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Institute Update

Test System Monitoring and Good Laboratory Practices at IIVS

The expanding use of *in vitro* methods by industry and regulatory agencies has resulted in an increased need to apply Good Laboratory Practice (GLP) regulations to these systems. Recently, the Organization for Economic Cooperative Development (OECD) published advisories to clarify the application of the GLP principles to *in vitro* studies.

Positive controls (red tape) and negative controls (blue tape) as prepared for the BCOP assay.

Since opening in 1997, IIVS has actively pursued creating a culture of quality that expands beyond the performance of assays in our laboratory. This culture is necessary to give confidence to a maturing field and will ultimately ease the progression of *in vitro* methods into the regulatory arena. For example, we feel it is crucial to carefully monitor each test system to assure that it is performing within acceptable limits during every study. To this end, IIVS runs a set of assay controls (comprised of both a positive and negative control) with EVERY assay we perform—whether the protocol is GLP or not. A positive control is a substance which is expected to cause a known response in a test system. The magnitude of the response is chosen so that a failure on either side of the expected effect can be detected. Thus on any given day we can determine if our assays are performing with significantly more or less sensitivity than the historical average. The negative control is run to measure the range of test system response when an inactive test material is present. Negative controls, or blanks, are substances such as distilled water, saline, or media that are expected to cause little change in the test system on their own. All manipulations specified in the protocol are carried out on the test system exposed to either type of control material.

Another example of our commitment to quality is our vendor audit program. Since testing facilities must verify the quality of the test components they use, IIVS conducts yearly vendor and sub-contractor audits. During these

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BITS & PIECES

- Visit us at the 2006 Annual SOT Meeting Expo in San Diego, CA. Booth #1425.
- BCOP Histology Info Session at SOT on Wednesday March 8th, 1:30—2:30 Room 11A
- John Harbell to present at the 6th International Conference on Early Toxicity Screening in June
- **John Harbell elected to position of Vice-President of the Society of In Vitro Biology!**

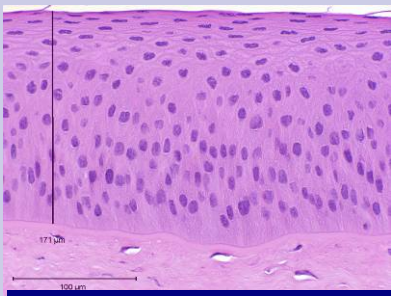
Inside this issue:

IIVS Continues Scientific Outreach Programs

Over the past 8 years, IIVS has been involved in the optimization and validation of a wide range of cell-based bioassays, developed to address toxicity and potency endpoints. As part of our outreach program, we have worked to share these experiences with other organizations through participation on expert advisory panels, providing hands-on training sessions, and presentations at scientific meetings. For example, **Hans Raabe** will describe the conclusions of our recent *in vitro* skin penetration workshop at the Perspectives in Percutaneous Penetration 10th International Conference in La Grande Motte, France. Another example is the upcoming presentation (ISE 6th International Conference) by **John Harbell** on the necessity for *in vitro* bioassay consistency during the progression from validation to regulatory acceptance. IIVS outreach activities are intended to facilitate acceptance and expanded use of *in vitro* assays by regulatory agencies. For more information , please visit our web site at www.iivs.org.

Using Histological Evaluation to Enhance the BCOP Assay for Ocular Irritation Information Session

This year we are hosting a special **Information Session on Wednesday from 1:30-2:30pm in room 11A** in the convention center**.** Please plan to join us for the latest information from **Drs. John Harbell (IIVS) and Deepta Ghate, M.D. (Emory University)** on the benefits of adding an histological analysis of corneal damage to *in vitro* organotypic assays such as the traditional Bovine Corneal Opacity and Permeability assay. The BCOP assay is widely used to assess ocular irritation. Although the standard endpoints are generally predictive, damage caused through certain modes of action is sometimes missed. This one hour presentation will provide participants with information on the structure of the cornea (Dr. Ghate) and on how histological evaluation enhances irritation predictions by allowing direct measure of depth and area of injury. Histological analysis also allows for a characterization of the specific lesions induced by the various test articles' modes of action (Dr. Harbell). **Dr. Rodger Curren** will provide the introduction to the presentations. For more information on this session, please stop by our SOT booth.



Photograph of the epithelium of a negative control cornea

Important SOT Information

- Booth #1425
  - M 8:30-4:30
  - T, W 9:30-4:30
- Info Session
  - W 1:30-2:30
  - Room 11A

SOT members enjoying themselves at a fiesta happy hour party in San Diego

Join Us In San Diego for the 2006 Society of Toxicology Meeting

With mild temperatures, gleaming white beaches and fabulous Mexican food, San Diego is a perfect setting for the 45th annual meeting of the Society of Toxicology (March 5th-9th). Take this opportunity to meet with our technical staff to discuss current projects, learn about new applications of *in vitro* test methods or hear an update of current regulatory and committee work. Stop by **booth #1425** during exhibit hours (9:30am-4:30pm Monday, 8:30-4:30 Tuesday and Wednesday) to see us. Once again we will have a special item for you to take home as our gift.

…and don't miss our co-authored session and posters…

Presentation Co-Author—Monday: Alternative Models for Assessment of Toxicity 9:30am-12:00pm

- Xenobiotic Metabolizing Enzyme (XME) Expression in the EpiDerm™ In Vitro Human Skin Equivalent: Utility for Assessing Dermal Biotransformation of Pharmaceuticals, Cosmetics and Environmental Chemicals

Posters Monday: Genotoxicity/DNA Repair 1:30-4:30pm

- Evaluation of a Novel Micronucleus Assay Using a Human 3-D Skin Model, EpiDerm™

Tuesday: Risk Assessment Methods—Regulatory/Policy 9am-12pm

- The Importance of Supplier Qualification for Vendors of Materials Used in In Vitro Assays

Wednesday: Alternative Models for Assessment of Ocular and Dermal Toxicity 9am-12pm

- Application of Histological Evaluation to Enhance the Bovine Corneal Opacity and Permeability (BCOP) Assay
- Fragrance Impact on Marketed Air Freshener Products by BCOP Assay and Histology

Alternatives to Mammalian Models 1:30-4:30pm

- Use of an Adenosine Triphosphate Cytotoxicity (ATP) Assay in Normal Human Epidermal Keratinocytes to Predict Systemic Toxicity In Vitro
- Reducing Animal Use in Acute Systemic Toxicity Testing by Using in Vitro Cytotoxicity Assays for Estimating Start Doses
- The Use of Mouse Fibroblasts (3T3) and Normal Human Epidermal Keratinocytes (NHK) Cytotoxicity Assays for Estimating Acute Oral Toxicity of Formulations and Mixtures
- Reproducibility Analyses for In Vitro Neutral Red Uptake Methods from a Validation Study to Evaluate In Vitro Cytotoxicity Assays for Estimating Rodent Acute Systemic Toxicity

Thank You for Your Support

IIVS is probably best known for its product testing capabilities. Every year we help hundreds of clients use non-animal methods to assess the efficacy and safety of their products.

Many people are less familiar with our educational and outreach programs that energize the worldwide use and acceptance of alternative methods. Through product testing we have acquired extensive first hand knowledge of the performance of *in vitro* methods with a variety of products. This information makes IIVS unique in its ability to advocate for the appropriate uses of *in vitro* methods by industry, regulatory agencies and animal welfare groups around the world. These communications take a variety of forms: from peer-reviewed manuscripts to college seminars to hands-on training sessions for regulatory agency personnel. Unlike our testing services, these educational and outreach programs are funded solely by the generous contributions of our supporters. Without this assistance, IIVS could never provide the extensive programs which we feel are essential to the continued growth of the field. IIVS would like to thank our Sponsors and Contributors (see right panel) who - through their continued monetary and philosophical support – have joined with us to accelerate the acceptance of *in vitro* methods.

Sustaining Sponsors

- Colgate-Palmolive
- Johnson & Johnson
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Contributors

- Combined Federal Campaign
- Dial
- Doris Day Animal League
- Institute for Ethical Research
- People for the Ethical Treatment of Animals

Test System Monitoring and GLPs at IIVS

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audits, vendor facilities are inspected, employees are interviewed, training programs and equipment maintenance are examined, and lot or batch specific documentation is reviewed. Reports of these yearly inspections are created and retained at IIVS to provide documented evidence of our review of each vendor's overall in-house quality program. Combining our assay control historical database with this test system monitoring program gives us even greater confidence in the quality and reproducibility of the test systems we use.

We believe it is extremely important to continue this comprehensive quality assurance program which helps us provide the best available data to clients and regulatory agencies, thus hastening the scientific acceptance of *in vitro* methods.

For more information on the Quality Assurance or GLP programs at IIVS, please see the recently presented posters under Publications at www.iivs.org).

SAP Member Highlight—Dr. Daniel Bagley

Dr. Daniel Bagley of the Colgate-Palmolive Company has been a valuable member of the SAP since our founding in 1997. In addition to his everyday responsibilities as Senior Worldwide Director of Product Safety, Dermal Clinicals and Statistics, Dr. Bagley is responsible for leading Colgate's efforts to identify, use and gain regulatory acceptance of alternative methods. Colgate has committed more than one million dollars annually to this process which keeps Dan actively involved in overseeing numerous internal and external research programs for the development of new safety and efficacy tests. He also serves as Colgate's liaison to U.S. and European organizations working in the field. His group's efforts have contributed significantly to Colgate-Palmolive's moratorium on all animal testing of their personal care products designed for adults. IIVS greatly appreciates Dan's knowledge and expertise which he readily shares with the advisory committee.

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Advancing Science & Animal Welfare Together

2006 Annual SOT Meeting Tox Expo San Diego, CA. Booth #1425.

Founded in 1997, IIVS is a non-profit science-based organization dedicated to the advancement of alternative, non-animal testing methods. IIVS seeks to refine the science, broaden the use, and increase the acceptance of in vitro *testing worldwide.*

To learn more about IIVS, or how you can support our programs, please visit us at www.iivs.org.

It is only with the generous support of industry, the animal protection community, and the general public that we can continue to make a difference in acceptance of in vitro *methods.*

"What's New at Our House"

Welcome to our new Study Director Janet Luczak! Janet brings to IIVS over 20 years of experience in GLP-compliant contract laboratory services in the application of assay systems for evaluation of materials used in humans. Janet first worked with some of the current IIVS crew while at Microbiological Associates (now BioReliance Corp.). She then traveled to Primedica, and next to Charles River Laboratories where she was most recently Director of Business Development. In this role she had responsibility for client services, sales, and business development for the Biopharmaceutical Services Division. The first assay that Janet will take over Study Director responsibilities for will be the Bovine Cornea Opacity and Permeability Assay (BCOP). Janet can be reached by phone at **301-963-4946** or by email at **jluczak@iivs.org**. You should be hearing from Janet soon concerning your current or planned BCOP studies.

Another biologist joins the ranks at IIVS. Jennifer Nash graduated in 2002 from Virginia Polytechnic Institute and State University with a Bachelor of Science in Engineering Science and Mechanics. Jennifer then began a Master's degree program in Bioengineering at Georgia Institute of Technology studying the mechanical and biochemical properties of the chordae tendineae of the mitral valve. She completed her Master's in 2004. Continuing her cardiac research at the University of Maryland School of Medicine, she conducted strain analysis and protein expression on myocardial tissue following myocardial infarctions. Jennifer joined the Institute for In Vitro Sciences as a biologist in January 2006. As a new member of the laboratory team, Jennifer is currently trained to run the Bovine Corneal Opacity and Permeability Assay.

A new booth! It was time to update our image a bit, so a new booth debuts at the upcoming SOT meeting. Please stop by and give us your comments!