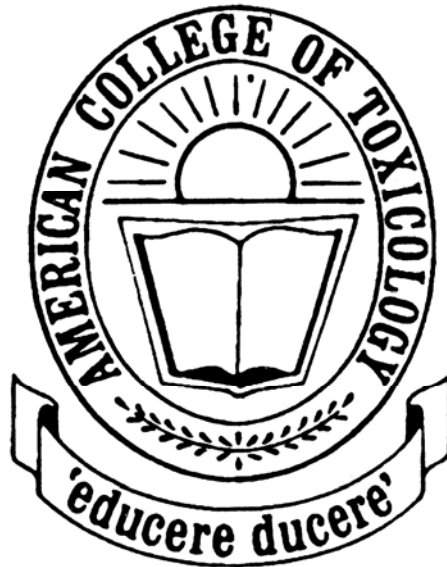


**THIRTY-FIRST ANNUAL MEETING
OF THE
AMERICAN COLLEGE OF TOXICOLOGY**

EDUCATION COURSES

November 7, 2010



**Baltimore Marriott Waterfront Hotel
700 Aliceanna Street
Baltimore, MD 21202**

**Reservations – Tel: 760-322-6000 - 800-266-9432 –
www.marriott.com/BWIWF
Deadline for Hotel Reservations – October 5, 2010
Deadline for Advanced Registration – October 5 2010**

CONTINUING EDUCATION COURSES

NOVEMBER 7, 2010

REGISTRATION LIMITED

SUNDAY MORNING – 11/7/10

*Pharmacologist/Toxicologist Supervisor, US
FDA, CDER/OAP/DAVP, Silver Spring, MD*

8:00 – 11:30 COURSE #1

STUDY DIRECTOR TRAINING

*Chair: Barbara J. Mounho, Ph.D., DABT,
Scientific Director, Amgen Inc., Thousand
Oaks, CA*

This continuing education course is intended to provide an introduction to a study director's responsibilities and review both logistical-, regulatory- and scientific-related aspects of toxicology studies. The course will be divided into two parts (morning and afternoon sessions). The course will focus on the practicalities of study director responsibilities for study conduct, oversight, protocols, animal models, and final reports. This course will also review the evolution and scope of the GLP regulations and what a study director should do/not do during an FDA inspection, as well as how to manage challenges a study director can encounter in toxicology studies and how to appropriately communicate study deviations to a sponsor. This is an excellent course for newer study directors, but sure to be informative for the more experienced as well.

Drug development is a term used to define the entire process of bringing a new drug or device to the market. It is an integrated, multidisciplinary endeavor that includes drug discovery, chemistry, pharmacology, nonclinical safety testing, manufacturing, clinical trials, and regulatory submissions. This workshop will provide an overview of the contributions from each area, with a focus on safety assessment, and some of the challenges that can arise. The workshop will also cover the information that should be included in INDs and NDAs submitted to FDA as well as advice on how to write a good IND/NDA.

8:00 – 11:30 COURSE #3

DEVELOPMENTAL AND REPRODUCTIVE TOXICOLOGY (Basic Course)

*Co-Chairs: Robert M. Parker, Ph.D., DABT,
Director, Dev & Repro Toxicology,
Huntingdon Life Sciences, East Millstone,
NJ and Rochelle W. Tyl, Ph.D., DABT, RTI
International, Center for Life Sciences and
Toxicology, Research Triangle Park, NC*

Developmental and Reproductive Toxicity (DART) studies are among the most complex and difficult in the field of toxicology. DART studies entail multiple and interrelated endpoints and systems that are rapidly changing in characteristics and in their responses to toxic insults over time. Developmental toxicity will be viewed in a broad

8:00 – 11:30 COURSE #2

DRUG DEVELOPMENT 101

*Co-Chairs: Lorrene Alice Buckley, Ph.D.,
DABT, Research Fellow, Eli Lilly and
Company, Indianapolis, IN and Hanan N.
Ghantous, Ph.D., DABT,*

context, including aspects of postnatal development and multigenerational effects. In addition, DART studies routinely generate large data sets and require special statistical analysis. However, because of the decline in DART training programs, data from developmental toxicity studies are often managed or interpreted by individuals with limited backgrounds in these fields.

The objective of the basic course in Developmental and Reproductive Toxicology is to provide an overview of:

- female reproductive system including oogenesis and ovarian toxicity;
- male reproductive system including spermatogenesis and testicular toxicity;
- mating, fertility, placentation and early development,
- regulatory agency (agrochemical and pharmaceutical) promulgated study designs; and
- DART risk assessment.

8:00 – 11:30 COURSE #4

THE DESIGN AND PERFORMANCE OF PRE-IND GENOTOXICITY STUDIES AND PRE-NDA

Chair: Elias Zahalka, Ph.D., MBA, Director of Toxicology Operations, BioReliance Corp., Rockville, MD

The course will review the regulatory requirements for genetic toxicology testing and the test systems available for mutagenicity testing. Complementing of test systems within a genetic toxicology battery of tests will be discussed, with regard to demonstration of mechanism of action and assessment of risk. Additionally, the course will review the recent technologies available to assess the potential mutagenicity of a compound, as well as subsequent follow-up study

options. Interpretation of positive results in genetic toxicology studies will also be addressed.

8:00 – 11:30 COURSE #5

“BACKGROUND’ PATHOLOGY IN NONCLINICAL STUDIES: WHAT IS IT AND WHAT DOES IT MEAN?

Chair: Daniel J. Patrick, DVM, DACVP, Principal Pathologist, MPI Research, Mattawan, MI

Nonclinical animal models are generally considered to be a “clean” and consistent background of normal anatomy and physiology within which to evaluate the potential toxicity of putative therapeutic agents. But, spontaneous background findings both physiological and pathological manifest in these models and can be quite variable in character, incidence and severity within and between studies. Although an experienced toxicologic pathologist is accustomed to identifying and differentiating these changes from test article-related effects, the distinction is occasionally unclear due to random distribution across dose groups or overlap with those associated with test article treatment. This session will describe some of the more common non-proliferative and proliferative background changes in rodent and non-rodent nonclinical animal models. The presentation will also outline approaches used by the pathologist to build a weight of evidence for or against attributing the morphologic or clinical pathologic change to administration of the test article. The aim is to provide the regulatory reviewer an understanding of these changes and their context in nonclinical safety assessment.

SUNDAY AFTERNOON – 11/1/09

1:00 – 4:30 COURSE #6

STUDY MONITORING COURSE *Chair: Paul L. Roney, Ph.D., DABT, Senior Consultant, Toxicology, Kendle International Inc., Rockville, MD*

With the increased emphasis on outsourcing toxicology studies to specialty Contract Research Organizations (CRO), toxicologists are being asked to monitor studies being conducted outside of their organizations. In this capacity, they must ensure that the toxicology program is conducted properly and in a cost effective manner. This presents a particular challenge to the toxicologist because many toxicologists have no training in managing these types of programs. This course will provide the participants with the tools they need succeed in this endeavor. Specifically, this course will discuss what factors the toxicologist needs to consider when selecting a CRO including bid solicitation and bid analysis (cheapest is not always best). It will also discuss the interactions between the Study Monitor and the CRO before, during and after the study. It includes a CRO's Study Director's perspective of what makes an effective team between the Study Monitor and the Study Director. It will conclude with a discussion of the legal obligations between you and the CRO. This course is a must for any toxicologist who is responsible for outsourcing toxicology studies, no matter what sort of company he/she works for.

1:00 – 4:30 **COURSE #7**

CONSIDERATIONS WITH REGARD TO NHP USE IN NON- CLINICAL SAFETY ASSESSMENT

Chair: Lorrene Alice Buckley, Ph.D., DABT, Research Fellow, Eli Lilly and Company, Indianapolis, IN and Kathryn Chapman, Ph.D., Pharmaceutical Programme Manager, NC3Rs.

Species selection represents a major challenge in designing nonclinical safety assessment testing of biopharmaceuticals (eg., monoclonal antibodies, mAbs). Frequently, the only pharmacologically relevant species for nonclinical testing of mAb in drug development is the non-human primate (NHP). This situation has resulted in a significant increase in the number of these animals used in nonclinical safety assessment. Coupled with a rapidly increasing number of mAbs in development, there is an urgent need to investigate alternative approaches and strategies for the safety assessment of mAbs. This course, which builds upon a basic understanding of biopharmaceutical development, will overview approaches considered in a collaborative consortium of industry, CRO, and regulatory scientists (the NC3Rs working group) and engage the audience to identify opportunities to alternative approaches to nonclinical testing and minimize NHP use in mAb development

1:00 – 4:30 **COURSE #8**

ADRENAL TOXICOLOGY

Chair: Philip W. Harvey, Covance Laboratories Inc., Harrogate, United Kingdom and Christopher Springall, M.D., VP Non-Clinical Safety Assessment, Covance Laboratories, Inc., Harrogate, United Kingdom

The adrenal is recognized as the most frequent target in the endocrine system for toxicity, based on surveys of in vivo toxicity studies. In addition to being a frequent and significant target for pharmaceuticals, the adrenal is a key target for environmental species. Mechanisms of adrenal toxicity are varied and an understanding of those mechanisms is vital to correct interpretation of findings in toxicity

studies. The rise of in vitro systems to predict and investigate toxicity is a highly topical subject that is passing in to mainstream toxicology evaluation. This program will provide an overview of adrenal toxicology and explore various mechanisms with known examples and strategies to evaluate adrenal toxicology. It will particularly focus on the differential diagnostic requirements to establish the cause of adrenocortical hypertrophy, whether stress or direct pharmacotoxicology leading to insufficiency. It will cover in detail the use of the H295R cell line for examining mechanisms of adrenocortical toxicity (currently validated by US EPA for sex steroid endocrine disruptor endpoints). Mechanisms of adrenocortical and adrenomedullary toxicity will be examined and illustrated with histopathology. The significance of the adrenal gland as a major target for endocrine toxicology/endocrine disruption will be explored, including in the context of broader environmental considerations.

1:00 – 4:30 COURSE #9

DESIGN AND PERFORMANCE OF CARCINOGENICITY STUDIES

Chair: Elias Zahalka, Ph.D., MBA, Director of Toxicology Operations, BioReliance Corp., Rockville, MD

The course will review the regulatory requirements for carcinogenicity testing and the function of the carcinogenicity assessment committee (CAC) at the FDA in support of compound assessment. A review of the two approaches for carcinogenicity assessment based on the ICH guideline will be discussed. The design, conduct and data interpretation of the two year studies in two rodent species and the alternative approach using one long term study in rats and one short term study in mice using transgenic animals

will be reviewed. Additionally, the most common transgenic mice models (rasH2, P53 and TgAC) used in assessing the potential carcinogenicity of compounds and the background tumor data associated with each model will be discussed.

1:00 – 4:30 COURSE #10

LEACHABLES AND EXTRACTABLES: BEST PRACTICES TO IDENTIFY AND QUALIFY LEACHABLES IN DRUG PRODUCTS

Co-Chairs: Douglas J. Ball, M.S., DABT, Research Fellow, Pfizer Global R&D, Groton CT and Jackie Kunzler, MS, MBA, DABT, Sr. Research Manager, Baxter Healthcare Corporation, Round Lake IL

Analytical techniques are increasingly sophisticated and capable of detecting and identifying chemicals at picogram quantities. However, it is generally accepted that there are levels of many chemicals below which the risks to human health are so negligible as to be of no consequence. This rationale has been a strong impetus for development of safety and analytical thresholds for regulating chemicals to which humans are exposed. Safety thresholds have a history of use in regulatory applications, most notably in guidelines for food packaging. Such thresholds have been developed for application for extractables and leachables in orally inhaled and nasal drug products (OINDP). In OINDP, the drug substance is usually contained in a delivery device that may contain polymers, elastomers, and other components from which minute quantities of material may migrate (leach) into the product and be delivered to the sensitive surfaces of the respiratory and/or nasal tract along with the therapeutic agent. While every effort is taken to reduce the levels of these leachables, complete removal is not possible. Because leachables are

non-drug-related impurities, there is an increased concern for human risk of leachable exposure on a daily basis. Similar situations for the presence of leachables exists for other drug products such as parenterals and ophthalmics. This continuing education course will address concepts, background, historical use and development of safety thresholds and how they are applied to analytical evaluation in OINDP and how these concepts are being applied to parenteral and ophthalmic drug products.

