



DACC NEWS

Volume 27, Number 3, September 2011

ANIMAL CLINICAL CHEMISTRY

A DIVISION OF AACC



DACC Fall Meeting *October 21, 2011, Raritan, NJ*

Message from the Chair

It's been a very interesting summer. Hot and wet, and then there was Irene! I hope everyone that was in her path has recovered. The summer highlight was the AACC Annual Meeting which was held in Atlanta, Georgia.



We kicked off the week at the Annual Meeting with the DACC Lunch and Learn on Monday July 25th. The theme of the meeting was "Case Studies". Our guest speaker was Peter O'Brien presenting "Case Studies of Predictive & Translational Safety Biomarkers for

Various Organ Toxicities". This was followed by member case studies presented by Kay Criswell "Utilization of the Sysmex Hematology Analyzer for Bone Marrow Evaluation in Rats", Lila Ramaiah presenting on drug-induced hematotoxicity "Anemia in a Monkey", Chris Perigard presenting a coagulation case study "What's with the Prolonged APTT?", and Susan Haley presenting "Clinical Pathology

In This Issue:

[Pg.2 Announcing 2011 Travel Award Winner](#)

[Pg.4 Fall Symposium Program Schedule](#)

[Pg.6 Fall Meeting Presentation Abstracts](#)

[Pg.10 Tribute to Ingrid Austin](#)

[Pg.11 Regulatory Reminder -Hepatotoxicity](#)

[Pg.12 Regulatory Update -Genomic BMs](#)

[Pg.15 Images from the 2011 Lunch & Learn](#)

Laboratory Operations and Staffing". It was a wonderful afternoon of continuing education and networking. After a brief rest, we gathered at Pitty Pat's Porch for a reception dinner honoring Dr. Peter O'Brien as the recipient of the DACC's 2011 Award for Outstanding Contribution to Animal Clinical Chemistry. We have to thank Siemens's Healthcare Diagnostics for sponsoring the award and the fabulous event. The DACC also co-sponsored a symposium entitled "Clinical Translational Science: Providing Innovative Diagnostic Tools" on Tuesday July 26.

One of the outstanding continuing education opportunities of the AACC Annual Meeting is the Poster Sessions. Animal research posters by AACC/DACC members were



slated at both the Animal and Hematology Sessions. Each year the DACC selects an outstanding poster for special recognition. This year the poster award recipient is Jeffrey Bock, from Pfizer for his poster "Comparison of the Sysmex XT-2000iV, Flow Cytometry, and Microscopic Bone Marrow Differentials in Wistar Rats". Congratulations! The award will be represented at the DACC Fall Meeting.

Well, Summer is over and we begin to look forward to the traditional Fall meetings like AAPS, ACT, ASVCP, and of course the DACC Fall Meeting. The DACC Fall Meeting is set for October 21.

It will be co-hosted by J&J and Huntingdon Life Sciences at the J&J Raritan New Jersey facility. The theme of the meeting is Hepatotoxicity and the planning committee has once again pulled together a great full day symposium. I hope you can be there for education, networking, and fun! An exciting year so far and we'll end the year in the same fashion. As this is my last message to the membership as the division Chair, I want to thank everyone who contributed to another successful year. Not to be corny but a chain is only as strong as its weakest link, and the DACC has none. It has been an honor to serve as this division's chair. Stay safe everyone.

❖ *Barbara*

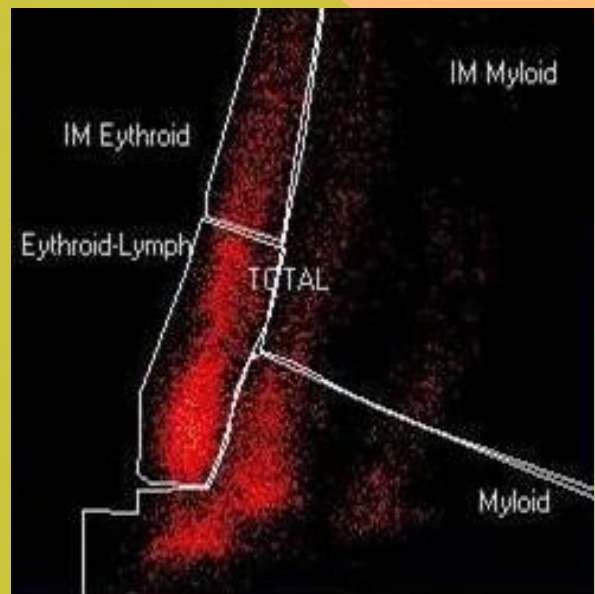
Announcing the Winner of the DACC 2011 Travel Award for the Best Poster Presented at the Annual Meeting

Congratulations to This Year's Winner Jeffrey Bock of Pfizer Global Research & Development, Groton Laboratories, for His Group's Poster Titled
"Comparison of Sysmex Flow Cytometric and Microscopic Bone Marrow Differentials in Wistar Rats"

Bone Marrow Differentials By Flow Cytometry

The poster, authored by Jeff and his Pfizer colleagues Kay Criswell and Richard Giovanelli, illustrated that implementation of automated bone marrow analysis in rodent safety studies greatly improves consistency and timeliness of data compared to both microscopic and flow cytometric analysis. They concluded that the Sysmex XT-2000iV demonstrates the ability to detect relevant hematological changes in bone marrow specific cell lineages, and that it provides advantages of increased throughput as well as confirmed accuracy and reproducibility.

Great Work!!



A
BIG
DACC
THANKS!

To:
**Johnson & Johnson
Pharmaceutical Research
& Development**
and
Huntingdon Life Sciences

For Co-Hosting the 2011 DACC Fall Meeting at J&J's Raritan, New Jersey Facility and for Providing Printed Handouts, Breakfast and Lunch to the Attendees

To:
Sysmex America, Inc.

For Their Contributions to the DACC Mixer/Buffer Dinner and Meet the Speakers Reception the Night Prior to the 2011 Fall Meeting



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Jiri Aubrecht, Pharm –Pfizer, Inc.
Gregory Bannish –Huntingdon Life Sciences
Eric Blomme –Abbot Laboratories
Mary Carsillo, –Millennium
Mark Collinge –Pfizer, Inc.
Alison Harrill –Hamner Institutes for Health Sciences
Jon Kimball –The Potter-Hawkins Group
Thomas Li –Hoffmann-La Roche, Inc.
Michael Linn –Hoffmann-La Roche, Inc.
Carmen Raventos-Suarez –Pfizer, Inc.
Shelli Schomaker –Pfizer, Inc.
Eric Schultze –Lilly Research Labs
Sharon Sokolowski –Pfizer, Inc.
Jessica Whritenour –Pfizer, Inc.



2011 DACC Fall Meeting

Hepatotoxicity: Mechanisms, Predictivity, and Biomarkers

Thursday – October 20

DACC Executive Committee Meeting

5:00pm – 6:30pm

Tuscany Room, Holiday Inn Express Hotel and Suites, Bridgewater/Branchburg, NJ

Open to All Members! Come Join in the Planning of DACC Activities!

DACC Meet the Speakers and Poster Travel Award Reception/Mixer

Great Room, Holiday Inn Express Hotel and Suites

6:30pm – 8:30pm

Supported by **Sysmex America, Inc.**

Free!

RSVP to Barb at litzenbb@princeton.huntingdon.com

Friday – October 21

Registration and Continental Breakfast

8:00am – 8:30am

Johnson & Johnson Pharmaceutical Research & Development

1000 US Route 202 South, Raritan, NJ

Welcome & Introductions

8:30am – 8:45am

Barbara Litzenberger, Welcoming Address, DACC Chair, Huntingdon Life Sciences

Kay Criswell, Symposium Moderator, DACC Chair-Elect, Pfizer Global Research & Development

Mechanisms of Acetaminophen Hepatotoxicity: New Insights Into the Mouse and Human Pathophysiology

8:45am – 9:25am

Hartmut Jaeschke, PhD, ATS, Professor Department of Pharmacology, Toxicology and Therapeutics
University of Kansas Medical Center

Inflammatory Stress and Models of Idiosyncratic Hepatotoxicity

Robert A. Roth, PhD, DABT, Professor Dept. of Pharmacology and Toxicology 9:25am – 10:05am

Center for Integrative Toxicology, Michigan State University

Break

10:05am – 10:30am

Potential Models for Investigating the Role of the Immune System in Drug-Induced Liver Injury

10:30am – 11:10am

Jessica Whritenour, PhD, Principal Scientist Immunotoxicology

Pfizer, Inc., Groton, CT

Translational Pharmacogenetics: Improving Toxicity Risk Prediction by Using Genetically Defined Rodents

11:10am – 11:50am

Alison Harrill, PhD, Research Investigator

Institute for Drug Safety Sciences, Hamner Institutes for Health Sciences

2011 DACC Fall Meeting Hepatotoxicity: Mechanisms, Predictivity, and Biomarkers

Friday – October 21

Lunch

11:50am – 1:00pm

In Vitro Models for Assessing Hepatic Toxicity Hazards

1:00pm – 1:40pm

Michael Aleo, PhD, Research Fellow
Pfizer Inc., Groton, CT

Current Toolbox for the Prediction of Hepatotoxicity

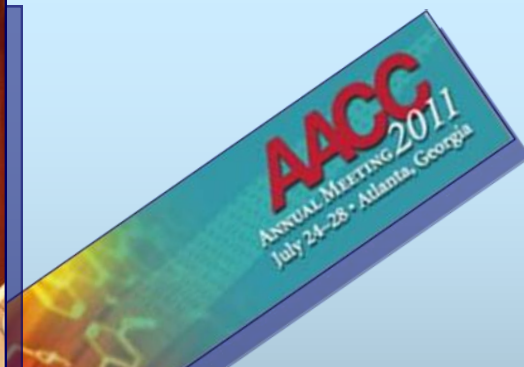
1:40pm – 2:20pm

Eric A. Blomme, DVM, PhD, DACVP, Senior Project Leader
Abbot Laboratories, Chicago, IL

Progress Towards Qualification of Hepatic Biomarkers by the Predictive Safety Testing Consortium

2:20pm – 3:00pm

Shelli Schomaker, BA, Principal Scientist
Biomarkers, Pfizer Inc., Groton, CT



Meeting Abstracts

DACC Fall Meeting Friday, October 21, 2011

Mechanisms of Acetaminophen Hepatotoxicity: New Insights Into the Mouse and Human Pathophysiology

Hartmut Jaeschke, PhD, ATS, Professor
Department of Pharmacology, Toxicology and Therapeutics
The University of Kansas Medical Center

Acetaminophen (APAP) hepatotoxicity is the most frequent cause of acute liver failure in the western world. APAP is also the most studied model hepatotoxin and it is popular as a test system to evaluate potential hepatoprotective agents. It is well established that APAP toxicity is initiated by the formation of a reactive metabolite, which can be detoxified by glutathione, but also leads to protein binding. Although these events are critical to initiate the toxicity, they are insufficient to cause cell death. The presentation will discuss the propagation events in mouse hepatocytes and in vivo including mitochondrial dysfunction, reactive oxygen and peroxynitrite formation, the c-Jun-N-terminal kinase activation

loop, the mitochondrial membrane permeability transition pore, mechanisms of nuclear DNA damage and the defense mechanisms including MnSOD activity and autophagy that control the development of cell necrosis. In addition, mechanisms of APAP-induced cell death in the human HepaRG cell line will be presented. Finally, data from biomarker-based investigations of the mechanisms of APAP-induced liver injury in overdosed patients will be discussed. Together, these studies provide evidence for the relevance of mouse models and certain human cell lines for studies of APAP hepatotoxicity mechanisms in humans. ❖

Inflammatory Stress and Models of Idiosyncratic Hepatotoxicity

Robert A. Roth, PhD, DABT, Professor
Department of Pharmacology and Toxicology, Center for Integrative Toxicology
Michigan State University

Idiosyncratic, drug-induced liver injury (IDILI) remains not only a public health concern but a major problem for drug development. IDILI reactions are currently not predicted by current preclinical testing paradigms and often are not recognized until an offending drug has reached the market. The F.D.A. typically will call for removal of such a drug or inclusion of a "black box warning." Thus, despite much effort and financial investment in drug development, IDILI remains a major issue for pharmaceutical companies. Because these reactions are typically rare, the underlying causes are not understood, and predictive models have been slow to appear. Among the several hypotheses that have emerged to explain IDILI is the "inflammatory stress hypothesis," which proposes that an inflammatory episode occur-

ring during drug therapy renders an otherwise non-toxic drug hepatotoxic. Indeed, for several drugs associated with human IDILI, a modest inflammatory stress in rodents renders the liver sensitive to injury from drug exposure. This enhanced sensitivity is associated with expression of proinflammatory cytokines as well as other mediators of inflammation and with enhanced sensitivity of hepatocytes to the cytotoxic effects of inflammatory factors. In particular, prolonged generation of tumor necrosis factor-alpha (TNF) appears to be important for the development of injury. Understanding mechanisms of drug-inflammation interactions could lead to models effective in predicting preclinically the potential of some drug candidates to cause IDILI in humans. ❖

Register for the Fall Meeting **ONLINE** at the AACC website:

<http://direct.aacc.org/ProductCatalog/Product.aspx?ID=6735>

Reserve a Room at Holiday Inn Express Hotel and Suites

947 US Highway 202 North, Branchburg, NJ, 908-252-1000

www.hiexpress.com/hotels/us/en/branchburg/bjenj/hoteldetail

Discount Group Code: "DCC"



Meeting Abstracts

DACC Fall Meeting Friday, October 21, 2011

Potential Models for Investigating the Role of the Immune System in Drug Induced Liver Injury

Jessica Whritenour, PhD, Principal Scientist, Immunotoxicology
Pfizer, Inc., Groton, CT

Several clinical features suggest that the immune system may play a role in the pathogenesis of drug induced liver injury (DILI). Such features include the presence of a rash, fever, and/or peripheral eosinophilia, a delay in the occurrence of symptoms, and a rapid response upon drug re-exposure. Proposed mechanisms to explain the role of the adaptive immune system in DILI include the hapten and danger hypotheses and the pharmacological interactions concept, however, no one mechanism sufficiently explains every DILI scenario. The lack of animal models coupled with the idiosyncratic nature of the response has made it difficult to identify risk factors and biomarkers for human risk assessment. In an attempt to address these knowledge gaps, an in vivo mouse model of allergic DILI is being developed to

better understand the mechanism(s) and to help identify key risk factors that may eventually be developed into predictive tools. Predictive models to assess the potential of a drug to produce a hypersensitivity response are also being explored, and results from these studies may provide additional mechanistic information relevant to allergic DILI. While these methods are still in the early stages of development, the success of these projects will have a significant impact on human risk assessment and drug development. This presentation will provide an overview of the mechanisms by which drugs can produce allergic DILI and introduce some of the models that are in development for predicting hypersensitivity reactions and their potential utility for predicting allergic DILI. ❖

Translational Pharmacogenetics: Improving Toxicity Risk Prediction by Using Genetically Defined Rodents

Alison Harrill, PhD, Hamner-University of North Carolina, Institute for Drug Safety Sciences
The Hamner Institutes for Health Sciences, Research Triangle Park, NC

Despite advances in nonclinical testing strategies, unpredicted, yet serious, adverse drug reactions (ADRs) continue to be observed during clinical testing or post-marketing surveillance. In part, the failure to understand and predict certain clinical ADRs may be due to the failure to appreciate and exploit the genetic architecture of nonclinical species. Recent examples from the literature have shown that genetic variation can be predictive of toxicity risk in clinical populations. In response, the FDA's recently released strategic plan - entitled Advancing Regulatory Science at FDA - calls for the characterization of "genetic factors that may be associated with adverse events". Mouse diversity panels (MDPs) are genetically diverse sets of inbred mouse strains that may have utility in population-based risk assessment. MDP experiments have been successfully employed to detect genetic susceptibility factors to drug-induced liver toxicity in humans and have the additional potential to determine population-based biomarkers of effect. By combining extensive genetic databases, rationally designed mouse strain panels (e.g. the Collaborative Cross), and toxicity assessment, there is the potential for improved prediction

and mechanistic understanding of drug toxicity using a combined pharmacogenetic approach. Our laboratory has successfully demonstrated the use of the MDP approach to identify genetic risk factors of acetaminophen-induced liver injury, a finding that was later validated in independent clinical cohorts. In this presentation, an example will be presented of a case in which the classical MDP was utilized for mechanistic understanding of toxicity that caused failure of a compound in late stage clinical trials due to safety concerns. DB289, a drug developed for the treatment of human African trypanosomiasis (sleeping sickness) and withdrawn from late stage clinical trials due to renal failure in healthy volunteers, was evaluated using the mouse population-based approach. In this study, the combination of the MDP approach and novel biomarker analyses demonstrated that sensitive mouse strains indicated the potential for the kidney toxicity in contrast to classical rodent testing that had not indicated this potential. Taken together, these data support the potential of the MDP as an improved pharmaceutical safety testing strategy to detect and prevent target organ toxicities in clinical populations. ❖

Meeting Abstracts

DACC Fall Meeting Friday, October 21, 2011

In Vitro Models for Assessing Hepatic Toxicity Hazard

Michael D. Aleo, PhD, Research Fellow, Drug Safety R&D
Pfizer Global R&D, Groton, CT

Drug-induced liver injury (DILI) is a global public health concern and is the most common reason why drugs are removed from clinical development, not approved by regulatory agencies, or withdrawn from the marketplace after their approval. The present material demonstrates the use of two in vitro assays to assess potential hepatotoxicity hazard of pharmaceuticals. The first part of the presentation will focus on use of a cell-based assay to assess three relevant mechanisms of hepatic parenchymal cell injury (mitochondrial membrane potential, generation of reactive oxygen species, and reductions in intracellular glutathione levels) using high content cellular imaging of cryopreserved human hepatocytes. A retrospective analysis of 344 pharmaceuticals and chemicals shows a reasonable degree of sensitivity and high degree of specificity for prediction of liver

injury in humans (Xu et al., *Toxicol. Sci.* 105: 97-105, 2008). The second part of the presentation will focus on the evaluation of a whole organism model to assess potential of pharmaceuticals to cause liver injury in zebrafish. In theory these in vitro predictions can augment the performance of the traditional combined preclinical animal testing paradigm by identifying human-specific hepatotoxicants. Proper use and interpretation of results may be useful in selection of experimental pharmaceuticals with less potential to cause human hepatotoxicity. Technical and practical considerations regarding the complexities of implementing and interpreting the results of cell-based and whole organism screening assays during the drug discovery process will be highlighted. ❖

Current Toolbox for the Prediction of Hepatotoxicity

Eric Blomme, DVM, PhD, DACVP, Director, Investigative Toxicology and Pathology
Abbott Laboratories, Chicago, IL

Hepatotoxicity represents a significant cause of failure in drug discovery and development, and methods to better predict and characterize this toxicity would be highly desirable to increase the probability of success in pharmaceutical R&D. This presentation will provide an overview of the current

status of several technologies for hepatotoxicity prediction that can be used in drug discovery for compound characterization. The strengths, limitations and application of these technologies during lead optimization and candidate selection will be illustrated using selected examples. ❖

Dr. Peter O'Brien Receives the 2011 DACC Award for Outstanding Contribution to Animal Clinical Chemistry

The presentation of this 19th annual DACC award was on July 25, 2011 at the AACC Annual Meeting in Atlanta and was generously supported by Siemens Healthcare Diagnostics.

Dr. P. O'Brien, *BSc, DVM, MS, DVSc, PhD, FRCPath, Diplomate ECVCP*, is a Veterinary Clinical Pathologist and Conway Fellow at the School of Agriculture in the Department of Food Science and Veterinary Medicine at the University College Dublin, Ireland.



Meeting Abstracts

DACC Fall Meeting Friday, October 21, 2011

Progress Towards Qualification of Hepatic Biomarkers by the Predictive Safety Testing Consortium

Shelli Schomaker, Safety Biomarkers, Drug Safety Research & Development
Pfizer Global R&D, Groton, CT

Hepatotoxicity remains a major challenge in drug discovery and development and a major reason for withdrawal of drugs from the market. While alanine aminotransferase (ALT) activity remains the gold standard clinical chemistry marker of liver injury, additional biomarkers are sought to improve the overall sensitivity and specificity for the detection of liver function in preclinical and clinical studies. Both the pharmaceutical industry and regulatory agencies recognize the importance of and are committing resources to the development of novel biomarkers of drug toxicity and safety. The Critical Path Institute's Predictive Safety Testing Consortium (PSTC), a collaboration among 16 pharmaceutical companies with FDA and EMEA participation, has the goal of qualifying preclinical and clinical safety biomarkers for regulatory acceptance. Pfizer and other member companies have used the consortium mechanism to bring forward putative safety biomarkers that have been derived from the literature or discovered in their internal laboratories that have significant sup-

porting data and biological rationale. The initial goal of the qualification is to demonstrate the potential advantages of these markers (singly or in a panel) for the detection of liver damage in comparison to ALT in the context of acute drug-induced liver injury in rats. This presentation will focus on the advances the Hepatotoxicity Working Group of the PSTC has made towards the preclinical and clinical qualification of four serum biomarkers of hepatotoxicity: glutamate dehydrogenase, paraoxonase, purine nucleoside phosphorylase, and malate dehydrogenase. Newly endorsed biomarkers just entering the qualification process will also be highlighted. The overall value of this PSTC effort extends beyond sharing of costs and intellectual resources as it will also enable a more rapid safety biomarker qualification with direct engagement of regulatory agencies. This will result in the development and subsequent acceptance of more reliable biomarkers of toxicity that can be utilized for the safe conduct of preclinical and clinical studies. ❖

The DACC Needs YOUR Vote!

Your participation in the upcoming DACC election is important to assuring continued management quality of your Division's business and educational activities.

2011 DACC Election Will Begin This Fall (FULL MEMBERS ONLY)

Cast Your Vote Online

Candidate for Chair-Elect:

Rich Giovanelli, Pfizer

Candidates for Secretary:

Dave Adams, GlaxoSmithKline

Johanna Wisniewski, Pfizer

Candidates for Nominating Committee:

Rosemary Nicklaus, Roche

Joseph Sansone

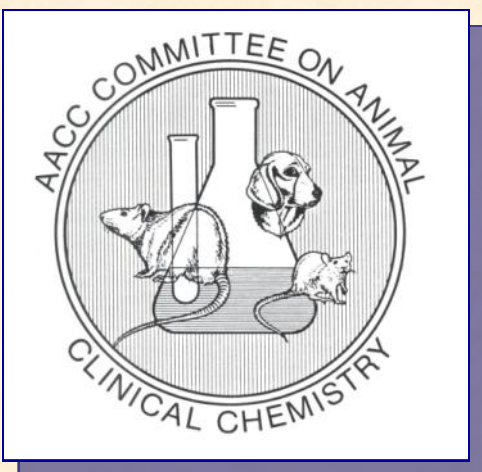
Instructions for voting **ONLINE** in DACC's 2011 election will be sent by the AACC in the near future to DACC members eligible to vote. If you have any questions regarding the balloting, please contact Renée Pearson, DACC Secretary, at 703-663-0768 or Dr.Renee@verizon.net

Ingrid's Birthday Gift

Long ago and far away in a laboratory that has long since been reduced to rubble, the employees of a large photographic company were engaged in the study of chemical toxicity. The laboratory had been around for a very long time. Since the great depression in fact, and as such had many traditions. One of those traditions was that every employee received, on their birthday, a card signed by everyone in the laboratory. It would be waiting for them on their desk or laboratory bench when they arrived in the morning. The other part of the tradition was there would be doughnuts for all. However, it was the duty of the birthday boy or girl to supply them. But you did get to choose the doughnuts.

This was the way it was when I arrived to take my place as an employee. By then the birthday cards had become unique. No longer were they purchased at a store. Instead, everyone got the same card, hand drawn in pen and ink. These were made by the talented young lady shown in the photo whose name was **Ingrid Austin** (right). She was a histology technician who made text book quality slides and pursued a hobby of fine art and photography. Ingrid continued to provide these cards through our transition into a new laboratory and until the end of her life.

Well, the time came after the formation of the *Laboratory Animal Clinical Analysis Group (LACAG)* in 1976 that the organization needed a logo for the newsletter. After searching around for ideas and trying to draw a few ourselves, I remembered Ingrid's birthday cards. I pulled one out and it was perfect. The graphic was just what we needed. Ingrid agreed to let us use it and her creation (below) has been the pictorial symbol of LACAG and later the DACC ever since.

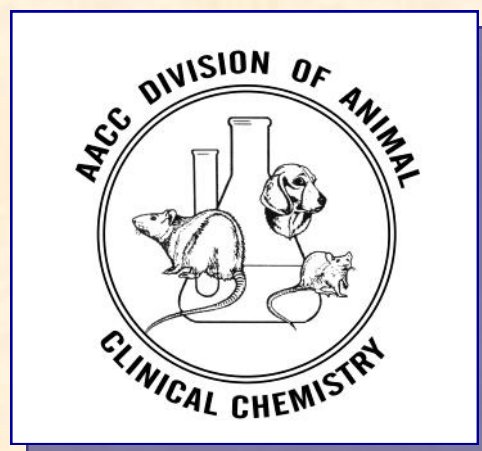


Over time, the image became fuzzy due to

constant reproduction. Recently, the logo has been re-sharpened (below). Occasionally, attempts have been made to stylize it such as on the cover page of the LACAG application for AACC Division status. It has also appeared in modified form and colors on numerous AACC annual meeting buttons. The first of these was a blue and gold lapel button given out in 1989. It would be eleven years before it would be displayed

again, this time on the 2000 San Francisco meeting button.

Ingrid's original graphic design remains unchanged and it is a pleasure, honor, and duty to give her credit for her creativity and willingness to share her birthday card with us on the DACC's 35th birthday. ❖ *By Bob Emmons*



★ **REGULATORY HEPATOTOXICITY REMINDER** ★

FDA Guidance Document Regarding Drug-Induced Liver Injury

In light of DACC Fall Meeting focusing on Hepatotoxicity and issues related to mechanisms of acute and chronic liver injury, preclinical predictive assays and models currently in use or being evaluated to reduce clinical hepatotoxicity in late-stage clinical trials, the use of routine and exploratory biomarkers, and the evaluation of consortium activities to develop new hepatic biomarkers, it seems appropriate to remind ourselves of the regulatory (Agency's) issues and recommendations related to drug-induced liver injury.

Despite extensive preclinical testing, drug-induced liver injury is still a major cause of attrition of compounds in late-stage development. Understanding mechanisms of liver injury and developing new assay, models, and biomarkers to more accurately predict hepatotoxicity at earlier stages of drug development remains a critical issue.

In **July of 2009**, the Food and Drug Administration (FDA) released a guidance document describing nonbinding recommendations:

Guidance for Industry “Drug-Induced Liver Injury: Premarketing Clinical Evaluation”

www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM174090.pdf

“ . . . to assist the pharmaceutical industry and other investigators who are conducting new drug development in *assessing the potential* for a drug to cause **severe** liver injury (i.e., irreversible liver failure that is fatal or requires liver transplantation). In particular, the guidance addresses how laboratory measurements that signal the potential for such drug-induced liver injury (DILI) can be obtained and evaluated during drug development. This evaluation is important because most drugs that cause severe DILI do so infrequently; typical drug development databases with up to a few thousand subjects exposed to a new drug will not show any cases” This guidance does not address issues of preclinical evaluation for signals of DILI, nor the detection and assessment of DILI after drug approval and marketing. This guidance document was developed within the Division of Gastroenterology Products in the Office of New Drugs, the Office of Medical Policy, and the Office of Surveillance and Epidemiology in CDER in cooperation with CBER.

Although the scope of this guidance is targeted for clinical development programs, the background and translational aspects of the rationales discussed make this document an important and relevant resource for all preclinical development projects. It should be remembered that the FDA's current thinking and recommendations on a topic are reflected in published guidances.

❖ *Jon P. Kimball, DACC's Regulatory Affairs & Intersociety Liaison*



U.S. Food and Drug Administration
Protecting and Promoting Your Health

★ REGULATORY AFFAIRS UPDATE ★

FDA Releases Guidance Document Regarding Qualification of Genomic Biomarkers

On **August 10, 2011**, the Food and Drug Administration (FDA) released a guidance document describing recommendations regarding context, structure and format of regulatory submissions for qualification of genomic biomarkers. This guidance document notes that biomarkers have great potential for drug development. For example, they can guide dose selection and provide safer and more effective therapies. A qualification submission can include information for a single genomic biomarker, or for multiple genomic biomarkers used as classifiers. The guidance document focuses on genomic biomarkers, but it is noted that the principles described in the guidance document are applicable to other biomarker categories such as genomics, proteomics, imaging and a combination of biomarkers.

Drug development and regulatory review is challenging, complex and changing at an unprecedented pace. Industry (pharma) and the FDA, while being different enterprises, have a common goal of reliance on biomarkers to empower people to make better decisions. Drug developers and regulators may choose to use biomarkers differently given their respective missions, but together we now have to face the challenge that there is an increasingly sophisticated array of technology to discover and develop new biomarkers.

Guidance for Industry

“E16 Biomarkers Related to Drug or Biotechnology Product Development: Context, Structure, and Format of Qualification Submissions”

www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm267449.pdf

This guidance document was developed within the Efficacy Working Group of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The guidance is provided to facilitate a consistent format for the submission of data to the end of easy review and exchange of assessments. The guidance document notes that qualification is a conclusion that within the stated parameters, a biomarker can be relied upon to adequately reflect a biological process, response, or event, and support use of the biomarker during drug or biotechnology product development, from discovery through post approval.

The scope of this guidance is the context, structure, and format of qualification submissions for clinical and *nonclinical* genomic biomarkers related to development of drug or biotechnology products including translational medicine approaches, pharmacokinetics, pharmacodynamics, and efficacy and safety aspects. FDA guidance documents, including this guidance, contain Nonbinding Recommendations and do not establish legally enforceable responsibilities. However, the FDA's current thinking and recommendations on a topic are reflected in published guidances.

❖ *Jon P. Kimball, DACC's Regulatory Affairs & Intersociety Liaison*



U.S. Food and Drug Administration
Protecting and Promoting Your Health

Call for Nominations

2012 Division of Animal Clinical Chemistry Award for Outstanding Contributions to Animal Clinical Chemistry

The DACC has established a Division Award which recognizes Outstanding Contributions in the field of Animal Clinical Chemistry. This Award consists of a plaque, an honorarium and a reception for the individual so honored, and is usually presented at the AACC Annual Meeting. The DACC Awards Committee would like to invite all members and friends of the DACC to nominate such an honoree.

The Award is to recognize the achievements of an individual who has made significant contributions in the field of animal clinical chemistry in its broadest sense including teaching, training, practicing and research. Activities and achievements of this person, which have significantly benefited the science and advancement of this discipline, as well as enhanced the public awareness and understanding, are also taken into consideration.

The recipient of this prestigious award will be selected from nominations submitted by an AACC member or group of members such as division, local section, committee or commission. Nominations will also be considered from non-member individuals and organizations. Please submit your nomination by letter or e-mail. The submission should consist of a statement of the nominee's accomplishments and a current curriculum vitae and bibliography. Two seconding letters of support from colleagues detailing the candidate's accomplishments not given in the primary letter of nomination should be included. The latter will play an important role in the Awards Committee deliberations.

Previous recipients of the DACC award were:

Jiro J. Kaneko, DVM, PhD	1993	Douglas A. Neptun, BS, MT/ASCP	2003
Eitan Bogin, PhD	1994	Charles C. Capen, DVM, PhD	2004
Donald T. Forman, PhD	1995	John H. (Tim) Lumsden, DVM, DACVP	2005
Robert E. Emmons, BS	1996	Douglas J. Weiss, DVM, PhD, DACVP	2006
Walter F. Loeb, DVM, PhD	1997	W. Jean Dodds, DVM	2007
Thomas J. Reimers, PhD	1998	N. Leigh Anderson, PhD	2008
Jon P. Kimball, PhD	1999	Kay A. Criswell, PhD, DABT	2009
Dai T. Davies, PhD	2000	P. David Eckersall, BSc, MBA, PhD	2010
Walter E. Hoffmann, DVM, PhD	2001	Peter J. O'Brien, DVM, DVSc, PhD	2011
John W. Harvey, DVM, PhD	2002		

Nominations must be received no later than March 30, 2012.

Please submit completed nomination documents by email or surface mail to:

Jon P. Kimball, PhD, DACC Awards Committee

1732 Old Lystra Road, Chapel Hill, NC 27517, 919-967-4016, eMail: JonKimball@msn.com

**2012 Division of Animal Clinical Chemistry
Travel Award for DACC Best Poster Presentation
At the AACC Annual Meeting**

DACC Travel Award
Recognition Award for DACC Poster Presentations

The AACC Division of Animal Clinical Chemistry (DACC) Executive and Awards Committees have established a Travel Award to be given in recognition of outstanding research in the area of Animal Clinical Laboratory Medicine for an abstract accepted and a poster presented at the AACC Annual Meeting. This DACC Travel Award is for the presenters of the best abstract & poster by DACC members, associates, or trainees (in academia or industry) in multi-species Clinical Pathology that has been accepted and presented at the AACC Annual Meeting. Up to two posters & abstracts may be selected each year for this award based on merit and recommendation of the Abstract Review Committee.

The Travel Award consists of a certificate of scientific merit, a \$500 monetary cash award, and travel reimbursement (up to \$1000) to support the awardees' expenses to attend (registration fee waived) the DACC Fall Meeting.

The award abstract and accompanying poster will be displayed at the DACC Fall Meeting.

This Award is Sponsored by the DACC Executive and Awards Committees

***A REMINDER to Submit 2012 AACC Annual Meeting
Poster Abstracts***

***The DEADLINE for poster abstract submission is
February 27, 2012***

It has only been a short time since last summer's AACC Annual Meeting, but time flies when you are as busy as we all have been these past few months. And time will seem accelerate as we become involved in the approaching holiday season. Thus, this note is to serve as a reminder that **you only have a few months remaining to submit your DACC poster abstracts for next year's annual AACC meeting in July. Stay tuned for AACC announcements regarding online abstract submission procedures.**

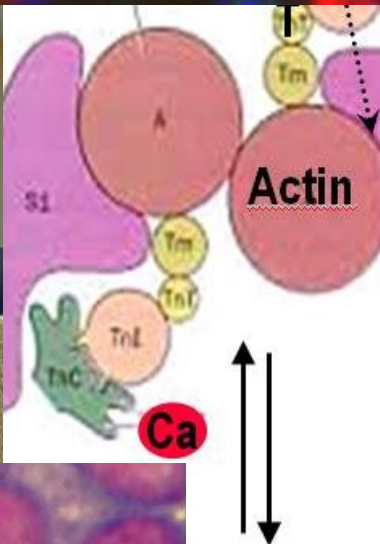


Be sure to submit your abstract to be included with those in the Animal Clinical Chemistry Division

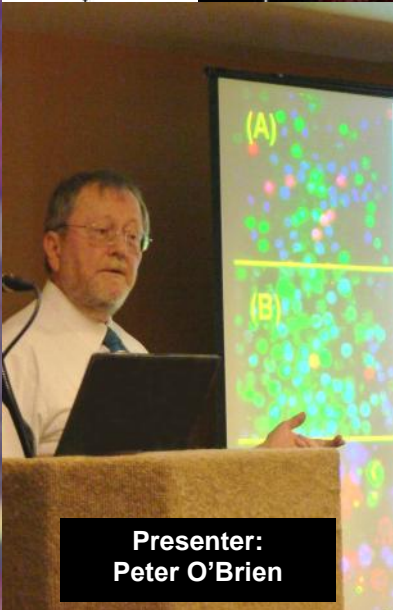
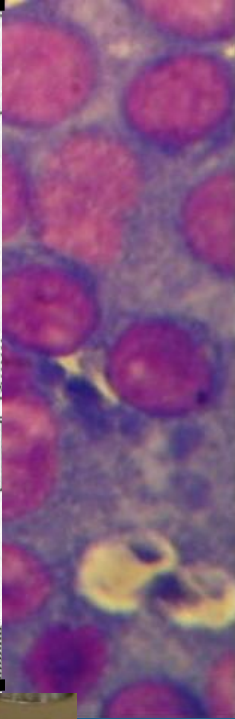
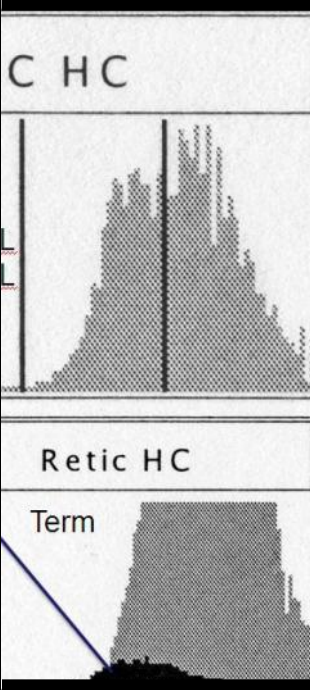
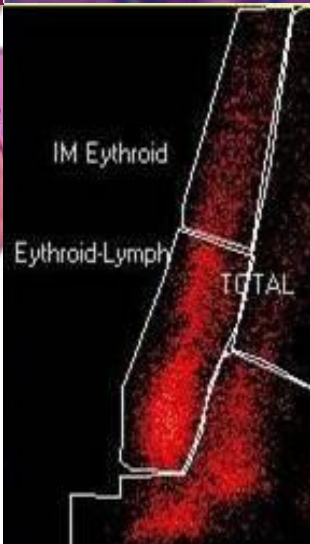


Images from the 2011 Annual Meeting
DACC Lunch and Learn "Case Studies"

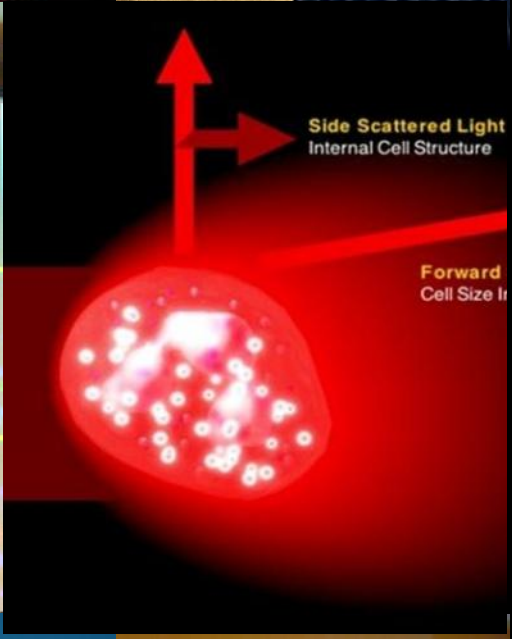
**Presenter:
Lila Ramaiah**



**Presenter:
Kay Criswell**



**Presenter:
Peter O'Brien**



**Presenter:
Chris Perigard**

What's with the Prolonged APTT?

...tati
...shana Pandya, MT (ASCP)



**Presenter:
Susan Haley**

Short Scripts

International Year of Chemistry 2011

Don't miss the excellent article in the September issue of Clinical Chemistry by Marek H. Dominiczak: "Laboratory -Its Meaning in Science and Culture"
www.clinchem.org/cgi/content/extract/57/7/1088



Volunteers are needed for DACC committees. Join your colleagues in determining the future direction of YOUR division.



**ACVP/ASVCP
ANNUAL MEETING
Nashville, TN
December 3-7, 2011**
[www.asvcp.org/meeting/2011/
preliminaryprogram.cfm](http://www.asvcp.org/meeting/2011/preliminaryprogram.cfm)



Meet the Speakers and Poster Travel Award Reception/Mixer

**Thursday 10/20/11 6:30pm in the Great Room
Holiday Inn Express Hotel and Suites
947 US Highway 202 North, Branchburg, NJ**

Free !! Send RSVP for the Reception to Barb at
litzenbb@princeton.huntingdon.com

**Co-Hosted by
Huntingdon Life Sciences and
Sysmex America, Inc.**



The 2011 DACC Election is SOON!
Please Vote This Year and Run for Office Next Year
The Election Process Depends on YOUR Vote !
Watch For Your Electronic Ballot Announcement!



DACC NEWS

AACC's Division of Animal Clinical Chemistry



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DACC 2011 Committees

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Karen Lynch (2012)
Kay Criswell (2013)
Dave Desmond (2014)
Mike Bieraugel (Exec Rep)

Membership

Joe Sansone (Chair)
Rosemary Nicklaus
Ana Maria Roncal-Lahman
Gail Walter

Scientific Program & Long Range Planning

Barbara Litzenberger
Kay Criswell
Mike Bieraugel
Rosemary Nicklaus
Doug Thudium

Fund Raising

Jon Kimball
Doug Neptun
Chris Perigard
Lila Ramaiah (Exec Rep)

Awards

Jon Kimball (Chair)
Jiro Kaneko
Bob Emmons
Doug Neptun

Spring*/Fall Meeting**

*Mike Bieraugel
**Kay Criswell

Annual Meeting

*Mike Bieraugel (2011)
*Barbara Litzenberger (2012)

Regulatory Affairs & Intersociety Liaison

Jon Kimball:
ISACB
Gail Walter:
ASVCP/SOT/STP

* Principal Organizer, with Help from the Executive and the Scientific Program & Long Range Planning Committees