Course Name and Number: BIMS 5327, TOXICOLOGY  
Credit Hours: 3 sem. Hrs (3:0)  
Instructor: Kenneth Ihenetu, PhD, FIBMS (London), NRCC (CC), SC(ASCP)  
Office: CS 130 G  
Hours: Wednesday 10-12 and by appointment  
Phone: 825-2359 (office)  
E-mail: Kenneth.ihenetu@tamucc.edu  
Room: CS 130 G

Prerequisite: As permitted by the Instructor.

INTRODUCTION

Toxicology is a profession requiring expertise in a number of biological and other scientific disciplines. Toxicologists working in specialist areas of toxicology should have knowledge of other aspects of the subject, in order to make decisions on chemical safety. In many instances, practitioners will have no specific qualifications in toxicology, although they may have qualifications in the discipline from which they entered toxicology (e.g. biology/pharmacology, biochemistry, pathology).

Toxicology is a continually developing science and practitioners require knowledge of current developments and an ability to integrate different parts of the subject. It is recognized that candidate may have deficiencies in their knowledge in certain basic areas and it is desirable that these be remedied as early as possible in their training program. Students are encouraged to attend courses designed to achieve the objectives of this training syllabus.

COURSE DESCRIPTION: The purpose of this course is to provide an understanding of the field of toxicology and how it is applied to safety and health in the workplace. The course will include the principles of toxicology; a review of human physiology and recognition of physiological effects of toxic agents; absorption, distribution, and elimination of toxic agents; TLV and LD concepts; use of medical technology; modes of contact and entry of toxic agents; dosage, time, and concentration effects; recognition of toxic agents; toxic effects on various organ systems (hematotoxicity, hepatotoxicity, nephrotoxicity, neurotoxicity, dermatotoxicity, pulmonotoxicity); study of occupational diseases, epidemiology, and risk assessment.

LEARNING OUTCOMES: At the end of the course:
1. Students will be able to design and apply appropriate in vivo and in vitro tests in order to investigate the toxicity of substances and assess the implications of the results.
2. Students will be able to analyze the application of toxicological methods in various specialist areas.
3. Students will be able to interpret data and to assess hazard and risk.
4. Students will be able to evaluate toxicity of unknown compounds, using a number of representative compounds as references.
5. Students will be able to analyze chemicals in pharmaceutical preparations, agriculture, food and consumer products, the workplace and the environment.

AUDIENCE DEFINED: This is a graduate course for students that have limited knowledge of toxicology or have not previously taken a course in Toxicology at the university level.

LABORATORIES: 
There are no labs required for this class.

CLASS POLICIES:
1. Failure to meet submission deadlines or missing examinations without one week prior notification will result in an “F” for the work in question. Work submitted late or a missed exam requires a written explanation from your physician.

2. Any student involved in providing false or misleading information, plagiarism, classroom misdemeanor, or academic dishonesty will be assigned an “F” for the work in question.

3. According to university policy, an “F” will be assigned if a student withdraws from the course without completing the proper forms for dropping a course.

**REQUIRED TEXT:**
Toxicology, The Basic Science of Poisons; Casarett and Doull

**SUPPLEMENTAL BIBLIOGRAPHY:**

3. Toxicology, The Basic Science of Poisons; Casarett and Doull  
5. Industrial Toxicology, Safety and Health Applications in the Workplace; Phillip L. Williams and James L. Burson

**COURSE GRADES AND REQUIREMENTS:**

The final mark will be calculated as an average from the following grades:

1. Three one hour exams, each worth 33 points, will emphasize lecture material, but may also include related quizzes, discussion and directed short projects.  
   Total number of Points: 100

The following scale will be used to report grades:

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<tr>
<th>Grade</th>
<th>Points</th>
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<tr>
<td>A</td>
<td>90 - 100</td>
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<td>B</td>
<td>80 - 89</td>
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<td>60 - 69</td>
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**ASSIGNMENTS/PROJECTS:** Assignments, unannounced quizzes and mini-projects will also be administered throughout the course.

**HONESTY**

As stated in the university catalog, "University students are expected to conduct themselves in accordance with the highest standards of academic honesty." Therefore, cheating will not be tolerated and will result in a failing grade for the course.
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<tr>
<th>July</th>
<th>Mon</th>
<th>2</th>
<th>Clinical manifestations of toxicity</th>
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<tbody>
<tr>
<td>Tues</td>
<td>3</td>
<td>Structural manifestations of toxicity</td>
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<td>Wed</td>
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<td>Holiday</td>
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<td>Thu</td>
<td>5</td>
<td>Mechanistic toxicology</td>
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<tr>
<th>July</th>
<th>Mon</th>
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<th>Toxicogeneomics</th>
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<tr>
<td>Tue</td>
<td>10</td>
<td>Principles of toxicokinetics</td>
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<td>Wed</td>
<td>11</td>
<td>Genetic toxicology</td>
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<td>Thu</td>
<td>12</td>
<td>Carcinogenesis and Exam 1</td>
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<tr>
<th>July</th>
<th>Mon</th>
<th>16</th>
<th>Biomonitoring</th>
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<tr>
<td>Tues</td>
<td>17</td>
<td>Reproductive toxicology</td>
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<tr>
<td>Wed</td>
<td>18</td>
<td>Research Methods in Toxicology discipline</td>
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<tr>
<td>Thu</td>
<td>19</td>
<td>Epidemiology</td>
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<tr>
<th>July</th>
<th>Mon</th>
<th>23</th>
<th>Toxicity test study design</th>
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<tr>
<td>Tue</td>
<td>24</td>
<td><em>In vitro and in silico</em> toxicology</td>
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<tr>
<td>Wed</td>
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<td>Behavioural toxicology and neurotoxicology</td>
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<tr>
<td>Thurs</td>
<td>26</td>
<td>Behavioural toxicology and neurotoxicology and Exam II</td>
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| Mon  | 30   | Immunotoxicology |
| Tue  | 31   | Radiation toxicology |

| Aug  | Wed  | 1       | Clinical toxicology |
|      | Thurs| 2       | Regulatory toxicology in different countries |
|      | Fri  | 3       | Final Exams |

**General Disclaimer:**
The instructor reserves the right to modify the schedule when necessary. These changes will be announced during regularly scheduled lecture periods. In case of absence during this announcement, it is the responsibility of the student to obtain the information as no effort will be made to contact students who were absent when the announcement was made.

**STUDENTS WITH DISABILITIES**
Texas A&M University-Corpus Christi complies with the Americans with Disabilities Act in making reasonable accommodations for qualified students with disabilities. If you need disability accommodations in this class, please see me as soon as possible. If you suspect that you may have a disability (physical impairment, learning disability, psychiatric disability, etc.), please contact the Services for Students with Disabilities Office (located in Driftwood 101) at 825-5816. It is important that you contact them in a timely fashion as it may take several days to review requests and prepare accommodations. Please have your accommodation letter and the necessary forms from Services for Students with Disabilities Office with you when you come to see me.
INSTRUCTION PROGRAMME

This comprises of 19 different topic areas. The student should be familiar with a representative examples as well as compounds of current toxicological interest, from both a histopathological and biochemical point of view.

**Topic Areas**

1. **Clinical manifestations of toxicity:** methods of monitoring, including clinical observations, clinical chemistry, haematology, other organ function tests:-
   
i) Weight change, clinical signs of toxicity, including functional observations, etc.;
   ii) Methods for the collection, handling and storage of blood and urine samples;
   iii) Hematological examination: morphology of blood cells, blood films, bone marrow aspirates, total and differential blood cell counts, coagulation tests;
   iv) Biochemical assessment of organ function including clinical chemistry, plasma and urinalysis as well as specific tests such as insulin clearance;
   v) Electrophysiological techniques (e.g. ECG, ECG & EMG);
   vi) Blood pressure, body temperature;
   vii) Use of biomarkers.

2. **Structural manifestations of toxicity:** Principles of pathological changes occurring in organs and tissues and recognition of gross pathological processes in major organs; the recognition of toxic responses; the distinction between acute and chronic effects; knowledge of pathological techniques such as fixing and staining, as well as a basic knowledge of microscopical procedures. Additionally the candidate should understand the basic techniques of histochemistry and immunocytochemistry.

   The range of pathological processes should include:-
   1) degenerative changes
   2) cell death (apoptosis and necrosis)
   3) inflammation, acute and chronic
   4) the adaptive changes of atrophy, hypertrophy, hyperplasia
   5) disorders of differentiation, metaplasia, dysplasia and neoplasia
   6) restructure and repair

   The Candidate should be familiar with the toxicological pathology of the following systems:
   i) skin
   ii) central and peripheral nervous system
   iii) eye, ear and other sense organs
   iv) endocrine organs
   v) cardiovascular system
   vi) alimentary tract
   vii) respiratory system
   viii) hepatic system
   ix) renal system
   x) reproduction system
   xi) immune system
   xii) hematopoietic system
   xiii) bone
   xiv) muscular system

3. **Mechanistic toxicology:** Disorders of cellular and molecular function and the mechanisms underlying common toxic effects. The role of metabolism in toxicity; structure activity relationships. An understanding of reversible reactions of chemicals with macromolecules, and the consequences of the dose response and concentration effect relationships and pharmacodynamic effects of chemicals. Receptor-mediated toxicity. The classification of pharmacological actions at the receptor level. The concept of target organ toxicity. Principles of programmed cell death (apoptosis). Mechanisms and consequences of altered gene expression as adaptive stress response and signal transduction. Use of genetically modified cells and organisms to explore mechanisms. Cell and in vivo imaging e.g. positron emission tomography (PET), confocal microscopy.


5. **Principles of toxicokinetics:** a knowledge of factors affecting the absorption, distribution, metabolism and excretion of toxic substances. The major routes and enzymes of xenobiotic metabolism. The sources
of variability in xenobiotic disposition, including species, strain, sex, environmental (e.g. enzyme induction) and pathophysiological factors. Pharmacogenetic differences in handling xenobiotics. Xenobiotic transporters, PBPK approaches.

6. Genetic toxicology: An understanding of the genetic control of germ cells and somatic cells. Assays for gene mutation in prokaryotes. In vivo and in vitro assays for DNA damage, gene mutation, chromosomal damage and genomic damage, dose-response relationships in eukaryotes, including the importance of xenobiotic metabolism in such systems. The design and interpretation of individual tests. Overall strategy for testing of chemicals.

7. Carcinogenesis: Mechanisms involved in tumour formation including multistage, i.e. initiation, promotion and progression; distinction between genotoxic and non-genotoxic carcinogens. Dose-response relationships. Role of oncogenes and tumour suppressor genes in the cell cycle and in apoptosis. Methods for determining the carcinogenic potential of chemicals including transgenic models. Biological and toxicological significance of the results of carcinogenicity studies. Mode of action and framework approaches.

8. Biomonitoring: Biomarkers of exposure, effect and susceptibility for carcinogens and other toxicants. The distinction between measures of acute and chronic exposure, and between spot samples and integrated measures. Principal techniques of exposure assessment, including urinary levels of compounds or a metabolite, adducts in urine, with blood or tissue proteins or DNA. Clinical measures of exposures. Limitation of these methods. Their role in risk assessment and extrapolation of animal data to man.


10. Research Methods in Toxicology discipline
   i) Concepts of statistics (distributions; parametric and non-parametric tests, multiple comparisons; sampling; summarising data; presenting data; hypothesis testing and study power).
   ii) Application of statistical analysis to toxicology studies (e.g. analysis of bench data; genotoxicity data; body weight, organ weight, haematology data, pathology data including methods for analysing tumour frequency). Confidence intervals.

11. Epidemiology: Difference between incidence and prevalence. Mortality and morbidity rates, sources of data, standardised and proportional rates, analytical and descriptive epidemiology. Cancer incidence and mortality rates for major anatomical sites. Retrospective and prospective studies, use of sampling techniques, selection of suitable populations, control groups, etc. Cross sectional, cohort, case control and intervention studies. Trends in cancer incidence and mortality. Monitoring of exposure in the environment and of biological uptake in exposed populations. The concept of molecular epidemiology, biomarkers of exposure, effect and susceptibility (see also 8).

12. Toxicity test study design: Acute toxicity studies including irritancy, sensitisation, and sub-chronic, long-term and lifetime studies. Opportunities for refinements of existing methods with respect to animal welfare considerations (the three “R”s) and development of in vitro alternatives. The importance of clear definitions and characterisation of the test substance. The construction of safety evaluation programmes for different categories of substance including biological and GM products. An understanding of experimental design and report writing (see also 21). Tiered-testing strategies.


14. Behavioural toxicology and neurotoxicology: A basic understanding of factors governing behaviour and the difference in behavioural patterns between experimental animals and humans, observational tests, sensory functions including otoxicity and ocular toxicity, motor function tests and more complex tests of behaviour. Interface between behavioural toxicology and neurotoxicology. Neurotransmitters and interference by foreign compounds with them.

15. Immunotoxicology: The structure and function of the immune system and the mechanisms whereby exposure to xenobiotics may influence the immune system. Including both induced immunological impairment, and adverse responses due to sensitisation or allergic responses to chemicals. Clinical manifestations of such reactions. Methods for assessing changes in immunological competence (functional assays and measurement of host resistance), and for contact sensitivity including local
lymph node assay (LLNA), respiratory sensitivity and allergy including to chemicals and GM proteins. The significance and interpretation of the results of such tests.

16. **Ecotoxicology:** An understanding of ecosystems and how xenobiotics may affect them, biological oxygen demand, the concept of food chains, bioaccumulation, persistence and toxicity (BPT), dispersal of xenobiotics into the environment, effects of chemicals on fish, birds and other wildlife. Appropriate biomarkers. Basic tests on Daphnia, earthworms, birds and fish. Awareness of major issues of concern.

17. **Radiation toxicology:** $\alpha$, $\beta$ and $\gamma$ radiation and X-rays; neutrons, toxicity of important radio-nuclides, high and low linear energy transfer (LET) and non-ionising radiation such as UV. Health effects of radiation exposure.


19. **Regulatory toxicology in different countries:** Good laboratory practice (GLP), quality assurance (QA) and control and labelling requirements. The regulatory position covering different areas of chemicals (e.g. industrial, agricultural and pharmaceutical) in the EU, USA and Japan and other countries. International (e.g. OECD and ICH) guidelines where relevant. The candidate should have some knowledge of regulations as they affect materials produced by biotechnological means e.g. novel foods,
Course Number: _BIMS 5590____  Instructor: _Kenneth Ihenetu____

Credit Hours: __3_____________  Semester: ___Summer II_____  Year: __2007____

Course Title: _Advanced Topics in Toxicology__________________________

1. Course Description (Approximately 25 words).

This course will provide candidates requisite knowledge to design and supervise appropriate tests _in vivo_ and _in vitro_ in order to investigate the toxicity of substances and to assess the implications of the results. Candidate will be expected to have an appreciation of the toxicity of a number of representative compounds and be able to apply their knowledge to the evaluation of chemicals in pharmaceutical preparations, agriculture, food and consumer products, the work place and the environment.

2. Attach course outline or syllabus and a statement of course goals or objectives.

    See attachment for course outline.

3. What group or groups of students is the course designed for?

    Graduate biology students who are interested in Biology, biomedical science, molecular and marine biology majors. Graduate students environmental science who are interested in environmental and regulatory toxicology are also encouraged to take the course.

4. What is your best estimate of potential enrollment? What is the estimate based on?

    5-10.

    Based on interested students in these majors.

5. What degree and/or teacher certification requirements will this course fulfill?

    Elective for MS degree in Biology, Marine Biology and Mariculture

6. Are present library and other university resources adequate to support this course?

    Yes.

7. Comments:

Department Action: Approve ____________

Reject ____________ Date: _______________
More information requested: ____________________

COMMENTS: