Practice Test questions:

1. What are the two areas of toxicology that a regulatory toxicologist must integrate in order to determine the "safety" of any chemical?

2. List routes of exposure in the order of most rapid response.

3. What is the standard dosing frequency for an **acute** dosage strategy? What is the standard dosing frequency for a **subacute** dosage strategy?

4. Why is elimination half-life critical in developing a dosing strategy?

1. Plot the Probit Dose-Response Curves for Chemicals A and B. (Hint: -1 SD units = 16% response; -2 units =4.5 % response; +1 SD= 84 %; +2 SD = 95.5%)

Dose (mg/kg)	%Responding	N.E.D.	Probit
A			
10	7	-1.8	
25	20	-0.8	
50	50	0	
75	67	+0.5	
100	84	+1	
B			
100	13	-1.25	
300	42	-0.25	
600	67	+0.5	
1000	84	+1.0	

2. Which chemical is more potent? Explain why?

If the ED50 for chemical A is 10 mg/kg, what is the Therapeutic Index for Chemical A and would it be classified as "safe"?

1. Describe two types of antagonism and provide examples of each.

2. List at least 2 assumptions necessary in deriving a dose-response relationship

4. What's the difference between an allergic reaction and an idiosyncratic response??

2. What's the difference between a toxin and toxicant (one sentence)?

3. What is one factor influencing transport of a toxicant to a target? What is one factor that influences transport of a toxicant away from the target?

4. What is the definition of an electrophile (one sentence)? Provide at least two examples.

Bonus: What are 3 types of reactions that an ultimate toxicant may have with the target molecule?

1. Draw a dose-response curve where chemical A is more efficacious and potent than chemical B.

3 and 4. Draw the pathway of spontaneous lipid peroxidation following H-abstraction.

2. How is superoxide anion *completely* detoxified (list all reactions)??

3. What are the 4 mechanisms of calcium elimination from the cell??

4. Acetaminophen inhibits the Ca^{2+}-ATPase in the cell membrane. Provide 2 mechanisms of how this covalent binding episode may alter cellular maintenance.

What are three repair mechanisms for damaged DNA??

1. What is the descriptive term that would define a mass of chemical in a volume of air that killed 50% of a population of rats following exposure by inhalation??

2. What are the two main classification of dose-response relationships--what's the difference??

3. Provide one mechanism (and the agent responsible) for the disruption of ATP synthesis.

4. What are the differences between necrosis and apoptosis?

2. Define Dispositional Tolerance and provide one example.

3. What are the three general mechanisms for free radical formation?

4. Chloroform does not appear to directly bind to DNA, but has been shown to be carcinogenic. Provide a detailed mechanism for carcinogenesis for this non-genotoxic chemical.

Provide the Henderson Hasselbach equation for a weak acid.

2.What are the three general mechanisms of Dysregulation of Gene expression??

3. What are two mechanisms of lipid repair (list all cofactors)??

4. Where would you expect a weak acid with a Pka of 3 to be absorbed in the GI tract? explain why.

What are three defenses of the blood-brain barrier??

1. Give an example of how a chemical may penetrate the blood brain barrier.

2. List three long-term storage depots in the body

3 and 4. Outline the etiology of three side reactions that may occur during tissue injury.

what are the differences between microsomal and cytolsoic epoxide hydrolases?

1. What is the difference between TGF α and TGF β??

2. Briefly describe the sequalae of fibrosis

3. What are the 4 sources of Fecal Excreta??

4. If you were given a mouse liver and told to measure cytosolic and microsomal epoxide hydrolase activity and differentiate the two activities, how would carry out this task??

What are three enzymes that oxidize ethanol?

1. Describe 4 general mechanisms of disrupting ATP synthesis

2. Describe 4 general mechanisms of causing sustained elevation of cytosolic Ca^{2+}.

3. 2,6 Dinitrobenzene is a rat liver tumorigen, yet it is rapidly glucuronidated in the liver of rats. Explain how this compound may cause liver injury when it is rapidly eliminated from the liver.

4. What are the two possible pathways of biotransformation for menadione in a typical hepatocyte?

What are 3 differences between FMO and P450?

In each region of the lung, describe the various "defenses" present that try to prevent absorption or particle deposition.

Why does a weak acid usually get absorbed in the stomach?

How does MPTP exert its toxicity? Describe pathways of bioactivation and the enzymes as well as cofactors involved.

What is the most abundant P450 isoform in the human liver?

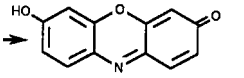
Provide examples of 4 reactions catalyzed by cytochrome P450

Provide an example of a flavin-containing monooxygenase-catalyzed oxygenation forming an electrophilic metabolite.

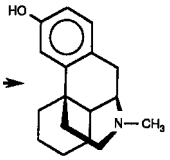
What is the function of p53?

What are three general mechanisms for increasing P450 activity or content?

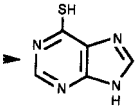
Provide the starting compounds and specifc isoforms responsible for catalysis:



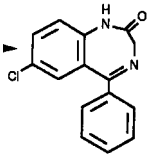
Resorufin



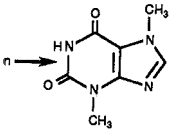
Dextrorphan



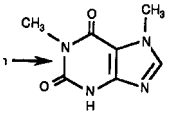
6-Mercaptopurine



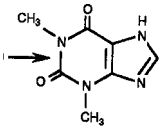
Nordiazepam



Theobromine



Paraxanthine



Theophylline

If toxicant X bound pyruvate dehydrogenase and inactivated it, what effect would this interaction have on cellular maintenance?

What is the name of the protein that forms a heteodimer complex with the Ah receptor and carries it to the XRE in the nucleus??

There are 5 classes of P450 inducers. **BRIEFLY** discuss (in outline) the mechanisms of 2 of these classes.

List 3 compounds bioactivated by sulfotransferases

Draw a typical dose response curve for an essential nutrient and indicate the thresold of safety.

List 3 electrophilic metabolites, the parent and the enzymes catalyzing toxication.

Provide 3 separate enzymatic mechanisms for toxicity (i.e. bladder cancer) of 2-aminofluorene (aryl amine).

What is the mitochondrial enzyme that converts cyanide to the less toxic thiocyanate??

A metabolite of hexachlorobutadiene has been shown to permeabilize the inner membrane of the mitochondria. With your knowledge of biotransformation pathways and mechanisms of cell injury, predict the active metabolite and the ramifications of enhanced mitochondrial membrane permeability. (Hint: this occurs predominantly in the kidney)

50 pts on biotransformation (include enzymes and location)

50 pts on cell injury

What are 3 advantages of physiologically based toxicokinetic models over classical models?

What are the differences between perfusion-limited and membrance-limited compartments??

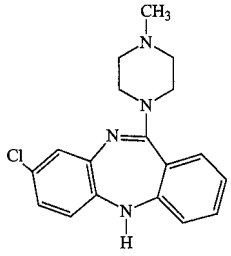
Provide one example of an idiosyncratic reaction involving biotransformation.

What are 4 of the most common parameters used in PBTKs??

N-nitrosodimethylamine is a carcinogenic precursor. Provide its mechanism of bioactivation and the specific enzymes involved in its biotransformation.

What are the dispostional processess and how do they relate to one another?

Provide 3 potential metabolites and the enzymes responsible for catalysis for the following drug:



Clozapine

List 3 tumor suppressor proteins

What are two advantages and two disadvantages of PBTKs over classical pharmacokinetic models?

What enzymatic activity would you use to assay for CYP2D6?? CYP1A1??

What are three general classes of receptors that promoters may interact with to enhance cell proliferation?

What are three Phase I enzyme reactions?

Draw a typical cross-section of human skin and label major components.

Draw dose response curves showing 2 compounds that are synergistic.

Provide mechanisms of repair for three different biomolecules or organelles.

Draw the cell division cycle.

What are three major types of Genetic damage.