Appendix A: Cohort A and Cohort B Learning Objectives (six-credit point unit)

LO1. Demonstrate an understanding of the body as a complex adaptive biological system in relation to biochemistry/biotechnology

LO2. Apply a sound understanding of the scientific basis of the use of medicines

LO3. Apply appropriate numeracy skills to the solution of pharmacy problems

LO4. Demonstrate an understanding of the pharmacological mechanisms of action and the properties drugs display as biologically active molecules in living systems

LO5. Demonstrate an understanding of pharmaceutical factors impacting on therapeutic efficacy

LO6. Apply an understanding of basic and applied sciences to the management and solution of pharmaceutical and clinical problems, including metabolism and enzymatic degradation of drugs

LO7. Demonstrate the ability to learn independently and take responsibility for your own learning.

Appendix B: Cohort C Learning Objectives (12-credit point unit)

LO1. Describe pharmacodynamic and pharmacokinetic principles and interpret pharmacodynamic and pharmacokinetic information.

LO2. Calculate relevant pharmacodynamic and pharmacokinetic parameters using appropriate equations.

LO3. Explain how genetic variations can influence the response to medicines and contribute to variability in response between individuals.

LO4. Explain basic reasons for variability in response to medicines in different individuals, including the effects of disease, demographics, genetics and other medicines.

LO5. Apply appropriate numeracy skills to solve pharmaceutical problems.

LO6. Apply knowledge of therapeutic principles to solve and manage pharmaceutical and clinical problems, including those relating to the metabolism and degradation of drugs.

LO7. Apply knowledge of therapeutic principles to communicate and provide appropriate information to patients and other health professionals.

LO8. Demonstrate responsibility for personal and professional development through independent learning and continuous reflection.

Appendix C: Workshop Questions

PHAR2813 Workshop 3

Q3. Which metabolic enzymes have a major impact on the pharmacokinetics of the drugs listed below and what is the clinical impact of particular genetic variants. Name at least one **inhibitor** and **inducer** of the relevant CYP isoform that would require a dose adjustment if co- administered with the named drug.

Drug Name	**CYP enzyme**	**Function of CYP enzyme and clinical effect of genetic variants**	**CYP inhibitor**	**CYP inducer**
Codeine				
Tamoxifen				
Warfarin				
Omeprazole				

Clopidogrel				
Clozapine				

Note: refer to lectures on Pharmacogenomics and drug interactions

Tip: Consider this handy reference: http://medicine.iupui.edu/clinpharm/ddis/main-table

Q6. Read the following cases and using the pharmacogenomics report provided answer the clinical questions [Hint: Access the CPIC website for further details on gene-drug recommendations].

Case 1: Selective Serotonin Reuptake Inhibitors
JC is a 27-year-old Caucasian male who has been diagnosed with obsessive compulsive disorder (OCD). JC was a diagnosed with OCD four years ago and most recently was taking clomipramine. A psychiatrist is now starting to use pharmacogenetic testing and orders a comprehensive panel for each of her patients. You are consulted to interpret the pharmacogenomic testing results as the psychiatrist is wanting to now use paroxetine in JC because he has experienced an adverse drug reaction to clomipramine.

Review the attached pharmacogenomic report and CPIC guidelines for paroxetine to answer the following questions about JC.

a) What is the main clearance pathway for paroxetine (e.g. renal clearance, metabolism)?

b) Based on JC pharmacogenomics, what is the anticipated effect on the clearance and plasma concentrations of paroxetine?

c) What is your recommendation to JC's psychiatrist based on the pharmacogenomic report?

Using the same pharmacogenomics report answer the questions for Case 2.

Case 2: Urate lowering therapy
XL is a 67-year-old East Asian male of Han-Chinese ancestry who has been diagnosed with gout. XL reports experiencing 6 gout flares in the last year and his last serum urate concentration obtained last week was 0.56 umol/L. His general practitioner decides to start him on allopurinol. The general practitioner is now starting to use pharmacogenetic testing and orders a comprehensive panel for each of his patients. You are consulted to interpret the pharmacogenomic testing results as the general practitioner is wanting to know whether allopurinol can be prescribed to XL. The pharmacogenomics report is available, allowing pre-emptive application of the information.

a) Based on XL's pharmacogenomic report what is your recommendation regarding initiation of allopurinol?

The general practitioner explains that XL has a younger brother who is also reporting occasional gout flares. The brother has not been initiated on allopurinol yet.

b) What is your recommendation regarding the need for pharmacogenomic testing for XL's brother?

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REPORT NUMBER-12279	SPECIMEN DETAILS	ORDERED BY
LAST NAME: C	**SPECIMEN TYPE:** Buccal Swab	
FIRST NAME: J	**COLLECTION DATE:** 10/3/2022	
DATE OF BIRTH: 13/2/1983	**RECEIVED DATE:** 12/3/2022	
	REPORT DATE: 14/3/2022	

Test Details

Gene	Genotype	Phenotype	Alleles Tested
CYP2C19	*1/*17	Rapid Metaboliser	*2, *3, *4, *4B, *5, *6, *7, *8, *9, *17
CYP2D6	*4/*4	Poor Metaboliser	*2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14A, *14B, *17, *29, *35, *41
CYP3A5	*3/*3	Poor Metaboliser	*1D, *2, *3, *3B, *3C, *6, *7, *8, *9
CYP3A4	*1/*1	Normal Metaboliser	*1B, *2, *3, *12, *17, *22
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity	-1639G>A
CYP4F2	*1/*1	Normal Function	*2, *3
CYP2C9	*1/*3	Intermediate Metaboliser	*2, *3, *4, *5, *6, *11
CYP2B6	*1/*1	Normal Metaboliser	*6, *9
CYP1A2	*1F/*1F	Normal Metaboliser - Higher Inducibility	*1C, *1D, *1F, *1K, *1L, *1V, *1W
SLCO1B1	521T>C T/T	Normal Function	521T>C, 388A>G
CFTR	R553X/R553X	Negative	Numerous
DPYD	c.[85T>C];[=]	Normal Metaboliser	Numerous
TPMT	*1/*1	Normal Metaboliser	*2, *3A, *3B, *3C, *4
NUDT15	*1/*1	Normal Metaboliser	*2, *3, *4, *5, *6, *7, *8, *9
UGT1A1	*1/*36	Normal Metaboliser	*6, *27, *28, *36, *37, *60, *80
G6PD	A- or A-/A-	Deficient	Numerous

Additional Test Results (added to this original report)

HLA-B*15:02	Positive	HLA-A*31:01	Negative
HLA-B*57:01	Negative		
HLA-B*58:01	Positive		

Limitation: This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Absence of a detectable gene mutation does not rule out the possibility that a patient has different phenotypes due to the presence of an undetected polymorphism or due to other factors such as drug-drug interactions, comorbidities and lifestyle habits.

Methodology: Array based assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.

Disclaimer: The University of Sydney developed the Genotype test. The performance characteristics of this test were determined by The University of Sydney. It has not been cleared or approved by the Therapeutic Goods Administration.

The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

[redacted]

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REPORT NUMBER-12279	SPECIMEN DETAILS	ORDERED BY
LAST NAME: L	**SPECIMEN TYPE:** Buccal Swab	
FIRST NAME: X	**COLLECTION DATE:** 10/3/2022	
DATE OF BIRTH: 10/8/1963	**RECEIVED DATE:** 12/3/2022	
	REPORT DATE: 14/3/2022	

Test Details

Gene	Genotype	Phenotype	Alleles Tested
CYP2C19	*1/*17	**Rapid** Metaboliser	*2, *3, *4, *4B, *5, *6, *7, *8, *9, *17
CYP2D6	*4/*4	**Poor** Metaboliser	*2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14A, *14B, *17, *29, *35, *41
CYP3A5	*3/*3	Poor Metaboliser	*1D, *2, *3, *3B, *3C, *6, *7, *8, *9
CYP3A4	*1/*1	Normal Metaboliser	*1B, *2, *3, *12, *17, *22
VKORC1	-1639G>A G/A	**Intermediate** Warfarin Sensitivity	-1639G>A
CYP4F2	*1/*1	**Normal Function**	*2, *3
CYP2C9	*1/*3	**Intermediate Metaboliser**	*2, *3, *4, *5, *6, *11
CYP2B6	*1/*1	Normal Metaboliser	*6, *9
CYP1A2	*1F/*1F	Normal Metaboliser - Higher Inducibility	*1C, *1D, *1F, *1K, *1L, *1V, *1W
SLCO1B1	521T>C T/T	**Normal** Function	521T>C, 388A>G
CFTR	R553X/R553X	**Negative**	Numerous
DPYD	c.[85T>C];[=]	**Normal Metaboliser**	Numerous
TPMT	*1/*1	**Normal Metaboliser**	*2, *3A, *3B, *3C, *4
NUDT15	*1/*1	**Normal Metaboliser**	*2, *3, *4, *5, *6, *7, *8, *9
UGT1A1	*1/*36	**Normal Metaboliser**	*6, *27, *28, *36, *37, *60, *80
G6PD	A- or A-/A-	**Deficient**	Numerous

Additional Test Results (added to this original report)

HLA-B*15:02	**Positive**	**HLA-A*31:01**	**Negative**
HLA-B*57:01	**Negative**		
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