Supplementary File 1

CYP2C19-Clopidogrel

This file was converted from the original .xls to .pdf format. To view the .xls tables please refer to the gene specific TPP Translation Tables as posted on the Pharmacogenomics Knowledge Base website https://www.pharmgkb.org/page/tppTables.

TPP PGx Clinical Decision Support

Gene	CYP2C19
Drug(s)	Clopidogrel
Pathway	https://www.pharmgkb.org/pathway/PA154424674

Purpose
This document summarizes the implementation of pharmacogenomics (PGx) clinical decision support (CDS) for members of the PGRN Translational Pharmacogenomics Project (TPP). This document is intended to facilitate similar implementations at other sites.

Organization And Content	
This document contains several worksheets (tabs), each of which captures information related to a specific aspect of PGx CDS. The information is organized into tables that are intended to enable a high-level comparison across sites. Additional, site-specific information may be provided separately.	
Worksheet Name	**Description**
README	Describes the the content and how to use this document
<gene> Haplotypes	Lists which alleles are tested at each site and their functional interpretation
<gene> Diplotypes	Reports how many of each diplotype were observed at each site
<drug> - Phenotypes	Translations for each site from diplotype to drug-specific phenotype
<drug> - Pretest CDS	High-level description of CDS that fires before a patient genotype is known or when a genotype test result is obtained
<drug> - Results Notif	Summarizes how patients and providers are notified of test results
<drug> - Posttest CDS	High-level description of CDS that fires after a patient genotype is known
Value Sets	Lists the consensus terms and definitions used in this document

How To Use This Document

The data on the Haplotypes and Diplotypes tabs provides background information about the genetic lab tests that are available at each site and the number of times each diplotype was observed. This may help sites considering new PGx CDS implementations as they consider the scope of their implementation.

The Phenotypes tab serves as the primary entry point into the genotype-to-phenotype-to-CDS translation process. The information in this worksheet can be used to inform decisions about how a given diplotype might be translated into a clinical phenotype.

The CDS tabs summarize the CDS implementation at each site for a given phenotype. The phenotypes on this tab will tie directly to those listed on the Phenotypes tabs. Due to the complex nature of CDS implementations, only high-level descriptions are provided. Additional data may be available separately.

Project Sites

PGRN Group	Medical Center	Principal Investigators
PAAR	University of Chicago	Mark Ratain, MD, Nancy J. Cox, Ph.D., M. Eileen Dolan, Ph.D
PAAR4Kids	St. Jude Children's Research Hospital	Mary V. Relling, PharmD
PAPI-2	University of Maryland, Baltimore, School o	Alan R. Shuldiner, MD
PAT	Vanderbilt University Medical Center	Dan M. Roden, MD
PEAR	University of Florida	Julie A. Johnson, PharmD
PharmGKB	Stanford University School of Medicine	Russ B. Altman, MD, PhD and Teri E. Klein, PhD
PHAT	Brigham and Women's Hospital/Harvard	Scott Weiss, MD, MS and Kelan Tantisira, MD, MPH
PHONT	Mayo Clinic	Christopher G. Chute, M.D., Dr.Ph.
PPII	Mayo Clinic	Richard Weinshilboum, MD, Liewei Wang, MD, PhD
XGEN	Ohio State University	Wolfgang Sadee DR.rer.nat., M.Pharmacy

Questions And Feedback

This document was created by the PGRN TPP Data Standardization Work Group (Robert Freimuth, PhD, Chair)
Questions and feedback can be directed to PharmGKB at http://www.pharmgkb.org/submit/startFeedback.action

CYP2C19

Genotype Test Status. The table shows which haplotype alleles are tested and reported at each site.
Valid values for testing status: Y, N (see the "Value Sets" tab)
Note: Some haplotypes may be tested but not reported (indicated as N in the table)
*Note: The *1 haplotype is inferred based on the absence of variants at interrogated sites*

	Genotype Test Status						
Haplotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAPI-2 (UMB)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
*1	Y	Y	Y	Y	Y	Y	Y
*2	Y	N	Y	Y	Y	Y	Y
*2A	N	Y	N	N	N	N	N
*2B	N	Y	N	N	N	N	N
*3	Y	Y	Y	Y	Y	Y	Y
*4	Y	Y	N	Y	Y	Y	Y
*5	Y	Y	N	Y	Y	N	Y
*6	Y	Y	N	Y	Y	Y	Y
*7	Y	Y	N	Y	N	Y	Y
*8	Y	Y	N	Y	Y	Y	Y
*9	Y	Y	N	N	N	Y	N
*10	N	Y	N	N	Y	Y	N
*11	N	N	N	N	N	Y	N
*12	Y	Y	N	Y	N	N	N
*13	N	Y	N	N	N	N	N
*14	N	Y	N	N	N	Y	N
*15	N	Y	N	N	N	N	N
*17	Y	Y	Y	Y	Y	Y	Y
Platform	Sequenom ADME panel + custom panel	Affymetrix DMET Plus, supplemented with CYP2D6 copy number assay	Nanosphere Verigene	Illumina BeadXpress/ADME	ABI Systems QuantStudio Custom Array	Sanger Sequencing	Affymetrix Genome-Wide Human SNP Array 6.0 and DMET Plus

Functional Interpretation. The table shows the functional interpretation of each CYP2C19 allele.
Valid values for functional interpretation: see the Value Sets tab
Haplotypes that are not assayed (see above) should have blank interpretations
Note: This table may be omitted for some genes (e.g., HLA-B)

	Functional Interpretation						
Haplotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAPI-2 (UMB)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
*1	Normal	Normal	Normal	Normal	Normal	Normal	Normal
*2	Decreased	Decreased	Decreased	Decreased	Decreased	Undetectable	Decreased
*2A		Decreased					
*2B		Decreased					
*3	Decreased	Decreased	Decreased	Decreased	Decreased	Undetectable	Decreased
*4	Decreased	Decreased		Decreased	Decreased	Undetectable	Decreased
*5	Decreased	Decreased		Decreased	Decreased		Decreased
*6	Decreased	Decreased		Decreased	Decreased	Undetectable	Decreased
*7	Decreased	Decreased		Decreased		Undetectable	Decreased
*8	Decreased	Decreased		Decreased	Decreased	Decreased	Decreased
*9	Uncharacterized	Uncharacterized				Decreased	
*10		Uncharacterized			Uncharacterized	Decreased	
*11						Uncharacterized	
*12	Uncharacterized	Uncharacterized		Uncharacterized			
*13		Uncharacterized					
*14		Uncharacterized				Uncharacterized	
*15		Uncharacterized					
*17	Increased	Increased	Increased	Increased	Increased	Increased	Increased

CYP2C19

Diplotype Counts. The number of samples observed with each diplotype is shown.
It is anticipated that these counts will be updated approximately once per year
Counts for diplotypes that were assayed but not observed should be reported as 0 (zero), whereas counts for diplotypes that were not assayed should be left blank

			Diplotype Counts						
Haplotype1	Haplotype2	Diplotype	PAAR (U Chicago) as of 10/1/13	PAAR4Kids (St. Jude) as of 02/28/2014	PAPI-2 (UMB) as of 3/10/2014	PAT (Vanderbilt) as of Sept 2013	PEAR (U FL) as of 2/28/2014	PPII (Mayo Clinic) as of 9/5/2012	XGEN (OSU) as of Aug 2013
*1	*1	*1/*1	230	517	96	5670	503	174	84
*1	*2	*1/*2	125		50	2659	218	78	34
*1	*2A	*1/*2A		250					
*1	*2B	*1/*2B		28					
*1	*3	*1/*3	0	0	1	11	1	0	0
*1	*4	*1/*4	0	1		37	2	0	0
*1	*5	*1/*5	0	0		0	0		0
*1	*6	*1/*6	0	0		5	11	0	0
*1	*7	*1/*7	0	0		0		0	0
*1	*8	*1/*8	0	4		53	3	0	1
*1	*9	*1/*9	0	23			3	0	
*1	*10	*1/*10		2			37	0	
*1	*11	*1/*11						0	
*1	*12	*1/*12	0	0		7			
*1	*13	*1/*13		11					
*1	*14	*1/*14		0				0	
*1	*15	*1/*15		16					
*1	*17	*1/*17	115	339	72	3814	303	103	64
*2	*2	*2/*2	10		4	354	17	12	3
*2	*2A	*2/*2A							
*2	*2B	*2/*2B							
*2	*3	*2/*3	0		0	7	2	0	0
*2	*4	*2/*4	0			11	0	1	0
*2	*5	*2/*5	0			0	0		0
*2	*6	*2/*6	0			1	0	0	0
*2	*7	*2/*7	0			0		0	0
*2	*8	*2/*8	0			11	0	0	1
*2	*9	*2/*9	0					0	
*2	*10	*2/*10					1	0	
*2	*11	*2/*11						3	
*2	*12	*2/*12	0			0			
*2	*13	*2/*13							
*2	*14	*2/*14						0	
*2	*15	*2/*15							
*2	*17	*2/*17	28		21	942	63	0	12
*2A	*2A	*2A/*2A		29					
*2A	*2B	*2A/*2B		4					
*2A	*3	*2A/*3		2					
*2A	*4	*2A/*4		1					
*2A	*5	*2A/*5		0					
*2A	*6	*2A/*6		1					
*2A	*7	*2A/*7		0					
*2A	*8	*2A/*8		0					
*2A	*9	*2A/*9		10					
*2A	*10	*2A/*10		0					
*2A	*11	*2A/*11							
*2A	*12	*2A/*12		0					
*2A	*13	*2A/*13		3					
*2A	*14	*2A/*14		0					
*2A	*15	*2A/*15		8					
*2A	*17	*2A/*17		77					
*2B	*2B	*2B/*2B		0					
*2B	*3	*2B/*3		0					
*2B	*4	*2B/*4		0					
*2B	*5	*2B/*5		0					
*2B	*6	*2B/*6		0					
*2B	*7	*2B/*7		0					
*2B	*8	*2B/*8		1					
*2B	*9	*2B/*9		0					
*2B	*10	*2B/*10		0					
*2B	*11	*2B/*11							
*2B	*12	*2B/*12		0					
*2B	*13	*2B/*13		0					
*2B	*14	*2B/*14		0					
*2B	*15	*2B/*15		1					
*2B	*17	*2B/*17		9					
*3	*3	*3/*3	0	0	0	2	0	0	0
*3	*4	*3/*4	0	0		1	0	0	0
*3	*5	*3/*5	0	0		0	0		0
*3	*6	*3/*6	0	0		0	0	0	0
*3	*7	*3/*7	0	0		0		0	0
*3	*8	*3/*8	0	0		0	0	0	0
*3	*9	*3/*9	0	0				0	
*3	*10	*3/*10		0			0	0	
*3	*11	*3/*11						0	
*3	*12	*3/*12	0	0		0			
*3	*13	*3/*13		0					
*3	*14	*3/*14		0				0	
*3	*15	*3/*15		0					
*3	*17	*3/*17	0	0	0	0	0	0	0

Haplotype1	Haplotype2	Diplotype	PAAR (U Chicago) as of 10/1/13	PAAR4Kids (St. Jude) as of 02/28/2014	PAPI-2 (UMB) as of 3/10/2014	PAT (Vanderbilt) as of Sept 2013	PEAR (U FL) as of 2/28/2014	PPII (Mayo Clinic) as of 9/5/2012	XGEN (OSU) as of Aug 2013
*4	*4	*4/*4	0	0		0	0	0	0
*4	*5	*4/*5	0	0		0	0		0
*4	*6	*4/*6	0	0		0	0	0	0
*4	*7	*4/*7	0	0		0		0	0
*4	*8	*4/*8	0	0		0	0	0	0
*4	*9	*4/*9	0	0				0	
*4	*10	*4/*10		0			0	0	
*4	*11	*4/*11						0	
*4	*12	*4/*12	0	0		0			
*4	*13	*4/*13		0					
*4	*14	*4/*14		0				0	
*4	*15	*4/*15		0					
*4	*17	*4/*17	1	0		16	2	0	1
*5	*5	*5/*5	0	0		0	0		0
*5	*6	*5/*6	0	0		0	52		0
*5	*7	*5/*7	0	0		0			0
*5	*8	*5/*8	0	0		0	8		0
*5	*9	*5/*9	0	0					
*5	*10	*5/*10		0			0		
*5	*11	*5/*11							
*5	*12	*5/*12	0	0		0			
*5	*13	*5/*13		0					
*5	*14	*5/*14		0					
*5	*15	*5/*15		0					
*5	*17	*5/*17	0	0		1	0		0
*6	*6	*6/*6	0	0		0	0	0	0
*6	*7	*6/*7	0	0		0		0	0
*6	*8	*6/*8	0	0		0	0	0	0
*6	*9	*6/*9	0	0				0	
*6	*10	*6/*10		0			0	0	
*6	*11	*6/*11						0	
*6	*12	*6/*12	0	0		0			
*6	*13	*6/*13		0					
*6	*14	*6/*14		0				0	
*6	*15	*6/*15		0					
*6	*17	*6/*17	0	0		3	0	0	0
*7	*7	*7/*7	0	0		0		0	0
*7	*8	*7/*8	0	0		0		0	0
*7	*9	*7/*9	0	0				0	
*7	*10	*7/*10		0				0	
*7	*11	*7/*11						0	
*7	*12	*7/*12	0	0		0			
*7	*13	*7/*13		0					
*7	*14	*7/*14		0				0	
*7	*15	*7/*15		0					
*7	*17	*7/*17	0	0		0		0	0
*8	*8	*8/*8	0	0		1	0	0	0
*8	*9	*8/*9	0	0				0	
*8	*10	*8/*10		0			0	0	
*8	*11	*8/*11						0	
*8	*12	*8/*12	0	0		0			
*8	*13	*8/*13		0					
*8	*14	*8/*14		0				0	
*8	*15	*8/*15		0					
*8	*17	*8/*17	0	0		20	1	0	0
*9	*9	*9/*9	0	0				0	
*9	*10	*9/*10		0				0	
*9	*11	*9/*11						0	
*9	*12	*9/*12	0	0					
*9	*13	*9/*13		3					
*9	*14	*9/*14						0	
*9	*15	*9/*15		1					
*9	*17	*9/*17	0	2				0	
*10	*10	*10/*10		0			0	0	
*10	*11	*10/*11						0	
*10	*12	*10/*12		0					
*10	*13	*10/*13		0					
*10	*14	*10/*14		0				0	
*10	*15	*10/*15		0					
*10	*17	*10/*17		0			0	0	
*11	*11	*11/*11						0	
*11	*12	*11/*12							
*11	*13	*11/*13							
*11	*14	*11/*14						0	
*11	*15	*11/*15							
*11	*17	*11/*17						0	
*12	*12	*12/*12	0	0		0			
*12	*13	*12/*13		0					
*12	*14	*12/*14		0					
*12	*15	*12/*15		0					
*12	*17	*12/*17	0	0		3			
*13	*13	*13/*13		0					
*13	*14	*13/*14		0					
*13	*15	*13/*15		0					
*13	*17	*13/*17		6			1		
*14	*14	*14/*14		0				0	
*14	*15	*14/*15		0					
*14	*17	*14/*17		0				0	
*15	*15	*15/*15		0					
*15	*17	*15/*17		13					
*17	*17	*17/*17	29	68	8	664	59	19	3

Haplotype1	Haplotype2	Diplotype	PAAR (U Chicago) as of 10/1/13	PAAR4Kids (St. Jude) as of 02/28/2014	PAPI-2 (UMB) as of 3/10/2014	PAT (Vanderbilt) as of Sept 2013	PEAR (U FL) as of 2/28/2014	PPII (Mayo Clinic) as of 9/5/2012	XGEN (OSU) as of Aug 2013
*1	Unchar Variant	*1/Unchar Variant	4					3	
*2	Unchar Variant	*2/Unchar Variant	1					1	
*2A	Unchar Variant	*2A/Unchar Variant							
*2B	Unchar Variant	*2B/Unchar Variant							
*3	Unchar Variant	*3/Unchar Variant						0	
*4	Unchar Variant	*4/Unchar Variant						0	
*5	Unchar Variant	*5/Unchar Variant							
*6	Unchar Variant	*6/Unchar Variant						0	
*7	Unchar Variant	*7/Unchar Variant						0	
*8	Unchar Variant	*8/Unchar Variant						0	
*9	Unchar Variant	*9/Unchar Variant						0	
*10	Unchar Variant	*10/Unchar Variant						0	
*11	Unchar Variant	*11/Unchar Variant						0	
*12	Unchar Variant	*12/Unchar Variant							
*13	Unchar Variant	*13/Unchar Variant							
*14	Unchar Variant	*14/Unchar Variant						0	
*15	Unchar Variant	*15/Unchar Variant							
*17	Unchar Variant	*17/Unchar Variant	19					0	
		Ambiguous call				13		22	
		No call	45	1		2			0
		Totals	607	1431	252	14308	1287	416	203

CYP2C19

Drug-Specific Phenotypes. The interpreted phenotype is shown for each diplotype that is possible, based on the known alleles for this gene.
Note: Diplotype phenotypes may be site-specific (differences between sites are acceptable)
Note: The values for phenotype are specified on the "value sets" tab. Diplotypes that are not tested should be left blank.

	Phenotypes for Clopidogrel						
Diplotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAPI-2 (UMB)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
*1/*1	EM	EM	EM	EM	EM	EM	EM
*1/*2	IM	IM	IM	IM	IM	IM	IM
*1/*2A		IM					
*1/*2B		IM					
*1/*3	IM	IM	IM	IM	IM		IM
*1/*4	IM	IM		IM	IM		IM
*1/*5	IM	IM		IM	IM		IM
*1/*6	IM	IM		IM	IM		IM
*1/*7	IM	IM		IM			IM
*1/*8	IM	IM		IM	IM		IM
*1/*9	Indeterminate	Indeterminate					
*1/*10		Indeterminate			Indeterminate		
*1/*11							
*1/*12	Indeterminate	Indeterminate		Indeterminate			
*1/*13		Indeterminate					
*1/*14		Indeterminate					
*1/*15		Indeterminate					
*1/*17	UM	UM	UM	EM	UM	Possible UM	UM
*2/*2	PM	PM	PM	PM	PM	PM	PM
*2/*2A		PM					
*2/*2B		PM					
*2/*3	PM	PM	PM	PM	PM		PM
*2/*4	PM	PM		PM	PM	PM	PM
*2/*5	PM	PM		PM	PM		PM
*2/*6	PM	PM		PM	PM		PM
*2/*7	PM	PM		PM			PM
*2/*8	PM	PM		PM	PM		PM
*2/*9	Indeterminate	Indeterminate					
*2/*10		Indeterminate			Indeterminate		
*2/*11						IM	
*2/*12	Indeterminate	Indeterminate		Indeterminate			
*2/*13		Indeterminate					
*2/*14		Indeterminate					
*2/*15		Indeterminate					
*2/*17	IM	IM	IM	Indeterminate	IM		IM
*2A/*2A		PM					
*2A/*2B		PM					
*2A/*3		PM					
*2A/*4		PM					
*2A/*5		PM					
*2A/*6		PM					
*2A/*7		PM					
*2A/*8		PM					
*2A/*9		Indeterminate					
*2A/*10		Indeterminate					
*2A/*11							
*2A/*12		Indeterminate					
*2A/*13		Indeterminate					
*2A/*14		Indeterminate					
*2A/*15		Indeterminate					
*2A/*17		IM					
*2B/*2B		PM					
*2B/*3		PM					
*2B/*4		PM					
*2B/*5		PM					
*2B/*6		PM					
*2B/*7		PM					
*2B/*8		PM					
*2B/*9		Indeterminate					
*2B/*10		Indeterminate					
*2B/*11							
*2B/*12		Indeterminate					
*2B/*13		Indeterminate					
*2B/*14		Indeterminate					
*2B/*15		Indeterminate					
*2B/*17		IM					

Diplotype	PAAR (U Chicago)	PAAR4Kids (St. Jude)	PAPI-2 (UMB)	PAT (Vanderbilt)	PEAR (U FL)	PPII (Mayo Clinic)	XGEN (OSU)
*3/*3	PM	PM	PM	PM	PM		PM
*3/*4	PM	PM		PM	PM		PM
*3/*5	PM	PM		PM	PM		PM
*3/*6	PM	PM		PM	PM		PM
*3/*7	PM	PM		PM			PM
*3/*8	PM	PM		PM	PM		PM
*3/*9	Indeterminate	Indeterminate					
*3/*10		Indeterminate			Indeterminate		
*3/*11							
*3/*12	Indeterminate	Indeterminate		Indeterminate			
*3/*13		Indeterminate					
*3/*14		Indeterminate					
*3/*15		Indeterminate					
*3/*17	IM	Indeterminate	IM	Indeterminate	IM		IM
*4/*4	PM	PM		PM	PM		PM
*4/*5	PM	PM		PM	PM		PM
*4/*6	PM	PM		PM	PM		PM
*4/*7	PM	PM		PM			PM
*4/*8	PM	PM		PM	PM		PM
*4/*9	Indeterminate	Indeterminate					
*4/*10		Indeterminate			Indeterminate		
*4/*11							
*4/*12	Indeterminate	Indeterminate		Indeterminate			
*4/*13		Indeterminate					
*4/*14		Indeterminate					
*4/*15		Indeterminate					
*4/*17	IM	Indeterminate		Indeterminate	IM		IM
*5/*5	PM	PM		PM	PM		PM
*5/*6	PM	PM		PM	PM		PM
*5/*7	PM	PM		PM			PM
*5/*8	PM	PM		PM	PM		PM
*5/*9	Indeterminate	Indeterminate					
*5/*10		Indeterminate			Indeterminate		
*5/*11							
*5/*12	Indeterminate	Indeterminate		Indeterminate			
*5/*13		Indeterminate					
*5/*14		Indeterminate					
*5/*15		Indeterminate					
*5/*17	IM	Indeterminate		Indeterminate	IM		IM
*6/*6	PM	PM		PM	PM		PM
*6/*7	PM	PM		PM			PM
*6/*8	PM	PM		PM	PM		PM
*6/*9	Indeterminate	Indeterminate					
*6/*10		Indeterminate			Indeterminate		
*6/*11							
*6/*12	Indeterminate	Indeterminate		Indeterminate			
*6/*13		Indeterminate					
*6/*14		Indeterminate					
*6/*15		Indeterminate					
*6/*17	IM	Indeterminate		Indeterminate	IM		IM
*7/*7	PM	PM		PM			PM
*7/*8	PM	PM		PM			PM
*7/*9	Indeterminate	Indeterminate					
*7/*10		Indeterminate					
*7/*11							
*7/*12	Indeterminate	Indeterminate		Indeterminate			
*7/*13		Indeterminate					
*7/*14		Indeterminate					
*7/*15		Indeterminate					
*7/*17	IM	Indeterminate		Indeterminate			IM
*8/*8	PM	PM		PM	PM		PM
*8/*9	Indeterminate	Indeterminate					
*8/*10		Indeterminate			Indeterminate		
*8/*11							
*8/*12	Indeterminate	Indeterminate		Indeterminate			
*8/*13		Indeterminate					
*8/*14		Indeterminate					
*8/*15		Indeterminate					
*8/*17	IM	Indeterminate		Indeterminate	IM		IM
*9/*9	Indeterminate	Indeterminate					
*9/*10		Indeterminate					
*9/*11							
*9/*12	Indeterminate	Indeterminate					
*9/*13		Indeterminate					
*9/*14		Indeterminate					
*9/*15		Indeterminate					
*9/*17	Indeterminate	Indeterminate					

Diplotype	PAAR (U Chicago)	PAAR4Kids (St. Jude)	PAPI-2 (UMB)	PAT (Vanderbilt)	PEAR (U FL)	PPII (Mayo Clinic)	XGEN (OSU)
*10/*10		Indeterminate			Indeterminate		
*10/*11							
*10/*12		Indeterminate					
*10/*13		Indeterminate					
*10/*14		Indeterminate					
*10/*15		Indeterminate					
*10/*17		Indeterminate			Indeterminate		
*11/*11							
*11/*12							
*11/*13							
*11/*14							
*11/*15							
*11/*17							
*12/*12	Indeterminate	Indeterminate		Indeterminate			
*12/*13		Indeterminate					
*12/*14		Indeterminate					
*12/*15		Indeterminate					
*12/*17	Indeterminate	Indeterminate		Indeterminate			
*13/*13		Indeterminate					
*13/*14		Indeterminate					
*13/*15		Indeterminate					
*13/*17		Indeterminate					
*14/*14		Indeterminate					
*14/*15		Indeterminate					
*14/*17		Indeterminate					
*15/*15		Indeterminate					
*15/*17		Indeterminate					
*17/*17	UM	UM	UM	UM	UM	UM	UM
*1/Unchar Variant	Indeterminate	Indeterminate					
*2/Unchar Variant	Indeterminate	Indeterminate					
*2A/Unchar Variant		Indeterminate					
*2B/Unchar Variant		Indeterminate					
*3/Unchar Variant	Indeterminate	Indeterminate					
*4/Unchar Variant	Indeterminate	Indeterminate					
*5/Unchar Variant	Indeterminate	Indeterminate					
*6/Unchar Variant	Indeterminate	Indeterminate					
*7/Unchar Variant	Indeterminate	Indeterminate					
*8/Unchar Variant	Indeterminate	Indeterminate					
*9/Unchar Variant	Indeterminate	Indeterminate					
*10/Unchar Variant		Indeterminate					
*11/Unchar Variant							
*12/Unchar Variant	Indeterminate	Indeterminate					
*13/Unchar Variant		Indeterminate					
*14/Unchar Variant		Indeterminate					
*15/Unchar Variant		Indeterminate					
*17/Unchar Variant	Indeterminate	Indeterminate					

CYP2C19 + Clopidogrel

CDS Summaries
Additional detail may be provided through site-specific workflow diagrams and supplementary information
Note: If CDS has not been implemented for this scenario, the cells are left empty

Trigger Context	The context in which the rule fires. Examples: inpatient order, outpatient order, predictive score
CDS Type	The type of CDS provided. See the Value Sets tab for examples.
Pre-Order Genetic Testing	Indicates whether genetic testing is required prior to the drug order. See the Value Sets tab.

Drug is ordered or indicated but no genotype result is on file							
	PAAR (U Chicago)	**PAAR4Kids (St. Jude)**	**PAPI-2 (UMB)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
Trigger Context	All patients (preemptive)	All orders		Predictive Score; Ordersets			Research protocol
CDS Type	Passive	Active		Active + Passive			Active + Passive
Pre-Order Genetic Testing	Recommended	Recommended		Recommended			Required

CYP2C19 + Clopidogrel

Summary of Results Notification
Additional detail may be provided through site-specific workflow diagrams and supplementary information

Phenotypes correspond to the value set. See the "Value Sets" tab for details.
Types of notification are defined on the "Value Sets" tab.

Provider notification of a genotype test result							
Phenotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAPI-2 (UMB)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
UM	Passive	Active + Passive	Passive	Passive	Passive		Active + Passive
EM	Passive	Passive	Passive	Passive	Passive		Active + Passive
IM	Passive	Active + Passive	Active + Passive	Passive	Active + Passive		Active + Passive
PM	Passive	Active + Passive	Active + Passive	Passive	Active + Passive		Active + Passive
Indeterminate	Passive	Passive		Passive	Passive		
Possible UM		Active + Passive					
Possible IM		Active + Passive					
Possible PM		Active + Passive					

Patient notification of a genotype test result							
Phenotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAPI-2 (UMB)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
UM	Active	Active	Active	Passive	None		Active + Passive
EM	Active	Active	Active	Passive	None		Active + Passive
IM	Active	Active	Active + Passive	Passive	None		Active + Passive
PM	Active	Active	Active + Passive	Passive	None		Active + Passive
Indeterminate	Active	None		Passive	None		
Possible UM		Active					
Possible IM		Active					
Possible PM		Active					

CYP2C19 + Clopidogrel

CDS Summaries
Additional detail may be provided through site-specific workflow diagrams and supplementary informatio

Note: See the Value Sets tab for examples of CDS Type.
Note: Recommendation(s) should be a concatenated list of 1-2 word summaries. Examples include "Drug Change, Dose Change, Monitorin

Drug is ordered, genotype test result is on file														
	PAAR (U Chicago)		PAAR4Kids (St. Jude)		PAPI-2 (UMB)		PAT (Vanderbilt)		PEAR (U FL)		PPII (Mayo Clinic)		XGEN (OSU)	
Phenotype	CDS Type	Recommendation(s)	CDS Type	Recommendation(s)	CDS Type	Recommendation(s)	CDS Type	Recommendation(s)	CDS Type	Recommendation(s)	CDS Type	Recommendation(s)	CDS Type	Recommendation(s)
UM	Passive	No change	Passive	No change	Passive	No change	Passive	No change	Passive	No change			Active + Passive	No recommendation
EM	Passive	No change	Passive	No change	Passive	No change	Passive	No change	Passive	No change			Active + Passive	No recommendation
IM	Passive	Drug change	Active + Passive	Drug change	Active + Passive	Drug or dose change	Active + Passive	Drug change	Active + Passive	Drug change			Active + Passive	No recommendation
PM	Passive	Drug change	Active + Passive	Drug change	Active + Passive	Drug change	Active + Passive	Drug change	Active + Passive	Drug change			Active + Passive	No recommendation
Indeterminate	Passive	No change	Passive	No change			Passive	No change	Passive	No change				
Possible UM			Passive	No change										
Possible IM			Active + Passive	Drug change										
Possible PM			Active + Passive	Drug change										

Value Sets

Genotype Test Status		
Abbreviation	**Term**	**Definition**
Y	Yes	Allele is tested
N	No	Allele is not tested

Functional Interpretation		
Abbreviation	**Term**	**Definition**
	Increased	The allele is associated with increased activity/function relative to the reference (wild-type) allele.
	Normal	The allele is associated with activity/function similar to the reference (wild-type) allele.
	Decreased	The allele is associated with decreased activity/function relative to the reference (wild-type) allele.
	Undetectable	The allele is associated with no detectable activity/function relative to the reference (wild-type) allele.
	Varies by substrate	The impact of the allele on activity/function varies by substrate. Details will be provided separately.
	Uncharacterized	The activity/function associated with the allele has not yet been characterized or the data are ambiguous.

Phenotype Terms for CYP2C19 + Clopidogrel			
Abbreviation	**Term**	**Definition***	**Examples of Diplotypes***
UM	Ultrarapid metabolizer	Increased enzyme function compared to extensive metabolizer	*17/*17, *1/*17
EM	Extensive metabolizer	Metabolism that is usually exhibited by the plurality of tested patients	*1/*1
IM	Intermediate metabolizer	Enzyme function is decreased compared to extensive metabolizer and increased compared to poor metabolizer	*1/*2A, *2A/*17
PM	Poor metabolizer	Little or no enzyme function	*3/*3
Indeterminate	Indeterminate	Based on genetic test results, the metabolism status cannot be assigned	*1/*9
Possible UM	Possible ultrarapid metabolizer	Genetic test results that indicate the patient might be an ultrarapid metabolizer; the test results cannot distinguish between UM and EM status, but the patient is not a PM	
Possible IM	Possible intermediate metabolizer	Genetic test results that indicate the patient might be an intermediate metabolizer; the test results cannot distinguish between IM and EM status, but the patient is not a PM and is not a UM	
Possible PM	Possible poor metabolizer	Genetic test results that indicate the patient might be a poor metabolizer; the test results cannot distinguish between PM and other statuses, but the patient is not a UM	

** The rules given in the definition may have site-specific exceptions*

The value set above was derived from the following value set from LOINC:

LOINC code	51971-0
LOINC component	Drug metabolism analysis overall interpretation
LOINC code	**LOINC answer text**
LA10315-2	Ultrarapid metabolizer
LA10316-0	Extensive metabolizer
LA10317-8	Intermediate metabolizer
LA9657-3	Poor metabolizer
LA9663-1	Inconclusive

Value Sets

CDS Type			
Abbreviation	**Term**	**Definition**	**Examples**
	Active	Specific messages are sent, but are not stored in the EHR for future (passive) reference	Popup alert, phone call, USPS letter, verbal communication
	Active + Passive	Specific messages are sent, information is also available on demand.	Email, EHR inbox; examples include those listed for "Active" and "Passive"
	Passive	No specific messages are sent, information is available on demand.	Test results and interpretations/consults via the EHR or patient portal

Pre-Order Genetic Testing		
Abbreviation	**Term**	**Definition**
	Recommended	Testing is recommended prior to drug order
	Required	Testing is required prior to drug order, institutional hard stop

Provider Notification			
Abbreviation	**Term**	**Definition**	**Examples**
	Active + Passive	Specific messages are sent, information is also available on demand.	Verbal communication, email, EHR inbox; examples include those listed for "Active" and "Passive"
	Passive	No specific messages are sent, information is available on demand.	Test results and interpretations/consults via the EHR

Patient Notification			
Abbreviation	**Term**	**Definition**	**Examples**
	Active	Specific messages are sent, but are not stored in the EHR for future (passive) reference	Verbal communication, phone call, USPS letter
	Passive	No specific messages are sent, information is available on demand.	Test results and interpretations/consults via the patient portal
	Active + Passive	Specific messages are sent, information is also available on demand.	Email; examples include those listed for "Active" and "Passive"
	None	Patient is not notified of the results.	

Post-Test Recommendation		
Abbreviation	**Term**	**Definition**
	No recommendation	No recommendation is provided
	No change	Follow normal prescription practices
	Drug change	Recommend use of a different drug
	Dose change	Recommend a dose adjustment for this drug
	Drug or dose change	Recommend a change in drug and/or dose (the particular recommendation may be explicit or left to clinical judgement)

Supplementary File 2

TPMT-Thiopurines

This file was converted from the original .xls to .pdf format. To view the .xls tables please refer to the gene specific TPP Translation Tables as posted on the Pharmacogenomics Knowledge Base website https://www.pharmgkb.org/page/tppTables.

TPP PGx Clinical Decision Support

Gene	TPMT
Drug(s)	Thiopurines
Pathway	http://www.pharmgkb.org/pathway/PA2040

Purpose
This document summarizes the implementation of pharmacogenomics (PGx) clinical decision support (CDS) for members of the PGRN Translational Pharmacogenomics Project (TPP). This document is intended to facilitate similar implementations at other sites.

Organization And Content

This document contains several worksheets (tabs), each of which captures information related to a specific aspect of PGx CDS. The information is organized into tables that are intended to enable a high-level comparison across sites. Additional, site-specific information may be provided separately.

Worksheet Name	**Description**
README	Describes the the content and how to use this document
<gene> Haplotypes	Lists which alleles are tested at each site and their functional interpretation
<gene> Diplotypes	Reports how many of each diplotype were observed at each site
<drug> - Phenotypes	Translations for each site from diplotype to drug-specific phenotype
<drug> - Pretest CDS	High-level description of CDS that fires before a patient genotype is known or when a genotype test result is obtained
<drug> - Results Notif	Summarizes how patients and providers are notified of test results
<drug> - Posttest CDS	High-level description of CDS that fires after a patient genotype is known
Value Sets	Lists the consensus terms and definitions used in this document

How To Use This Document

The data on the Haplotypes and Diplotypes tabs provides background information about the genetic lab tests that are available at each site and the number of times each diplotype was observed. This may help sites considering new PGx CDS implementations as they consider the scope of their implementation.

The Phenotypes tab serves as the primary entry point into the genotype-to-phenotype-to-CDS translation process. The information in this worksheet can be used to inform decisions about how a given diplotype might be translated into a clinical phenotype.

The CDS tabs summarize the CDS implementation at each site for a given phenotype. The phenotypes on this tab will tie directly to those listed on the Phenotypes tabs. Due to the complex nature of CDS implementations, only high-level descriptions are provided. Additional data may be available separately.

Project Sites

PGRN Group	Medical Center	Principal Investigators
PAAR	University of Chicago	Mark Ratain, MD, Nancy J. Cox, Ph.D., M. Eileen Dolan, Ph.D
PAAR4Kids	St. Jude Children's Research Hospital	Mary V. Relling, PharmD
PAPI-2	University of Maryland, Baltimore, School of	Alan R. Shuldiner, MD
PAT	Vanderbilt University Medical Center	Dan M. Roden, MD
PEAR	University of Florida	Julie A. Johnson, PharmD
PharmGKB	Stanford University School of Medicine	Russ B. Altman, MD, PhD and Teri E. Klein, PhD
PHAT	Brigham and Women's Hospital/Harvard	Scott Weiss, MD, MS and Kelan Tantisira, MD, MPH
PHONT	Mayo Clinic	Christopher G. Chute, M.D., Dr.Ph.
PPII	Mayo Clinic	Richard Weinshilboum, MD, Liewei Wang, MD, PhD
XGEN	Ohio State University	Peter Embi, MD

Questions And Feedback

This document was created by the PGRN TPP Data Standardization Work Group (Robert Freimuth, PhD, Chair)
Questions and feedback can be directed to PharmGKB at http://www.pharmgkb.org/submit/startFeedback.action

TPMT

Haplotype definitions are maintained by the TPMT nomenclature committee and are available at: http://www.imh.liu.se/tpmtalleles?l=en

Genotype Test Status. The table shows which haplotype alleles are tested and reported at each site.

Valid values for testing status: Y, N (see the "Value Sets" tab)

Note: Some haplotypes may be tested but not reported (indicated as N in the table)

*Note: The *1 haplotype is inferred based on the absence of variants at interrogated sites*

	Genotype Test Status					
Haplotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
*1	Y	Y	Y	Y	Y	Y
*1A	N	N	N	N	N	N
*1S	N	N	N	N	N	N
*2	Y	Y	Y	Y	Y	Y
*3A	Y	Y	Y	Y	Y	Y
*3B	Y	Y	Y	Y	Y	Y
*3C	Y	Y	Y	Y	Y	Y
*3D	Y	Y	N	N	N	N
*3E	N	N	N	N	N	N
*4	N	Y	Y	N	N	Y
*5	N	N	N	N	N	N
*6	N	N	N	N	N	N
*7	N	N	N	N	N	N
*8	Y	Y	Y	N	N	N
*9	N	N	N	N	N	N
*10	N	N	N	N	N	N
*11	N	N	N	N	N	N
*12	N	N	N	N	N	N
*13	N	N	N	N	N	N
*14	N	N	N	N	N	N
*15	N	N	N	N	N	N
*16	N	N	N	N	N	N
*17	N	N	N	N	N	N
*18	N	N	N	N	N	N
*19	N	N	N	N	N	N
*20	N	N	N	N	N	N
*21	N	N	N	N	N	N
*22	N	N	N	N	N	N
*23	N	N	N	N	N	N
*24	N	Y	N	N	N	N
*25	N	N	N	N	N	N
*26	N	N	N	N	N	N
*27	N	N	N	N	N	N
*28	N	N	N	N	N	N
*29	N	N	N	N	N	N
*30	N	N	N	N	N	N
*31	N	N	N	N	N	N
*32	N	N	N	N	N	N
*33	N	N	N	N	N	N
*34	N	N	N	N	N	N
*35	N	N	N	N	N	N
*36	N	N	N	N	N	N
*37	N	N	N	N	N	N
Platform	Sequenom	Affymetrix DMET Plus, supplemented with CYP2D6 copy number assay	Illumina ADME VeraCode	Life Technologies ViiA 7	PCR 5'-Nuclease End-Point Allelic Discrimination Analysis	Affymetrix DMET Plus

Functional Interpretation. The table shows the functional interpretation of each allele.
Valid values for functional interpretation: see the Value Sets tab
Haplotypes that are not assayed (see above) should have blank interpretations
Note: This table may be omitted for some genes (e.g., HLA-B)

	Functional Interpretation					
Haplotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
*1	Normal	Normal	Normal	Normal	Normal	
*1A						
*1S						
*2	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable	Decreased
*3A	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable	Decreased
*3B	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable	Decreased
*3C	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable	Decreased
*3D	Uncharacterized	Undetectable				
*3E						
*4		Undetectable	Indeterminate			Decreased
*5						
*6						
*7						
*8	Decreased	Indeterminate	Indeterminate			
*9						
*10						
*11						
*12						
*13						
*14						
*15						
*16						
*17						
*18						
*19						
*20						
*21						
*22						
*23						
*24		Normal				
*25						
*26						
*27						
*28						
*29						
*30						
*31						
*32						
*33						
*34						
*35						
*36						
*37						

TPMT

Diplotype Counts. The number of samples observed with each diplotype is shown.
It is anticipated that these counts will be updated approximately once per year
Counts for diplotypes that were assayed but not observed should be reported as 0 (zero), whereas counts for diplotypes that were not assayed should be left blank

‡ *Due to technological limitations of the genotyping test, it is not possible to distinguish between the diplotypes of *1/*3A vs *3B/*3C. Based on the relative frequency of *3A vs the *3B and *3C alleles, it is assumed that the diplotype is *1/*3A; however, there is a small chance (< 1 in 100,000) that this patient's diplotype is instead a compound heterozygote (*3B/*3C).*

Note: The list of diplotypes shown in this table has been restricted to only those that have been observed by the reporting sites.

			Diplotype Counts					
Haplotype1	**Haplotype2**	**Diplotype**	**PAAR (U Chicago) as of 7/21/14**	**PAAR4Kids (St. Jude) as of 07/21/2014**	**PAT (Vanderbilt) as of 7/30/14**	**PEAR (U FL) as of**	**PPII (Mayo Clinic) as of 8/22/14**	**XGEN (OSU) as of July 2014**
*1	*1	*1/*1	635	1754	12522		473	197
*1	*2	*1/*2	3	3	76		0	0
*1	*3A	*1/*3A	42	73	955		41	11
*1	*3B	*1/*3B	1	0	3		0	0
*1	*3C	*1/*3C	14	90	250		0	0
*1	*3D	*1/*3D	0	0				
*1	*4	*1/*4		0	77			0
*1	*8	*1/*8	12	45	79			
*1	*24	*1/*24		46				
*2	*2	*2/*2	0	0	0		0	0
*2	*3A	*2/*3A	0	1	4		0	0
*2	*3B	*2/*3B	0	0	0		0	0
*2	*3C	*2/*3C	0	0	1		0	0
*2	*3D	*2/*3D	0	0				
*2	*4	*2/*4		0	0			0
*2	*8	*2/*8	0	0	0			
*2	*24	*2/*24		0				
*3A	*3A	*3A/*3A	1	2	21		0	0
*3A	*3B	*3A/*3B	0	0	0		0	0
*3A	*3C	*3A/*3C	0	0	6		0	0
*3A	*3D	*3A/*3D	0	0				
*3A	*4	*3A/*4		0	0			0
*3A	*8	*3A/*8	0	1	1			
*3A	*24	*3A/*24		1				
*3B	*3B	*3B/*3B	0	0	0		0	0
*3B	*3C	*3B/*3C	0	0	0		0	0
*3B	*3D	*3B/*3D	0	0				
*3B	*4	*3B/*4		0	0			0
*3B	*8	*3B/*8	0	0	0			
*3B	*24	*3B/*24		0				
*3C	*3C	*3C/*3C	0	0	5		0	0
*3C	*3D	*3C/*3D	0	0				
*3C	*4	*3C/*4		0	0			0
*3C	*8	*3C/*8	1	1	8			
*3C	*24	*3C/*24		4				
*3D	*3D	*3D/*3D	0	0				
*3D	*4	*3D/*4		0				
*3D	*8	*3D/*8	0	0				
*3D	*24	*3D/*24		0				
*4	*4	*4/*4		0	0			0
*4	*8	*4/*8		0	0			
*4	*24	*4/*24		0				
*8	*8	*8/*8	0	0	1			
*8	*24	*8/*24		1				
*24	*24	*24/*24		0				
*1	Unchar Variant	*1/Unchar Variant	0	0	0		0	0
*2	Unchar Variant	*2/Unchar Variant	0	0	0		0	0
*3A	Unchar Variant	*3A/Unchar Variant	0	0	0		0	0
*3B	Unchar Variant	*3B/Unchar Variant	0	0	0		0	0
*3C	Unchar Variant	*3C/Unchar Variant	0	0	0		0	0
*3D	Unchar Variant	*3D/Unchar Variant	0	0				
*4	Unchar Variant	*4/Unchar Variant		0	0			0
*8	Unchar Variant	*8/Unchar Variant	0	0	0			
*24	Unchar Variant	*24/Unchar Variant		0				
		Ambiguous call	1	12				
		No call	26	1	547			
		Totals	736	2035	14556	0	514	208

TPMT

Drug-Specific Phenotypes. The interpreted phenotype is shown for each diplotype that is possible, based on the known alleles for this gene.

Note: Diplotype phenotypes may be site-specific (differences between sites are acceptable)

Note: The values for phenotype are specified on the "value sets" tab. Diplotypes that are not tested should be left blank.

‡ Due to technological limitations of the genotyping test, it is not possible to distinguish between the diplotypes of *1/*3A vs *3B/*3C. Based on the relative frequency of *3A vs the *3B and *3C alleles, it is assumed that the diplotype is *1/*3A; however, there is a small chance (< 1 in 100,000) that this patient's diplotype is instead a compound heterozygote (*3B/*3C). Since the *3 alleles all confer significantly reduced activity, a patient with a *1/*3A diplotype would have a single reduced-function allele but a patient with *3B/*3C would have two reduced-function alleles. This has direct impact on the predicted phenotype of these two diplotypes (see table below).

	Phenotypes for Thiopurines					
Diplotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
*1/*1	Normal/High	Normal/High	Normal/High	Normal/High	Normal/High	Normal/High
*1/*2	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate
*1/*3A ‡	Intermediate	Intermediate	Low/Absent	Intermediate	Intermediate	Indeterminate
*1/*3B	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate
*1/*3C	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate
*1/*3D		Intermediate				
*1/*4		Intermediate	Indeterminate			Intermediate
*1/*8	Intermediate	Possible Intermed.	Indeterminate			
*1/*24		Normal/High				
*2/*2		Low/Absent	Low/Absent		Low/Absent	
*2/*3A		Low/Absent	Low/Absent	Low/Absent	Low/Absent	Low/Absent
*2/*3B		Low/Absent	Low/Absent	Low/Absent	Low/Absent	Low/Absent
*2/*3C		Low/Absent	Low/Absent	Low/Absent	Low/Absent	Low/Absent
*2/*3D		Low/Absent				
*2/*4		Low/Absent	Low/Absent			Low/Absent
*2/*8		Possible Low/Absent	Indeterminate			
*2/*24		Intermediate				
*3A/*3A		Low/Absent	Low/Absent		Low/Absent	
*3A/*3B	Low/Absent	Low/Absent	Low/Absent	Low/Absent	Low/Absent	Low/Absent
*3A/*3C	Low/Absent	Low/Absent	Low/Absent	Low/Absent	Low/Absent	Low/Absent
*3A/*3D		Intermediate				
*3A/*4		Low/Absent	Indeterminate			Low/Absent
*3A/*8		Possible Low/Absent	Indeterminate			
*3A/*24		Intermediate				
*3B/*3B		Low/Absent	Low/Absent		Low/Absent	
*3B/*3C ‡		Low/Absent	Low/Absent	Low/Absent	Low/Absent	Indeterminate
*3B/*3D		Low/Absent				
*3B/*4		Low/Absent	Indeterminate			Low/Absent
*3B/*8		Possible Low/Absent	Indeterminate			
*3B/*24		Intermediate				
*3C/*3C		Low/Absent	Low/Absent		Low/Absent	
*3C/*3D		Low/Absent				
*3C/*4		Low/Absent	Indeterminate			Low/Absent
*3C/*8	Low/Absent	Possible Low/Absent	Indeterminate			
*3C/*24		Intermediate				
*3D/*3D		Low/Absent				
*3D/*4		Low/Absent				
*3D/*8		Possible Low/Absent				
*3D/*24		Intermediate				
*4/*4		Low/Absent	Indeterminate			
*4/*8		Possible Low/Absent	Indeterminate			
*4/*24		Intermediate				
*8/*8		Possible Low/Absent	Indeterminate			
*8/*24		Possible Intermed.				
*24/*24		Normal/High				
*1/Unchar Variant		Indeterminate				
*2/Unchar Variant		Intermediate				
*3A/Unchar Variant		Intermediate				
*3B/Unchar Variant		Intermediate				
*3C/Unchar Variant		Intermediate				
*3D/Unchar Variant		Intermediate				
*4/Unchar Variant		Intermediate				
*8/Unchar Variant		Intermediate				
*24/Unchar Variant		Intermediate				

TPMT + Thiopurines

CDS Summaries
Additional detail may be provided through site-specific workflow diagrams and supplementary information
Note: If CDS has not been implemented for this scenario, the cells are left empty

Trigger Context	The context in which the rule fires. Examples: inpatient order, outpatient order, predictive score
CDS Type	The type of CDS provided. See the Value Sets tab for examples.
Pre-Order Genetic Testing	Indicates whether genetic testing is required prior to the drug order. See the Value Sets tab.

Drug is ordered or indicated but no genotype result is on file						
	PAAR (U Chicago)	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
Trigger Context	Preemptive, all enrolled patients	All orders		Inpatient orders	All new orders only; as of 8/2014 rule for phenotype test is implemented, rule for genotype test is being implemented	Research protocol
CDS Type	Passive	Active		Active	Active + Passive	Active + Passive
Pre-Order Genetic Testing	Recommended	Recommended		Recommended	Recommended	Required

Pre-order test is recommended, but can be either phenotype or genotype (based on patient context)

TPMT + Thiopurines

Summary of Results Notification
Additional detail may be provided through site-specific workflow diagrams and supplementary information
Note: If a phenotype term is not in use, the cell will be left blank.

Phenotypes correspond to the value set. See the "Value Sets" tab for details.
Types of notification are defined on the "Value Sets" tab.

Provider notification of a genotype test result						
Phenotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
Normal/High	Passive	Passive	Passive	Passive	Passive	Passive
Intermediate	Passive	Active + Passive	Passive	Active + Passive	Active + Passive	Active + Passive
Low/Absent	Passive	Active + Passive	Passive	Active + Passive	Active + Passive	Active + Passive
Indeterminate	Passive	Passive	Passive	Passive		Active + Passive
Possible Intermed.		Active + Passive				
Possible Low/Absent		Active + Passive				

Patient notification of a genotype test result						
Phenotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
Normal/High	None	Active	Passive	None	Passive	Active + Passive
Intermediate	None	Active	Passive	None	Passive	Active + Passive
Low/Absent	None	Active	Passive	None	Passive	Active + Passive
Indeterminate	None	None	Passive	None		Active + Passive
Possible Intermed.		Active				
Possible Low/Absent		Active				

TPMT + Thiopurines

CDS Summaries
Additional detail may be provided through site-specific workflow diagrams and supplementary information

Note: See the Value Sets tab for examples of CDS Type.

Azathioprine:

Azathioprine is ordered, genotype test result is on file																		
	PAAR (U Chicago)			PAAR4Kids (St. Jude)			PAT (Vanderbilt)			PEAR (U FL)			PPII (Mayo Clinic)			XGEN (OSU)		
Phenotype	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**
Normal/High	Passive	No change	No change	Passive	No change	No change	Passive	No change	No change	Passive	No change	No change	Passive	No recommendation	No recommendation	Passive	No recommendation	No recommendation
Intermediate	Passive	Dose change	Dose change	Active+ Passive	Dose change	Dose change	Active + Passive	Dose change	Dose change	Active + Passive	Dose change	No recommendation	Active + Passive	Drug or dose change	Dose change	Active + Passive	Drug or dose change	Drug or dose change
Low/Absent	Passive	Drug or dose change	Drug change	Active+ Passive	Drug or dose change	Drug change	Active + Passive	Drug or dose change	Drug or dose change	Active + Passive	Drug or dose change	No recommendation	Active + Passive	Drug or dose change	Drug change	Active + Passive	Drug or dose change	Drug or dose change
Indeterminate	Passive	No recommendation	No recommendation	Passive	No change	No change	Passive	No change	No change	Passive	No recommendation	No recommendation				Active + Passive	Drug or dose change	Drug or dose change
Possible Intermed.				Active+ Passive	Dose change	Dose change												
Possible Low/Absent				Active+ Passive	Drug or dose change	Drug change												

Note: alerts are context-independent, but AME content is fully specified

Mercaptopurine:

Mercaptopurine is ordered, genotype test result is on file																		
	PAAR			PAAR4Kids			PAT			PEAR			PPII			XGEN		
Phenotype	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**
Normal/High	Passive	No change	No change	Passive	No change	No change	Passive	No change	No change	Passive	No change	No change	Passive	No recommendation	No recommendation	Passive	No recommendation	No recommendation
Intermediate	Passive	Dose change	Dose change	Active+ Passive	Dose change	Dose change	Active + Passive	Dose change	Dose change	Active + Passive	Dose change	Dose change	Active + Passive	Dose change	Dose change	Active + Passive	Drug or dose change	Drug or dose change
Low/Absent	Passive	Drug or dose change	Drug change	Active+ Passive	Dose change	Drug change	Active + Passive	Drug or dose change	Drug or dose change	Active + Passive	Drug change	Dose change	Active + Passive	Dose change	Drug change	Active + Passive	Drug or dose change	Drug or dose change
Indeterminate	Passive	No recommendation	No recommendation	Passive	No change	No change	Passive	No change	No change	Passive	No recommendation	No recommendation				Active + Passive	Drug or dose change	Drug or dose change
Possible Intermed.				Active+ Passive	Dose change	Dose change												
Possible Low/Absent				Active+ Passive	Dose change	Drug change												

Thioguanine:

Thioguanine is ordered, genotype test result is on file																		
	PAAR			PAAR4Kids			PAT			PEAR			PPII			XGEN		
Phenotype	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**	**CDS Type**	**Recommendation(s) for Malignancy**	**Recommendation(s) for Non-Malignancy**
Normal/High				Passive	No change	No change	Passive	No change	No change	Passive	No change	No change	Passive	No recommendation	No recommendation	Passive	No recommendation	No recommendation
Intermediate				Active+ Passive	Drug or dose change	Dose change	Active + Passive	Dose change	Dose change	Active + Passive	Dose change	Dose change	Active + Passive	Dose change	Dose change	Active + Passive	Drug or dose change	Drug or dose change
Low/Absent				Active+ Passive	Drug or dose change	Drug change	Active + Passive	Drug or dose change	Drug or dose change	Active + Passive	Drug change	Dose change	Active + Passive	Dose change	Drug change	Active + Passive	Drug or dose change	Drug or dose change
Indeterminate				Passive	No change	No change	Passive	No change	No change	Passive	No recommendation	No recommendation				Active + Passive	Drug or dose change	Drug or dose change
Possible Intermed.				Active+ Passive	Drug or dose change	Dose change												
Possible Low/Absent				Active+ Passive	Drug or dose change	Drug change												

Value Sets

Genotype Test Status		
Abbreviation	**Term**	**Definition**
Y	Yes	Allele is tested
N	No	Allele is not tested

Functional Interpretation		
Abbreviation	**Term**	**Definition**
	Increased	The allele is associated with increased activity/function relative to the reference (wild-type) allele.
	Normal	The allele is associated with activity/function similar to the reference (wild-type) allele.
	Decreased	The allele is associated with decreased activity/function relative to the reference (wild-type) allele.
	Undetectable	The allele is associated with no detectable activity/function relative to the reference (wild-type) allele.
	Varies by substrate	The impact of the allele on activity/function varies by substrate. Details will be provided separately.
	Indeterminate	The data for the activity/function associated with the allele are ambiguous, conflicting, or otherwise difficult to interpret.
	Uncharacterized	The activity/function associated with the allele is not yet characterized.

Note: CPIC is in the process of developing standardized phenotype terms. The terms below may change in the future based on those activities.

Phenotype Terms for TPMT + Thiopurines			
Abbreviation	**Term**	**Definition***	**Examples of Diplotypes***
Normal/High	Normal (high) Activity	Metabolism that is usually exhibited by the plurality of tested patients	*1/*1
Intermediate	Intermediate Activity	Enzyme function is decreased compared to patients with high activity and increased compared to patients with low or absent activity	*1/*3A
Low/Absent	Low or Absent Activity	Little or no enzyme function	*3A/*3A
Indeterminate	Indeterminate	Based on genetic test results, the metabolism status cannot be assigned	
Possible Intermed.	Possible Intermediate Activity	Genetic test results that indicate the patient might have intermediate TPMT activity	
Possible Low/Absent	Possible Low or Absent Activity	Genetic test results that indicate the patient might have little or no enzyme function	

** The rules given in the definition may have site-specific exceptions*

The value set above was derived from the following value set from LOINC:

LOINC code	51971-0
LOINC component	Drug metabolism analysis overall interpretation
LOINC code	**LOINC answer text**
LA10315-2	Ultrarapid metabolizer
LA10316-0	Extensive metabolizer
LA10317-8	Intermediate metabolizer
LA9657-3	Poor metabolizer
LA9663-1	Inconclusive

Value Sets

CDS Type			
Abbreviation	**Term**	**Definition**	**Examples**
	Active	Specific messages are sent, but are not stored in the EHR for future (passive) reference	Popup alert, phone call, USPS letter, verbal communication
	Active + Passive	Specific messages are sent, information is also available on demand.	Email, EHR inbox; examples include those listed for "Active" and "Passive"
	Passive	No specific messages are sent, information is available on demand.	Test results and interpretations/consults via the EHR or patient portal

Pre-Order Genetic Testing		
Abbreviation	**Term**	**Definition**
	Recommended	Testing is recommended prior to drug order
	Required	Testing is required prior to drug order, institutional hard stop

Provider Notification			
Abbreviation	**Term**	**Definition**	**Examples**
	Active + Passive	Specific messages are sent, information is also available on demand.	Verbal communication, email, EHR inbox; examples include those listed for "Active" and "Passive"
	Passive	No specific messages are sent, information is available on demand.	Test results and interpretations/consults via the EHR

Patient Notification			
Abbreviation	**Term**	**Definition**	**Examples**
	Active	Specific messages are sent, but are not stored in the EHR for future (passive) reference	Verbal communication, phone call, USPS letter
	Passive	No specific messages are sent, information is available on demand.	Test results and interpretations/consults via the patient portal
	Active + Passive	Specific messages are sent, information is also available on demand.	Email; examples include those listed for "Active" and "Passive"
	None	Patient is not notified of the results.	

Post-Test Recommendation		
Abbreviation	**Term**	**Definition**
	No recommendation	No recommendation is provided
	No change	Follow normal prescription practices
	Drug change	Recommend use of a different drug
	Dose change	Recommend a dose adjustment for this drug
	Drug or dose change	Recommend a change in drug and/or dose (the particular recommendation may be explicit or left to clinical judgement)

Supplementary File 3

SLCO1B1-Simvastatin

This file was converted from the original .xls to .pdf format. To view the .xls tables please refer to the gene specific TPP Translation Tables as posted on the Pharmacogenomics Knowledge Base website https://www.pharmgkb.org/page/tppTables.

TPP PGx Clinical Decision Support

Gene	SLCO1B1
Drug(s)	Simvastatin
Pathway	https://www.pharmgkb.org/pathway/PA145011109

Purpose
This document summarizes the implementation of pharmacogenomics (PGx) clinical decision support (CDS) for members of the PGRN Translational Pharmacogenomics Project (TPP). This document is intended to facilitate similar implementations at other sites.

Organization And Content	
This document contains several worksheets (tabs), each of which captures information related to a specific aspect of PGx CDS. The information is organized into tables that are intended to enable a high-level comparison across sites. Additional, site-specific information may be provided separately.	
Worksheet Name	**Description**
README	Describes the the content and how to use this document
<gene> Haplotypes	Lists which alleles are tested at each site and their functional interpretation
<gene> Diplotypes	Reports how many of each diplotype were observed at each site
<drug> - Phenotypes	Translations for each site from diplotype to drug-specific phenotype
<drug> - Pretest CDS	High-level description of CDS that fires before a patient genotype is known or when a genotype test result is obtained
<drug> - Results Notif	Summarizes how patients and providers are notified of test results
<drug> - Posttest CDS	High-level description of CDS that fires after a patient genotype is known
Value Sets	Lists the consensus terms and definitions used in this document

How To Use This Document

The data on the Haplotypes and Diplotypes tabs provides background information about the genetic lab tests that are available at each site and the number of times each diplotype was observed. This may help sites considering new PGx CDS implementations as they consider the scope of their implementation.

The Phenotypes tab serves as the primary entry point into the genotype-to-phenotype-to-CDS translation process. The information in this worksheet can be used to inform decisions about how a given diplotype might be translated into a clinical phenotype.

The CDS tabs summarize the CDS implementation at each site for a given phenotype. The phenotypes on this tab will tie directly to those listed on the Phenotypes tabs. Due to the complex nature of CDS implementations, only high-level descriptions are provided. Additional data may be available separately.

Project Sites

PGRN Group	Medical Center	Principal Investigators
PAAR	University of Chicago	Mark Ratain, MD, Nancy J. Cox, Ph.D., M. Eileen Dolan, Ph.D
PAAR4Kids	St. Jude Children's Research Hospital	Mary V. Relling, PharmD
PAPI-2	University of Maryland, Baltimore, School o	Alan R. Shuldiner, MD
PAT	Vanderbilt University Medical Center	Dan M. Roden, MD
PEAR	University of Florida	Julie A. Johnson, PharmD
PharmGKB	Stanford University School of Medicine	Russ B. Altman, MD, PhD and Teri E. Klein, PhD
PHAT	Brigham and Women's Hospital/Harvard	Scott Weiss, MD, MS and Kelan Tantisira, MD, MPH
PHONT	Mayo Clinic	Robert R. Freimuth, PhD
PPII	Mayo Clinic	Richard Weinshilboum, MD, Liewei Wang, MD, PhD
XGEN	Ohio State University	Peter Embi, MD

Questions And Feedback

This document was created by the PGRN TPP Data Standardization Work Group (Robert Freimuth, PhD, Chair)
Questions and feedback can be directed to PharmGKB at http://www.pharmgkb.org/submit/startFeedback.action

SLCO1B1

Haplotypes SLCO1B1*1a - *14 were extracted from PMID:11477075 Table 1b, and mapped to rs numbers via Table 3 in PMID:21245207. *15 is from PMID:12130747. *16 is from PMID:12811365. *17 - *21 are from PMID:15226675. *22-36 are from PMID:22147369. See SLCO1B1_haplotypes tab for rsID mappings.

Genotype Test Status. The table shows which haplotype alleles are tested and reported at each site.

Valid values for testing status: Y, N (see the "Value Sets" tab)

Note: Some haplotypes may be tested but not reported (indicated as N in the table)

*Note: The *1 haplotype is inferred based on the absence of variants at interrogated sites. Assays that do not distinguish between *1A and *1B will report *1.*

	Genotype Test Status					
Haplotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
*1	Y					
*1A		Y			N	N
*1B		Y			N	N
*1C		N			N	N
*2		Y			N	N
*3		Y			N	N
*4		Y			N	N
*5	Y	Y			Y	Y
*6		Y			N	N
*7		Y			N	N
*8		Y			N	N
*9		Y			N	N
*10		Y			N	N
*11		Y			N	N
*12		Y			N	N
*13		Y			N	N
*14		Y			N	N
*15		Y			N	N
*16		Y			N	N
*17		Y			N	N
*18		Y			N	N
*19		N			N	N
*20		N			N	N
*21		Y			N	N
*22		N			N	N
*23		N			N	N
*24		N			N	N
*25		N			N	N
*26		N			N	N
*27		N			N	N
*28		N			N	N
*29		N			N	N
*30		N			N	N
*31		Y			N	N
*32		N			N	N
*33		N			N	N
*34		N			N	N
*35		N			N	N
*36		N			N	N
Platform	Sequenom	Affymetrix DMET Plus, supplemented with CYP2D6 copy number assay	Illumina ADME VeraCode	Life Technologies ViiA 7	PCR 5'-Nuclease End-Point Allelic Discrimination Analysis	Affymetrix DMET Plus

Functional Interpretation. The table shows the functional interpretation of each allele.

Valid values for functional interpretation: see the Value Sets tab

Haplotypes that are not assayed (see above) should have blank interpretations

Note: This table may be omitted for some genes (e.g., HLA-B)

*Note: The *1 haplotype is inferred based on the absence of variants at interrogated sites. Assays that do not distinguish between *1A and *1B will report *1.*

	Functional Interpretation					
Haplotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
*1	Normal				Normal	Normal
*1A		Normal				
*1B		Normal				
*1C						
*2		Indeterminate				
*3		Indeterminate				
*4		Indeterminate				
*5	Decreased	Decreased			Decreased	Decreased
*6		Indeterminate				
*7		Indeterminate				
*8		Indeterminate				
*9		Indeterminate				
*10		Indeterminate				
*11		Indeterminate				
*12		Indeterminate				
*13		Indeterminate				
*14		Indeterminate				
*15		Decreased				
*16		Indeterminate				
*17		Decreased				
*18		Indeterminate				
*19						
*20						
*21		Indeterminate				
*22						
*23						
*24						
*25						
*26						
*27						
*28						
*29						
*30						
*31		Decreased				
*32						
*33						
*34						
*35						
*36						

SLCO1B1

Diplotype Counts. The number of samples observed with each diplotype is shown.
It is anticipated that these counts will be updated approximately once per year
Counts for diplotypes that were assayed but not observed should be reported as 0 (zero), whereas counts for diplotypes that were not assayed should be left blank.

Note: The list of diplotypes shown in this table has been restricted to only those that have been observed by the reporting sites.
Note: The *5 allele is defined by rs4149056, but this variant is also present in the *15 and *17 alleles. Assays that detect only *5 will include patients that carry the *15 or *17 alleles.

			Diplotype Counts						
Haplotype1	Haplotype2	Diplotype	PAAR (U Chicago) as of 2/23/2015	PAAR4Kids (St. Jude) as of 05/11/2015	PAT (Vanderbilt) as of	PEAR (U FL) as of	PPII (Mayo Clinic) as of 2//2/2015	XGEN (OSU) as of 2/10/2015	
*1	*1	*1/*1	549				809	149	This section is used if the assay DOES NOT distinguish between *1A and *1B
*1	*2	*1/*2							
*1	*3	*1/*3							
*1	*4	*1/*4							
*1	*5	*1/*5	153				300	57	
*1	*6	*1/*6							
*1	*7	*1/*7							
*1	*8	*1/*8							
*1	*9	*1/*9							
*1	*10	*1/*10							
*1	*11	*1/*11							
*1	*12	*1/*12							
*1	*13	*1/*13							
*1	*14	*1/*14							
*1	*15	*1/*15							
*1	*16	*1/*16							
*1	*17	*1/*17							
*1	*18	*1/*18							
*1	*21	*1/*21							
*1A	*1A	*1A/*1A		467					‡ Due to technological limitations of the genotyping test, it is not possible to distinguish between the diplotypes of *1A/*15 and *1B/*5. The DMET chip cannot distinguish which chromosome the SNPs are on.Unlike TPMT, all of the diplotypes could be oberserved and it is not possible t speculate on the diplotype that might actually be carried by the patient.
*1A	*1B	*1A/*1B		463					
*1A	*2	*1A/*2		0					
*1A	*3	*1A/*3		0					
*1A	*4	*1A/*4		0					
*1A	*5	*1A/*5		49					
*1A	*6	*1A/*6		0					
*1A	*7	*1A/*7		0					
*1A	*8	*1A/*8		0					
*1A	*9	*1A/*9		0					
*1A	*10	*1A/*10		0					
*1A	*11	*1A/*11		0					
*1A	*12	*1A/*12		0					
*1A	*13	*1A/*13		0					
		*1A/*14,*1B/*4		254					
*1A	*14	*1A/*14							
		*1A/*15,*1B/*5‡		194					
*1A	*15	*1A/*15		0					
*1A	*16	*1A/*16		0					
*1A	*17	*1A/*17							
		*1A/*17,*5/*21		26					
*1A	*18	*1A/*18		0					
*1A	*21	*1A/*21		62					
*1A	*31	*1A/*31		0					
*1B	*1B	*1B/*1B		462					
*1B	*2	*1B/*2		0					
*1B	*3	*1B/*3		0					
*1B	*4	*1B/*4							
*1B	*5	*1B/*5							
*1B	*6	*1B/*6		0					
*1B	*7	*1B/*7		0					
*1B	*8	*1B/*8		0					
*1B	*9	*1B/*9		14					
*1B	*10	*1B/*10		0					
*1B	*11	*1B/*11		0					
*1B	*12	*1B/*12		0					
*1B	*13	*1B/*13		0					
*1B	*14	*1B/*14		119					
*1B	*15	*1B/*15		53					
*1B	*16	*1B/*16		0					
*1B	*17	*1B/*17							
		*1B/*17,*15/*21		20					
*1B	*18	*1B/*18		0					
*1B	*21	*1B/*21		28					
*1B	*31	*1B/*31		48					

Haplotype1	Haplotype2	Diplotype	PAAR (U Chicago) as of 2/23/2015	PAAR4Kids (St. Jude) as of 05/11/2015	PAT (Vanderbilt) as of	PEAR (U FL) as of	PPII (Mayo Clinic) as of 2//2/2015	XGEN (OSU) as of 2/10/2015
*2	*2	*2/*2		0				
*2	*3	*2/*3		0				
*2	*4	*2/*4		0				
*2	*5	*2/*5		0				
*2	*6	*2/*6		0				
*2	*7	*2/*7		0				
*2	*8	*2/*8		0				
*2	*9	*2/*9		0				
*2	*10	*2/*10		0				
*2	*11	*2/*11		0				
*2	*12	*2/*12		0				
*2	*13	*2/*13		0				
*2	*14	*2/*14		0				
*2	*15	*2/*15		0				
*2	*16	*2/*16		0				
*2	*17	*2/*17		0				
*2	*18	*2/*18		0				
*2	*21	*2/*21		0				
*2	*31	*2/*31		0				
*3	*3	*3/*3		0				
*3	*4	*3/*4		0				
*3	*5	*3/*5		0				
*3	*6	*3/*6		0				
*3	*7	*3/*7		0				
*3	*8	*3/*8		0				
*3	*9	*3/*9		0				
*3	*10	*3/*10		0				
*3	*11	*3/*11		0				
*3	*12	*3/*12		0				
*3	*13	*3/*13		0				
*3	*14	*3/*14		0				
*3	*15	*3/*15		0				
*3	*16	*3/*16		0				
*3	*17	*3/*17		0				
*3	*18	*3/*18		0				
*3	*21	*3/*21		0				
*3	*31	*3/*31		0				
*4	*4	*4/*4		0				
*4	*5	*4/*5		0				
*4	*6	*4/*6		0				
*4	*7	*4/*7		0				
*4	*8	*4/*8		0				
*4	*9	*4/*9		0				
*4	*10	*4/*10		0				
*4	*11	*4/*11		0				
*4	*12	*4/*12		0				
*4	*13	*4/*13		0				
*4	*14	*4/*14		0				
*4	*15	*4/*15						
		*4/*15,*5/*14		19				
*4	*16	*4/*16		0				
*4	*17	*4/*17		0				
*4	*18	*4/*18		0				
*4	*21	*4/*21		0				
*4	*31	*4/*31		0				
*5	*5	*5/*5	15	1			33	2
*5	*6	*5/*6		0				
*5	*7	*5/*7		0				
*5	*8	*5/*8		0				
*5	*9	*5/*9		0				
*5	*10	*5/*10		0				
*5	*11	*5/*11		0				
*5	*12	*5/*12		0				
*5	*13	*5/*13		0				
*5	*14	*5/*14						
*5	*15	*5/*15		0				
*5	*16	*5/*16		0				
*5	*17	*5/*17		1				
*5	*18	*5/*18		0				
*5	*21	*5/*21						
*5	*31	*5/*31		0				

Haplotype1	Haplotype2	Diplotype	PAAR (U Chicago) as of 2/23/2015	PAAR4Kids (St. Jude) as of 05/11/2015	PAT (Vanderbilt) as of	PEAR (U FL) as of	PPII (Mayo Clinic) as of 2//2/2015	XGEN (OSU) as of 2/10/2015
*6	*6	*6/*6		0				
*6	*7	*6/*7		0				
*6	*8	*6/*8		0				
*6	*9	*6/*9		0				
*6	*10	*6/*10		0				
*6	*11	*6/*11		0				
*6	*12	*6/*12		0				
*6	*13	*6/*13		0				
*6	*14	*6/*14		0				
*6	*15	*6/*15		0				
*6	*16	*6/*16		0				
*6	*17	*6/*17		0				
*6	*18	*6/*18		0				
*6	*21	*6/*21		0				
*6	*31	*6/*31		0				
*7	*7	*7/*7		0				
*7	*8	*7/*8		0				
*7	*9	*7/*9		0				
*7	*10	*7/*10		0				
*7	*11	*7/*11		0				
*7	*12	*7/*12		0				
*7	*13	*7/*13		0				
*7	*14	*7/*14		0				
*7	*15	*7/*15		0				
*7	*16	*7/*16		0				
*7	*17	*7/*17		0				
*7	*18	*7/*18		0				
*7	*21	*7/*21		0				
*7	*31	*7/*31		0				
*8	*8	*8/*8		0				
*8	*9	*8/*9		0				
*8	*10	*8/*10		0				
*8	*11	*8/*11		0				
*8	*12	*8/*12		0				
*8	*13	*8/*13		0				
*8	*14	*8/*14		0				
*8	*15	*8/*15		0				
*8	*16	*8/*16		0				
*8	*17	*8/*17		0				
*8	*18	*8/*18		0				
*8	*21	*8/*21		0				
*8	*31	*8/*31		0				
*9	*9	*9/*9		0				
*9	*10	*9/*10		0				
*9	*11	*9/*11		0				
*9	*12	*9/*12		0				
*9	*13	*9/*13		0				
*9	*14	*9/*14		0				
*9	*15	*9/*15		0				
*9	*16	*9/*16		0				
*9	*17	*9/*17		0				
*9	*18	*9/*18		0				
*9	*21	*9/*21		0				
*9	*31	*9/*31		0				
*10	*10	*10/*10		0				
*10	*11	*10/*11		0				
*10	*12	*10/*12		0				
*10	*13	*10/*13		0				
*10	*14	*10/*14		0				
*10	*15	*10/*15		0				
*10	*16	*10/*16		0				
*10	*17	*10/*17		0				
*10	*18	*10/*18		0				
*10	*21	*10/*21		0				
*10	*31	*10/*31		0				
*11	*11	*11/*11		0				
*11	*12	*11/*12		0				
*11	*13	*11/*13		0				
*11	*14	*11/*14		0				
*11	*15	*11/*15		0				
*11	*16	*11/*16		0				
*11	*17	*11/*17		0				
*11	*18	*11/*18		0				
*11	*21	*11/*21		0				
*11	*31	*11/*31		0				
*12	*12	*12/*12		0				
*12	*13	*12/*13		0				
*12	*14	*12/*14		0				
*12	*15	*12/*15		0				
*12	*16	*12/*16		0				
*12	*17	*12/*17		0				
*12	*18	*12/*18		0				
*12	*21	*12/*21		0				
*12	*31	*12/*31		0				

Haplotype1	Haplotype2	Diplotype	PAAR (U Chicago) as of 2/23/2015	PAAR4Kids (St. Jude) as of 05/11/2015	PAT (Vanderbilt) as of	PEAR (U FL) as of	PPII (Mayo Clinic) as of 2//2/2015	XGEN (OSU) as of 2/10/2015
*13	*13	*13/*13		0				
*13	*14	*13/*14		0				
*13	*15	*13/*15		0				
*13	*16	*13/*16		0				
*13	*17	*13/*17		0				
*13	*18	*13/*18		0				
*13	*21	*13/*21		0				
*13	*31	*13/*31		0				
*14	*14	*14/*14		37				
*14	*15	*14/*15		54				
*14	*16	*14/*16		0				
*14	*17	*14/*17		3				
*14	*18	*14/*18		0				
*14	*21	*14/*21		10				
*14	*31	*14/*31		0				
*15	*15	*15/*15		14				
*15	*16	*15/*16		0				
*15	*17	*15/*17		8				
*15	*18	*15/*18		0				
*15	*21	*15/*21						
*15	*31	*15/*31		0				
*16	*16	*16/*16		0				
*16	*17	*16/*17		0				
*16	*18	*16/*18		0				
*16	*21	*16/*21		0				
*16	*31	*16/*31		0				
*17	*17	*17/*17		0				
*17	*18	*17/*18		0				
*17	*21	*17/*21		1				
*17	*31	*17/*31		0				
*18	*18	*18/*18		0				
*18	*21	*18/*21		0				
*18	*31	*18/*31		0				
*21	*21	*21/*21		2				
*21	*31	*21/*31		0				
*31	*31	*31/*31		0				
*1	Unchar Variant	*1/Unchar Variant						
*1A	Unchar Variant	*1A/Unchar Variant						
*1B	Unchar Variant	*1B/Unchar Variant						
*2	Unchar Variant	*2/Unchar Variant						
*3	Unchar Variant	*3/Unchar Variant						
*4	Unchar Variant	*4/Unchar Variant						
*5	Unchar Variant	*5/Unchar Variant						
*6	Unchar Variant	*6/Unchar Variant						
*7	Unchar Variant	*7/Unchar Variant						
*8	Unchar Variant	*8/Unchar Variant						
*9	Unchar Variant	*9/Unchar Variant						
*10	Unchar Variant	*10/Unchar Variant						
*11	Unchar Variant	*11/Unchar Variant						
*12	Unchar Variant	*12/Unchar Variant						
*13	Unchar Variant	*13/Unchar Variant						
*14	Unchar Variant	*14/Unchar Variant						
*15	Unchar Variant	*15/Unchar Variant						
*16	Unchar Variant	*16/Unchar Variant						
*17	Unchar Variant	*17/Unchar Variant						
*18	Unchar Variant	*18/Unchar Variant						
*21	Unchar Variant	*21/Unchar Variant						
		Ambiguous call						
		No call	19	3				
		Totals	736	2412	0	0	1142	208

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Drug-Specific Phenotypes. The interpreted phenotype is shown for each diplotype that is possible, based on the known alleles for this gene.
Note: Diplotype phenotypes may be site-specific (differences between sites are acceptable)
Note: The values for phenotype are specified on the "value sets" tab. Diplotypes that are not tested should be left blank.

	Phenotypes for Simvastatin						
Diplotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**	
*1/*1	Normal/High				Normal/High	Normal/High	This section is used if the assay DOES NOT distinguish between *1A and *1B
*1/*2							
*1/*3							
*1/*4							
*1/*5	Intermediate				Intermediate	Intermediate	
*1/*6							
*1/*7							
*1/*8							
*1/*9							
*1/*10							
*1/*11							
*1/*12							
*1/*13							
*1/*14							
*1/*15							
*1/*16							
*1/*17							
*1/*18							
*1/*21							
*1A/*1A		Normal/High					This section is used if the assay DOES distinguish between *1A and *1B
*1A/*1B		Normal/High					
*1A/*2		Indeterminate					
*1A/*3		Indeterminate					
*1A/*4		Indeterminate					
*1A/*5		Intermediate					
*1A/*6		Indeterminate					
*1A/*7		Indeterminate					
*1A/*8		Indeterminate					
*1A/*9		Indeterminate					
*1A/*10		Indeterminate					
*1A/*11		Indeterminate					
*1A/*12		Indeterminate					
*1A/*13		Indeterminate					
*1A/*14		Indeterminate					
*1A/*15		Intermediate					
*1A/*16		Indeterminate					
*1A/*17		Indeterminate					
*1A/*18		Indeterminate					
*1A/*21		Indeterminate					
*1B/*1B		Normal/High					
*1B/*2		Indeterminate					
*1B/*3		Indeterminate					
*1B/*4		Indeterminate					
*1B/*5		Intermediate					
*1B/*6		Indeterminate					
*1B/*7		Indeterminate					
*1B/*8		Indeterminate					
*1B/*9		Indeterminate					
*1B/*10		Indeterminate					
*1B/*11		Indeterminate					
*1B/*12		Indeterminate					
*1B/*13		Indeterminate					
*1B/*14		Indeterminate					
*1B/*15		Intermediate					
*1B/*16		Indeterminate					
*1B/*17		Indeterminate					
*1B/*18		Indeterminate					
*1B/*21		Indeterminate					
*1B/*31		Intermediate					

Diplotype	PAAR (U Chicago)	PAAR4Kids (St. Jude)	PAT (Vanderbilt)	PEAR (U FL)	PPII (Mayo Clinic)	XGEN (OSU)
*2/*2		Indeterminate				
*2/*3		Indeterminate				
*2/*4		Indeterminate				
*2/*5		Indeterminate				
*2/*6		Indeterminate				
*2/*7		Indeterminate				
*2/*8		Indeterminate				
*2/*9		Indeterminate				
*2/*10		Indeterminate				
*2/*11		Indeterminate				
*2/*12		Indeterminate				
*2/*13		Indeterminate				
*2/*14		Indeterminate				
*2/*15		Indeterminate				
*2/*16		Indeterminate				
*2/*17		Indeterminate				
*2/*18		Indeterminate				
*2/*21		Indeterminate				
*3/*3		Indeterminate				
*3/*4		Indeterminate				
*3/*5		Indeterminate				
*3/*6		Indeterminate				
*3/*7		Indeterminate				
*3/*8		Indeterminate				
*3/*9		Indeterminate				
*3/*10		Indeterminate				
*3/*11		Indeterminate				
*3/*12		Indeterminate				
*3/*13		Indeterminate				
*3/*14		Indeterminate				
*3/*15		Indeterminate				
*3/*16		Indeterminate				
*3/*17		Indeterminate				
*3/*18		Indeterminate				
*3/*21		Indeterminate				
*4/*4		Indeterminate				
*4/*5		Indeterminate				
*4/*6		Indeterminate				
*4/*7		Indeterminate				
*4/*8		Indeterminate				
*4/*9		Indeterminate				
*4/*10		Indeterminate				
*4/*11		Indeterminate				
*4/*12		Indeterminate				
*4/*13		Indeterminate				
*4/*14		Indeterminate				
*4/*15		Indeterminate				
*4/*16		Indeterminate				
*4/*17		Indeterminate				
*4/*18		Indeterminate				
*4/*21		Indeterminate				
*5/*5	Low/Absent	Low/Absent			Low/Absent	Low/Absent
*5/*6		Indeterminate				
*5/*7		Indeterminate				
*5/*8		Indeterminate				
*5/*9		Indeterminate				
*5/*10		Indeterminate				
*5/*11		Indeterminate				
*5/*12		Indeterminate				
*5/*13		Indeterminate				
*5/*14		Indeterminate				
*5/*15		Low/Absent				
*5/*16		Indeterminate				
*5/*17		Low/Absent				
*5/*18		Indeterminate				
*5/*21		Indeterminate				
*6/*6		Indeterminate				
*6/*7		Indeterminate				
*6/*8		Indeterminate				
*6/*9		Indeterminate				
*6/*10		Indeterminate				
*6/*11		Indeterminate				
*6/*12		Indeterminate				
*6/*13		Indeterminate				
*6/*14		Indeterminate				
*6/*15		Indeterminate				
*6/*16		Indeterminate				
*6/*17		Indeterminate				
*6/*18		Indeterminate				
*6/*21		Indeterminate				

Diplotype	PAAR (U Chicago)	PAAR4Kids (St. Jude)	PAT (Vanderbilt)	PEAR (U FL)	PPII (Mayo Clinic)	XGEN (OSU)
*7/*7		Indeterminate				
*7/*8		Indeterminate				
*7/*9		Indeterminate				
*7/*10		Indeterminate				
*7/*11		Indeterminate				
*7/*12		Indeterminate				
*7/*13		Indeterminate				
*7/*14		Indeterminate				
*7/*15		Indeterminate				
*7/*16		Indeterminate				
*7/*17		Indeterminate				
*7/*18		Indeterminate				
*7/*21		Indeterminate				
*8/*8		Indeterminate				
*8/*9		Indeterminate				
*8/*10		Indeterminate				
*8/*11		Indeterminate				
*8/*12		Indeterminate				
*8/*13		Indeterminate				
*8/*14		Indeterminate				
*8/*15		Indeterminate				
*8/*16		Indeterminate				
*8/*17		Indeterminate				
*8/*18		Indeterminate				
*8/*21		Indeterminate				
*9/*9		Indeterminate				
*9/*10		Indeterminate				
*9/*11		Indeterminate				
*9/*12		Indeterminate				
*9/*13		Indeterminate				
*9/*14		Indeterminate				
*9/*15		Indeterminate				
*9/*16		Indeterminate				
*9/*17		Indeterminate				
*9/*18		Indeterminate				
*9/*21		Indeterminate				
*10/*10		Indeterminate				
*10/*11		Indeterminate				
*10/*12		Indeterminate				
*10/*13		Indeterminate				
*10/*14		Indeterminate				
*10/*15		Indeterminate				
*10/*16		Indeterminate				
*10/*17		Indeterminate				
*10/*18		Indeterminate				
*10/*21		Indeterminate				
*11/*11		Indeterminate				
*11/*12		Indeterminate				
*11/*13		Indeterminate				
*11/*14		Indeterminate				
*11/*15		Indeterminate				
*11/*16		Indeterminate				
*11/*17		Indeterminate				
*11/*18		Indeterminate				
*11/*21		Indeterminate				
*12/*12		Indeterminate				
*12/*13		Indeterminate				
*12/*14		Indeterminate				
*12/*15		Indeterminate				
*12/*16		Indeterminate				
*12/*17		Indeterminate				
*12/*18		Indeterminate				
*12/*21		Indeterminate				
*13/*13		Indeterminate				
*13/*14		Indeterminate				
*13/*15		Indeterminate				
*13/*16		Indeterminate				
*13/*17		Indeterminate				
*13/*18		Indeterminate				
*13/*21		Indeterminate				
*14/*14		Indeterminate				
*14/*15		Indeterminate				
*14/*16		Indeterminate				
*14/*17		Indeterminate				
*14/*18		Indeterminate				
*14/*21		Indeterminate				
*15/*15		Low/Absent				
*15/*16		Indeterminate				
*15/*17		Low/Absent				
*15/*18		Indeterminate				
*15/*21		Indeterminate				
*16/*16		Indeterminate				
*16/*17		Indeterminate				
*16/*18		Indeterminate				
*16/*21		Indeterminate				
*17/*17		Low/Absent				
*17/*18		Indeterminate				
*17/*21		Indeterminate				
*18/*18		Indeterminate				
*18/*21		Indeterminate				
*21/*21		Indeterminate				

Diplotype	PAAR (U Chicago)	PAAR4Kids (St. Jude)	PAT (Vanderbilt)	PEAR (U FL)	PPII (Mayo Clinic)	XGEN (OSU)
*1A/Unchar Variant		Indeterminate				
*1B/Unchar Variant		Indeterminate				
*2/Unchar Variant		Indeterminate				
*3/Unchar Variant		Indeterminate				
*4/Unchar Variant		Indeterminate				
*5/Unchar Variant		Indeterminate				
*6/Unchar Variant		Indeterminate				
*7/Unchar Variant		Indeterminate				
*8/Unchar Variant		Indeterminate				
*9/Unchar Variant		Indeterminate				
*10/Unchar Variant		Indeterminate				
*11/Unchar Variant		Indeterminate				
*12/Unchar Variant		Indeterminate				
*13/Unchar Variant		Indeterminate				
*14/Unchar Variant		Indeterminate				
*15/Unchar Variant		Indeterminate				
*16/Unchar Variant		Indeterminate				
*17/Unchar Variant		Indeterminate				
*18/Unchar Variant		Indeterminate				
*21/Unchar Variant		Indeterminate				

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CDS Summaries
Additional detail may be provided through site-specific workflow diagrams and supplementary information
Note: If CDS has not been implemented for this scenario, the cells are left empty

Trigger Context	The context in which the rule fires. Examples: inpatient order, outpatient order, predictive score
CDS Type	The type of CDS provided. See the Value Sets tab for examples.
Pre-Order Genetic Testing	Indicates whether genetic testing is required prior to the drug order. See the Value Sets tab.

Drug is ordered or indicated but no genotype result is on file						
	PAAR (U Chicago)	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
Trigger Context	Preemptive	All orders			Order confirmation screen if test results are on file	Research protocol
CDS Type	Passive	Active				Passive
Pre-Order Genetic Testing	Recommended	Recommended				Required

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Summary of Results Notification
Additional detail may be provided through site-specific workflow diagrams and supplementary information
Note: If a phenotype term is not in use, the cell will be left blank.

Phenotypes correspond to the value set. See the "Value Sets" tab for details.
Types of notification are defined on the "Value Sets" tab.

Provider notification of a genotype test result						
Phenotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
Normal/High	Passive	Passive			Passive	
Intermediate	Passive	Active + Passive			Active + Passive	
Low/Absent	Passive	Active + Passive			Active + Passive	
Indeterminate		Passive				
Possible Intermed.		Active + Passive				
Possible Low/Absent		Active + Passive				

Patient notification of a genotype test result						
Phenotype	**PAAR (U Chicago)**	**PAAR4Kids (St. Jude)**	**PAT (Vanderbilt)**	**PEAR (U FL)**	**PPII (Mayo Clinic)**	**XGEN (OSU)**
Normal/High	None	Active			Passive	
Intermediate	None	Active			Passive	
Low/Absent	None	Active			Passive	
Indeterminate		None				
Possible Intermed.		Active				
Possible Low/Absent		Active				

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CDS Summaries
Additional detail may be provided through site-specific workflow diagrams and supplementary information

Note: See the Value Sets tab for examples of CDS Type.

Simvastatin

Simvastatin is ordered, genotype test result is on file												
	PAAR (U Chicago)		PAAR4Kids (St. Jude)		PAT (Vanderbilt)		PEAR (U FL)		PPII (Mayo Clinic)		XGEN (OSU)	
Phenotype	**CDS Type**	**Recommendation(s)**	**CDS Type**	**Recommendation(s)**	**CDS Type**	**Recommendation(s)**	**CDS Type**	**Recommendation(s)**	**CDS Type**	**Recommendation(s)**	**CDS Type**	**Recommendation(s)**
Normal/High	Passive	No change	Passive	No change					Passive	No recommendation	Passive	No recommendation
Intermediate	Passive	Drug or dose change	Active + Passive	Drug or dose change					Active + Passive	Drug or dose change	Active + Passive	No recommendation
Low/Absent	Passive	Drug or dose change	Active + Passive	Drug or dose change					Active + Passive	Drug or dose change	Active + Passive	No recommendation
Indeterminate			Passive	No recommendation								
Possible Intermed.			Active + Passive	Drug or dose change								
Possible Low/Absent			Active + Passive	Drug or dose change								

Value Sets

Genotype Test Status		
Abbreviation	**Term**	**Definition**
Y	Yes	Allele is tested
N	No	Allele is not tested

Functional Interpretation		
Abbreviation	**Term**	**Definition**
	Increased	The allele is associated with increased activity/function relative to the reference (wild-type) allele.
	Normal	The allele is associated with activity/function similar to the reference (wild-type) allele.
	Decreased	The allele is associated with decreased activity/function relative to the reference (wild-type) allele.
	Undetectable	The allele is associated with no detectable activity/function relative to the reference (wild-type) allele.
	Varies by substrate	The impact of the allele on activity/function varies by substrate. Details will be provided separately.
	Indeterminate	The data for the activity/function associated with the allele are ambiguous, conflicting, or otherwise difficult to interpret.
	Uncharacterized	The activity/function associated with the allele is not yet characterized.

Note: CPIC is in the process of developing standardized phenotype terms. The terms below may change in the future based on those activities.

Phenotype Terms for TPMT + Thiopurines			
Abbreviation	**Term**	**Definition***	**Examples of Diplotypes***
Normal/High	Normal (high) Activity	Metabolism that is usually exhibited by the plurality of tested patients	
Intermediate	Intermediate Activity	Enzyme function is decreased compared to patients with high activity and increased compared to patients with low or absent activity	
Low/Absent	Low or Absent Activity	Little or no enzyme function	
Indeterminate	Indeterminate	Based on genetic test results, the metabolism status cannot be assigned	
Possible Intermed.	Possible Intermediate Activity	Genetic test results that indicate the patient might have intermediate TPMT activity	
Possible Low/Absent	Possible Low or Absent Activity	Genetic test results that indicate the patient might have little or no enzyme function	

** The rules given in the definition may have site-specific exceptions*

Value Sets

CDS Type			
Abbreviation	**Term**	**Definition**	**Examples**
	Active	Specific messages are sent, but are not stored in the EHR for future (passive) reference	Popup alert, phone call, USPS letter, verbal communication
	Active + Passive	Specific messages are sent, information is also available on demand.	Email, EHR inbox; examples include those listed for "Active" and "Passive"
	Passive	No specific messages are sent, information is available on demand.	Test results and interpretations/consults via the EHR or patient portal

Pre-Order Genetic Testing		
Abbreviation	**Term**	**Definition**
	Recommended	Testing is recommended prior to drug order
	Required	Testing is required prior to drug order, institutional hard stop

Provider Notification			
Abbreviation	**Term**	**Definition**	**Examples**
	Active + Passive	Specific messages are sent, information is also available on demand.	Verbal communication, email, EHR inbox; examples include those listed for "Active" and "Passive"
	Passive	No specific messages are sent, information is available on demand.	Test results and interpretations/consults via the EHR

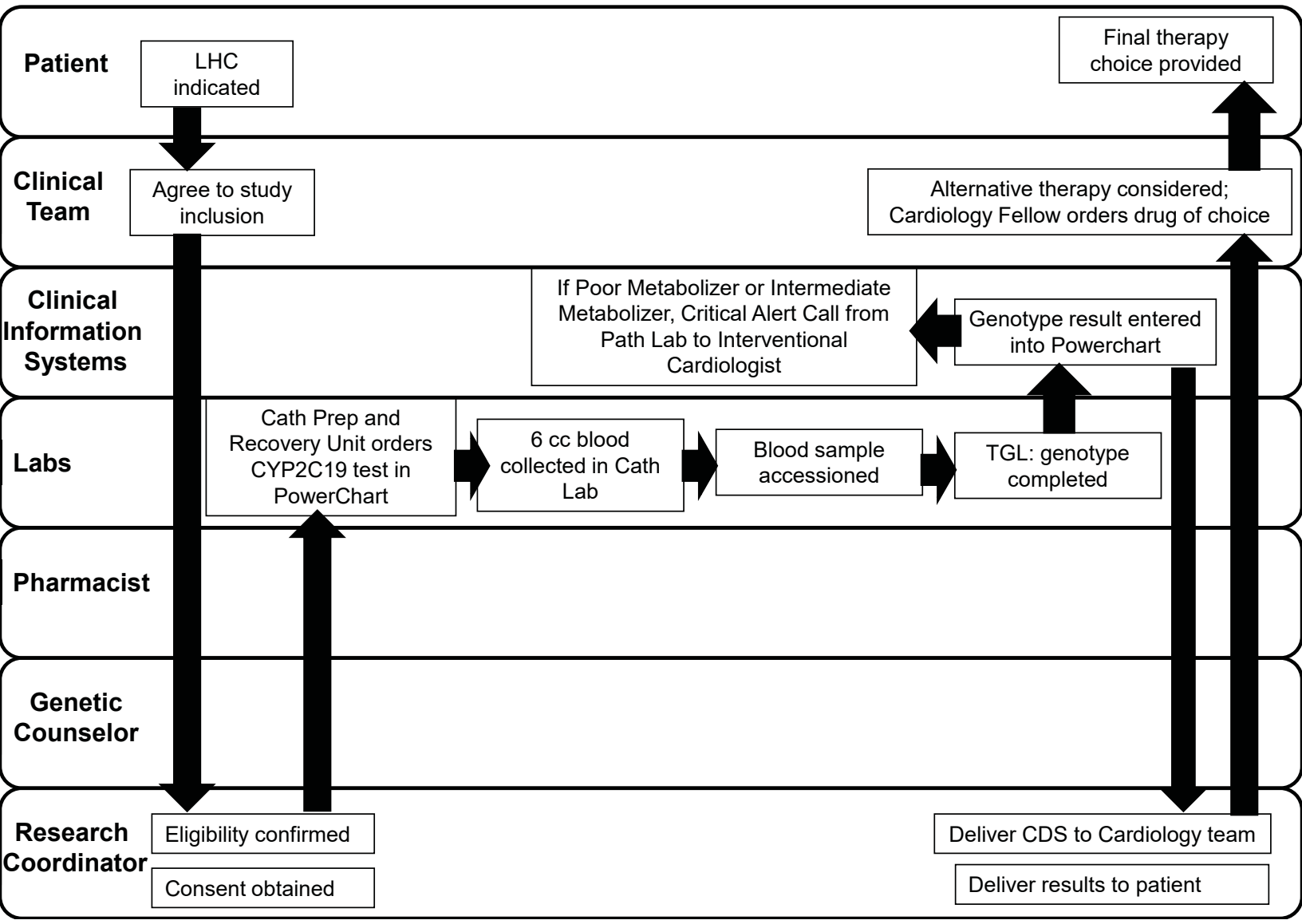
Patient Notification			
Abbreviation	**Term**	**Definition**	**Examples**
	Active	Specific messages are sent, but are not stored in the EHR for future (passive) reference	Verbal communication, phone call, USPS letter
	Passive	No specific messages are sent, information is available on demand.	Test results and interpretations/consults via the patient portal
	Active + Passive	Specific messages are sent, information is also available on demand.	Email; examples include those listed for "Active" and "Passive"
	None	Patient is not notified of the results.	

Post-Test Recommendation		
Abbreviation	**Term**	**Definition**
	No recommendation	No recommendation is provided
	No change	Follow normal prescription practices
	Drug change	Recommend use of a different drug
	Dose change	Recommend a dose adjustment for this drug
	Drug or dose change	Recommend a change in drug and/or dose (the particular recommendation may be explicit or left to clinical judgement)

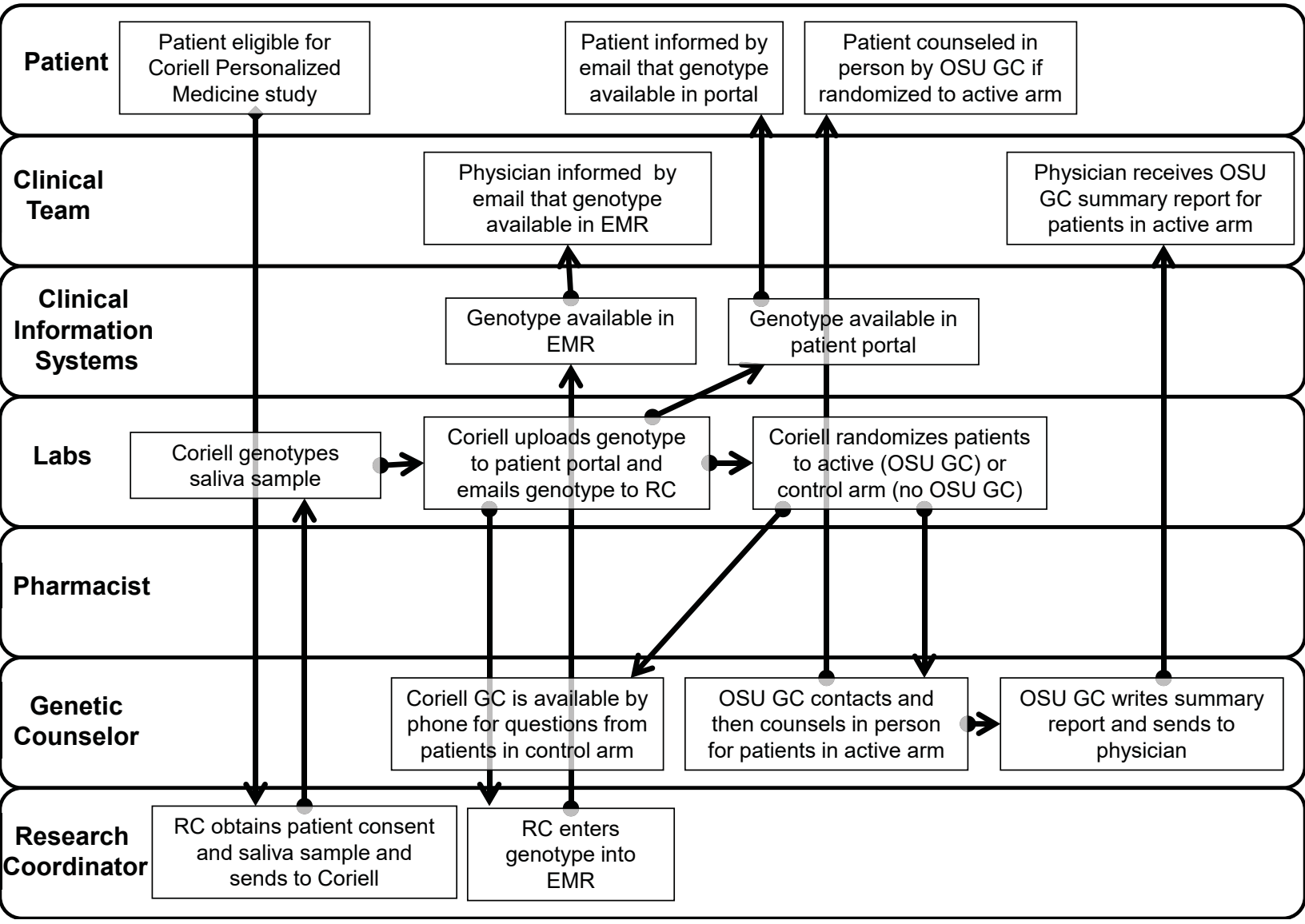
Supplementary File 4

Workflow Diagrams

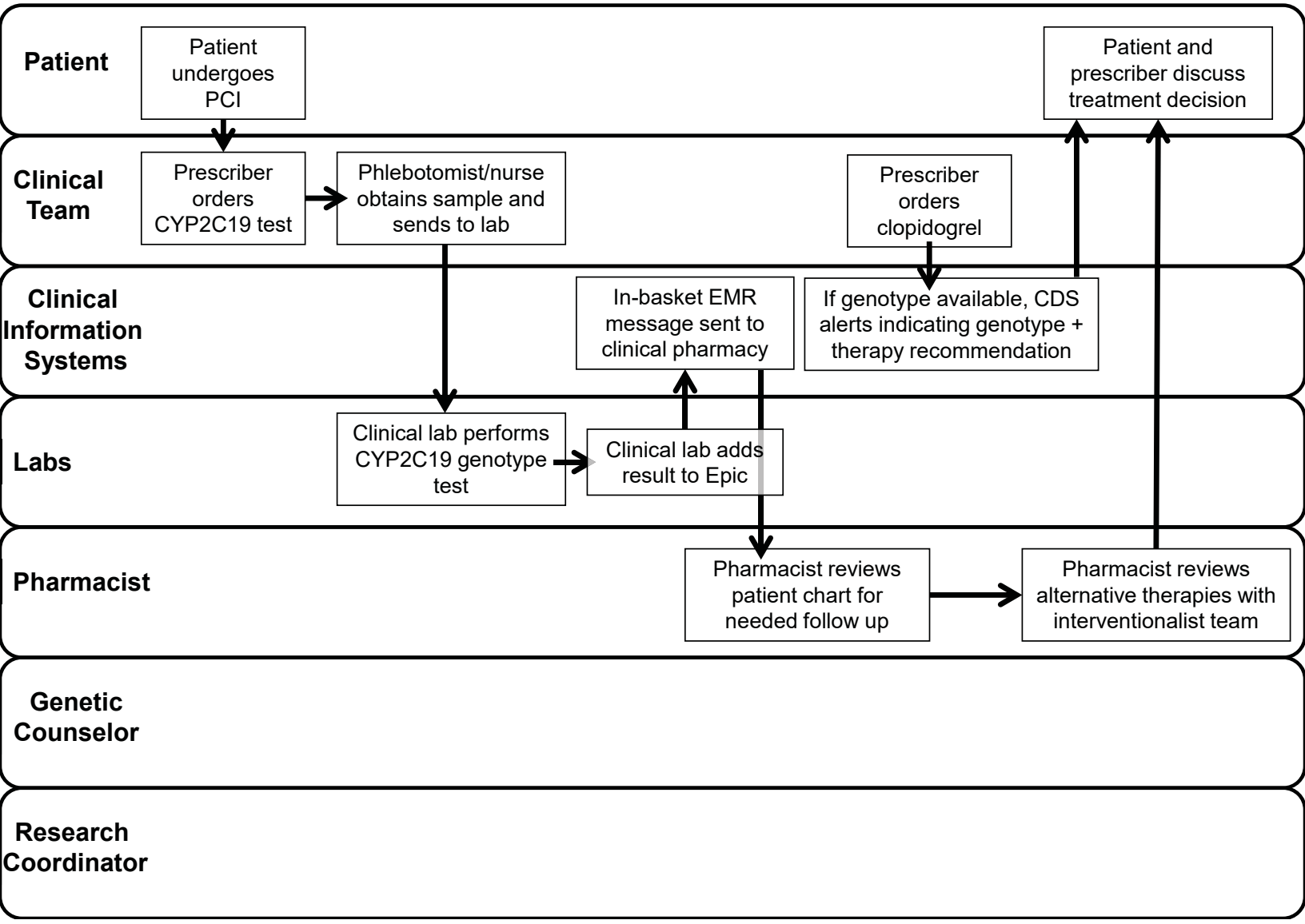
SITE: University of Maryland **GENE/DRUG:** CYP2C19/clopidogrel **TYPE:** Research



SITE: Ohio State University **GENE/DRUG:** CYP2C19/clopidogrel **TYPE:** Research



SITE: University of Florida **GENE/DRUG:** CYP2C19/clopidogrel **TYPE:** Clinical



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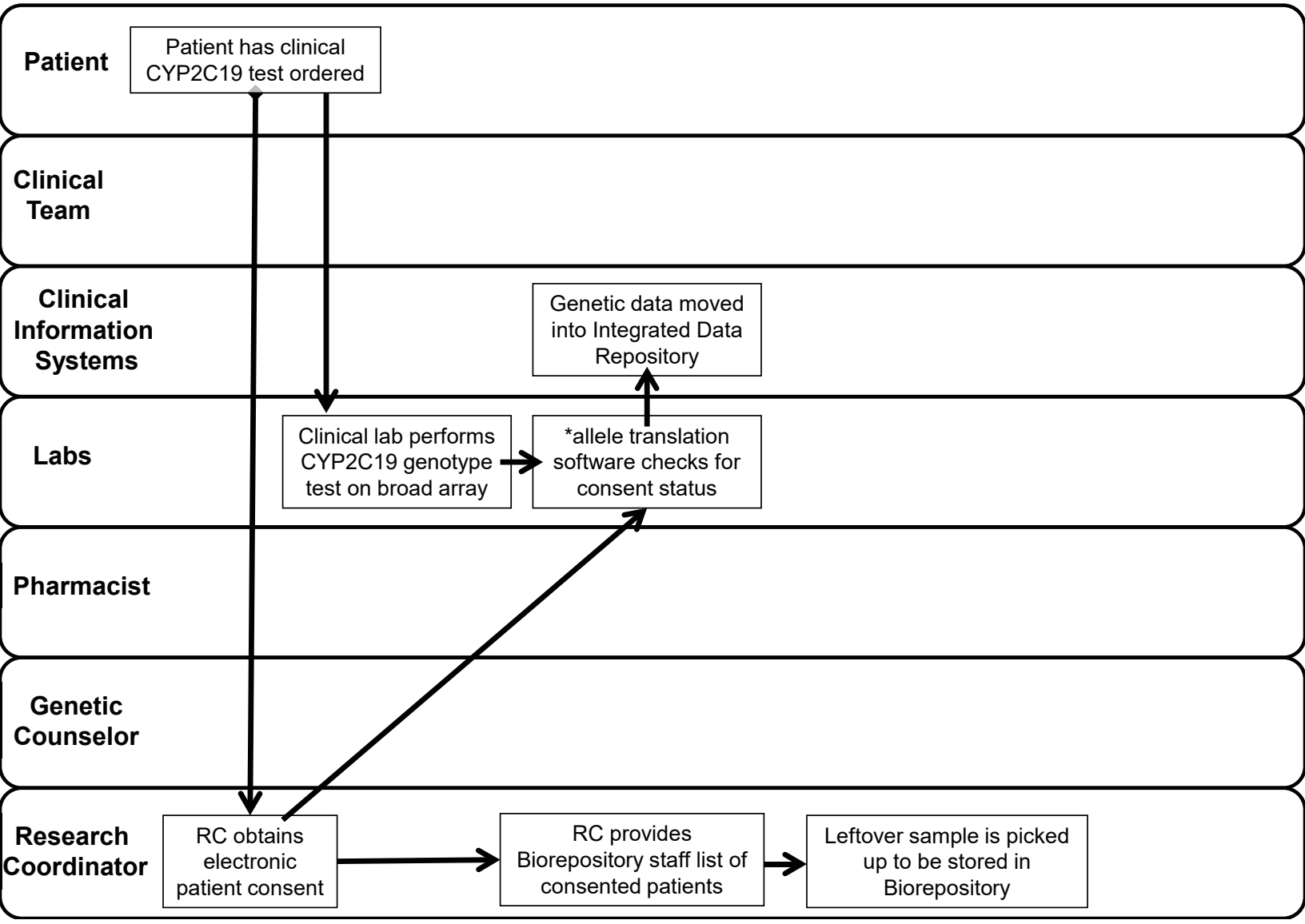
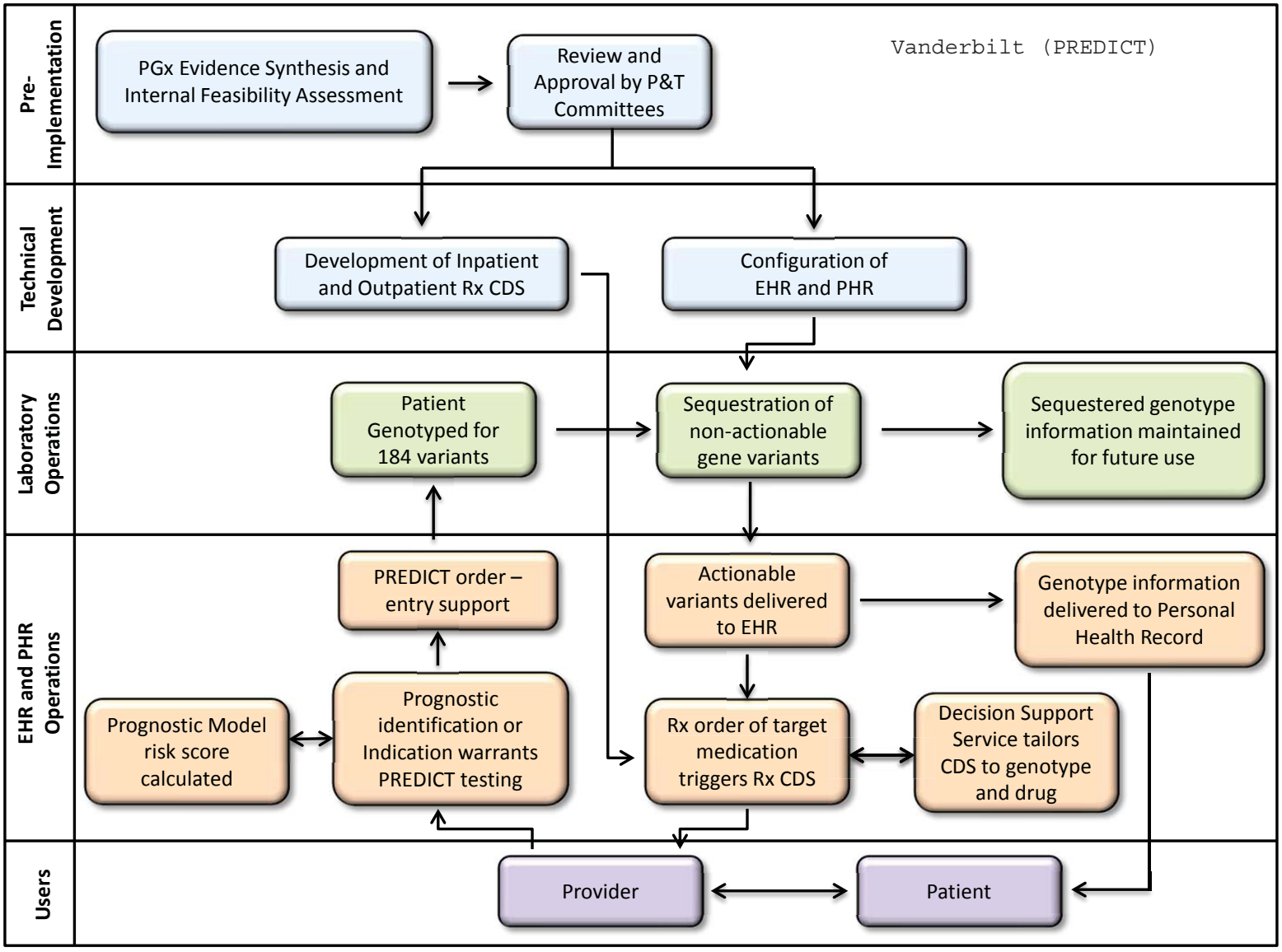
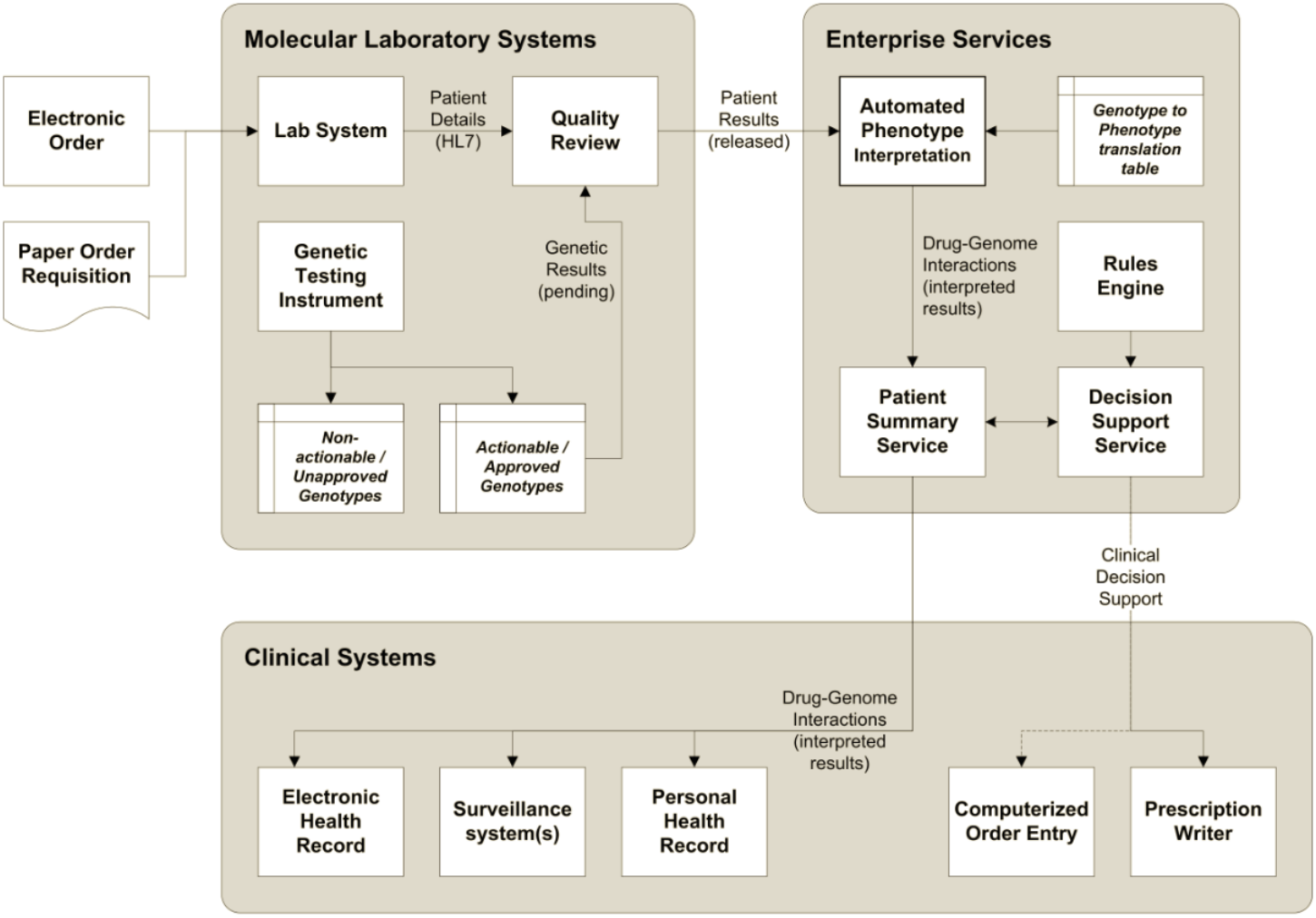




Peterson JF et al. Genet Med. 2013 Oct;15(10):833-841.

Vanderbilt (PREDICT)

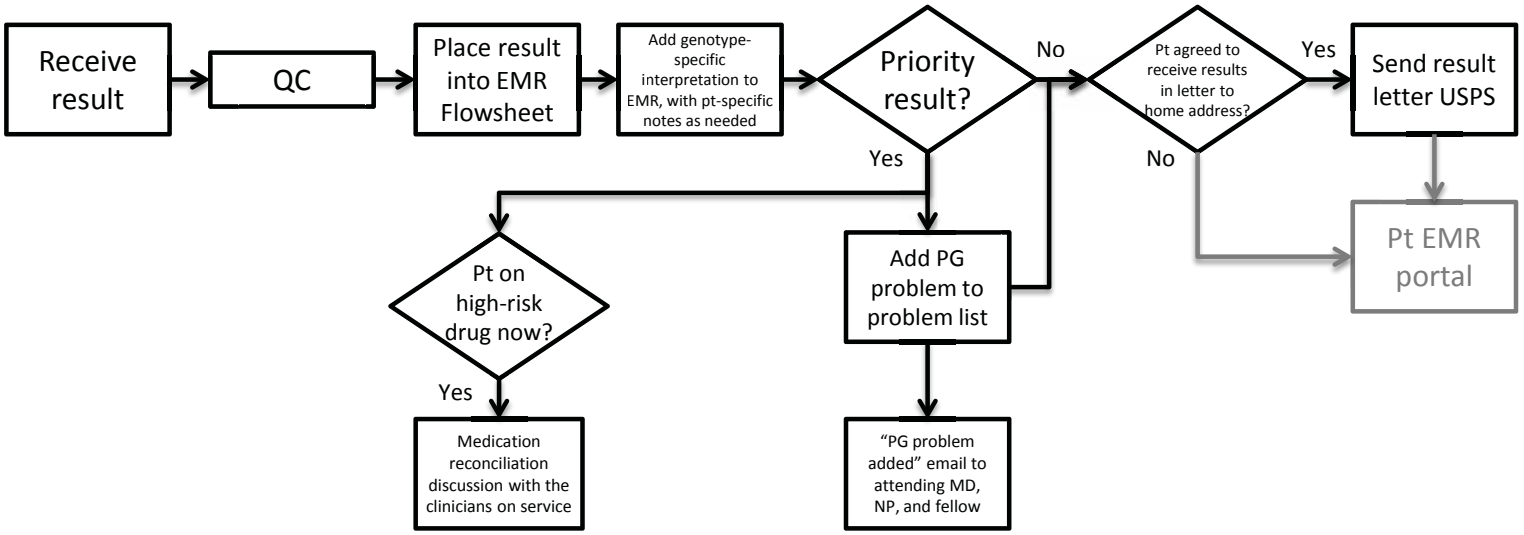
PREDICT Result Reporting Architecture



Peterson JF et al. Genet Med. 2013 Oct;15(10):833-841.

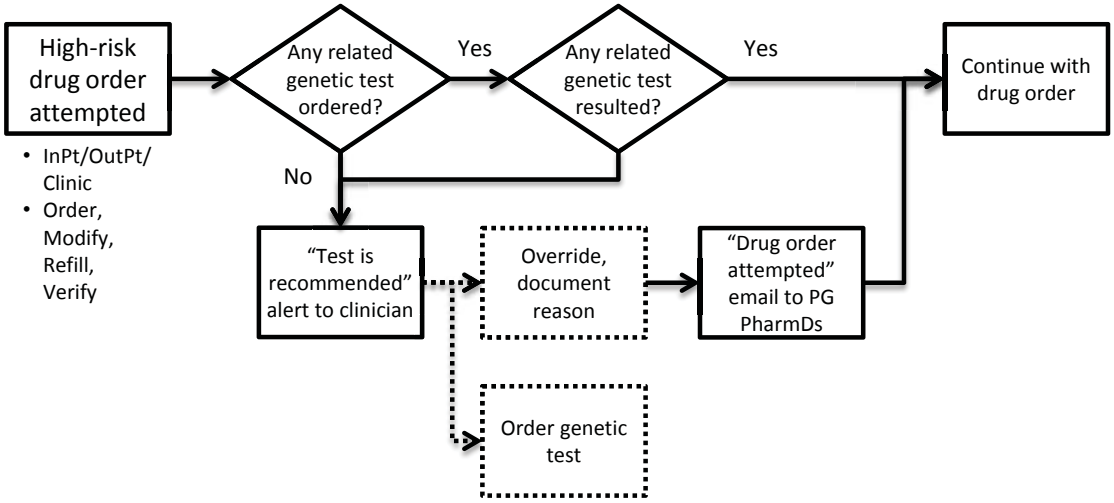
St. Jude

All PGen Results Interpreted

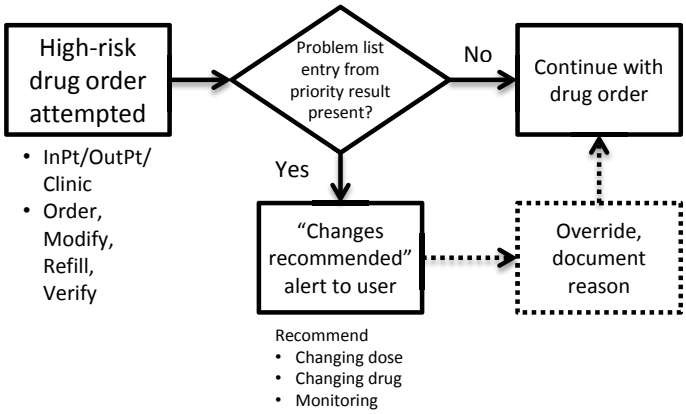


St. Jude

Pre-test: drug order attempt, no genetic tests; general case



Post-test: drug order attempt, genetic results available; general case



Advertised lines of support information

- Contact PG PharmD; phone, email
- www.stjude.org/pg4kds; www.pharmgkb.org
- PG Formulary (linked from hospital formulary)
- Contact PK research nurses; phone, email