MODEL EXAM QUESTIONS FOR PRACTISING (TOX-20303)

1. Introduction: History and Scope of Toxicology

1) What is toxicology? (Indicate the **one** best answer).

- ○ The field that studies the adverse effects on humans and animals.
- ○ The field that studies the adverse effects of chemicals on living organisms.
- ○ The field that studies the adverse effects of chemicals and micro organisms.
- ○ The field that studies the risk-benefit balance of chemicals for living organisms.

2) Indicate which persons played an important role in the history of toxicology. (Indicate **all** that apply).

- ☐ Atropa belladona
- ☐ Paracelsus
- ☐ Van ‘t Hoff
- ☐ St Anthony
- ☐ Orfila

3) Indicate which chemicals played an important role in the history of modern toxicology. (Indicate **all** that apply).

- ☐ Mercury
- ☐ Dioxins
- ☐ DDT
- ☐ Alcohol
- ☐ Softenon

4) Fill in the blanks. (Write your answer on the dots).

a) The concept of dose in toxicology was introduced in by ……
b) The target organ concept was introduced in toxicology by ……. …
c) The affair with …….. introduced emphasis on teratology and reproduction toxicology in safety testing of drugs and chemicals.
d) Modern toxicology especially developed because of the many new drugs, pesticides, munitions and industrial chemicals developed during the periods of the …… and ……

2. Principles of Toxicology

5) Give the right sequential order of the following steps. (Number the steps from 1 to 4 on the dots).

Risk assessment ……
Hazard identification ……
Risk management ……
Hazard characterisation ……

6) Indicate what is true about the process of risk evaluation as defined by the FAO and WHO. (Indicate **all** that apply).

- ☐ Risk assessment consists of risk characterisation, exposure assessment, risk management and risk communication.
- ☐ Risk assessment integrates hazard characterisation and exposure assessment.
- ☐ Risk management is part of risk assessment.
- ☐ Exposure assessment follows hazard characterization.
- ☐ Risk management follows risk assessment.

7) Match each description with its corresponding term. The terms may be used only once.

Description	Number of Term
A. Integrating hazard characteristics with exposure data.	……
B. The probability that an adverse effect will occur.	……
C. Integrating risk assessment with social, economic and political aspects.	……
D. The molecular structure affected by a toxic agent.	……
E. A potential danger of a compound or a process.	……

Term
1. risk assessment
2. hazard
3. receptor
4. risk
5. risk management

8) What is true about the process of risk assessment? (Indicate the **one** best answer).

- ○ Acute exposure and chronic exposure to a chemical result in effects on the same target organ.
- ○ DNA can be a toxicological receptor.
- ○ A dose response curve is important to establish the LD50 which is an important parameter in modern toxicological risk assessment.
- ○ The LD50 is a constant parameter reflecting the acute toxicity of a chemical for different species.

3. Mechanisms of Toxicity

9) Match each type of chemical with its corresponding term describing a mechanism of toxicity. The terms may be used **more than once or not at all.**

Term
1. electron abstraction
2. hydrogen abstraction
3. covalent binding
4. agonist action
5. modulating action

Type of chemical	Number of Term
A. Compound causing lipid peroxidation.	……
B. Electrophile causing a DNA mutation.	……
C. Compound causing methemoglobinemia.	……
D. Compound inhibiting acetylcholinesterase.	……
E. Compound binding and activating an acetylcholine receptor in the same way as done by acetylcholine.	……

10) What is true about mechanisms of toxicity? (Indicate **all** that apply).

- ☐ Methemglobinemia is caused by chemicals that cause electron transfer that oxidizes the Fe in hemoglobin from Fe^{2+} to Fe^{3+}.
- ☐ Reactive oxygen species (ROS) damage only unsaturated membrane lipids.
- ☐ Sarin and soman act by binding to the acetylcholine receptor.
- ☐ An antagonist does not require structural similarity to the natural ligand to block the receptor.
- ☐ Inhibition of oxygen binding to hemoglobin by CO is an example of non covalent binding causing toxicity.

11) Which are chemicals acting by non-covalent interactions? (Indicate the **one** best answer).

- ○ Sarin, soman, and acetylcholine agonists.
- ○ Benzo(a)pyrene and other genotoxic agents modifying DNA.
- ○ Tetrodotoxin, saxitoxin and curare.
- ○ Nitrate, reactive oxygen species and carbon monoxide.

12) What is true about reactive oxygen species (ROS)? (Indicate **all** that apply).

- ☐ In the Haber-Weiss reaction superoxide anions and hydrogen peroxide are converted to hydroxyl radicals.
- ☐ Reactive oxygen species cause formation of covalent DNA adducts.
- ☐ Reactive oxygen species are toxic because they are able to cause hydrogen abstraction.
- ☐ Reactive oxygen species are toxic because they cause non-covalent interactions with neurotransmitter receptor proteins.
- ☐ Reactive oxygen species are toxic because they cause methemoglobinemia.

4. Absorption, Distribution and Excretion of Toxicants

13) What is true for ADME characteristics? (Indicate the **one** best answer).

- ○ ADME characteristics describe all what happens to a compound when it has entered the body.
- ○ ADME characteristics describe the toxicodynamic phase.
- ○ ADME characteristics determine the bioavailability of a compound upon oral intake.
- ○ ADME characteristics describe how a compound becomes toxic including the mechanism of action.

14) Fill in the blanks. (Write your answer on the dots).

a) The process in which compounds pass cell membranes against a concentration gradient is called …….
b) The phase in which the toxic effect of a chemical or its metabolite is generated is called …… phase.
c) Absorption of gasses is dependent on their …….
d) Absorption of particles is especially dependent on their ……..……

15) Match each description with its corresponding term. The terms may be used only once.

Description	Number of Term
A. Process requiring energy	……
B. ADME characteristics	……
C. Transport by a carrier not using ATP	……
D. Process preventing systemic effects	……
E. Reaction with the toxicological receptor	……

Term
1. facilitated diffusion
2. toxicokinetics
3. first pass effect
4. toxicodynamics
5. active transport

16) What is true about absorption of toxicant by the lungs? (Indicate **all** that apply).

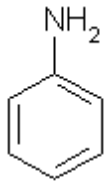
- ☐ The mucociliary escalator plays a role.
- ☐ The first pass effect plays a role.
- ☐ Particle water solubility plays a role.
- ☐ Ionization plays an important role.
- ☐ Diffusion through cell membranes is rate limiting.

5. Biotransformation of Xenobiotics

17) What is true about the biotransformation of xenobiotics? (Indicate **all** that apply).

- ☐ Phase I modification can follow phase II conjugation.
- ☐ Phase I modification makes a compound water soluble.
- ☐ Phase I modification results in bioactivation of a xenobiotic.
- ☐ Hydrophilic metabolites do not require phase I or phase II metabolism to be excreted in the urine.
- ☐ Biotransformation can be part of the mechanism of toxicity of a chemical.

18) What type of biotransformation reactions can play a role in the mammalian metabolism of aniline? (Indicate the **one** best answer).



aniline

- ○ N-Acetylation, hydroxylation, glucuronidation.
- ○ Epoxidation, methylation, sulfation.
- ○ Glutathione conjugation, reduction, N-hydroxylation.
- ○ Nitroreduction, glycine conjugation, aromatic ring opening.

19) What type of biotransformation reactions are phase I reactions? (Indicate the **one** best answer

- ○ N-Acetylation, glucuronidation, epoxidation.
- ○ Hydroxylation, sulfation, glutathione conjugation.
- ○ Methylation, N-oxidation, nitroreduction.
- ○ Heteroatom dealkylation, epoxidation, hydroxylation.

20) Fill in the blanks. (Write your answer on the dots).

a) The process in which compounds are modified into metabolites that are more toxic than the parent compound is called …….
b) The most important enzyme system for the phase I biotransformation reaction is ……
c) The most important enzymes for phase II metabolism of xenobiotics with hydroxyl groups are ……..…. and ……
d) The mechanism for phase I hydroxylation of aliphatics by P450 proceeding by H-radical abstraction followed by OH-radical coupling to the aliphatic radical is called the …… mechanism.

6. Toxicokinetics

21) What is true about toxicokinetics? (Indicate **all** that apply).

- ☐ Toxicokinetics describes dose-response curves.
- ☐ Toxicokinetics describes plasma concentrations as a function of time.
- ☐ Toxicokinetics describes models for bioavailability.
- ☐ Toxicokinetics is part of the toxicodynamic phase.
- ☐ Toxicokinetics includes PBK modelling.

22) What are advantages of PBK modelling over classical toxicokinetic modelling? (Indicate **all** that apply).

- ☐ PBK models can predict the concentration of a chemical in all relevant organs.
- ☐ PBK models can calculate the apparent volume of distribution.
- ☐ PBK models can be used to predict interspecies differences.
- ☐ PBK models can be used to predict chronic toxicity.
- ☐ PBK models can be used to model plasma levels.

23) Match each description with its corresponding term. The terms may be used only once.

Description	Number of Term
A. Kinetic model in which plasma levels and tissue levels of a chemical are modelled to be similar.	……
B. Kinetic model in which all relevant tissues are described as separate compartments.	……
C. Kinetic model in which the amount of compound eliminated is constant over time.	……
D. Kinetic model in which the rate of elimination of a compound is proportional to the amount of the compound in the body.	……
E. The amount of drug in the body divided by the plasma drug concentration.	……

Term
1. PBK model
2. one compartment model
3. 0-order kinetics
4. apparent volume of distribution
5. 1^{st} order kinetics

24) What parameters are used as input in PBK models? (Indicate the **one** best answer).

- ○ Apparent volume of distribution, plasma concentrations, dose administered.
- ○ Plasma concentrations, urinary levels, metabolite levels.
- ○ Blood flow rates, tissue volumes, kinetic parameters for biotransformation.
- ○ Tissue concentrations, species dependent parameters, first order elimination constants.

7. Genetic Toxicology

25) What is true about mutagenesis? (Indicate **all** that apply).

- ☐ Mutagenesis consistently predicts carcinogenesis.
- ☐ Mutagenesis includes initiation, promotion and progression.
- ☐ Mutagenesis occurs more often in germ cells than in somatic cells .
- ☐ Mutagenesis can result from oxidative stress.
- ☐ Mutagenesis is a reversible process.

26) Match each description with its corresponding term. The terms may be used only once.

Description	Number of Term
A. Enzymatic un-do of damage.	……
B. Removal of damaged base followed by DNA polymerase and DNA ligase activity.	……
C. Incorporation of random nucleotides to fill up a lesion.	……
D. Repair of action of DNA polymerase III resulting in 1 wrong base pair incorporated per 10^8 bases synthesized.	……

Term
1. mismatch repair
2. error prone repair
3. excision repair
4. reversal of damage

27) What are chromosome aberrations, i.e. changes at the individual chromosome level? (Indicate **all** that apply).

- ☐ Aneuploidy
- ☐ Frameshift mutations
- ☐ Basepair substitutions
- ☐ Translocations
- ☐ Sister chromatid exchanges

28) What is true about gene mutations? (Indicate the **one** best answer).

- ○ Genetic abnormalities resulting from mutations can be placed in two categories: frameshift mutations and chromosome aberrations.
- ○ Changes in the number of chromosomes, aneuploidy or polyploidy are not considered genetic abnormalities resulting from mutations.
- ○ Transitions and transversions are frameshift mutations.
- ○ Most chemical carcinogens with cancer initiating activity are also mutagenic.

8. Chemical Carcinogenesis

29) What are important cancer inducing factors? (Indicate **all** that apply).
- ☐ RNA viruses
- ☐ Ionizing radiation
- ☐ Pesticides
- ☐ Food colours
- ☐ Genetic factors

30) What is true about induction of cancer by asbestos? (Indicate the **one** best answer).
- ○ It requires metabolic biotransformation (bioactivation) by macrophages.
- ○ It occurs in lungs and liver and results in mesothelioma's.
- ○ It is initiated by the fact that asbestos fibres become surrounded by glycoprotein and cannot be adequately removed by macrophages.
- ○ It only occurs in combination with heavy smoking.

31) What are important classes of cancer inducing chemicals? (Indicate **all** that apply).
- ☐ Nitrosamines
- ☐ Films and fibres
- ☐ Polycyclic aromatic hydrocarbons
- ☐ Bacterial toxins
- ☐ Mycotoxins

32) Fill in the blanks. (Write your answer on the dots).
a) The process of carcinogenesis requires often more than one mutation and is therefore considered a ……. process.
b) The process of carcinogenesis requires activation of …….. -genes and inactivation of …….. -genes.
c) The three stages in the process of carcinogenesis are called ……, ……, and …….

9) Toxicity testing *in vitro* and *in vivo*

33) Match each description on the left with its corresponding term on the right. The terms may be used only once.

Description	Number of Term
A. Single dose test	……
B. 90 days test	……
C. 28 days test	……
D. Carcinogenicity test	……
E. Skin irritation test	……

Term
1. semi-chronic test
2. chronic test
3. acute test
4. short term test
5. specific test

34) What is true about the ADI or TDI? (Indicate **all** that apply).

- ☐ The ADI is for non-genotoxic compounds, the TDI for genotoxic compounds.
- ☐ The ADI is used for additives and therefore larger safety factors are used to derive it from the NOAEL.
- ☐ The ADI may vary depending on the study from which the NOAEL is taken.
- ☐ The ADI and TDI are health based safety limits and independent from the experimental design of the animal study from which they are derived.
- ☐ The TDI for a compound is generally higher than its ADI.

35) What is true about *in vitro* testing? (Indicate **all** that apply).

- ☐ *In vitro* test alternatives for all *in vivo* end parameters will be available in the near future.
- ☐ Present *in vitro* tests can predict the carcinogenic potential of a compound.
- ☐ The HGPRT test predicts genotoxicty for mammalian cells.
- ☐ The Mouse Lymphoma tk assay can predict both gene mutations as well as several chromosomal adverse effects.
- ☐ *In vitro* toxicity testing is most useful for genotoxicity and toxicokinetics.

36) What are *in vitro* tests for detecting gene mutations? (Indicate **all** that apply).

- ☐ Mouse Lymphoma tk assay
- ☐ S9 incubations
- ☐ Micronucleus test
- ☐ SCE test
- ☐ HGPRT test

10) Toxicity testing: Alternatives

37) Indicate which 3 toxicity tests require the highest number of experimental animals.

- ☐ Acute oral toxicity tests.
- ☐ Two generation reproductive toxicity tests.
- ☐ Developmental toxicity tests.
- ☐ Further in vivo mutagenicity tests.
- ☐ Carcinogenicity tests.

38) What is true about the 3Rs? (Indicate **all** that apply).

- ☐ The 3Rs indicate 3 orders of magnitude reduction in the number of experimental animals needed for safety testing.
- ☐ The 3Rs stand for Reduction Replacement and Refinement of animal testing.
- ☐ The 3Rs stand for Reach Regulated Replacement of animal testing.
- ☐ The 3Rs are relevant for all types of toxicity testing.
- ☐ The 3Rs are highly relevant for reproductive toxicity testing.

39) What is true about REACH? (Indicate **all** that apply).

- ☐ Implementation of REACH will reduce the number of animal experiments because it includes alternative testing strategies.
- ☐ REACH is restricted to all industrial chemicals used in the European Union.
- ☐ REACH aims at evaluation of the risk of 30 000 chemicals within the next 11 years.
- ☐ REACH stands for Regulation, Elimination and Authorisation of Chemicals
- ☐ REACH was initialized because for many industrial chemicals toxicity data were not available.

40) What techniques are expected to contribute to development of alternatives for animal testing? (Indicate **all** that apply).

- ☐ Omics technologies
- ☐ Computational toxicology
- ☐ Quantitative structure activity relationship approaches
- ☐ In vitro tests
- ☐ Microdosing in humans

11) Toxicological risk assessment

41) What are is true about environmental risk assessment? (Indicate **all** that apply).

- ☐ In the quotient method the Predicted estimated concentration (PEC) is compared to the Predicted no effect concentration (PNEC).
- ☐ The PNEC is the equivalent of the NOAEL in food safety assessment.
- ☐ The PNEC is the equivalent of the ADI in food safety assessment.
- ☐ The PEC is equivalent to the LOAEL in food safety assessment.
- ☐ The same uncertainty factors are used as in risk assessment of other chemicals.

42) What is true about human risk assessment? (Indicate **all** that apply).

- ☐ Well conducted epidemiological studies can provide convincing evidence for human risk.
- ☐ Ames tests provide insight in human cancer risks.
- ☐ Interspecies and intraspecies differences are not taken into account when calculating cancer risks by linear extrapolation from animal data.
- ☐ For quantitative risk assessment the benchmark dose (BMD) approach provides an estimate that is less dependent on the experimental set-up than the NOAEL approach.
- ☐ Exposure assessment is often a key area of uncertainty in human risk assessment.

43) What is the best description for the benchmark dose? (Indicate the **one** best answer).

- ○ A dose that equals the NOAEL.
- ○ The dose that results in a defined, for example 10%, response.
- ○ The dose that defines the sensitivity of a part of the population.
- ○ A dose that defines the margin of safety, taking the statistical uncertainty into account.

44) The role of safety factors is to take into account… (Indicate **all** that apply).

- ☐ …differences in life style factors and genetic variation.
- ☐ …differences between species.
- ☐ …differences in methods for exposure assessment.
- ☐ …sub-optimal study designs.
- ☐ …differences in intake levels.

12) Forensic Toxicology

45) - 48) No examples available

13. Toxicology of the liver

49) What are chemicals that cause liver toxicity? (Indicate the **one** best answer).

- ○ Dioxins, PCBs and furans.
- ○ Acetaminophen and bromobenzene.
- ○ Fatty acids and mycotoxins.
- ○ Alcohol and bile acids.

50) Which types of effect on the liver are chemically induced? (Indicate **all** that apply).

- ☐ steatosis
- ☐ glomerular injury
- ☐ emphysema
- ☐ lymphatic necrosis
- ☐ cirrhosis

51) What is true about toxic effects of chemicals on the liver? (Indicate **all** that apply).

- ☐ The toxic effect is often increased because activated macrophages excrete reactive oxygen species.
- ☐ Kupffer cells, the fixed macrophages in the liver are most sensitive to chemical compounds because they have the most active metabolism of xenobiotics.
- ☐ Most compounds that cause toxic effects on the liver interact with bile formation.
- ☐ Zone 3 hepatocytes are especially sensitive to chemicals that require bioactivation by cytochromes P450.
- ☐ Porphyria results from chemicals that interfere with heme biosynthesis.

52) Indicate what is true about the mechanism of liver damage caused by aflatoxin. (Indicate **all** that apply).

- ☐ The ultimate toxic effect is liver necrosis.
- ☐ Aflatoxin requires bioactivation before it can exert its adverse effect on the liver.
- ☐ Mutation of the gene for the p53 tumor suppressor gene may play a role in the mechanism of toxic action.
- ☐ Mutation of the ras oncogene plays a role in the mechanism of toxic action.
- ☐ The ultimate toxic effect is mesothelioma.

14. Toxic responses of the kidney

53) What is true about toxic effects of chemicals on the kidney? (Indicate **all** that apply).

- ☐ The kidney is extra susceptible to toxic injury because non- toxic concentrations in plasma may reach toxic concentrations in the kidney.
- ☐ The glomerulus is the part of the kidney most sensitive to toxic damage.
- ☐ Chemicals that require bioactivation are toxic to the kidney upon metabolism in the liver.
- ☐ Beta-lyase is an enzyme involved in bioactivation of several kidney toxins.
- ☐ The distal tubule is the most common site for renal injury by chemicals.

54) Give the right sequential order of the following steps. (Number the steps from 1 to 5 on the dots).

Transport to the kidney ……
Conversion by glutathione S-transferases ……
Conversion by beta-lyase ……
Transport to the liver ……
Conversion in the mercapturic acid pathway ……

55) What are the most important enzymes for bioactivation of halogenated hydrocarbons causing kidney toxicity? (Indicate the **one** best answer)

- ○ Cytochromes P450, dehalogenases, epoxide hydroxlases.
- ○ Beta-lyase, cytochrome P450s, glutathione S-transferases.
- ○ Mercapturic acid pathway enzymes.
- ○ The correct answer is not given.

56) Match each description with its corresponding chemical. The terms may be used only once.

Description	Number of Term
A. Therapeutic agents for which use levels are limited by nephrotoxicity.	……
B. Chemical that requires cytochrome P450 bioactivation to become toxic.	……
C. Chemical requiring beta-lyase activity to become nephrotoxic.	……
D. Chemical causing nephrotoxicity produced by a fungus.	……
E. Chemical that becomes nephrotoxic because it accumulates in the kidney.	……

Term
1. chloroform
2. ochratoxin A
3. cadmium
4. halogenated hydrocarbon
5. aminoglycoside antibiotics

15. Toxic responses of the respiratory system

57) What are important types of lung toxicity? (Indicate the **one** best answer).

- ○ Cancer, mesothelioma, and chirrosis.
- ○ Silicosis, inflammation, and hypersensitivity.
- ○ Inflammation, methemoglobinemia, and asbestosis.
- ○ Emphysema, fibrosis, and edema.

58) Fill in the blanks. (Write your answer on the dots).

a) The cells in the alveoli most sensitive to chemical damage are the …..... pneumocytes, and when damaged they can be replaced by …….. pneumocytes.
b) The Clara cells in the lung are of importance for toxicity because they contain the highest level of …….
c) A factor determining how deep gasses can penetrate into the lungs is their …… ……
d) A factor determining how deep particles can penetrate into the lungs is …… …….

59) Indicate which compounds may cause lung toxicity. (Indicate **all** that apply).

- ☐ Asbestos
- ☐ Dioxins
- ☐ Radon
- ☐ CO
- ☐ Mustard gas

60) Match each description with the name of the toxic effect described. The chemicals may be used only once.

Description of the toxic effect	Number of Term
A. Accumulation of macrophages.	……
B. Accumulation of water.	……
C. Accumulation of collagen.	……
D. Accumulation of damage to alveolar walls.	……
E. Accumulation of malignant tissue.	……

Chemical
1. emphysema
2. oedema
3. mesothelioma
4. inflammation
5. fibrosis

16. Toxicology of heart and vascular system

61) Indicate what are the targets for direct effects on the heart function. (Indicate **all** that apply).

- ☐ Effects on neurotransmitters
- ☐ Effects on calcium channels
- ☐ Effects on Na/K pumps
- ☐ Effects on oxidative phosphorylation
- ☐ Effects on the electron transport system in the mitochondria

62) Match each description with the name of the toxic effect described. The chemicals may be used only once.

Description of the toxic effect	Number of Term
A. effects on contraction frequency of the heart	……
B. effects on heart rhythm	……
C. effects on contraction intensity of the heart	……
D. effects on excitability of the heart	……
E. effects on impulse conductivity of the heart	……

Chemical
1. inotropy
2. chronotropy
3. bathmotropy
4. dromotropy
5. arrhytmia

63) Which are chemicals known for their heart toxicity? (Indicate **all** that apply).

- ☐ Digitalis glycosides
- ☐ Adriamycin
- ☐ Polycyclic hydrocarbons
- ☐ Polyunsaturated fatty acids
- ☐ Chlorinated dioxins

64) Indicate what is true about cardiovascular toxicity. (Indicate **all** that apply).

- ☐ The mechanism by which aterosclerosis develops is generally agreed upon.
- ☐ The somatic mutation theory predicts that atherosclerotic plaques represent malignant tumor sites.
- ☐ In the response to injury theory endothelial cells develop into atherosclerotic plaques.
- ☐ Atherosclerotic plaque formation may represent an effect resulting from immune stimulation.
- ☐ Vasoconstriction and vasodilatation are early stages in the development of atherosclerosis.

17. Toxic response of the Endocrine System

65) What is true about endocrine disruption? (Indicate **all** that apply).

- ☐ Compounds causing endocrine disruption originate from a very narrow class of chemical compounds.
- ☐ Compounds causing endocrine disruption are present in our food and environment.
- ☐ Compounds causing endocrine disruption are toxic to one of the hormone producing organs.
- ☐ Compounds causing endocrine disruption can be a risk factor for cancer incidences.
- ☐ Compounds causing endocrine disruption may cause developmental toxicity.

66) What are effects that can be caused by endocrine disruptors? (Indicate **all** that apply).

- ☐ Skin rashes.
- ☐ Increased chances on liver cancer.
- ☐ Increased chances on breast cancer.
- ☐ Imposex.
- ☐ Reduced chances on pregnancy.

67) Give the right sequential order of the following steps. (Number the steps from 1 to 5 on the dots).

Tumor development. ……
Activation of gene expression. ……
Exposure to an endocrine disruptor. ……
Activation of cell proliferation. ……
Activation of the estrogen receptor. ……

68) Match each description on the left with its corresponding term on the right. The terms may be used only once.

Description	Number of Term
A. Synthetic estrogen.	……
B. Mycoestrogen.	……
C. Metabolite with estrogen activity.	……
D. Phytoestrogen.	……
E. Industrial chemical with estrogen activity.	……

Term
1. zearalenone
2. genistein
3. hydroxy-PCB
4. diethylstilbestrol (DES)
5. bisphenol A

18. Toxic responses of the nervous system

69) Indicate what is true about neurotoxicity. (Indicate **all** that apply).
- ☐ Neurons are especially sensitive towards the consequences of CO or cyanide poisoning.
- ☐ For neurotoxicity chronic effects are of larger concern than acute effects.
- ☐ Methylmercury causes neurotoxicity and thereby loss of coordination (ataxia).
- ☐ Neuronopathy may cause a stocking and glove like distribution of effects.
- ☐ Neuronopathy of dopaminergic neurons may cause Parkinson like effects.

70) Fill in the blanks. (Write your answer on the dots).
a) Minamata disease is caused by the chemical compound ……..
b) A stocking-and-glove like distribution of neurotoxic effect can be due to a type of neurotoxicity that is also called …….
c) Neurotoxicity caused by effects of chemicals on the myelin layer produced by the myelinating cells is called……
d) Neurotoxicity caused by an adverse effect directly on the central cell body of the neuron is also called …….……..…

71) What are compounds causing neurotransmission associated toxicity? (Indicate the **one** best answer).
- ○ Methyl mercury, cocaine, and botulinum toxin.
- ○ Saxitoxin, sarin, and curare.
- ○ Tetrodotoxin, TOCP (triortho cresyl phosphate), and CS_2 (carbon disulfide).
- ○ Organophosphorous esters, gamma-diketones, and lead (Pb).

72) Indicate which effects represent neurotransmission toxicity. (Indicate **all** that apply).
- ☐ Effects on neurotransmitter biosynthesis
- ☐ Effects on neurotransmitter release
- ☐ Effects on the post synaptic receptor
- ☐ Effects on acetylcholine esterase
- ☐ Effects on sodium (Na^+) channels

19. Toxic responses of the skin

73) What are characteristic toxic effects of chemicals on the skin? (Indicate the **one** best answer).

- ○ Contact dermatitis, skin necrosis, skin colourisation.
- ○ Atopic contact dermatitis, urticaria, phototoxicity.
- ○ Acne, steatosis, skin cancer.
- ○ Hydratation, oedema, melanoma.

74) What is true about toxic effects of chemicals on the skin? (Indicate **all** that apply).

- ☐ The skin is highly sensitive because it has a large surface where exposure can occur.
- ☐ The skin is highly sensitive because it is easily penetrated by water soluble compounds.
- ☐ The skin is especially sensitive to corrosive agents.
- ☐ UV light can play a role in the skin toxicity of chemical compounds.
- ☐ Toxic effects on the skin may occur due to systemic exposure.

75) Fill in the blanks (Write your answer on the dots).

a. The two types of contact dermatitis that can be caused by chemical compounds are called …….. and ……. ..…… contact dermatitis.
b. Necrosis without secondary inflammation caused by extremely corrosive agents is also called ….……. …….
c. The type of skin toxicity caused by psoralenes in combination with UV-A is called ……..……
d. The very characteristic skin toxicity caused by dioxins is called ……. …….

76) Which compounds are known for their skin toxicity? (Indicate **all** that apply).

- ☐ TCDD
- ☐ Sarin
- ☐ Arsenic
- ☐ Methylmercury
- ☐ PAHs

20. Developmental toxicology

77) What is true about developmental toxicology? (Indicate **all** that apply).

- ☐ Mutation can be a mechanism underlying developmental toxicity.
- ☐ Decreased nutrient supply can be a mechanism underlying developmental toxicity.
- ☐ Developmental toxicity of a chemical is usually reflected by growth retardation at low dose and lethalithy at high dose.
- ☐ The majority of the birth defects are caused by exposure to radiation, drugs, chemicals or maternal metabolic imbalances.
- ☐ Developmental toxicity can result from effects on the placenta only.

78) Match each description with its corresponding chemical. The terms may be used only once.

Description	Number of Term
A. Teratogenic chemotherapeutic agent that causes DNA crosslinks.	……
B. Vitamin A analogue with teratogenic potential.	……
C. Teratogenic because of placental toxicity.	……
D. Chemical that introduced the concept of developmental toxicity in the field of safety testing.	……
E. Teratogenic chemical causing vaginal cancer in female offspring and also effects in male second generation.	……

Term
1. cylcophosphamide
2. thalidomide
3. cadmium
4. isotretinoin
5. DES (diethylstilbestrol)

79) Indicate which principles are part of Wilson's general principles of teratology. (Indicate **all** that apply).

- ☐ Susceptibility toward teratogenic agents depends on the genotype of the conceptus.
- ☐ Susceptibility varies with the developmental stage at time of exposure.
- ☐ There is no threshold and no NOAEL for teratogenic effects.
- ☐ With increasing concentration of the teratogen observed effects change from growth retardation to malformations to death.
- ☐ There is homology in development and thus in developmental stages for different organisms.

80) What is the most important principle underlying the investigation of the developmental toxicity of chemical compounds for men by doing animal experiments? (Indicate the **one** best answer)

- ○ Susceptibility varies only marginally with the species investigated.
- ○ There is homology in development for different mammalian species.
- ○ Dose response curves show the same characteristics in different mammalian species.
- ○ Mechanisms of teratogenicity are similar in different mammalian species.