PHA2022 Drugs in Society

MONASH UNIVERSITY · UNDERGRADUATE · SEMESTER 2, 2026

Full guide + ask Sia about PHA2022

SIDE 1/2 FINAL PRIORITIES · DEFINITIONS · FORMULAS · DECISION RULES · COMPARISONS

EXAM REVISION SHEET

Examination **20%** · **2 h 10 min**

01 · Exam map

COURSE.JSON · BRIEF

Lab 30 | Team 25 | Tests 25 | Exam 20

ASSESSMENT	WEIGHT	FORMAT / STATUS
Laboratory and workshop activities	30%	Exercise component; threshold hurdle
Team assignment	25%	Balanced drug-controversy project
In-semester quizzes and tests	25%	Includes mid-semester test and PeerWise activity
Examination	20%	2 hours 10 minutes; not listed as a separate threshold hurdle

Permitted materials: not confirmed for this offering in the course materials we hold — check the exam instructions on the LMS. *[BRIEF]*

02 · Six-boundary answer

FRONT · FAQ

target + drug → exposure/time → response → bounded decision → evidence + context

Trace every claim across scale changes; each arrow needs evidence.

RECITABLE FRAME

```
Target → concentration → exposure over
time → measured response → evidence
design → bounded drug or social
decision.
```

CATEGORY ERROR	REPAIR
Concentration = dose	Add route, bioavailability, distribution and clearance.
Binding = benefit	Name signalling, endpoint and patient outcome.
Association = cause	Ask design, comparator and alternatives.
Significance = importance	Give magnitude, uncertainty and consequence.
Approval = certainty	Keep indication, population and rare harm bounded.

EXAM TIP *State the observation that would reverse your conclusion: unexpected accumulation, reduced maximum, patient-relevant null result, displaced harm or failed control.*

09 · Laboratory evidence

C6 · PP 1–2

setup/ctl → raw data → estimate ± → bounded

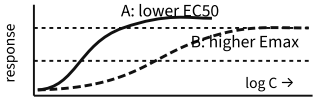
reproduce calculation + claim

Traceability connects setup to inference.

CONTROL / REPEAT	WHAT IT DIAGNOSES
Vehicle / negative	Baseline, solvent and handling effects.

03 · Dose–response dimensions

C1 · PP 1–3



Horizontal position answers potency; vertical maximum answers efficacy.

GRADED MODEL

```
E = Emax × C/(EC50 + C)
EC50 = concentration giving half of
that drug's measured maximum.
```

DIMENSION	READ / INFER	DO NOT INFER
Potency	Concentration or dose needed for a specified effect; horizontal position.	Maximum, safety or therapeutic value.
Efficacy	Achievable response in the defined system; Emax.	Affinity, required dose or toxicity.
Affinity	Binding tendency.	System response where coupling/reserve differ.
Window	Exposure range with desired effect without unacceptable toxicity.	One fixed ratio valid in every patient.

AGONISM AND ANTAGONISM

- ***Full agonist:*** reaches the system's higher maximum. ***Partial agonist:*** lower maximum even at high concentration.
- ***Competitive antagonist:*** in the simplified equilibrium model, surmountable; more agonist restores the maximum and shifts the curve right.
- ***Non-competitive or irreversible effect:*** may reduce the achievable maximum.
- ***Receptor reserve:*** full effect can precede full occupancy; EC50 need not equal a binding-affinity parameter.

CHECK *Name assay, preparation, endpoint, time, units, variability and the rival-mechanism experiment.*

04 · Graded vs quantal

C1

	GRADED	QUANTAL
Observation	Continuous response in a preparation	Individual reaches a defined event: yes/no
Summary	EC50, Emax	ED50 or TD50: half the studied population

graded size → event yes/no → population %

same shape ≠ same unit/inference

Define what each point represents before naming its midpoint.

05 · Exposure over time

C2 · PP 1–2

dose/rt → F + V → CL + t½ → C(t)

input → distribution → elimination

predict peak/trough/mean/time

Parameters answer different questions; do not collapse them into "levels".

PARAMETER	MEANING	WHERE IT BITES
Bioavailability F	Fraction of dose reaching systemic circulation in available form.	Systemic input; oral exposure may fall through absorption or first-pass metabolism.
Apparent V	Amount in body relative to measured plasma concentration.	Distribution and loading requirement; not a literal container.
Clearance CL	Elimination rate proportional to concentration.	Maintenance input and average exposure.
Half-life	Time for amount/concentration to halve under stated kinetics.	Accumulation, washout and time to a new steady state.

LINEAR FIRST-ORDER RELATION

```
t½ ≈ 0.693 × V/CL
If V stable and CL halves: t½ doubles;
same dose rate gives about twice
average steady exposure.
```

CL falls → t½ rises → accum. ↑ → maint. Δ

predict, then choose regimen

Lower clearance changes concentration–time behaviour before the dosing plan.

FIRST ORDER VS ZERO ORDER

FIRST ORDER	ZERO ORDER
Constant fraction removed per unit time; half-life constant if V and CL stable.	Roughly constant amount removed; small dose increases may produce disproportionate accumulation.

REGIMEN DECISIONS

- Loading is driven mainly by target concentration, V and F; maintenance replaces what clearance removes.
- Longer half-life means longer approach to steady state and washout, commonly several half-lives; it does not alone set the eventual mean concentration.
- Interval changes alter peak–trough fluctuation even when average input is similar.
- A concentration needs sampling time, analyte and distribution context; plasma may lag or differ from effect site.

06 · Repeated use

C3 · PP 1–3

drug exposure → adaptation → future use → learned context → response/risk

Pharmacology and learning interact, but each requires its own observation.

TERM	REQUIRED OBSERVATION	CLASSIC WRONG MOVE
Tolerance	Reduced response to same exposure, or more exposure for prior response.	Treating it as one shield across all effects.
Dependence	Withdrawal or impaired function after reduction.	Equating supervised dependence with addiction.
Reinforcement	Consequence increases future behaviour.	Equating it only with pleasure.
Sensitisation	Increased response with repeated exposure.	Assuming it cannot coexist with tolerance to another effect.
Substance-use disorder	Broader pattern of impaired control, priority, risk and consequence.	Inferring it from tolerance or dependence alone.

tol. loss → context Δ → pot. + co → OD risk

stack mechanisms; avoid blame

Changed conditions can amplify response to a remembered dose.

MECHANISMS THAT MUST STAY SEPARATE

- ***Pharmacodynamic tolerance:*** receptor/signalling adaptation. ***Pharmacokinetic:*** faster handling. ***Behavioural:*** learned compensation or changed performance.
- Tolerance is effect-specific: desired effect, impairment and respiratory depression may adapt at different rates; dose escalation can narrow the safety margin.
- Familiar cues may trigger compensatory responses. Unfamiliar context can remove some compensation; abstinence can also lower pharmacological tolerance.
- Rapid delivery can strengthen the behaviour–consequence link and increase peaks and acute harm; compare route with dose, F and time course.

CASE SCAFFOLD

```
Drug effect + time course + learned cue
+ behavioural consequence + adaptation
+ social condition → mechanism-linked
prevention or care.
```

WITHDRAWAL TIMING	BOUNDARY
Short half-life can mean quicker decline and earlier symptoms; a long-acting active metabolite can delay them.	Severity also depends on dose, duration, adaptation and individual condition.

07 · Benefit, harm, society

C4 · PP 1–2

baseline → relative → absolute → decision

population · follow-up · severity

uncertainty · equity · revision

A ratio becomes useful only after baseline and decision context are restored.

RISK LANGUAGE

```
Absolute risk = outcome probability in
a defined population/time.
Relative risk = risk in one group ÷
risk in the comparison group.
```

RR = 2.0 → 1 → 2 /10,000 → severity ±

relative + absolute + context

Repair a dramatic ratio by restoring its absolute and social context.

QUESTION	WHAT A COMPLETE ANSWER STATES
How large?	Relative and absolute change; baseline; confidence/uncertainty.
For whom?	Population represented; subgroups; distribution of benefit and harm.
Caused by exposure?	Design, comparator, confounding by indication/severity/co-use/access/behaviour.
What decision?	Approve, restrict, subsidise, warn, monitor, decriminalise or reduce harm.
What may shift?	Incentives, substitution, purity, stigma, help-seeking, legitimate access, equity.
When revise?	Implementation indicator, equity consequence and pre-stated update observation.

POLICY EVIDENCE

- Randomised trials answer some questions; cohort, case-control, interrupted time-series and natural experiments contribute different evidence when randomisation is infeasible or unethical.
- Before–after comparison can mix policy with trends, publicity, reformulation or simultaneous services. Series designs test level/slope; controlled series adds a comparison.
- Check anticipation, spillover and measurement changes; convergence across designs plus a plausible implementation mechanism strengthens the claim.

HARM REDUCTION AND BALANCE

CONCEPT	DECISION RULE
Harm reduction	Reduce preventable consequence without requiring immediate elimination of all use; judge outcomes, not slogans.
Balance	Represent strong evidence, material benefit/harm, uncertainty and values proportionally; unequal claims need not receive equal time.

08 · Development decisions

C5 · PP 1–3

target+mdl → dose/safe → ctrl eff. → post-M

each stage answers one uncertainty

phase ≠ population/design/outcome

Development is a sequence of stop–go decisions, not guaranteed progress.

STOP–GO QUESTION	IF UNRESOLVED
Target engaged at tolerable exposure?	Refine candidate, exposure or safety evidence.
Model predicts relevant human mechanism?	Choose a model with the missing feature; repetition alone cannot repair poor translation.
Human dose justified?	Add PK, PD, tolerability and exposure matching.
Trial isolates efficacy?	Audit randomisation, concealment, blinding, comparator, attrition and missingness.
Endpoint meaningful?	Measure validated surrogate or direct symptoms, function or survival.
Benefit outweighs harm here?	Bound indication, population, duration, uncertainty and monitoring.

assigned → marker Δ → benefit ? → next RCT

activity ≠ automatic benefit

A causal marker change can coexist with unresolved patient outcomes.

DESIGN DISTINCTIONS

- ***Randomisation*** reduces systematic allocation differences; ***concealment*** prevents foreknowledge; ***blinding*** reduces performance/assessment bias.
- Placebo controls expectations and study procedures when ethical; active comparator asks whether the candidate improves on current care.
- Intention-to-treat preserves assigned groups and estimates assignment under observed adherence/switching. Per-protocol addresses an adherent subset and may reintroduce selection.
- Prespecified primary outcomes protect against selective emphasis; subgroup differences require interaction evidence and often replication.

SURROGATE AND SAFETY BOUNDARIES

OBSERVATION	SUPPORTED CLAIM	NOT YET SUPPORTED
Marker changes in a randomised short trial	Assigned drug caused marker change under trial conditions.	Patients feel, function or survive better if surrogate unvalidated.
Post-market report	Signal requiring investigation.	Incidence rate or proof from raw case count.
Approval	Defined benefit–risk decision for an indication.	Universal superiority or absence of rare harm.

PHA2022 Drugs in Society · Self-test drills

MONASH UNIVERSITY · WORKED PATHS · JUDGEMENT CARDS · CLASSIC TRAPS

Full guide + ask Sia about PHA2022

SIDE 2/2 FOUR APPLICATIONS · WHICH-IS-TRUE · IF X → Y · SHORT-ANSWER FRAMES · EXAM-MORNING PLAN

ACTIVE RECALL

Original study practice · answers shown

10 · Drill 1: potency ≠ efficacy

C1 WORKED

Drug A: 1 µM · max 60 — needed: 50

Drug B: 10 µM · max 100 — needed: 80

Same assay: A sits left but plateaus lower; required response changes the choice.

PROMPT

```
Drug A: EC50 1 µM, Emax 60. Drug B:
EC50 10 µM, Emax 100. Compare at
required responses of 50 and 80 units.
```

STEP	ANSWER PATH
1 · Endpoint	Same measured assay response and conditions.
2 · Horizontal	A has lower EC50 → A is more potent.
3 · Vertical	B has higher Emax → B has greater efficacy.
4 · Required effect	At 50, either may work in this assay. At 80, A cannot reach the target regardless of concentration.
5 · Boundary	No safer/preferable clinical choice without exposure, adverse-response and patient evidence.

WHICH IS TRUE?

CLAIM	VERDICT	WHY
A is "stronger".	Reject	Dimension unnamed.
A is more potent.	True	Lower concentration reaches half its own maximum.
A is more efficacious.	False	Its maximum is lower.
B must be safer.	False	Safety is a different curve/evidence set.

SAY ALOUD *"A is more potent in this assay; B has greater efficacy; preference needs required effect, exposure and harm evidence."*

11 · Curve judgement cards

C1

right shift → max same/↓? → test mech.

curve first; receptor story second

Mechanism must discriminate the observed shift and maximum.

IF YOU SEE…	DO THIS
Right shift, same Emax	Consider simplified competitive antagonism; test surmountability.
Lower maximum	Consider partial agonism or non-competitive/irreversible effect.
Fitted EC50 outside tested range	Do not trust extra decimals; add discriminating concentrations.
Two sigmoids	Ask whether points are graded magnitudes or quantal proportions.

12 · Drill 2: clearance halves

C2 WORKED

CL × ½ → t½ × 2 → mean ×2 → maint. Δ

linear · V stable · F stable

longer to steady state · monitor

Direction first: reduced elimination raises exposure before a regimen is chosen.

PROMPT

```
A drug is mostly cleared unchanged by
the kidney. Total clearance halves;
dose, interval, V and F are initially
unchanged.
```

STEP	ANSWER PATH
1 · Exposure	At the same dose rate, average steady exposure approximately doubles under linear kinetics.
2 · Half-life	t½ ≈ 0.693V/CL → with stable V, half-life doubles.
3 · Time	Accumulation increases; new steady state and washout take longer.
4 · Maintenance	Reduce maintenance input, extend interval, monitor or consider an alternative; interval may widen peak–trough variation.
5 · Loading	May be less affected if target concentration, V and F are unchanged.

WHICH IS TRUE?

CLAIM	VERDICT	REPAIR
"Half-life fell because elimination slowed."	False	Lower CL lengthens half-life if V stable.
"Halve every dose immediately."	Incomplete	Name target exposure, interval, monitoring and assumptions.
"Loading and maintenance are identical decisions."	False	Loading relates mainly to target C, V, F; maintenance to elimination.
"Longer half-life sets higher final mean C."	False alone	Mean depends on input relative to CL.

INTERACTION CLASSIFIER

input | clearance | free/total | response

process → C–time → effect

Not every interaction is metabolism; identify the changed link.

CHANGED PROCESS	PREDICT FIRST
Absorption	Input and exposure profile.
Enzyme inhibition/induction	Clearance and concentration–time course.
Protein-binding change	Free versus total concentration.
Two sedatives, different targets	Response can rise without changing either plasma concentration.

13 · Drill 3: post-abstinence risk

C3 WORKED

tolerance has fallen | former dose | unfamiliar context | potency? + sedative

stacked effects → OD risk ↑

Several changed conditions can amplify response to a remembered dose.

PROMPT

```
A person resumes a former opioid dose
after abstinence, in an unfamiliar
setting, with another sedating drug.
```

STEP	ANSWER PATH
1 · Adaptation	Tolerance to respiratory depression may have fallen; the former dose can produce a larger effect.
2 · Context	Unfamiliar cues may provide less conditioned compensation.
3 · Exposure	Product strength and bioavailability may be uncertain.
4 · Co-use	Sedatives can produce additive or synergistic respiratory impairment.
5 · Response	Prioritise evidence-based overdose prevention and care; do not substitute blame for mechanism.

WHICH IS TRUE?

STATEMENT	VERDICT / REASON
Tolerance protects equally against every drug effect.	False: it is effect-specific and develops/recedes at different rates.
Dependence proves a substance-use disorder.	False: it can occur under supervised use; disorder requires a broader behavioural pattern.
Negative reinforcement can sustain use without pleasure.	True: relief of withdrawal or distress can increase future use.
Sensitisation and tolerance cannot coexist.	False: different measured effects may move in opposite directions.

IF YOU SEE X → DO Y

same dose: ↓ | stop → W/D | behav. + harm

tolerance ≠ dependence ≠ disorder

Different observations support different repeated-use concepts.

X	Y
Same dose, smaller response	Call tolerance only after ruling out exposure/product/assay change.
Symptoms after stopping	Identify dependence; connect timing to PK and adaptation.
Faster route	Predict tighter behaviour–consequence timing, higher peaks and acute harm.
Social factor	Name the pathway: exposure, reinforcement, vulnerability, care or recovery opportunity.

14 · Drill 4: repair the headline

C4 WORKED

RR 2.0 · rare severe outcome

1→2 /10k | +1 /10,000 | RR +100%

all true; not the whole decision

Relative doubling and a small absolute increase must be communicated together.

PROMPT

```
A cohort reports RR 2.0 for a severe
outcome: estimated annual risk rises
from 1 to 2 per 10,000 exposed people.
```

STEP	ANSWER PATH
1 · Baseline	1 case per 10,000 people per year in the comparison frame.
2 · Absolute	Increase = 1 per 10,000 per year in the studied population.
3 · Relative	RR 2.0 = relative doubling.
4 · Meaning	Severity can make a small absolute increase important; ratio alone does not show burden.
5 · Boundary	Add population represented, number exposed, uncertainty and potential confounding.

TWO BASELINE WORLDS

SAME 50% RELATIVE REDUCTION	BASELINE 40%	BASELINE 2%
New risk	20%	1%
Absolute reduction	20 percentage points	1 percentage point
Lesson	Same relative effect; radically different population consequence.	

POLICY JUDGEMENT CARD

decision | mech. | metric+eq. | revise if…

map intended + displaced outcomes

A recommendation is incomplete until implementation and revision are specified.

IF YOU SEE…	DO THIS
Dramatic ratio	Restore baseline, absolute change, time and severity.
Average benefit	Inspect subgroup benefit, harm and representation.
Raw safety reports	Separate signal detection from incidence; investigate reporting and exposure counts.
Simple before–after policy graph	Ask about secular trend, co-interventions, anticipation, spillover and measurement change.
"Balanced" presentation	Weight evidence proportionally; separate empirical, value and implementation disagreement.

FINISH *Name implementation indicator, equity consequence and the observation that would trigger revision.*

15 · Surrogate + translation drills

C5–C6 WORKED

random → marker ↓ → outcome ?

next: valid surrogate or direct outcome

Causal biomarker activity can coexist with unresolved clinical benefit.

PROMPT A

```
A randomised short trial shows a
substantial biomarker improvement.
Symptoms and function are unmeasured;
the biomarker is not validated for this
drug class.
```

WHAT FOLLOWS	WHAT DOES NOT
Randomisation strengthens the claim that assignment changed the marker under trial conditions.	Patients feel, function or survive better.
Activity may support target engagement and dose selection if adherence and measurement are sound.	The biological pathway necessarily improves a patient-relevant outcome.
Next trial: defensible comparator, direct outcome or validated surrogate, adequate duration and harms.	Universal benefit or safety from statistical significance alone.

cell C/t → body expos → dose + PK → benefit:risk

each scale adds unit + uncertainty

A cell concentration cannot be relabelled as a human dose.

PROMPT B

```
Cells remain viable after 10 µM
exposure for four hours; a team calls a
10-µM human dose safe.
```

SCALE	REPAIR
Assay	Supports viability for one concentration, duration, cell type and measurement.
Units	Micromolar is concentration, not administered amount.
Exposure	Human dose must produce exposure through absorption, distribution, metabolism and excretion.
Safety	Add organ exposure, toxicology, metabolites, off-target effects, longer duration, clinical observation and rare outcomes.
Rewrite	"Bounded preclinical cell-viability evidence; human safety not established."

17 · Exam-morning plan

STUDY STRATEGY

1. Retrieve the six-link trace from memory: target, concentration, exposure, response, evidence, decision.
2. Redraw the potency/efficacy axes and write t½ ≈ 0.693V/CL.
3. Say the five category repairs: concentration ≠ dose; binding ≠ benefit; association ≠ cause; significance ≠ importance; cell viability ≠ human safety.

16 · MCQ trap matrix

C1–C6

setup/ctl → raw data → estimate ± → bounded

audit each option through the chain

Reproducibility carries the answer from observation to bounded conclusion.

WHICH STATEMENT IS TRUE?	CORRECT CONTRAST
Lower EC50 proves greater clinical benefit.	False: potency is horizontal; benefit also needs attainable response, exposure and outcomes.
Competitive antagonism must reduce Emax.	False: simplified surmountable model shifts right with maximum restored.
Lower clearance raises steady exposure at the same dose rate.	True under linear kinetics.
Dependence and addiction are synonyms.	False: adaptation after reduction is not the broader disorder pattern.
RR alone communicates population burden.	False: restore baseline and absolute risk.
A changed surrogate necessarily improves function.	False unless validated for context/intervention or confirmed directly.
Technical repeats increase biological n.	False: they estimate within-unit measurement variation.
A positive control proves the drug caused the response.	False: it shows the assay can produce/detect a known response.
Approval removes uncertainty about rare harm.	False: post-market evidence continues benefit–risk evaluation.

SHORT-ANSWER FRAMES

QUESTION	HIGH-YIELD SENTENCE ORDER
Compare drugs	System/endpoint → horizontal potency → vertical efficacy → required effect → exposure/harm boundary.
Adjust dose	Changed parameter → direction of C–time → peak/trough/mean/timing → loading vs maintenance → monitor.
Repeated-use case	Effect-specific adaptation → abstinence/time → cue/context → route/co-use → mechanism-linked response.
Evaluate claim	Exact observation → design/comparator → magnitude + uncertainty → translation limit → next discriminating evidence.
Policy recommendation	Decision/population/time → relative + absolute outcomes → distribution/equity → implementation pathway → review trigger.

exact obs. → design/ctrl → effect ± → bound clm.

another reader can reconstruct

why the answer follows

The handoff test catches missing links and overclaiming.