



Precision Medicine Executive Summary

August 2023

PURPOSE

The purpose of this document is to provide an executive overview of the importance of a pharmacist led pharmacogenomic (PGx) solution and where NCPDP standards can support the forward movement of Precision Medicine. The intent is to look at current progress of PGx within the healthcare arena and where NCPDP solutions can be explored, modified or created to support the pharmacist led PGx workflow.

DEFINITIONS

Personalized Medicine: an approach to patients that considers their genetic make-up but with attention to their preferences, beliefs, attitudes, knowledge, and social context.

Pharmacogenetics: the study of how variations in individual genes influence drug response. It examines the impact of specific genetic variations, such as single nucleotide polymorphisms (SNPs), on drug metabolism, efficacy, and adverse reactions. Pharmacogenetics typically investigates the influence of variations in specific genes known to be involved in drug metabolism or response.

Pharmacogenomics (PGx): the study of how an individual's entire genetic makeup, including all their genes, influences their response to drugs. It involves analyzing the entire genome to identify genetic variations that may impact drug metabolism, efficacy, and safety. Pharmacogenomics takes a broader approach by considering the interaction of multiple genes and genetic pathways.

Precision Medicine: a model for health care delivery that relies heavily on data, analytics, and information - at the core of Personalized Medicine - is a key tool in the Personalized/Precision Medicine Toolbox –the study of how genes affect a person’s response to medications.

Value based care arrangements: a form of reimbursement that ties payments for care delivery to the quality of care provided and rewards providers for both efficiency and effectiveness.

Pharmacogenetics or Pharmacogenomics?

While the terms *pharmacogenetics* and *pharmacogenomics* are often used interchangeably, pharmacogenetics generally refers to the effects of a single genetic marker while pharmacogenomics is broader in context, referring to the collective influence of variability across the genome to modulate an individual's drug response profile.

For the purpose of this Executive Summary, we will use the broader context “Pharmacogenomics” or the abbreviation “PGx”.

UNDERSTANDING PRECISION MEDICINE

Precision medicine emphasizes tailoring medical interventions to individual characteristics, including genetic factors. “Pharmacogenomics can play an important role in identifying responders and non-responders to medications, avoiding adverse events, and optimizing drug dose” (FDA, 2023). By integrating PGx results into the standard of care, pharmacies contribute to the broader adoption of precision medicine principles. Through standardized implementation of PGx testing and interpretation, stakeholders can consistently leverage genetic information to optimize treatment decisions. This integration facilitates a more precise, patient-centered approach that aligns with the goals of precision medicine.

Individualized Medication Selection: PGx helps identify genetic variations that can impact how a person metabolizes and responds to medications. By considering a patient's genetic profile, healthcare providers can make more informed decisions about which medications are likely to be most effective and which may pose a higher risk of adverse reactions.

Dosing Optimization: PGx testing can guide the optimization of medication dosages based on genetic factors. Genetic variations may affect drug metabolism enzymes, leading to either rapid or slow metabolism of certain medications. This information enables healthcare providers to adjust dosages to achieve optimal therapeutic outcomes while minimizing the risk of side effects.

Avoidance of Adverse Drug Reactions: Some genetic variations can increase the risk of adverse drug reactions or toxicity to specific medications. PGx testing helps identify patients who may be at higher risk, allowing healthcare providers to choose alternative medications or adjust dosages to mitigate these risks and improve patient safety.

Treatment Response Prediction: PGx can provide insights into how an individual may respond to specific medications based on their genetic profile. This information can assist healthcare providers in selecting the most appropriate treatment options and avoiding unnecessary trial-and-error approaches, leading to more targeted and effective treatment plans.

Avoidance of Ineffective Treatments: Genetic variations may impact the efficacy of certain medications for specific individuals. PGx testing can help identify patients who are less likely to respond to certain drugs, allowing healthcare providers to choose alternative therapies that are more likely to be effective. This avoids wasting time and resources on treatments that may not provide optimal outcomes.

“Pharmacogenomics (PGx) is a field of medicine that studies how genetic variation contributes to different responses to drugs in different patients. The goal of PGx is to use a patient’s genetic information to guide medication therapy to help reduce adverse drug events and optimize drug efficacy (through appropriate drug selection and dosing). To date, there have been many drugs that have been found to have gene-drug interactions. There are currently more than 250 US Food and Drug Administration-approved drugs that include genetic information on their drug label. Of these, current guidelines have clinically actionable recommendations for more than 45 drugs based on drug-gene interactions. Drugs with recommendations cover many therapeutic classes that are commonly prescribed, including analgesics, antidepressants, antipsychotics, and antihypertensives.” (Steinbach, et. al., 2022)

Advancement of Research and Drug Development: PGx data gathered from patients can contribute to research and drug development efforts. By analyzing the genetic profiles and treatment responses of individuals, researchers can uncover new insights into the relationships between genes, medications, and disease outcomes. This knowledge informs the development of new drugs and treatment approaches in the field of precision medicine.

BENEFITS OF PRECISION MEDICINE WITHIN PHARMACY

PGx holds immense potential to be the catalyst for transitioning to value-based care and advancing precision medicine. By implementing pharmacist led PGx solutions into the workflow of the pharmacy with fully integrating PGx results, improvements in patient care may be realized.

Facilitation of Value-Based Care: Value-based care aims to improve patient outcomes while reducing healthcare costs. PGx aligns seamlessly with this objective by enabling targeted therapies, minimizing adverse events, and optimizing medication regimens. By integrating PGx into pharmacy workflow, key stakeholders can ensure that patients receive the right medication at the right dose, enhancing treatment efficacy and cost-effectiveness (Johnson, et. al., 2021). This integration enables the delivery of value-based care by focusing on personalized, evidence-based medicine.

Improved Patient Outcomes: With 79% of patients reporting pharmacists as a reliable source for healthcare information beyond prescriptions (Lagasse, 2022), and 61% of Americans envisioning primary care moving to pharmacies within 5 years (Rebelo, 2022), PGx could reach a larger number of patients if integrated within pharmacy workflows. By integrating PGx into the workflow of the pharmacy, pharmacists can access valuable genetic information at the point of care. This integration empowers pharmacists to optimize drug therapy, minimize adverse drug reactions, enhance treatment effectiveness, and ultimately improve patient outcomes. An informed and engaged patient population leads to a more effective standard of care.

“While there remain barriers to large-scale adoption of precision medicine and genetics testing, the benefits of these technologies – along with VBC models that emphasize prevention and holistic care – are becoming increasingly undeniable. It will only be a matter of time before VBC, precision medicine, and genetics testing will enter the mainstream of healthcare.” (King, 2021)

Enhanced Medication Safety and Cost-Effectiveness: Adverse drug reactions (ADRs) contribute significantly to patient harm and increased healthcare costs. PGx testing provides crucial insights into a patient's genetic predisposition to specific drug reactions, enabling proactive measures to prevent ADRs. By integrating PGx results into the standard of care, pharmacists can identify patients at higher risk of ADRs and adjust medication regimens accordingly, leading to enhanced medication safety. (Cacabelos, Cacabelos & Carril, 2019). Avoiding ineffective medications through PGx-guided therapy selection can contribute to cost savings by reducing trial-and-error prescribing.

Optimization of Medication Selection and Dosing: The integration of PGx into pharmacy workflow enables proactive precise medication selection and dosing based on individual genetic profiles. By incorporating PGx testing as part of routine clinical practice, pharmacists can determine the most effective medications and appropriate dosages for each patient. This optimization reduces the likelihood of suboptimal treatment outcomes, therapeutic failures, and medication-related complications. Ultimately, PGx within the pharmacy workflow leads to improved patient satisfaction, reduced hospitalizations, and better resource utilization. When therapeutic outcomes are not achieved, the results can be both costly and harmful. Estimates of between 25% and 50% of prescribed medications have been shown to miss the mark on a proper therapeutic result (Steinbach, et. al., 2022). This study found the cost to the U.S. to be as much as \$528.4 billion annually in increased medical expense.

VALUE OF STANDARDIZED PHARMACIST LED PGX SOLUTIONS

The value of integrating standardized PGx to the pharmacy workflow, and healthcare as a whole, lies in improved patient outcomes, enhanced medication safety and cost-effectiveness, facilitated clinical decision-making, and advanced research and knowledge. Standardized PGx practices establish a foundation for consistent, evidence-based utilization of genetic information, driving improvements in precision medicine and optimizing medication therapy for better patient care. By harnessing the power of PGx, pharmacists can provide patient-centered care that maximizes treatment effectiveness, safety, and patient satisfaction.

The establishment and adoption of standards creates consistency across the various stakeholders, which is crucial for PGx success. Effective data integration and interoperability of PGx information allows for consistent interpretation of:

- Reporting
- Clinical guidelines
- Education and training
- Regulatory compliance
- Ethical considerations
- Research standards

A CALL TO ACTION

PGx is gaining recognition and acceptance in clinical practice and legislation such as the “Right Drug Dose Now” Act proposed in 2022 (Liebert, Inc. Publishers, 2022). As more stakeholders recognize its potential to improve patient care, standardization becomes crucial to ensure consistent and reliable integration of pharmacogenomic information into routine clinical workflows. With the advancement in technology and the increasing role precision medicine is playing within healthcare, the time is now to get involved and be a part of the precision medicine revolution being driven by advancements in genomic technologies, data analytics, and the unraveling of the complexities involved in the business application of this amazing science.

NCPDP'S INVOLVEMENT

As the healthcare standards and solutions leader for the common good, NCPDP continues to focus on strengthening healthcare delivery through pharmacy. As directed by the NCPDP Board of Trustees and the Strategic Planning Committee (SPC), Precision Medicine is a current initiative for NCPDP with a focus on the utilization of standards and innovative solutions.

Under the Professional Pharmacy Services Work Group (WG), WG10, is the Pharmacogenomics Task Group. This group is active, open for input by all stakeholders regardless of NCPDP membership and will be involved in NCPDP precision medicine activity as progress is achieved and the expertise of that group is needed. Additionally, NCPDP has hosted two webinars focused on both precision medicine and pharmacogenomics. An upcoming webinar will feature panelists from throughout the industry discussing the future of integrating a pharmacist led PGx solution into the pharmacy workflow utilizing NCPDP standards.

NCPDP has an established Precision Medicine Subcommittee with a primary focus on achieving the strategic initiatives of the organization. In March 2023, NCPDP welcomed key influencers within the industry, to participate in a Precision Medicine Stakeholder Action Group (SAG). The goal of this meeting was to understand the challenges and opportunities related to pharmacist participation in Precision Medicine and help determine next steps for NCPDP related to modifying and/or creating standards and guidance. The group concluded that collectively working toward interoperability between providers, standardized solutions are needed to effectively incorporate PGx information into pharmacy information systems and processes, leading to safer and more personalized medication therapy.

There are multiple potential use cases that could be created for the ordering and fulfillment of a pharmacogenomic standardized solution service for all stakeholders. The Precision Medicine SAG was charged with exploring NCPDP standards utilizing industry experience, expertise and evaluating potential gaps and barriers to successful integration and implementation. The applicability of an existing standard may be dependent on the individual precision medicine use case. The adoption of NCPDP standards, along with the creation of applicable new standards, could bring value to the integration and exchange of pharmacogenomic data within the pharmacy workflow.

SAG Takeaways

During the SAG, participants were asked to join groups based on how they felt their organization best aligned. The industry segments included Payer/PBM, Pharmacy, PGx Organizations/Laboratories, and Vendor Solutions/Compendia. Each segment was tasked to collaborate on four questions; highlights from the questions and responses can be found in the table below. A few themes emerged from the discussions: ambiguity or lack of payment model, the need for greater education of all players within PGx, including the patient, a lack of PGx standards for labs and testing, and a lack of interoperability for PGx data, including who should house the data and timely access to it.

	Payer/PBM	Pharmacy	PGx Organizations/ Laboratories	Vendor Solutions/ Compendia
<i>What are the barriers for your segment?</i>	<p>How should reimbursement be handled?</p> <p>Limitations and coverage concerns.</p> <p>What should be covered and what are the costs?</p> <p>Lack of evidence for PGx and PM.</p> <p>How do you build benchmarks on fair reimbursement rates?</p> <p>What is the value of PGx to the payer and patients?</p>	<p>Education of pharmacists.</p> <p>How to get paid for services rendered.</p> <p>What are the liabilities and risks of providing this service?</p> <p>Lack of standardization of data across labs.</p> <p>How/where is the data stored and by whom?</p> <p>How will the data stay current?</p> <p>How is the data made interoperable?</p>	<p>Inconsistency in what is being tested.</p> <p>Inconsistent nomenclature.</p> <p>Developed test vs commercially available testing.</p> <p>State/regulatory policies and/or standards in how genetic information should be protected, shared and used.</p> <p>How to make the data interoperable.</p> <p>What happens when patients move health plans, providers?</p> <p>Labs cannot offer interpretations, need 3rd party.</p>	<p>Changes in knowledge or guidelines.</p> <p>How is the data made interoperable?</p> <p>Where is the data housed?</p> <p>How to get real-time updates.</p> <p>PGx data should be linked to a drug via compendia, similar to linking drug interactions.</p> <p>FDA ambiguity and enforcement.</p>

	Payer/PBM	Pharmacy	PGx Organizations/ Laboratories	Vendor Solutions/ Compendia
<i>What solutions may be available?</i>	<p>Value based contract to get everyone on board – prescriber, lab, pharmacist, payer.</p> <p>Pre-test confirmation/prior authorization before administering the test.</p> <p>Standards can provide a way to track & communicate data.</p> <p>Stratify the population to understand the greatest benefits to PGx.</p> <p>Payer focused pilot for industry collaboration (possibility to be funded by NCPDP Foundation)?</p>	<p>Data interoperability through use of NCPDP standards.</p> <p>Education - identification of education needed.</p> <p>Relevant research – opportunity for NCPDP Foundation-funded pilot(s).</p> <p>Consistent process between all parties supported by NCPDP standards.</p> <p>EDvocating to legislators – ensure the pharmacy/pharmacist has a right to play in PM, PGx.</p>	<p>Affordability and accessibility for the patient.</p> <p>Uniform consensus on tests.</p>	<p>Support the standard through:</p> <ol style="list-style-type: none"> 1. Interpretation of the data 2. Education 3. How to identify the patient/drug 4. Expand interoperability <p>Continue to expand, support & implement standards into workflow that is seamless to pharmacist & provider.</p> <p>Put together a strong educational plan – how standards can support.</p> <p>Use embedded transaction processing to make determinations for decision support.</p>

	Payer/PBM	Pharmacy	PGx Organizations/ Laboratories	Vendor Solutions/ Compendia
How can your segment support PGx?	<p>Confirm action has been taken.</p> <p>Identify the ways to communicate information.</p> <p>Improve clinical policy.</p> <p>Multiple payors come together to leverage adoption.</p> <p>Capturing and making PGx data available to their providers.</p>	<p>Move toward appointment-based encounters, clinical consultations and PGx.</p> <p>Education/professional development of the pharmacist.</p> <p>Advocating to legislators for PGx advancement and pharmacist participation in PGx.</p> <p>Incorporating PGx results into the pharmacy workflow. Increased pharmacist PGx credentialing.</p> <p>Enhanced PGx services through specialty pharmacy or limited distribution networks.</p>	<p>Baseline standard test between labs.</p> <p>Uniform consensus on tests.</p> <p>Have a PGx specialist at each clinic location.</p>	<p>Support HL7/FHIR.</p> <p>Standards for pharmacy vs medical.</p> <p>PMS/Switch to look for ways to make PGx data flow seamlessly.</p> <p>Use existing NCPDP standards to make PGx information interoperable.</p>

What Can Be Done Now Within NCPDP?

- Explore existing NCPDP standards including:
 - Telecom - Developed to provide a standard format for the electronic submission of third party drug claims and other transactions between pharmacy providers, insurance carriers, third-party administrators and other responsible parties.
 - Could be utilized to determine messages for payers
 - SCRIPT - Developed for transmitting prescription information electronically between prescribers, pharmacies, payers, and other entities.
 - Could be utilized to message back to the pharmacy within the SCRIPT Implementation Reporting (SIR) TG
 - RxChange – as a part of SCRIPT, the RxChange message is used to request a change to a prescription
 - Could be utilized to determine messages to help facilitate results
 - Electronic Prior Authorization (ePA) – as a part of SCRIPT, the process that is used to request coverage of a specific medication for a specific patient.
 - Could be utilized for data fields
 - Real-Time Prescription Benefit (RTPB) – Delivers patient-specific benefit and cost information.
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- Utilize NCPDP’s membership base of subject matter experts such as:
 - Work Group 2 | Product Identification
 - Product Review and Billing Unit Exception Task Group
- Continued collaborate with the other industry associations and stakeholders

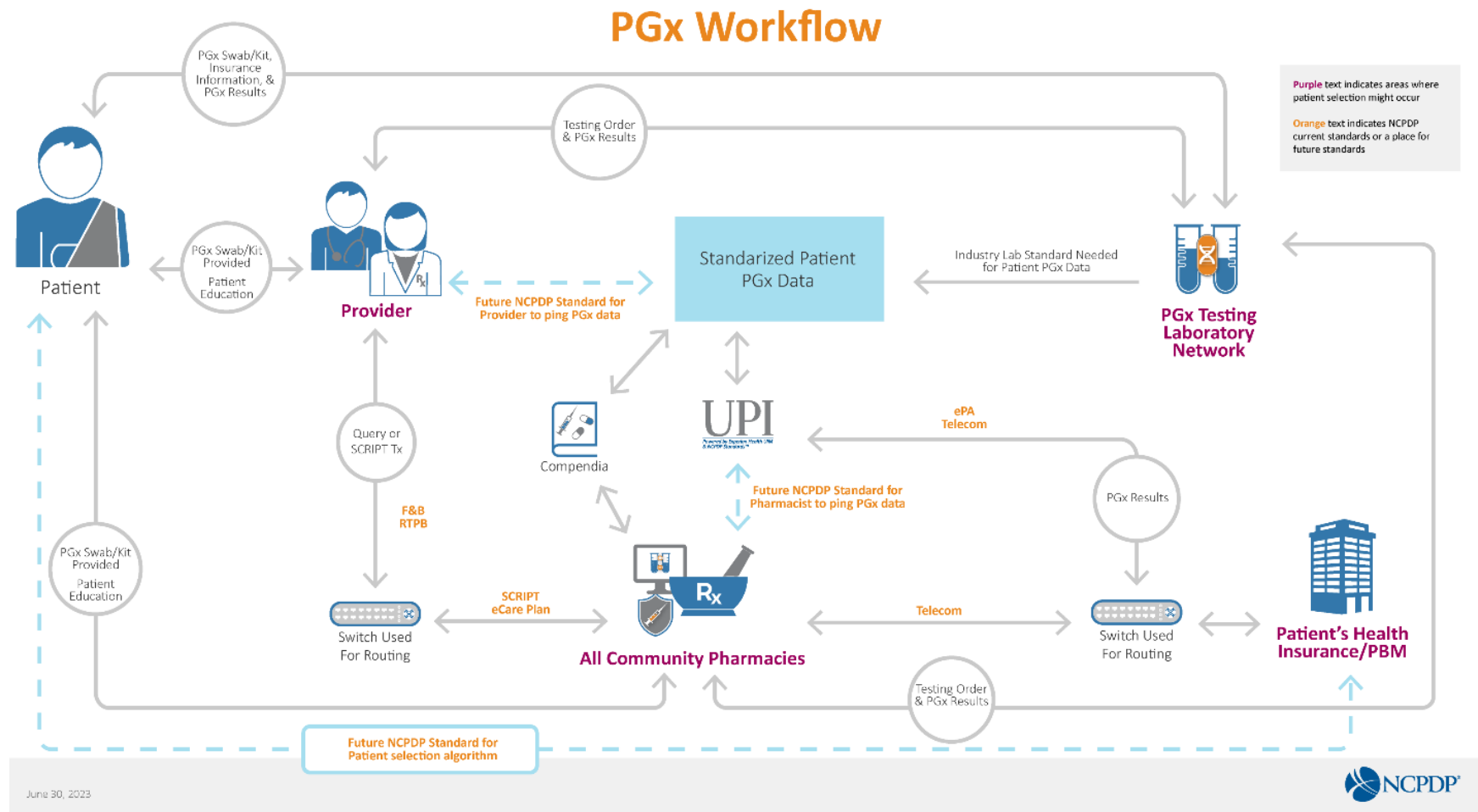
What Are Future Considerations?

This is a list of questions and/or areas to explore generated at the end of the NCPDP SAG by all industry stakeholders. While the answers are unclear at this time, this list provides direction for future research by NCPDP in collaboration with the industry.

- Where does the data live?
 - How is that data made available to other stakeholders?
- Pilot through the standards of SCRIPT, Telecom, ePA, & RTPB to see what is possible.
- Education throughout the healthcare arena
- Insights from research/pilots funded through the NCPDP Foundation
- Determine minimum data requirements/elements
- Collaboration with other Standards Development Organizations and government entities

PGx in Pharmacy Workflow

This NCPDP diagram showcases the possibilities of a pharmacist led PGx solution with the goal of bringing value by providing clarity, promoting collaboration, and highlighting the potential opportunities for stakeholder involvement. It facilitates discussion, understanding, implementation, and adoption of an innovative approach to personalized medication management, highlighting where NCPDP standards can be utilized, modified or created.



MOVING FORWARD

NCPDP continues to realize the value in, as well as the need for, the pharmacy industry to come together to address the opportunities surrounding PGx. By leveraging our industry expertise and knowledge gained from the SAG, NCPDP and key stakeholders can continue to work together to effectively communicate the importance and benefits of standardizing PGx in the pharmacist led workflow.

Areas for future exploration include a deep dive into NCPDP standards with the Pharmacogenomics TG and generation of a guidance document for the utilization of existing standards within the pharmacist led workflow. NCPDP may explore the benefits of creating a white paper, possibly in collaboration with industry stakeholder(s), as this is key to the success of standardized solutions for PGx.

The NCPDP Foundation is a 501(c)3 organization which provides grants for research that focus on advancing the use of standards-based information technology for better healthcare. Through the NCPDP Foundation, there is an opportunity for grant funding to research the use of NCPDP standards within Precision Medicine and, specifically, PGx. NCPDP Foundation grant research may also be able to provide further data on the benefits of pharmacist led PGx solutions.

COLLABORATION SUMMARY

Authors

Kristol Chism, R.Ph. | Director of Industry Relations | Optum Insight

Kristol brings a pharmacist's perspective to the Precision Medicine subcommittee and has contributed significantly to the advancement of this initiative within NCPDP. She is a leader within NCPDP due to her commitments including Precision Medicine subcommittee lead, co-lead of several task groups, Work Group 20 Lead, and Emerging Professional Fellow. Additionally, Kristol was the winner of the Rising Star Award in 2023.

Whitney Ellington | Senior Manager, Member & Product Marketing | NCPDP

With a background in maternal, fetal, and neonatal medicine, Whitney brings a medical perspective to the Precision Medicine subcommittee. She has several leadership roles within NCPDP including Precision Medicine subcommittee, Emerging Professionals, and oversight of NCPDP graphics and member communications. Whitney is currently working on her master's in public health and is a member of the Women in Healthcare, Phoenix Chapter.

Kelee Petzelt | Consultant, REMS Use Case Coordinator | Point of Care Partners

One of the leading experts in pharmacogenomics, Kelee was central to the creation of this document and the movement of pharmacogenomics within healthcare. Kelee has leadership roles within NCPDP including Precision Medicine subcommittee co-lead and Emerging Professionals event planning task group. She is highly involved as a guest speaker at industry events focused on pharmacogenomics. Kelee has contributed years of knowledge and resources to help move the Precision Medicine and pharmacogenomics initiative forward within NCPDP.

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RESOURCES

NCPDP Resources

Collaborative Workspace (access to join Task Groups (TG) and review meeting notes):

<https://dms.ncdp.org/>

Webinars can be accessed at: <https://www.ncdp.org/Webinars.aspx>

Membership Information: <https://www.ncdp.org/Membership.aspx>

Strategic Initiatives: <https://ncdp.org/Strategic-Initiatives.aspx>

Standards: <https://standards.ncdp.org/Access-to-Standards.aspx>

NCPDP Foundation: <http://ncdpfoundation.org/home.aspx>

PGx Information & Guidelines

Association for Molecular Pathology: eurekaalert.org/

Dutch Pharmacogenomics Working Group: [/pharmacogenomics-1/pharmacogenomics](http://pharmacogenomics-1/pharmacogenomics)

Canadian Pharmacogenomic Network for Medication Safety: cpnds.ubc.ca

European Pharmacogenomics Implementation Consortium: eu-pic.net/

CDC Public Health Genomics: cdc.gov/genomics/gtesting/index.htm

Food and Medication Administration: fda.gov/medications/science-and-research-medications/table-pharmacogenomic-biomarkers-medication-labeling

Clinical Pharmacogenetics Implementation Consortium: cpicpgx.org/guidelines

French Network of Pharmacogenetics:

sciencedirect.com/science/article/abs/pii/S0040595717300069?via%3Dihub

REFERENCES

- Cacabelos, Ramon, Cacabelos, Natalia & Carril, Juan. (April 2024). *The role of pharmacogenomics in adverse drug reactions*. National Library of Medicine; National Center for Biotechnology Information. Retrieved July 14, 2023 from: <https://doi.org/10.1080/17512433.2019.1597706>
- FDA. (February 10, 2023). Table of Pharmacogenomic Biomarkers in Drug Labeling. U.S. Food & Drug Administration. Retrieved July 19, 2023 from: <https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling>
- Johnson, Kevin, et. al. (January 2021). *Precision Medicine, AI, and the Future of Personalized Health Care*. National Library of Medicine; National Center for Biotechnology Information. Retrieved on July 14, 2023 from: <https://doi.org/10.1111%2Fcts.12884>
- King, Ron. (November 23, 2021). *How Precision Medicine and Genetic Testing Will Drive Value-based Care*. Managed Healthcare Executive. Retrieved July 14, 2023 from: <https://www.managedhealthcareexecutive.com/view/how-precision-medicine-and-genetic-testing-will-drive-value-based-care>
- Lagasse, Jeff. (January 18, 2022). *People placing more trust in pharmacists for care management: Patients had a high level of trust in pharmacists to complete most activities, including prescribing medications and providing counseling*. Healthcare Finance. Retrieved July 13, 2023 from: <https://www.healthcarefinancenews.com/news/people-placing-more-trust-pharmacists-care-management#:~:text=Patient%20respondents%20had%20a%20high,44%25>
- Rebelo, Andre. (December 7, 2022). *US survey signals big shifts in primary care to pharmacy and clinic settings as consumers seek lower medication and healthcare costs*. Wolters Kluwer. News and Press Releases. Retrieved July 13, 2023 from: <https://www.wolterskluwer.com/en/news/us-survey-signals-big-shifts-in-primary-care-to-pharmacy-and-clinic-settings>
- Steinback, Musetta, et. al. (April 2022). *Analysis of a panel-based pharmacogenomics testing program among members of a commercial and Medicare client of a pharmacy benefits manager*. Journal of Managed Care + Specialty Pharmacy (Volume 28; Issue 4). Retrieved July 14, 2023 from: <https://doi.org/10.18553/jmcp.2022.28.4.485>