INTERNATIONAL CONSORTIUM for INNOVATION & QUALITY in PHARMACEUTICAL DEVELOPMENT

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

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IQ CPLG/TALG PCS Working Group

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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.

	Deliverables	Milestones	Status
1	Webinar	Deliver an IQ webinar	IQ webinar planned for July 2020
2	Publication/white paper	Publish manuscripts/white paper	Work ongoing, manuscript outline under discussion
3	PCS and COVID correspondence article	IQ review is complete, 1st round of editorial feedback	Submitted to Nature Medicine Oct 2020
4	Conferences	Submitted abstract to ACCP, EBF presentation	Ongoing discussions around additional conferences to target

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.

www.future-science.com/doi/10.4155/bio-2020-0075

Patient-Centric Sampling Innovation

Traditional Venous Collection

Fingerstick Collection

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

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

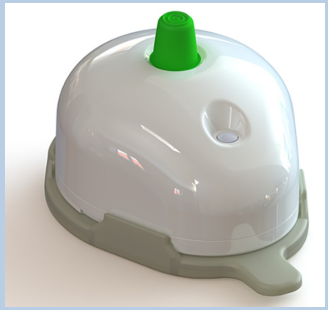
https://www.trajanscimed.com/pages/hemapen

Mobile Phlebotomy

www.sciencedirect.com/science/article/pii/S0167701217303287?via%3Dihub
ehp.niehs.nih.gov/doi/pdf/10.1289/ehp.6264

Capillary Collection

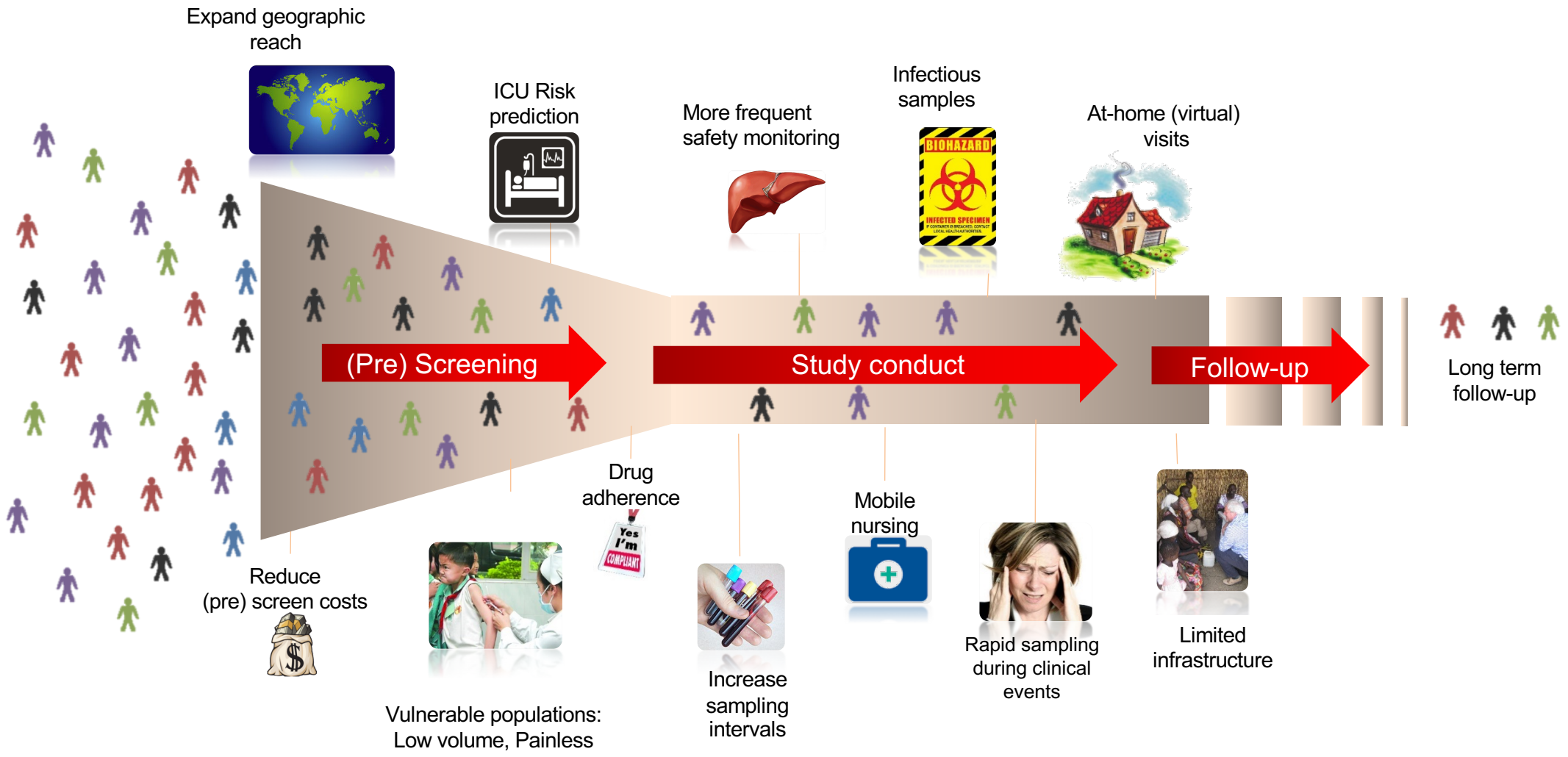
https://www.tassoinc.com/



http://www.7sbio.com/

https://www.drawbridgehealth.com/

PCS: Benefits to Patients and Sponsors



Before COVID-19

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[a] 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

[a]Tasso OnDemand Collection Device

Before COVID-19

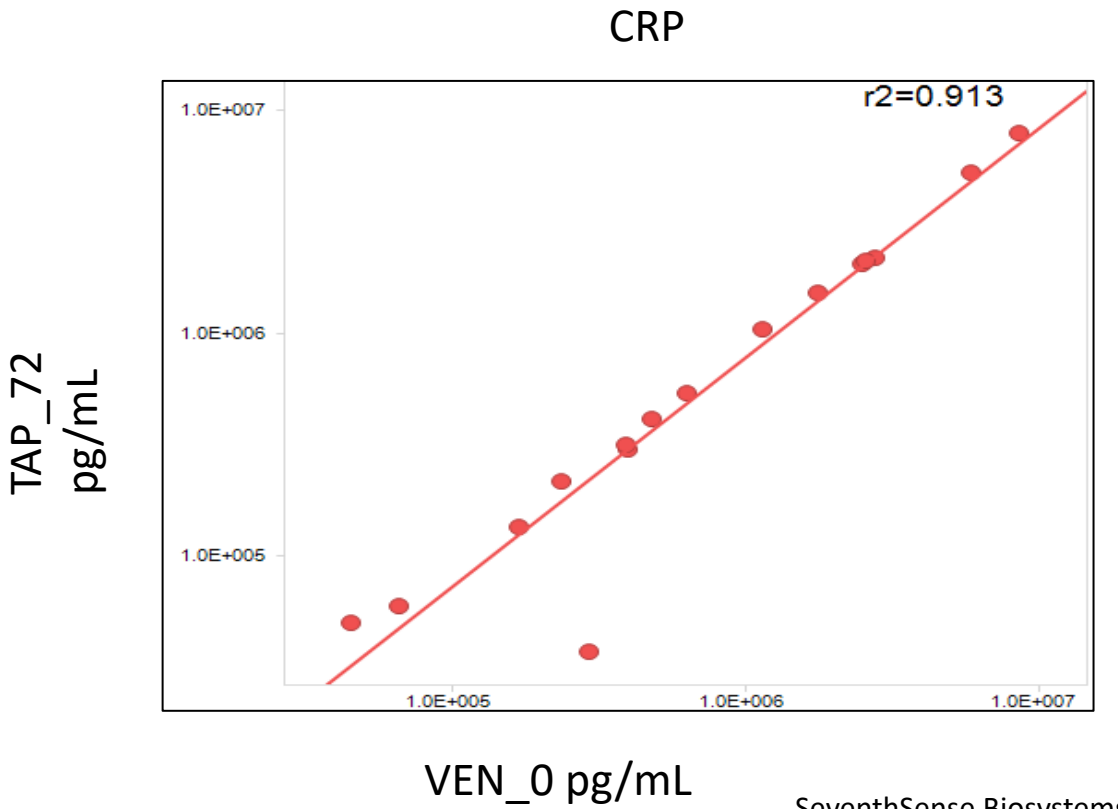
Case Study: Application for Biomarker Collection

- 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.

www.neoteryx.com/microsampling-news/ghent-university-scientists-use-vams-to-measure-a-novel-biomarker-for-alcohol-abuse

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

Before COVID-19



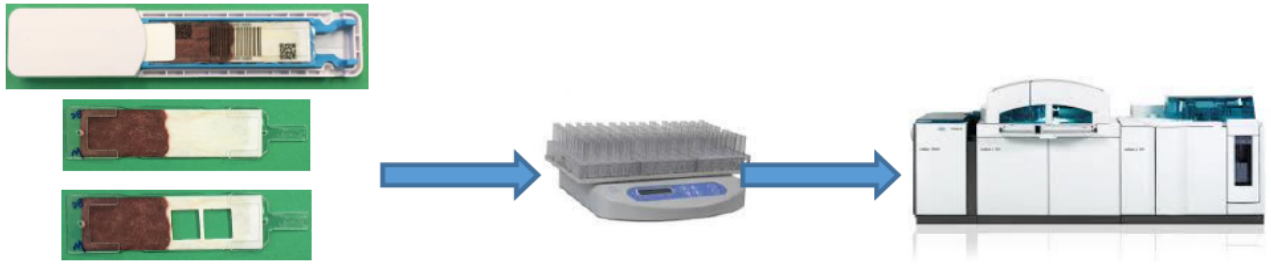
SeventhSense Biosystems TAP™
Venipuncture VEN

- Feasibility study in healthy volunteers to evaluate a novel micro sampling device[a] 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

Before COVID-19

Remote Safety Monitoring



Punch → Add diluent, Mix → Assay on Autoanalyzer

Desirable or Minimal Imprecision

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

Analyte	Variance (%CV)	Mean Bias to Phlebotomy (%)
HbA1c	6.3	0.5
ALT	8.9	0.1
AST	7.3	-0.5
Cholesterol	6.1	0.3
Creatinine	4.7	0.1
Glucose	4.7	-0.4
HDL	7.0	0.2
Triglycerides	6.5	0.1
TSH	5.7	-0.4
Vitamin D	7.8	0.3
LDL	6.6	0.1
BUN	8.0	-0.2
C-Peptide	4.7	0.1
Total PSA	5.4	0.4

Land O' Lakes Bioanalytical Conference 2019,
"Successful Implementation of Patient-Centric Sampling Technologies"

https://academic.oup.com/clinchem/article/66/6/821/5836762

Barriers

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

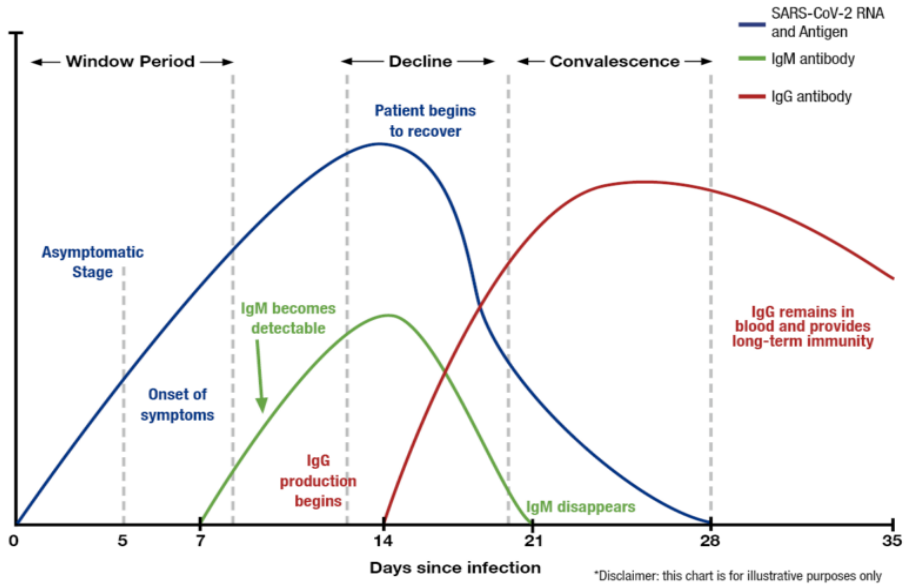
Patient Centric Sampling

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://hemaxis.com/services/covid19-testing/

https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas
https://www.kff.org/interactive/at-home-sars-cov-2-testing-what-are-the-options/
www.neoteryx.com/microsampling-news/neoteryx-provides-remote-blood-collection-kits-for-covid-19-research
www.niaid.nih.gov/news-events/nih-begins-study-quantify-undetected-cases-coronavirus-infection
https://www.fredhutch.org/en/research/divisions/vaccine-infectious-disease-division/research/infectious-disease-sciences/covid-watch.html

Patient Centric Sampling in the Pandemic

COVID-19

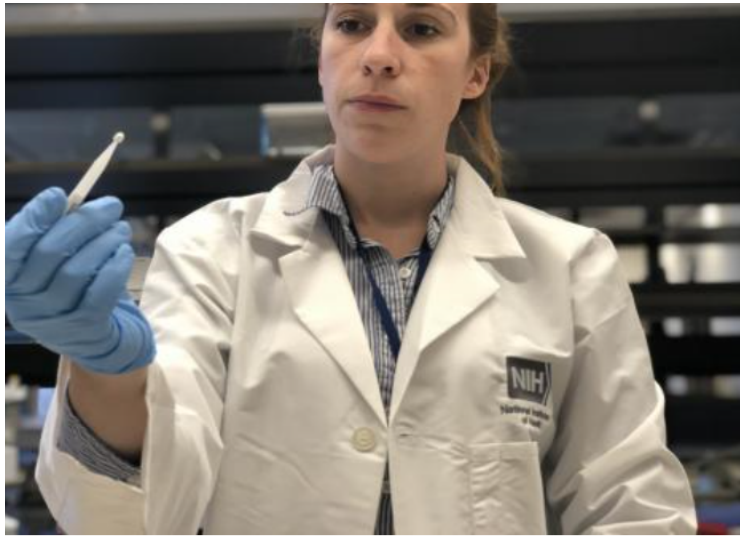
Current COVID testing

- 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/
https://pubmed.ncbi.nlm.nih.gov/32310815/#affiliation-1



www.neoteryx.com/microsampling-news/nih-begins-study-to-quantify-undetected-cases-of-coronavirus-infection

Case Studies: COVID-19 and Clinical Trials

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.

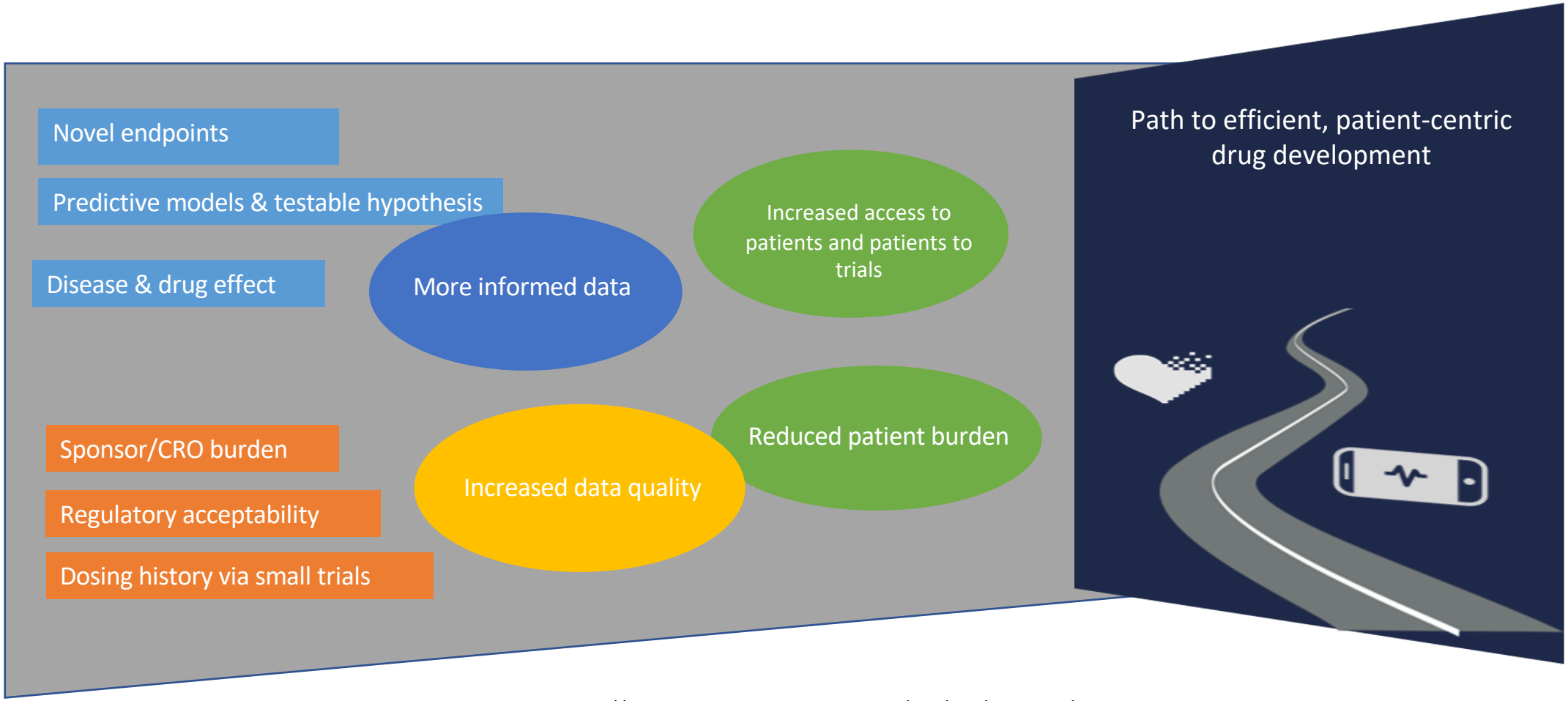
Solution: In all cases, home visits with a trained individual, often a nurse, were implemented to either deliver drug and supervise/assist with administration and/or collect remote samples for safety panels and drug concentrations, and/or conduct clinical evaluations.

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?



https://ascpt.onlinelibrary.wiley.com/doi/full/10.1002/cpt.1100
Kothare, et al. "Harnessing the Potential of Emerging Digital Health and Biological Sampling Technologies for Clinical Drug Development: Promise to Reality", CPT, Apr 2018.

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[a]

- 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/)

[a] www.e-b-f.eu/wp-content/uploads/2019/12/bcn2019-12-Neil-Spooner-on-behallf-of-the-AAPS-microsampling-team.pdf

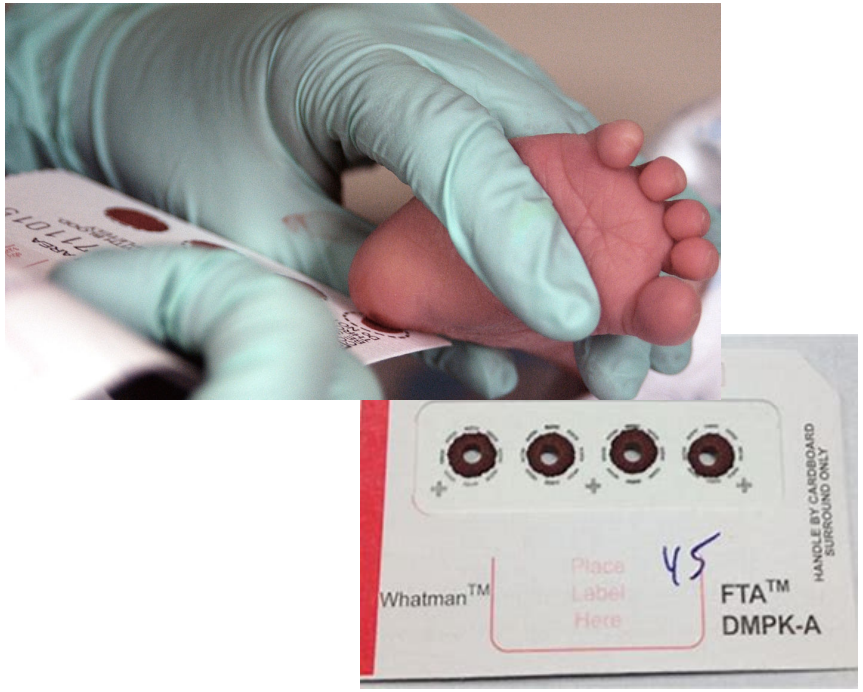
[b] www.future-science.com/doi/full/10.4155/bio-2019-0019

[c] www.aaps.org/education-and-research/workshops/micro-sampling

Historical Perspective: Dried Blood Spots

It can be done!

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



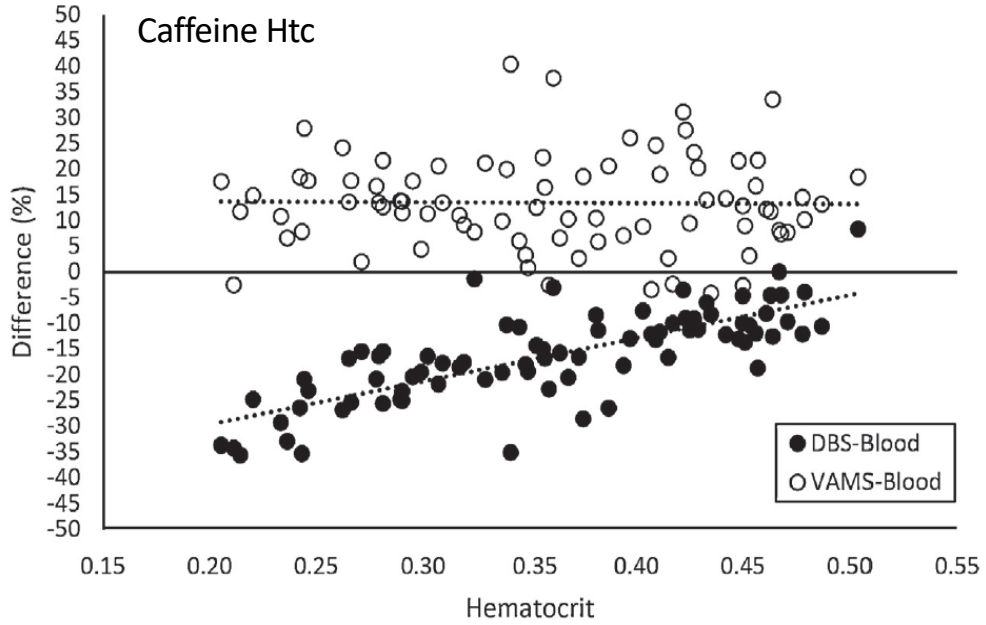
Successful Implementation Across the Pharmaceutical Industry

Stepping Forward with Volumetric Absorptive Microsampling (VAMS)

It can be done!

- 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



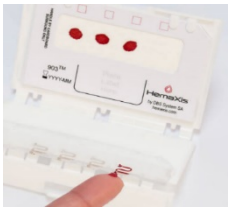
Patient Centric Sampling Devices

Devices

Product	TAP™	TASSO-M20™	BD Microtainer®
Company	Seventh Sense Biosystems	Tasso	BD
			
Current Status*	FDA 510(k) for HbA1c test FDA Class II CE marked	FDA Class I	FDA 510(k) for chemistry FDA Class II CE marked
Specification	Virtually painless, user-friendly self-collection of ~100µL whole blood	Simple, intuitive and virtually painless self-collection of dried blood with volume control	Collects blood (up to 500ul) 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

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

Patient Centric Sampling Devices

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

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