential information.
Patient Centric Sampling WG

**Leadership Groups:** TALG and CPLG  **Status:** Active (WG 2020-2022)

- **Mission:** Fill potential knowledge gaps in the field of patient centric sampling and provide a forum for cross-industry practitioners to share and define best practices on how to apply patient centric sampling to aid drug development

- **Objectives:**
  a) Increasing awareness and uptake across industries and b) Establish current state and best practice guidance for the novel approach of patient centric sampling

- **IQ Strategic Objectives:**
  The WG was transitioned from a DG at the beginning of 2020. The WG is having monthly teleconferences for discussing the various hot topics in addressing knowledge gaps in the novel area of patient centric sampling. A webinar has been scheduled for July 2020 with slides completed. Several work streams have been formed to brainstorm on topics and outlines for a manuscript or white paper aiming to provide best practice guidance of applying patient centric sampling in drug development.

<table>
<thead>
<tr>
<th>Deliverables</th>
<th>Milestones</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Webinar</td>
<td>Deliver an IQ webinar</td>
</tr>
<tr>
<td>2</td>
<td>Publication/white paper</td>
<td>Publish manuscripts/white paper</td>
</tr>
<tr>
<td>3</td>
<td>PCS and COVID correspondence article</td>
<td>IQ review is complete, 1st round of editorial feedback</td>
</tr>
<tr>
<td>4</td>
<td>Conferences</td>
<td>Submitted abstract to ACCP, EBF presentation</td>
</tr>
</tbody>
</table>

https://iqconsortium.org/
Patient Centric Sampling

The State of PCS in the Pharmaceutical Industry before the COVID-19 Pandemic
Where is the Innovation in Sampling?

The idea that biological sample collection in healthcare should center on the needs of the patient. New technology is reducing sample volume needs, providing less invasive collection techniques, and enabling collection of samples outside the traditional clinical setting making patient centric sampling a reality.

Patient-Centric Sampling Innovation

Traditional Venous Collection

Fingerstick Collection

Mobile Phlebotomy

Capillary Collection

https://cleancompetition.org/2016/05/11/whats-next-wednesday-dried-blood-spot-sampling/

https://www.neoteryx.com/mta-cartridge-blood-sampling-device-dbs

https://www.trajanscimed.com/pages/hemapen

https://www.7sbio.com/

http://www.tassoinc.com/

https://www.drawbridgehealth.com/


ehp.niehs.nih.gov/doi/pdf/10.1289/ehp.6264
PCS: Benefits to Patients and Sponsors

Expand geographic reach

ICU Risk prediction

More frequent safety monitoring

Infectious samples

At-home (virtual) visits

(Pre) Screening

Study conduct

Follow-up

Long term follow-up

Reduce (pre) screen costs

Vulnerable populations: Low volume, Painless

Drug adherence

Increase sampling intervals

Mobile nursing

Rapid sampling during clinical events

Limited infrastructure

Infectious samples at home (virtual) visits

Drug adherence

Increase sampling intervals

Mobile nursing

Rapid sampling during clinical events

Limited infrastructure

PCS: Benefits to Patients and Sponsors

Expand geographic reach

ICU Risk prediction

More frequent safety monitoring

Infectious samples

At-home (virtual) visits

(Pre) Screening

Study conduct

Follow-up

Long term follow-up

Reduce (pre) screen costs

Vulnerable populations: Low volume, Painless

Drug adherence

Increase sampling intervals

Mobile nursing

Rapid sampling during clinical events

Limited infrastructure

Infectious samples at home (virtual) visits

Drug adherence

Increase sampling intervals

Mobile nursing

Rapid sampling during clinical events

Limited infrastructure

Infectious samples at home (virtual) visits

Drug adherence

Increase sampling intervals

Mobile nursing

Rapid sampling during clinical events

Limited infrastructure

Infectious samples at home (virtual) visits

Drug adherence

Increase sampling intervals

Mobile nursing

Rapid sampling during clinical events

Limited infrastructure

Infectious samples at home (virtual) visits

Drug adherence

Increase sampling intervals

Mobile nursing

Rapid sampling during clinical events

Limited infrastructure

Infectious samples at home (virtual) visits

Drug adherence

Increase sampling intervals

Mobile nursing

Rapid sampling during clinical events

Limited infrastructure

Infectious samples at home (virtual) visits

Drug adherence

Increase sampling intervals

Mobile nursing

Rapid sampling during clinical events

Limited infrastructure

Infectious samples at home (virtual) visits

Drug adherence

Increase sampling intervals

Mobile nursing

Rapid sampling during clinical events

Limited infrastructure
Case Study: Application in Challenging Disease

- Duchenne Muscular Dystrophy (DMD) is a severe type of muscular dystrophy in ~ 1/5000 boys that begins with muscle weakness around age 4 and worsens quickly.
- There is no cure and life expectancy is limited to late twenties.
- Extremely painful and hard for DMD boys to provide conventional blood samples.
- The microsampling device<sup>a</sup> offers the possibility of remote patient sampling combined with painless sampling.
- A Phase 1b study in 2020 will compare conventional plasma PK samples with Tasso samples and the usability of the device in DMD boys.

<sup>a</sup>Tasso OnDemand Collection Device
Case Study: Application for Biomarker Collection

• Phosphatidylethanol Study Perform by Ghent University measured direct alcohol marker in proportion to the amount of alcohol used in the previous month.

• ~800 participants enrolled in ~4 days & asked to take 3 fingerstick blood samples in one month

• Training information was provided by email, hardcopy leaflet, and video.

• The team has received ISO 17025 certification for method that has been applied to judicial cases and for people to demonstrate sobriety.

Case Study: Evaluation of Micro Sampling Device for C-Reactive Protein (CRP) Plasma Levels

- Feasibility study in healthy volunteers to evaluate a novel micro sampling device enabling capillary blood collection
- Estimation of circulating inflammatory biomarker with both traditional liquid collection and alternative capillary blood collection using an ELISA method
- Obtained good correlation between both measurements

https://doi.org/10.4155/bio-2020-0063
Remote Safety Monitoring

Before COVID-19

Desirable or Minimal Imprecision

All < Minimal Total Error Budget (Bias + 1.65*CV)

Land O’ Lakes Bioanalytical Conference 2019,
“Successful Implementation of Patient-Centric Sampling Technologies”

https://academic.oup.com/clinchem/article/66/6/821/5836762
What’s getting in the way?

Logistical
• Technology access for in remote/underserved geographies
• Shipping requirements within a country
• Time and date stamp collection
• Patient compliance and sample quality
• Clinical site and patient training

Business/Regulatory Related
• Increases the cost of conducting the trial
• Increases the complexity of the protocol
• Import of device and regulatory approval in each country
• No definitive data that show return on investment

Bioanalytical Sample Analysis
• Sensitivity
• Stability and extractability in the dried state
Patient Centric Sampling

Impact of the COVID-19 Pandemic on PCS
Patient Centric Sampling in the Pandemic

Current COVID testing – proves it can be!
• Remote drive-by testing sites for molecular test
• At home collection of samples for molecular test with over 20 collection kits having EUA approval
• At home sample collection for COVID-19 serology testing
  NIH
  Fred Hutchinson Cancer Research
  University of Rochester
  UC San Diego
  Emory University

https://www.kff.org/interactive/at-home-sars-cov-2-testing-what-are-the-options/
Patient Centric Sampling in the Pandemic

Current COVID testing
• Participants provided positive feedback on at home collection of blood, saliva and oropharyngeal samples for COVID-19 diagnosis and serology
• The demand for devices that enable remote biological sample collection is impacting device manufacturer
  • Huge increases in device usage for COVID-19 testing and other healthcare testing
  • Increased investment
Impact on Clinical Trials
• Clinical sites have had to close down to ensure participant and staff safety
• Alternative at home sample collection to support social distancing in ongoing clinical trials
• PCS approaches can mitigate missing data due to the COVID-19 restrictions in ongoing clinical trials

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7406082/

**Background:** Sponsors provided case studies for trials that were shifting to patient centric approaches. Six case studies were provided from three different pharmaceutical companies. Many companies indicated that they are exploring alternative approaches to sampling.

**Study Details:** Global large late phase trials and small, early phase trials were represented. Studies included work in healthy volunteers and special populations. Shifts to different sampling approaches were taken mid-trial or at study start.

**Challenge:** Due to COVID-19, participants could no longer travel to sites. Sponsors and study participants have serious concerns around the risks due to the pandemic. This is a larger concern in populations at high risk for COVID-19 complications. However, clinical monitoring and sample collection is critical for safety and efficacy. Timelines for development can be very tight and delays due to the pandemic are difficult to tolerate.

**Solution:** In all cases, home visits with a trained individual, often a nurse, were implemented to either deliver drug and supervise/assist with administration and/or collect remote samples for safety panels and drug concentrations, and/or conduct clinical evaluations.

**Considerations:** Implementation was conducted at risk. Operational implementation can be challenging. Sample quality and integrity must be maintained.
COVID-19 and Clinical Trials

• Pandemic is changing the way sponsors are thinking about patient centric sampling
• Driving change in device usage across healthcare and fostering increased interest in pharma specifically.
• There are several cases of clinical trial teams shifting to mobile phlebotomy venous blood collection to provide critical data and maintain safe social distancing practices.
• Our IQ working group will seek to leverage the PCS lessons learned during the pandemic to understand the challenges and opportunities.
How do we move forward and what does success look like?

- Novel endpoints
- Predictive models & testable hypothesis
- Disease & drug effect
- More informed data
- Increased access to patients and patients to trials
- Reduced patient burden
- Increased data quality
- Sponsor/CRO burden
- Regulatory acceptability
- Dosing history via small trials

Path to efficient, patient-centric drug development

Thank you!
Back-up: IQ Patient Centric Sampling

Dried Blood Spot background – newborn screening, diabetes
PCS device details and background
PCS adoption barriers
Patient Centric Sampling: Building Collaborations

Share best practices in the pre-competitive space

- IQ PCS Working Group (https://iqconsortium.org/)
- AAPS Micro Sampling Discussion Group b,c
- European Bioanalysis Forum: Patient Centric / Home Sampling Team b
- Patient Centric Sampling Interest Group (https://cpsa-usa.com/2019/PCSIG.shtml)
- Transcelerate (https://www.transceleratebiopharmainc.com/)

---

c www.aaps.org/education-and-research/workshops/micro-sampling
Historical Perspective: Dried Blood Spots

- Simplifies collection and shipping
- Reduces trial geographical constraints
- Special populations – pediatrics, oncology, migraine

Successful Implementation Across the Pharmaceutical Industry
Stepping Forward with Volumetric Absorptive Microsampling (VAMS)

- A novel material that can accurately & precisely collect 10 or 20 µL of blood
- Diminishes hematocrit impact

www.neoteryx.com/mitra-cartridge-blood-sampling-device-dbs
## Patient Centric Sampling Devices

<table>
<thead>
<tr>
<th>Product</th>
<th>TAP™</th>
<th>TASSO-M20™</th>
<th>BD Microtainer®</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Company</strong></td>
<td>Seventh Sense Biosystems</td>
<td>Tasso</td>
<td>BD</td>
</tr>
<tr>
<td><strong>Current Status</strong>*</td>
<td>FDA 510(k) for HbA1c test</td>
<td>FDA Class I</td>
<td>FDA 510(k) for chemistry</td>
</tr>
<tr>
<td></td>
<td>FDA Class II</td>
<td></td>
<td>FDA Class II</td>
</tr>
<tr>
<td></td>
<td>CE marked</td>
<td></td>
<td>CE marked</td>
</tr>
<tr>
<td><strong>Specification</strong></td>
<td>Virtually painless, user-friendly self-collection of ~100µL whole blood</td>
<td>Simple, intuitive and virtually painless self-collection of dried blood with volume control</td>
<td>Collects blood (up to 500µl) from skin prick. Available with or without additives (serum/plasma separator gel, K2EDTA, Li-Heparin). Connectable with routine instruments (hematology, clinical chemistry) For use by research or healthcare professionals</td>
</tr>
</tbody>
</table>

* According to publically available online information as of Sept. 2020
# Patient Centric Sampling Devices

<table>
<thead>
<tr>
<th>Product</th>
<th>Mitra®</th>
<th>HemaXis DB</th>
<th>HemaPEN®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Company</td>
<td>Neoteryx</td>
<td>DBS System</td>
<td>Trajan</td>
</tr>
<tr>
<td>Current Status*</td>
<td>FDA Class I CE marked</td>
<td>FDA Class I CE marked</td>
<td>FDA Class I CE marked</td>
</tr>
<tr>
<td>Specification</td>
<td>User-friendly format for unassisted remote collection Accurate and precise dried blood collection with volume control</td>
<td>Accurate and precise blood on standard Dried Blood Spots (DBS) paper cards with volume control.</td>
<td>Minimally invasive Accurate and precise blood volumetric collection K2 EDTA Whole blood Registered for use by research personnel and healthcare professionals</td>
</tr>
</tbody>
</table>

* According to publically available online information as of Sept. 2020