IMPLEMENTATION OF CLINICAL PHARMACOGENOMICS ACROSS A MULTI-STATE HEALTH SYSTEM

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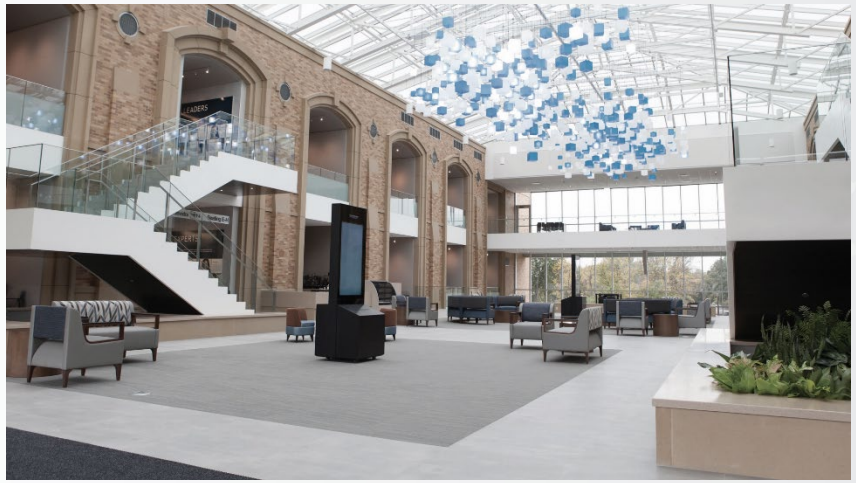
Clinical Pharmacogenomics Pharmacist and Clinical PGx PGY2 Residency Program Director, Sanford Health

SANFORD imagenetics®

OBJECTIVE

Describe methods used to implement pharmacogenomics into a large rural healthcare system.



Sanford Health

Sanford Health is one of the largest rural health systems in the United States and is dedicated to:

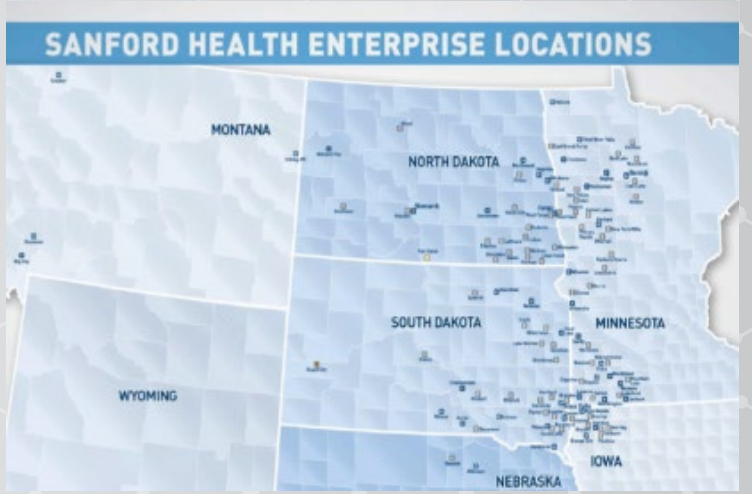
- integrated delivery of health care
- genomic medicine
- senior care and services
- global clinics
- research
- affordable insurance

SANFORD HEALTH

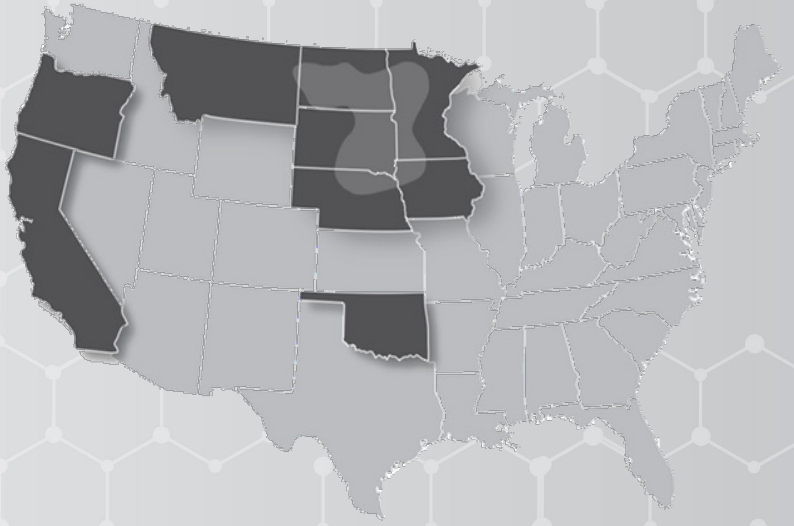
Sanford Health

Predominantly the upper Midwest

- Spans across 9 states



Geographical footprint of over 250,000 square miles

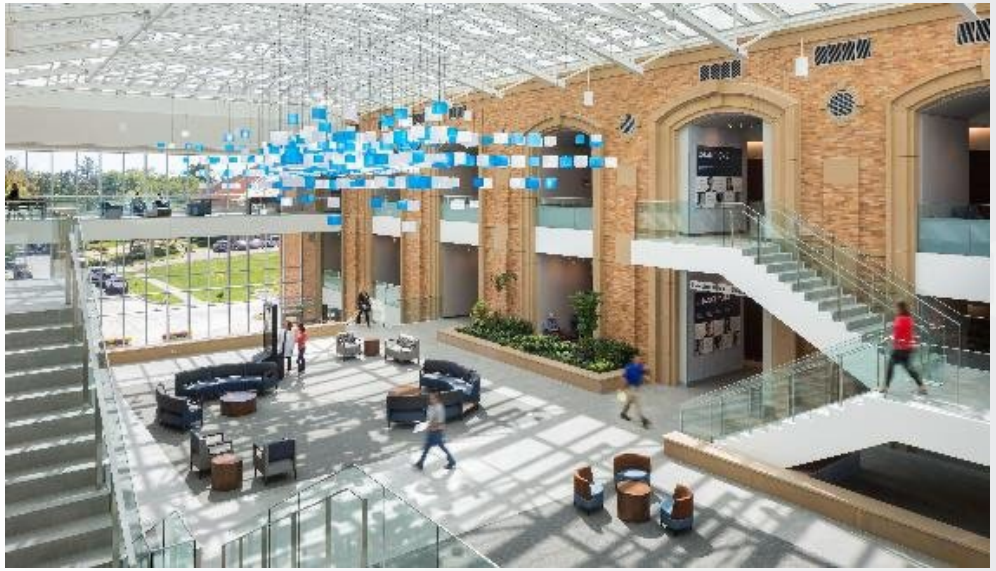


- >2 million patients
- 44 medical centers and 482 clinics
- >48,000 employees and 1,350 physicians

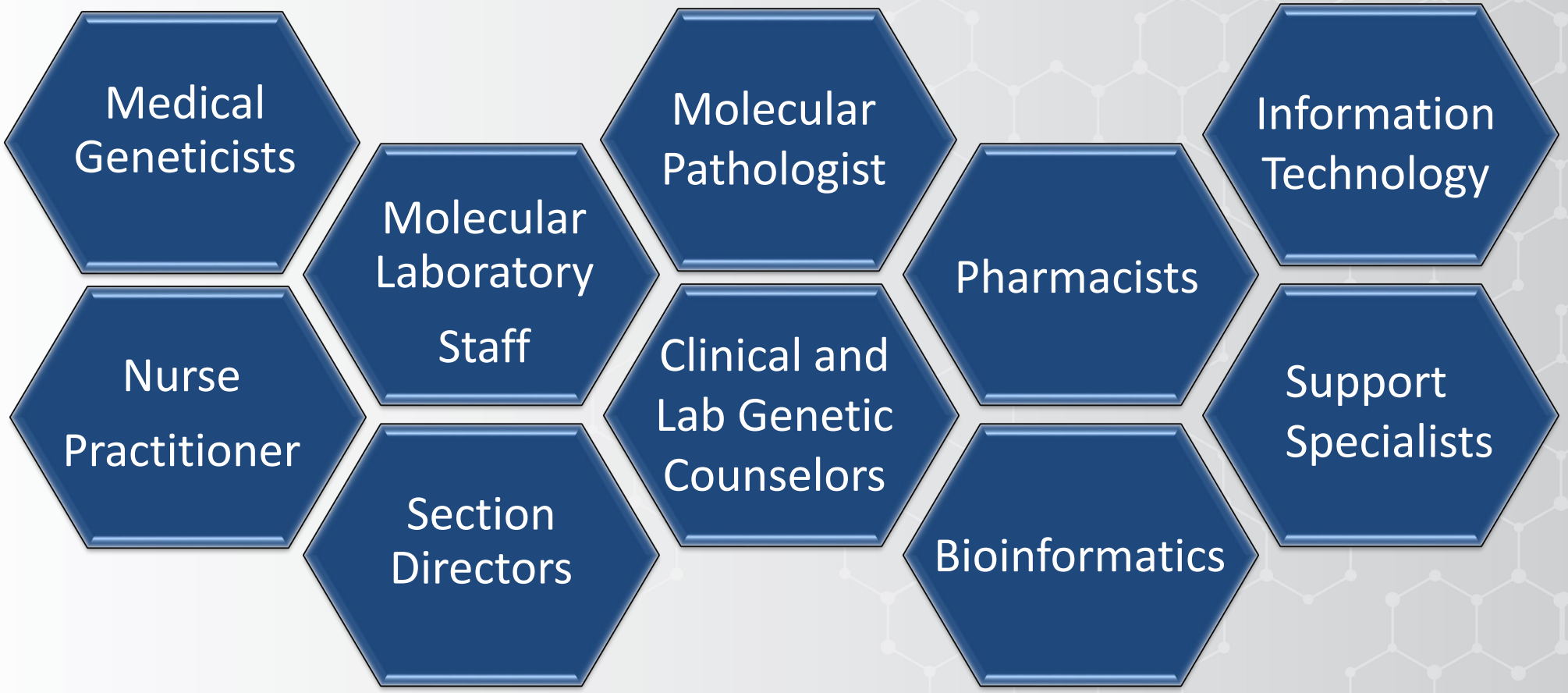
History of Imagenetics

Established in 2014 after a $125 million gift from philanthropist Denny Sanford

Internal Medicine and Genetics = Imagenetics



Multi-disciplinary Team



PGX PHARMACIST TIMELINE

- 2014
  - Natasha Petry is still employed by Internal Medicine department– starts working with Dr. Russ Wilke
- 2017/2018
  - **April Schultz** hired as manager (later promoted to Director of Operations and PGx services) – 1.0 FTE
  - **Jordan Baye** hired as 0.5 FTE South Dakota State University Faculty and 0.5 FTE Imagenetics
  - **Natasha Petry** hired as 0.5 FTE North Dakota State University Faculty and 0.5 FTE Imagenetics
- 2019
  - **Amanda Massmann** and **Joel Van Heukelom** hired each at 1.0 FTE (Amanda later promoted to clinical lead and Joel to supervisor)
- 2020
  - **Kristen Jacobsen** hired as Clinical PGx pharmacist (1.0 FTE)

Pillars of Sanford Imagenetics

Clinical Care

PGx Initiatives

Single Gene Testing

- *CYP2C19* – cath lab

PGx Panel Initiatives

- Psychiatry
  - Sanford Employee Health Plan
- Transplant
- Veterans
- Medicare Align

Population Screening

- Sanford Chip
  - Specific requirements
  - PGx panel
  - Medically Actionable Predisposition

In House Medical Genetics Lab

CAP Accredited

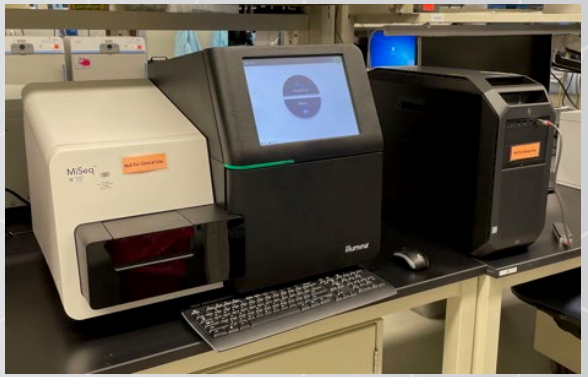
Digital Droplet PCR (ddPCR) for *CYP2D6* copy number assessment

Ease of ordering PGx testing

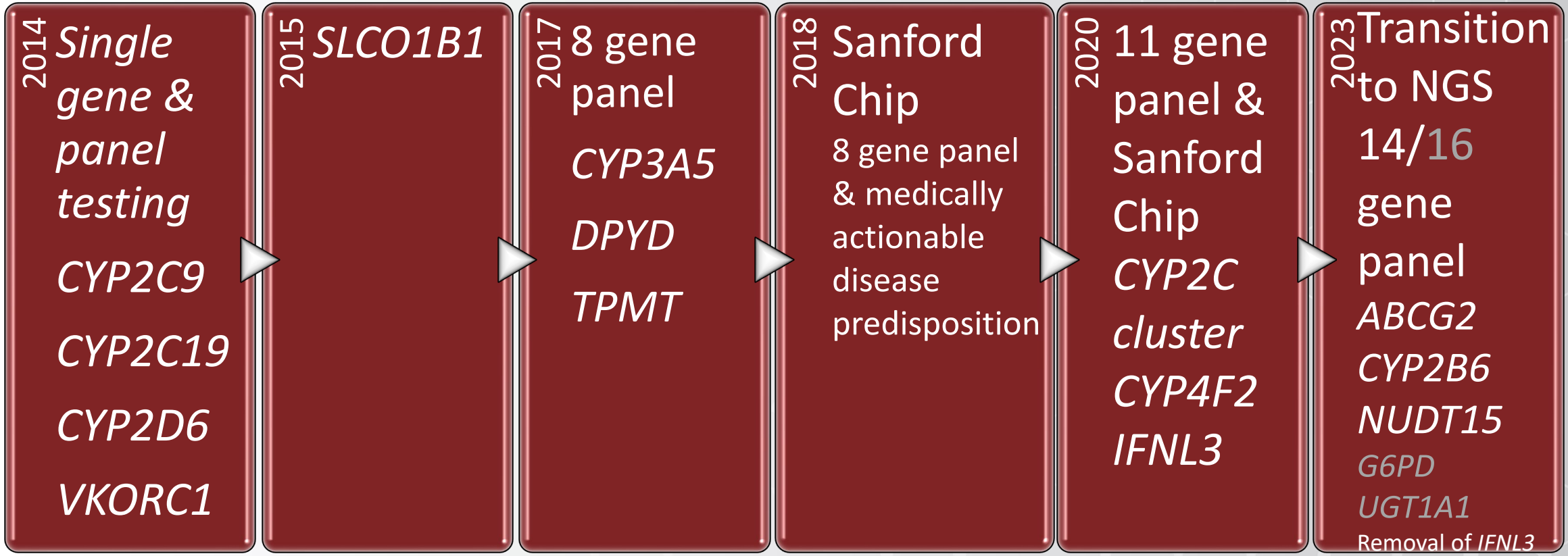
Translating Research to Clinical Screening and Diagnostics

Expanding Diagnostic Testing Capabilities

Support research activities in a CLIA/ CAP environment



Evolution of PGx testing



Patient name: 3_2, Rows
DOB: 04/01/1990

SANFORD Laboratories

MRN:	Row3_2	Test Name:	COMPREHENSIVE PHARMACOGENETICS PANEL
Sex:	female	Ordering Provider:	Shubhi
Specimen ID:	Row3_2	Date Collected:	11/01/2023
Specimen Type:	blood	Date Resulted:	11/21/2023

Patients should not stop their medication(s) or make any changes to their medication(s) without consulting with their provider first.

DRUG-GENE ASSOCIATION

MEDICATION CATEGORY	BASED ON PHARMACOGENETICS STANDARD DOSING PER YOUR PROVIDER	BASED ON PHARMACOGENETICS PROVIDER MAY DISCUSS ALTERNATIVES
Anti-infective	Abacavir (Ziagen) Atazanavir (Reyataz) Efavirenz (Sustiva; Atripla) Voriconazole (Vfend)	Dapsone (Aczone) Nitrofurantoin (Macrobid; Macrodantin) Primaquine (Primaquine) Tafenoquine (Arakoda; Krintafel)
Anticoagulant	Warfarin (Coumadin; Jantoven)	
Antiplatelet		Clopidogrel (Plavix)
Cholesterol		Atorvastatin (Lipitor) Fluvastatin (Lescol XL) Lovastatin (Mevacor) Pitavastatin (Livalo) Pravastatin (Pravachol) Rosuvastatin (Crestor) Simvastatin (Zocor)
Gastrointestinal	Metoclopramide (Reglan) Ondansetron (Zofran)	Dexlansoprazole (Dexilant) Lansoprazole (Prevacid) Omeprazole (Prilosec) Pantoprazole (Protonix)

Patient name: 3_2, Rows
DOB: 04/01/1990

SANFORD Laboratories

PHARMACOGENETIC RESULTS

GENE	RESULTS	PHENOTYPE
CYP2B6	*1/*22	Rapid Metabolizer
CYP2C19	*1/*9	Likely Intermediate Metabolizer
CYP2C9	*1/*8 Activity Score: 1.5	Intermediate Metabolizer
CYP2D6	*10/*10 Activity Score: 0.5	Intermediate Metabolizer
CYP3A5	*1/*1	Normal Metabolizer
G6PD	B/Canton	Decreased or Normal Function
*HLA-B *57:01 screen*	See Comment	Unknown Phenotype
NUDT15	*3/*6	Poor Metabolizer
SLCO1B1	*1/*5	Decreased Function
TPMT	*1/*3A	Intermediate Metabolizer
UGT1A1	See Comment	Unknown Phenotype

GENE	VARIANTS	ZYGOSITY	PHENOTYPE
ABCG2 (NM_004827.3)	c.421C>A (p.Q141K)	Homozygous	Poor Function
CYP2C cluster (NC_000010.10)	No Variants Detected	Homozygous	Low Sensitivity
CYP4F2 (NC_000019.9)	No Variants Detected	Homozygous	Normal Function
DPYD (NM_000110.4)	No Variants Detected Activity Score: 2	Homozygous	Normal Metabolizer
VKORC1 (NM_024006.5)	No Variants Detected	Homozygous	Low Warfarin Sensitivity

Electronically signed by: Massmann, Amanda Date signed: 11/21/2023
Medical Laboratory Director: Rachel Starks, MD, PhD CLIA number: 43D0658889
Sanford Medical Genetics Laboratory 1321 W 22nd Street, Sioux Falls, SD, 57105 (605) 312-GENE (4363) Page: 3

Patient name: 3_2, Rows
DOB: 04/01/1990

SANFORD Laboratories

Regions excluded due to inadequate sequencing coverage rs2395029

The panel includes the following targets:

ABCG2
rs2231142 G>T

CYP2B6
rs34223104 T>C
rs3745274 G>T
rs28399499 T>C
rs3211371 C>T

CYP2C Cluster
rs12777823 G>A

CYP2C19
rs4244285 G>A
rs4986893 G>A
rs28399504 A>G
rs12248560 C>T
rs56337013 C>T
rs72552267 G>A
rs72558186 T>A
rs41291556 T>C
rs17884712 G>A
rs6413438 C>T
rs12769205 A>G
rs375781227 G>A
rs118203759 C>G
rs118203757 G>A
rs140278421 G>C
rs192154563 C>T

CYP2C9
rs1799853 C>T
rs1057910 A>C
rs28371686 C>G
rs9332131 AA>A
rs7900194 G>A
rs28371685 C>T
rs9332239 C>T
rs72558187 T>C
rs72558190 C>A
rs56165452 T>C
rs72558192 A>G

CYP2D6
rs1135840 G>C
rs72549346 CAC>CACAC
rs72549347 G>A
rs59421388 C>T
rs28371725 C>T
rs79292917 C>T
rs5030867 T>G
rs16947 A>G
rs5030656 CTTCT>CT
rs72549352 G(7)>G(8)
rs35742686 T>-
rs3892097 C>T
rs5030865 C>T, A
rs5030655 A>-
rs61736512 C>T
rs1135822 A>T
rs28371706 G>A, T
rs774671100 A>AA
rs5030862 C>T
rs1065852 G>A

CYP3A5
rs41303343 A>AA
rs10264272 C>T
rs776746 C>T

CYP4F2
rs2108622 C>T

DPYD
rs1801268 C>A
rs67376798 T>A
rs3918290 C>T
rs72549303 CG>G
rs55886062 A>C
rs56038477 C>T
rs78060119 C>A
rs75017182 G>C
rs1801266 G>A
rs115232898 T>C
rs72549309 ATGA[2]>ATGA

G6PD
rs72554664 C>T
rs72554665 C>G,A
rs5030869 C>T
rs76723693 A>G
rs137852330 G>A
rs5030868 G>A
rs267606836 G>A
rs1050829 T>C
rs267606835 G>C
rs1050828 C>T

HLA-B*57-01
rs2395029 T>G

NUDT15
rs746071566 GAGTCG(3)>GAGTCG(2),GAGTCG(4)
rs116855232 C>T
rs147390019 G>A
rs186364861 G>A
rs766023281 G>C
[GRCh37/hg19] chr13:48611985 A>G

SLCO1B1
rs2306283 A>G
rs11045819 C>A
rs4149056 T>C

TPMT
rs1142345 T>C,G
rs1800584 C>T
rs74423290 G>C
rs9333570 C>T
rs1800460 C>T
rs72552738 C>T
rs1800462 C>G
rs267607275 A>G
rs9333569 T>C

UGT1A1
rs3064744 TA(7)>TA(6),TA(8),TA(9)
rs4148323 G>A
rs35350960 C>A

VKORC1
rs9923231 C>T

Electronically signed by: Massmann, Amanda Date signed: 11/21/2023
Medical Laboratory Director: Rachel Starks, MD, PhD CLIA number: 43D0658889
Sanford Medical Genetics Laboratory 1321 W 22nd Street, Sioux Falls, SD, 57105 (605) 312-GENE (4363) Page: 4

PGx Clinical Service

PGx Clinic (pre and post visits)

Clinical Decision Support

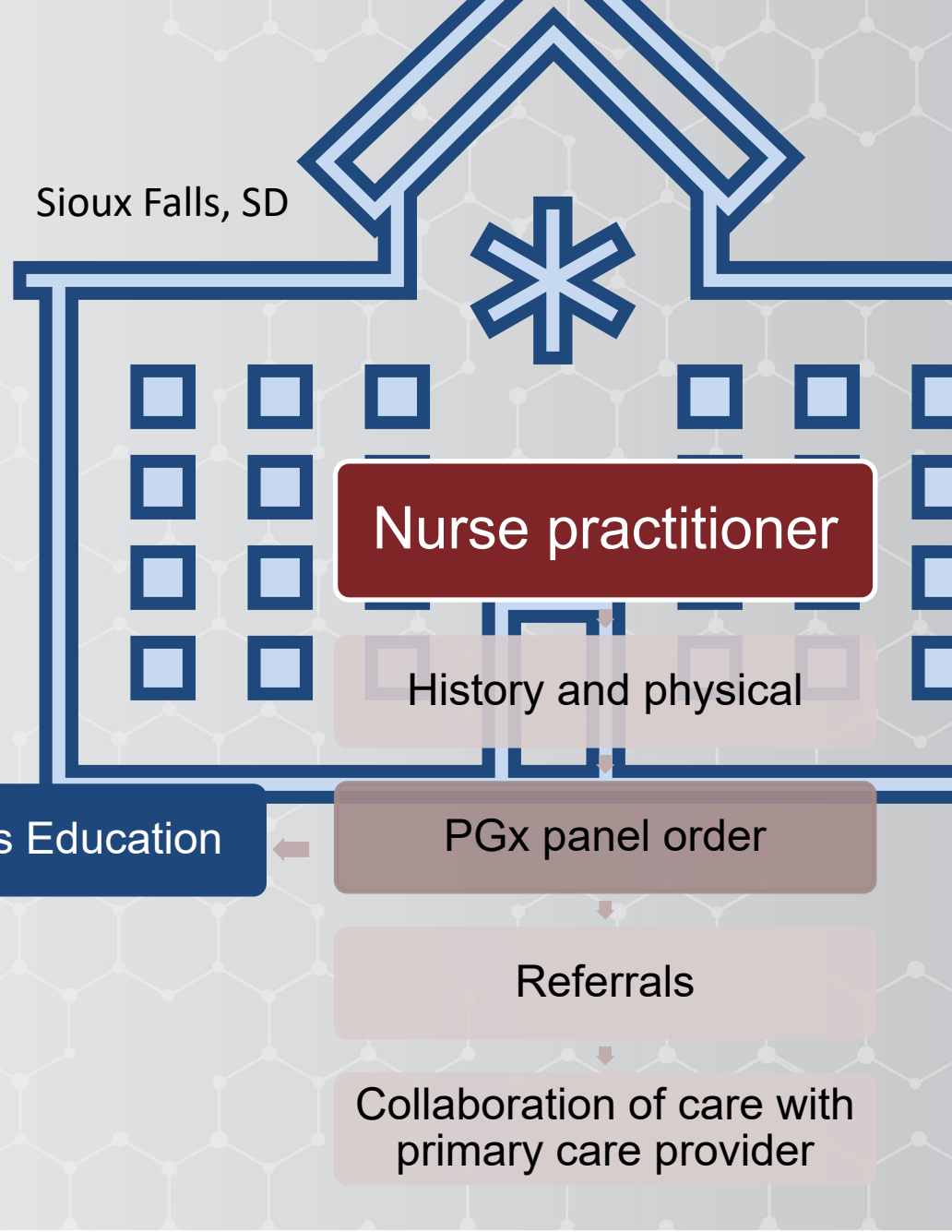
Patient Portal Result Messages

Clinical Note within EMR

Actionable Notes Routed to Providers

All PGx Results Reviewed

PGx Clinic **Model**



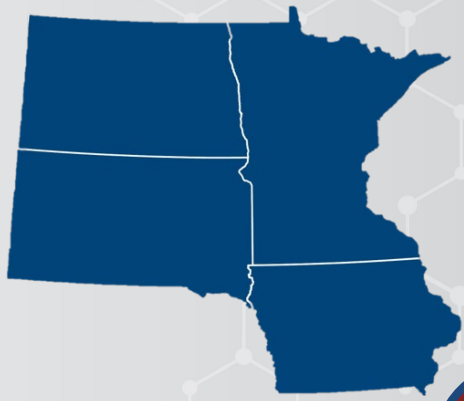
Nurse

- Review of medication list
- "Basics of PGx" video

Pharmacist

- Research consent
- Comprehensive medication reconciliation and history
- PGx overview

PGx Virtual Clinic **Model**



Pharmacist

Comprehensive medication reconciliation and history

PGx overview

PGx Results Education

Research consent

Nurse practitioner

History and Review of Systems

PGx panel order

Referrals

Collaboration of care with primary care provider

Discrete Data

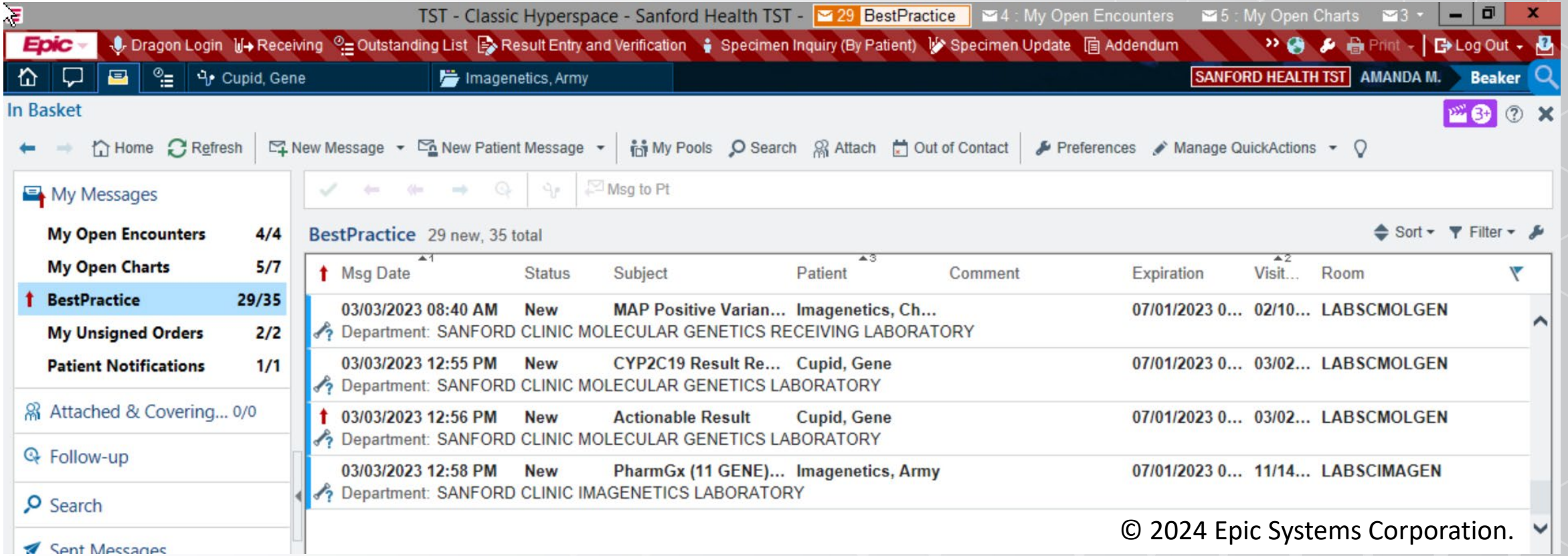
- Data is stored in a particular manner that can be easily retrieved and turned into relevant information

- Laboratory components may include:
  - Genotype/diplotype
  - Phenotype
  - Activity score

Screenshot before transition to updated panel

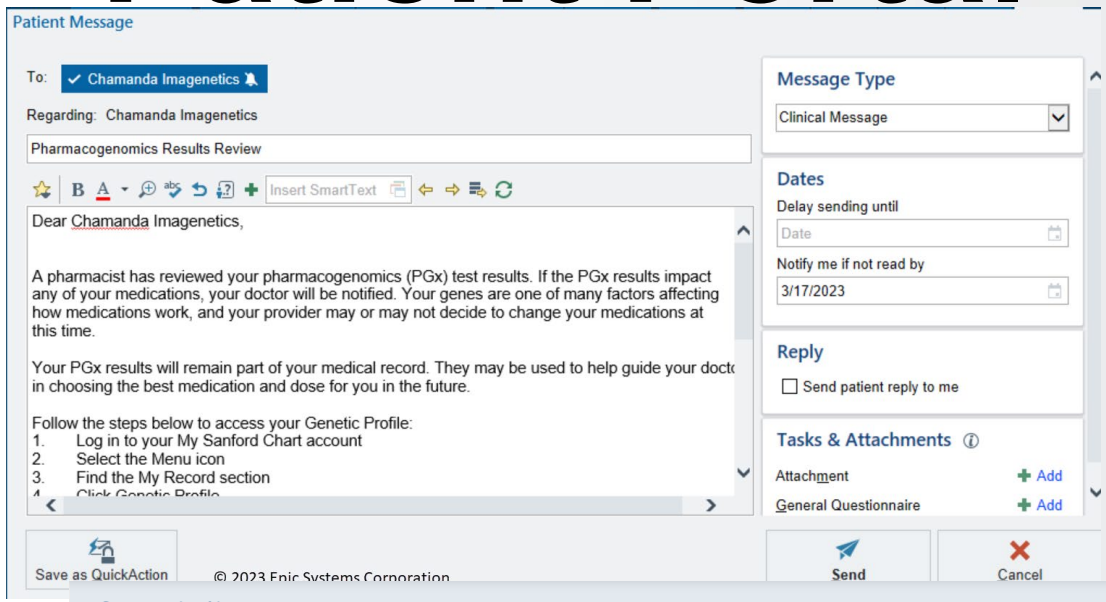
GENETICS	
MISCELLANEOUS GENETIC ...	
PHARMGX PANEL (11 GENE)	
CYP2C Cluster Phenotype	High Sensit...
CYP2C Cluster Genotype	g.96405502...
CYP2C19 Phenotype	Rapid Meta...
CYP2C19 Genotype	*1/*17
CYP2D6 Phenotype	Intermediat...
CYP2D6 Genotype	*2/*3
CYP2D6 Activity Score	Activity Sco...
CYP2C9 Phenotype	Normal Met...
CYP2C9 Genotype	*1/*1
CYP2C9 Activity Score	Activity Sco...
VKORC1 Phenotype	High Warfa...
VKORC1 Genotype	-1639G>A ...
CYP3A5 Phenotype	Poor Metab...
CYP3A5 Genotype	*3/*3
CYP4F2 Phenotype	Normal Acti...
CYP4F2 Genotype	c.1297G>A ...
DPYD Phenotype	Normal Met...
DPYD Activity Score	Activity Sco...
IFNL3 Phenotype	Favorable ...
IFNL3 Genotype	rs12979860...
SLCO1B1 Phenotype	Normal Fun...
SLCO1B1 Genotype	*1/*1
TPMT Phenotype	Normal Met...
TPMT Genotype	*1/*1

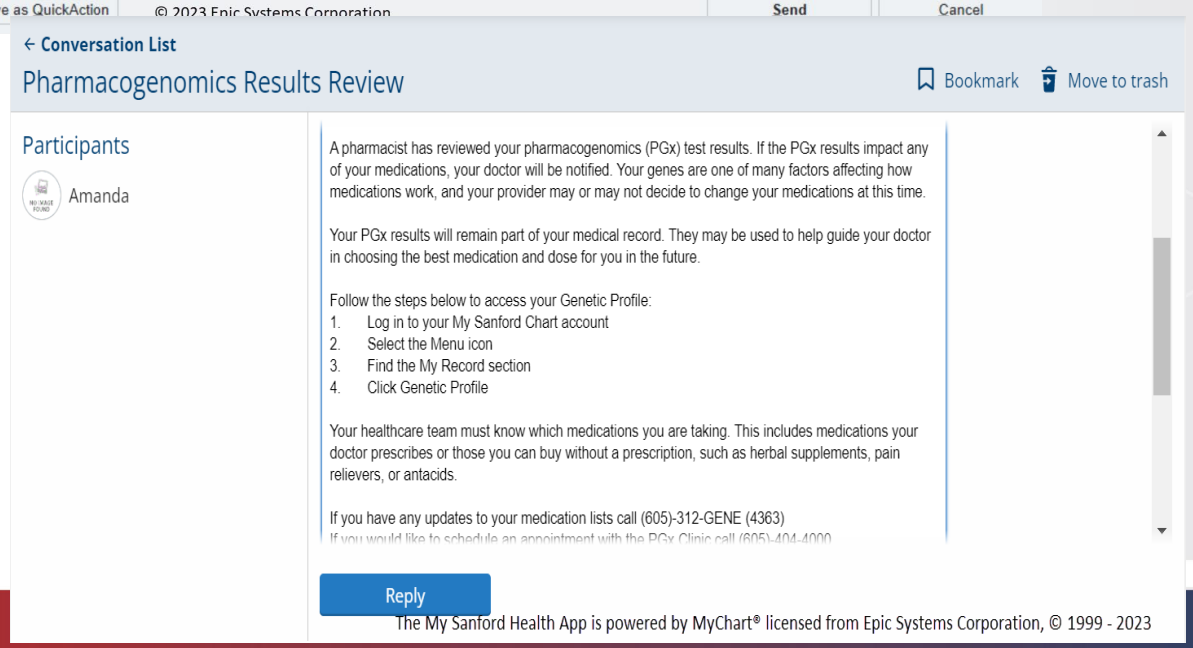
PGx Result Notification

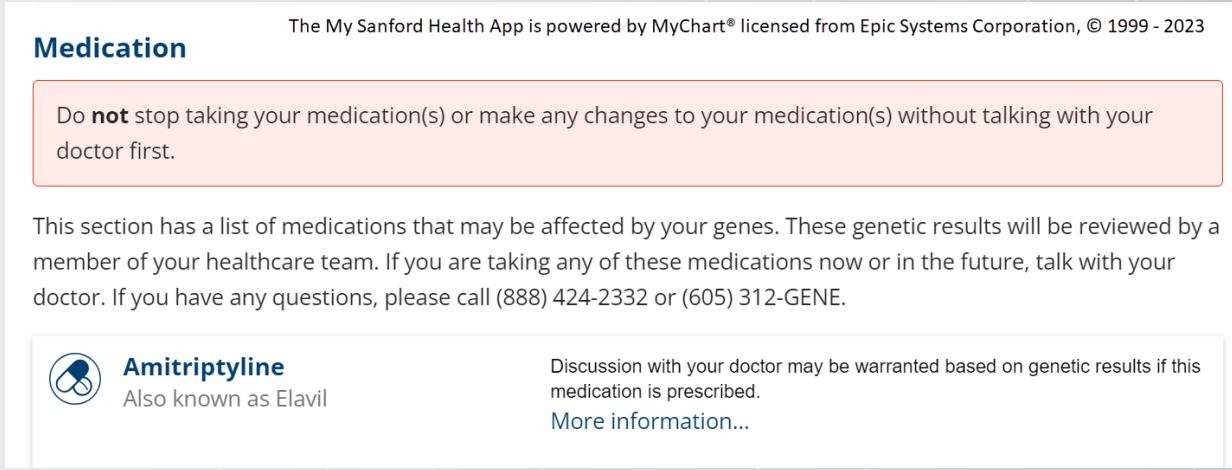


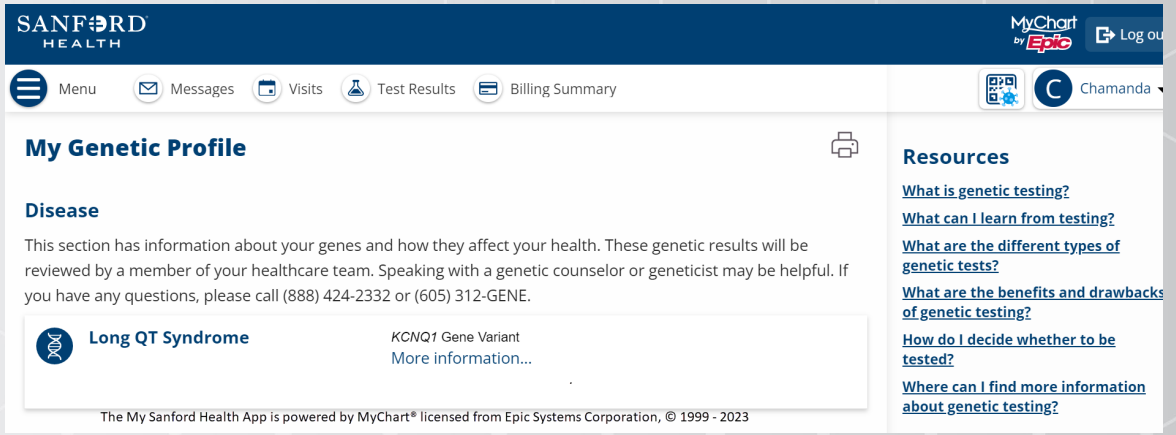
Genomic Indicators

Patient Portal

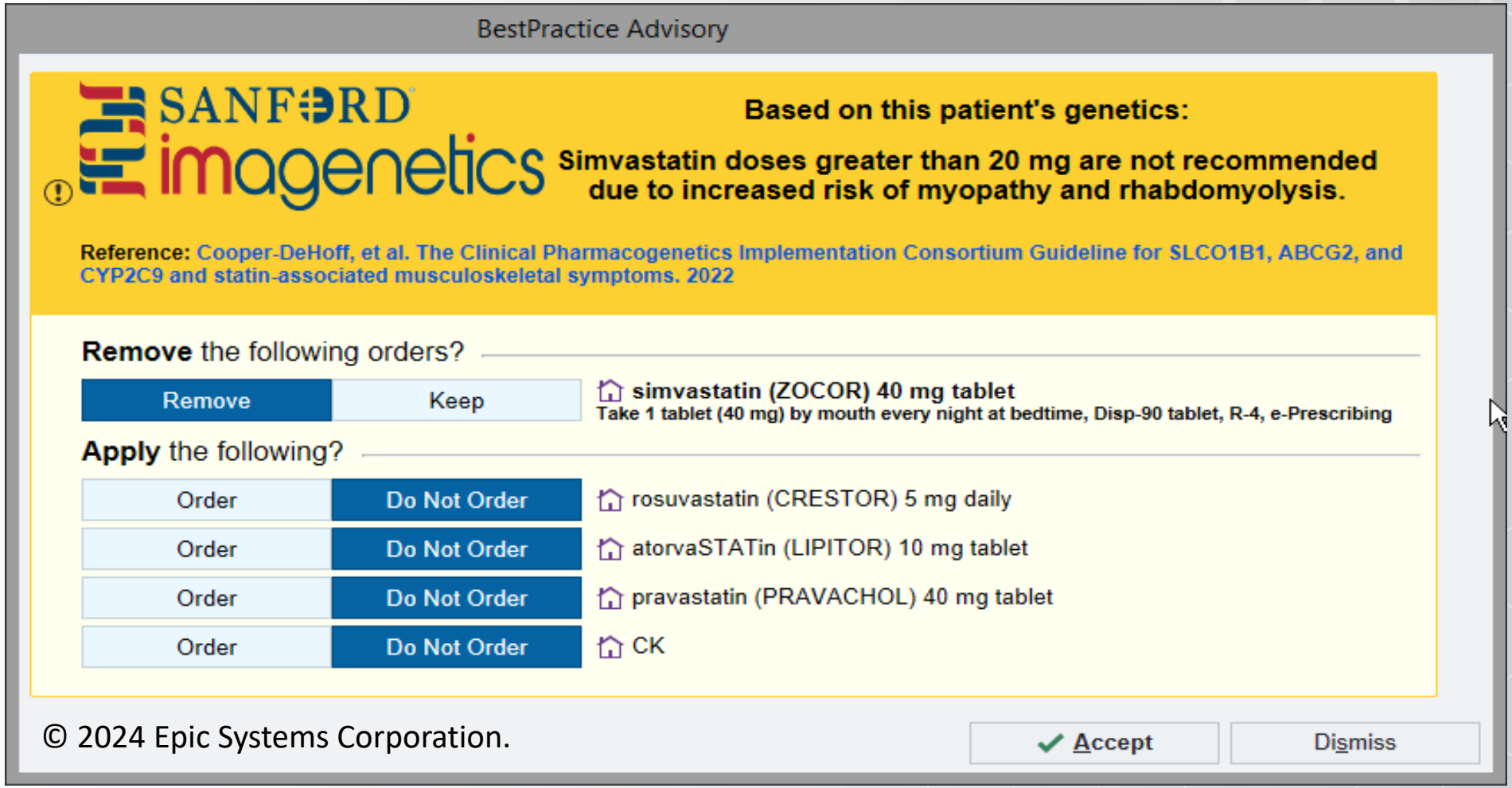




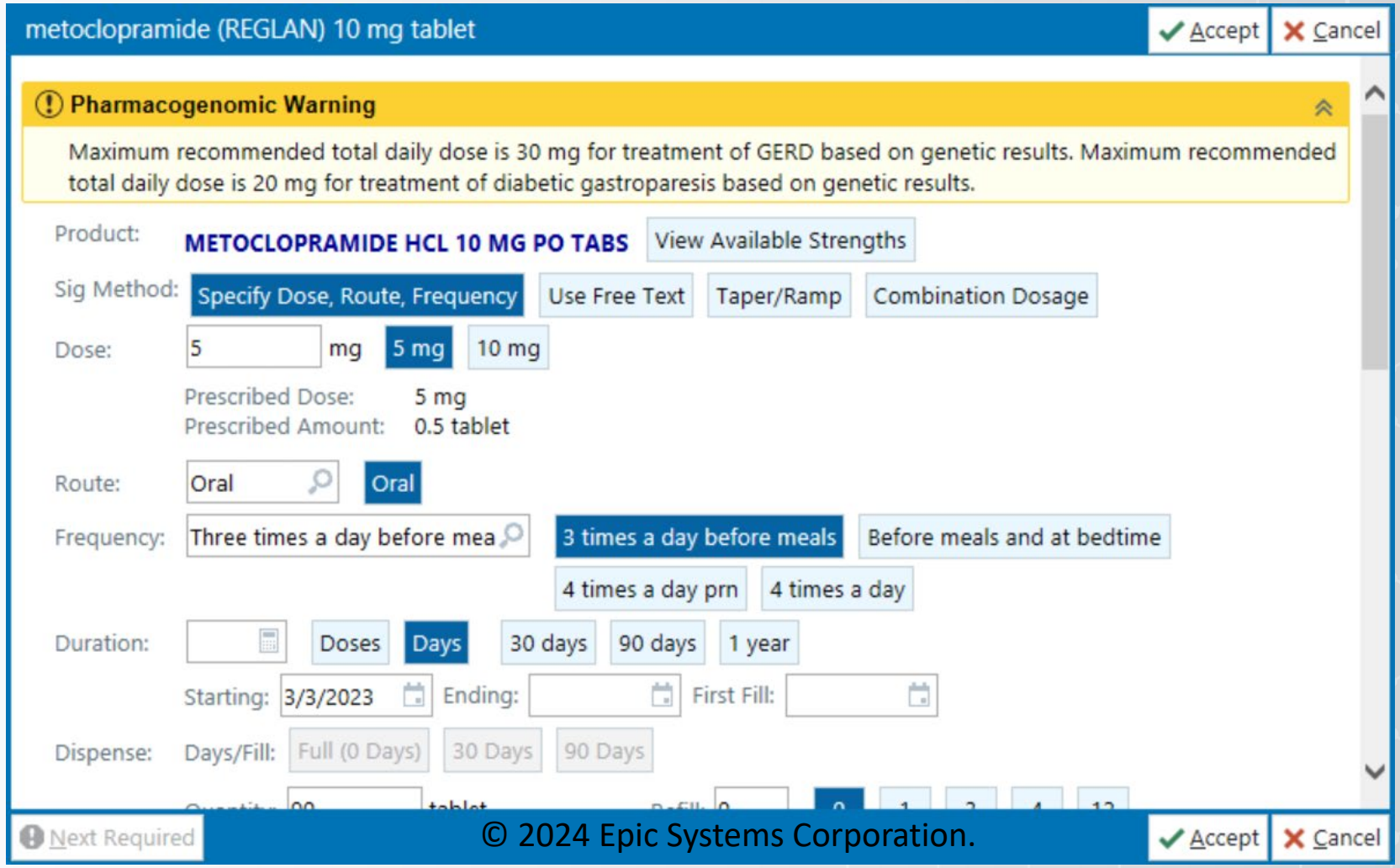




Interruptive Alerts



Non-interruptive Alerts



Education

Educational Tools & Approaches

Internal

- In-services & Champions
- Internal Website
- Modules
- Pocket Cards

External

- Community Lectures
- External Website
- Patient Instructions through the EMR
- Medication Specific Resources

Residency Program

PGY2 – CLINICAL PHARMACOGENOMICS PHARMACY RESIDENCY

Preparing pharmacy residents to be leaders in pharmacogenomics while providing exceptional patient care opportunities in the clinical setting.

FAST FACTS

- 1 resident position
- ASHP-accredited
- Start date July 1, 2024 (flexible)
- Longitudinal rotations with opportunities to explore electives in areas of interest!

PROGRAM STRUCTURE

Required Longitudinal Experiences:

- Orientation
- Administration
- Clinical Decision Support
- Clinical Pharmacogenomics I
- Clinical Pharmacogenomics II
- Education
- Research

Following the orientation learning experience, residency learning experiences are generally longitudinal and built upon the three pillars of Imagenetics: Clinical Care, Education, and Research. Experiences related to the three pillars include:

Clinical Care

- Provide evidence-based interpretation of PGx results to optimize pharmacotherapy
- Staff multidisciplinary PGx clinic
- Assist with clinical decision support maintenance and updates
- Address PGx-related drug info questions

Education

- Contribute to educational materials for patients and healthcare providers
- Teach and precept students, PGY1 residents, and other learners
- Obtain teaching certificate

Research

- Evaluate PGx drug literature and statistics
- Conduct a year-long research project

QUALIFICATIONS

All residency candidates must meet the following prerequisites:

- Earned a PharmD degree from an accredited college of pharmacy
- Hold an active pharmacy license, or be eligible for licensure in South Dakota
- Be participating in or have completed an American Society of Health-System Pharmacists (ASHP) accredited PGY1 residency program or one in the ASHP accreditation process.

APPLICATION

Application materials and deadline will be managed through PhORCAS:

- Letter of interest
  - Address clinical areas of interest and reasons for pursuing PGY2 in PGx
- Curriculum Vitae
- Academic transcripts
- Three reference submissions

Applicants considered for a position will be invited for an interview with pharmacy administration, preceptors, and current residents. They will be required to review and present a brief case study.

PROGRAM CONTACT INFORMATION

Natasha Petry, PharmD, MPH, BCACP
Residency Program Director
PGY2 Clinical Pharmacogenomics

natasha.petry@sanfordhealth.org
(701) 234-6016

Sanford Imagenetics
1321 W. 22nd Street
Sioux Falls, SD 57105

SANFORD imagenetics

STIPEND AND BENEFITS

The stipend is competitive and updated annually. Residents are provided paid health and vision insurance and 20 days of Allowed Time Away (ATA), which are separate from paid holidays off. All required travel expenses are also covered.

SANFORD HEALTH

Sanford Health, one of the largest health systems in the United States, is dedicated to the integrated delivery of health care, genomic medicine, senior care and services, global clinics, research and affordable insurance.

Sanford USD Medical Center is the largest hospital in South Dakota (545 patient beds) and academic teaching institution for the University of South Dakota Sanford School of Medicine. Sanford USDMC provides an exciting learning environment to disciplines including medicine, pharmacy and nursing.

ABOUT SIOUX FALLS, SOUTH DAKOTA

With over 200,000 people, Sioux Falls is a great place to live. This vibrant city offers everything from parks and entertainment to shopping and music. With easy access to outdoor activities like biking, boating, hunting and fishing, there is something for everyone. Sioux Falls strives to maintain one of the healthiest environments in which to live, work and raise a family.

FOR MORE INFORMATION

Websites:

- Imagenetics: imagenetics.sanfordhealth.org
- PGY2 Residency: www.sanfordhealth.org/residency-programs/pharmacy-residency

Scan the QR codes to access more information or ask a question:

Other Training Opportunities

- APPE
- IPPE

NDSU NORTH DAKOTA STATE UNIVERSITY

Other schools upon request

- PGY1 Resident Electives
  - Sioux Falls Sanford
  - Fargo Sanford

- High school student shadowing

- NIH Laboratory Genetics and Genomics Fellowship elective

Research

Selected Publications

› Pharmacogenomics. 2019 Aug;20(12):903-913. doi: 10.2217/pgs-2019-0043.

Implementation of wide-scale pharmacogenetic testing in primary care

Natasha Petry [1 2], Jordan Baye [1 2 3], Aissa Aifaoui [1], Russell A Wilke [4 5], Roxana A Lupu [4 5], John Savageau [6], Britni Gapp [6], Amanda Massmann [1], Deidre Hahn [2], Catherine Hajek [1 5], April Schultz [1 5]

› Front Genet. 2021 Mar 12;12:626845. doi: 10.3389/fgene.2021.626845. eCollection 2021.

Precision Population Medicine in Primary Care: The Sanford Chip Experience

Kurt D Christensen [1 2 3], Megan Bell [4], Carrie L B Zawatsky [5 6], Lauren N Galbraith [1], Robert C Green [3 5 6 7], Allison M Hutchinson [4], Leila Jamal [8 9], Jessica L LeBlanc [1], Jennifer R Leonhard [10], Michelle Moore [4], Lisa Mullineaux [11], Natasha Petry [12 13], Dylan M Platt [4], Sherin Shaaban [14 15], April Schultz [4 16], Bethany D Tucker [4], Joel Van Heukelom [4 16], Elizabeth Wheeler [4], Emilie S Zoltick [1], Catherine Hajek [4 16]; Imagenetics Metrics Team

Collaborators, Affiliations + expand

PMID: 33777099 PMCID: PMC7994529 DOI: 10.3389/fgene.2021.626845

Free PMC article

Abstract

Genetic testing has the potential to revolutionize primary care, but few health systems have developed the infrastructure to support precision population medicine applications or attempted to evaluate its impact on patient and provider outcomes. In 2018, Sanford Health, the nation's largest rural nonprofit health care system, began offering genetic testing to its primary care patients. To date, more than 11,000 patients have participated in the Sanford Chip Program, over 90% of whom have been identified with at least one informative pharmacogenomic variant, and about 1.5% of whom have been identified with a medically actionable predisposition for disease. This manuscript describes the rationale for offering the Sanford Chip, the programs and infrastructure implemented to support it, and evolving plans for research to evaluate its real-world impact.

Keywords: decision support systems, clinical; genetic counseling; genetic testing; pharmacogenomic

› Genet Med. 2022 Jan;24(1):214-224. doi: 10.1016/j.gim.2021.08.008. Epub 2021 Nov 30.

Improved provider preparedness through an 8-part genetics and genomic education program

Catherine Hajek [1], Allison M Hutchinson [2], Lauren N Galbraith [3], Robert C Green [4], Michael F Murray [5], Natasha Petry [6], Charlene L Preys [7], Carrie L B Zawatsky [8], Emilie S Zoltick [3], Kurt D Christensen [9]; Imagenetics METRICS Team

Collaborators, Affiliations + expand

PMID: 34906462 PMCID: PMC9121992 DOI: 10.1016/j.gim.2021.08.008

› Pharmacogenomics. 2020 Nov;21(17):1207-1215. doi: 10.2217/pgs-2020-0088. Epub 2020 Oct 29.

Malignant hyperthermia susceptibility: utilization of genetic results in an electronic medical record to increase safety

Jordan F Baye [1 2 3], Natasha J Petry [1 4], Shauna L Jacobson [5], Michelle M Moore [1], Bethany Tucker [1], Sherin Shaaban [6], Amanda K Massmann [1 3], Nicole M Clark [1], April J Schultz [1 3]

Affiliations + expand

PMID: 33118445 DOI: 10.2217/pgs-2020-0088

Abstract

Aim: This manuscript describes implementation of clinical decision support for providers concerned with perioperative complications of malignant hyperthermia susceptibility. **Materials & methods:** Clinical decision support for malignant hyperthermia susceptibility was implemented in 2018 based around our pre-emptive genotyping platform. We completed a brief descriptive review of patients who underwent pre-emptive testing, focused particularly on *RYR1* and *CACNA1S* genes. **Results:** To date, we have completed pre-emptive genetic testing on more than 10,000 patients; 13 patients having been identified as a carrier of a pathogenic or likely pathogenic variant of *RYR1* or *CACNA1S*. **Conclusion:** An alert system for malignant hyperthermia susceptibility - as an extension of our pre-emptive genomics platform - was implemented successfully. Implementation strategies and lessons learned are discussed herein.

Keywords: clinical decision support; inhalation anesthetics; malignant hyperthermia; malignant hyperthermia susceptibility; personalized medicine; pharmacogenomics.

Lessons Learned

Barriers

- Technology Integration / Updates
- Lack of Insurance Coverage
- Education Initiatives
- Communication Across Multiple Disciplines
- Physical Distance
- Maintenance

Strengths

Emphasis on physician-patient relationship

Foundation of education

Primarily clinical focus

(not research)

Clinical evaluation is both prospective and retrospective

In-house lab imputes discrete genomics data in EMR

Implementation efforts focused on evidence-based sources

Effective use of technology within a rural footprint

Support from administration

Sanford Imagenetics Team

Pharmacogenomics

April Schultz, PharmD
Joel Van Heukelom, PharmD, MBA
Amanda Massmann, PharmD
Kristen Jacobsen, PharmD
Natasha Petry, PharmD, MPH, BCACP
Jordan Baye, PharmD, MA, BCPS
Jennifer Morgan, DNP, APRN-CNP

Administration

Elizabeth Wheeler, MPH
Jessica Aguilar, FACHE
Rochelle Odenbrett, MT (ASCP), MBA
Heather Oakland, MHSA

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Acknowledgements

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Thank you for the invitation to speak today!

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