Fellow DTSS members,

We are now just about halfway in the annual cycle of DTSS, delimited by SOT annual meeting 2014 in Phoenix, and the upcoming SOT annual meeting in San Diego March 22-26, 2015. The SOT annual meeting is also the venue for our annual DTSS members’ meeting. This is an occasion for toxicologists with an interest in the toxicology of the skin to meet scientific colleagues and friends and to discuss both scientific and general topics. This year the DTSS annual meeting will be on Wednesday 25 March, so all DTSS members, please mark your calendars.

Lots of things are happening in the field of dermal toxicology, both on a scientific and regulatory level: A new ICH S10 guideline on Photosafety evaluation of pharmaceuticals has recently reached ICH Step 4 and is under implementation in the various regions. This guideline is obviously relevant for drugs applied to the skin. The SOT 2014 annual meeting had an interesting session on phototoxicity testing of pharmaceuticals without the use of animals, organized by Lew Kinter and Abigail Jacobs and co-sponsored by DTSS, where different strategies for mainly in vitro-based testing for phototoxic potential of both dermal and systemically applied pharmaceuticals were presented. Generally, as judged from the presentations and posters on dermal toxicology at the SOT meetings it is evident that new and improved in vitro-based methods play an increasing role in the safety evaluation of drugs.
or chemicals that come in contact with the skin, be it methods to assess transdermal penetration, local skin (or eye) irritation, or phototoxicity. Also, in vitro methods that could provide a realistic assessment of chemicals for allergic skin sensitization potential are being researched. In the European Union the safety of cosmetic products is now being assessed without the use of animal testing, and safety evaluation of chemicals under the European Union’s REACH process intends to use as few laboratory animals as possible. Members of DTSS are clearly taking part in this research for such new methods.

When this newsletter is published, the deadline for submission of abstracts for SOT 2015 has just passed. I hope that many DTSS members have submitted abstracts, so there will a good selection of dermal toxicology posters and presentations at the upcoming SOT 2015. Please note: The Late Breaking Abstract submission period will be from December 5, 2014 to January 12, 2015. I also strongly encourage all members to consider generating scientific session proposals with dermal toxicology content for future SOT meetings, since this would clearly increase the value of the SOT meetings for the DTSS members. The next deadline for submitting session proposals is 30 April 2015 but it is probably not too soon to start putting your ideas and speakers together. Finally, I would like to draw your attention to the awards that are given out by DTSS in collaboration with our sponsors at the annual DTSS member meeting. Please, visit the DTSS website for further details about the various awards and submit your application by 31 January 2015.

I would like to use this occasion to thank my fellow DTSS officers for the work they are doing for our members: John Graham as Past President and Councilor, Jeff Yourick as Vice President, Doug Learn as Vice President-Elect, Jill Harvilchuck as Secretary/Treasurer, Adrienne Black and Neera Tewari-Singh as Councilors, Shuxi Qiao as student representative and Anil Jain as post-doc representative.

Thank you for your continued support of DTSS and I look forward to seeing everyone in San Diego!

Sincerely,
Jens Thing Mortensen, DVM, DABT, ERT
President 2014-15, Dermal Toxicology Specialty Section
The Mission of DTSS

The objectives of the Dermal Toxicology Specialty Section (DTSS) are to provide a forum for the interaction of individuals involved in risk assessment, pharmacokinetics, dermal penetration/absorption, hypersensitivity and dermal toxicity, regulatory issues, basic skin biology and other professionals working in the field of dermal research. Members who wish to receive more information on the specialty section should contact Jens Mortensen or any of the other Officers by e-mail.

DTSS Activities include:

• Presents/sponsors programs and educational activities;

• Acts as a resource to the SOT in dermal toxicology;

• Relates developments in dermal toxicology to SOT activities; and

• Stimulates growth in the science of dermal toxicology.
ICH HARMONISED TRIPARTITE GUIDELINE
PHOTOSAFETY EVALUATION OF PHARMACEUTICALS
S10

Having reached Step 4 of the ICH Process at the ICH Steering Committee meeting on 13 November 2013 this guideline is recommended for adoption to the three regulatory parties to ICH.

Excerpt from the document related to dermal routes:

Please refer to the complete document for more detail (http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Safety/S10/S10_Step_4.pdf)

Recommendations for Pharmaceuticals Given via Dermal Routes
5.2.1 Assessment of Phototoxicity Potential

If the active substance and excipients do not have MEC values greater than 1000 L mol\(^{-1}\) cm\(^{-1}\) (between 290 and 700 nm), no further photosafety testing is recommended and no phototoxicity is anticipated in humans. For compounds with MEC values of 1000 L mol\(^{-1}\) cm\(^{-1}\) or higher, negative photoreactivity test results (e.g., a ROS assay) can support a decision that no further photosafety assessment is warranted (see Note 5 for exception). If further assessment is warranted, available data on the phototoxicity of chemical class-related compounds should be evaluated, as this could inform on the approach to be taken.

Tissue distribution is not a consideration for the phototoxicity of dermal products. Dermal products are administered directly to the skin and hence, unless they are applied to areas not usually exposed to light, are assumed to be present in light-exposed tissues.

5.2.2 Experimental Evaluation of Phototoxicity and Photoallergy
The 3T3 NRU-PT can be used to assess individually the phototoxicity potential of the API and any new excipient(s), provided that appropriate testing conditions can be achieved (e.g., test concentrations not limited by poor solubility, relevant UVB dose can be applied). In cases where no phototoxic component has been identified in vitro, the overall phototoxicity potential of the clinical formulation can be regarded as low. (continued on next page)
Some properties of the clinical formulation that could influence the potential phototoxic response (e.g., penetration into skin, intracellular uptake) cannot be evaluated using the 3T3 NRU-PT alone. Therefore, confirmation of the overall negative result in an evaluation using the clinical formulation and/or monitoring during clinical trials can still be warranted. Reconstructed human skin models can be used to assess the phototoxicity potential of clinical formulations. Under adequate test conditions (see Section 3.3), a negative result in a reconstructed human skin assay indicates that the direct phototoxicity potential of the formulation can be regarded as low. In this case, generally no further phototoxicity testing is recommended (see Note 5 for exception).

If an appropriate in vitro assay is not available, the initial test could be an in vivo phototoxicity test on the clinical formulation. A negative result in an appropriately conducted in vivo animal phototoxicity study would be sufficient evidence that the formulation is not directly phototoxic and no further phototoxicity testing is recommended (see Note 5 for exception). Alternatively, the phototoxicity potential can be assessed in the clinical setting.

For dermal products where the API or any new excipient has a MEC value greater than 1000 L mol-1 cm-1 at any wavelength between 290 and 700 nm, a photoallergy assessment is generally warranted in addition to phototoxicity testing. As the predictivity of nonclinical photoallergy tests is unknown, this would typically be a clinical assessment using the to-be-marketed formulation and conducted during Phase 3.

Photosafety evaluation of the clinical formulation delivered via dermal patches can follow the above described principles for clinical dermal formulations. For transdermal patches, the principles for both dermal and systemic drugs should be applied. In addition, the intended clinical use (e.g., skin area recommended for use, duration of application) and the properties of the patch matrix (e.g., being opaque to UV and visible light) should be considered for the overall risk assessment.
Upcoming Conferences & Events


- January 31, 2015: Deadline for Early Bird Registration for SOT meeting
- February 19, 2015: Deadline for Housing Registration for SOT meeting
- February 28, 2015: Deadline for Standard Registration for SOT meeting
- After February 28, 2015: Final Registration period for SOT Meeting


June 8, 2015: Satellite meeting: International Society for Biophysics and Imaging of the Skin, Vancouver, Canada (http://isbs2015.doodlekit.com/)

Food and Drug Administration
Center for Food Safety and Applied Nutrition (CFSAN)
Guidance for Industry
Safety of Nanomaterials in Cosmetic Products
June 2014

CFSAN Finalized this Guidance for Industry in June 2014. There is plenty of dermal/skin application in this guidance that might be of interest to DTSS members:

**Summary of Recommendations**

In summary, nanomaterials can have chemical, physical, and biological properties that differ from those of larger scale particles with the same chemical composition, and the use of nanomaterials in cosmetic products may raise questions about the safety of the product for its intended use. As with any cosmetic product that has new or altered properties, data needs and testing methods should be evaluated to address any unique properties and function of the nanomaterials used in the cosmetic products as well as the questions that continue to remain about the applicability of traditional safety testing methods to products that involve nanotechnology. We recommend that the safety assessment for cosmetic products using nanomaterials should address several important factors, including:

- the physicochemical characteristics,
- agglomeration and size distribution of nanomaterials under the conditions of toxicity testing and as expected in the final product,
- impurities,
- potential routes of exposure to the nanomaterials,
- potential for aggregation and agglomeration of nanoparticles in the final product,
- dosimetry for *in vitro* and *in vivo* toxicology studies, and
- *in vitro* and *in vivo* toxicological data on nanomaterial ingredients and their impurities, dermal penetration, potential inhalation, irritation (skin and eye) and sensitization studies, mutagenicity/genotoxicity studies.

We expect that the science surrounding nanomaterials will continue to evolve and be used in the development of new testing methods.
The safety of a cosmetic product should be evaluated by analyzing the physicochemical properties and the relevant toxicological endpoints of each ingredient in relation to the expected exposure resulting from the intended use of the finished product. If you wish to use a nanomaterial in a cosmetic product, either a new material or an altered version of an already marketed ingredient, we encourage you to meet with us to discuss the test methods and data needed to substantiate the product’s safety, including short-term toxicity and other long-term toxicity data, as appropriate. We welcome your questions relating to the use of nanomaterials in cosmetic products.

(disclaimer: Guidance documents represent FDA’s current thinking on a topic. They do not create or confer any rights for or on any person and do not operate to bind FDA or the public. Manufacturers can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations.)
Membership and Award Opportunities

DTSS Members – Would you like to become more active in DTSS?
If you have any suggestions or recommendations on how to make our specialty section better or better able to serve your needs, please email your suggestions to:

jnstthing@gmail.com

Membership Drive and Award Opportunities

As always, we encourage you to apply for membership at this website: http://www.toxicology.org/ISOT/SS/dtss/membership.html. DTSS members have the opportunity to apply for a number of DTSS sponsored awards. The Best Paper Award is awarded in recognition of an exceptional recent peer-reviewed publication in the field of dermal toxicology and pharmacology. The Sinclair Student Abstract Award and the Stratacor Postdoctoral Abstract Award recognize outstanding student and postdoctoral candidates for their contribution to dermal toxicology. Two Battelle Student Research Awards are awarded to graduate students for use in research projects involving dermal toxicology. The DTSS 2015 award winners will be announced at the 2015 SOT Annual Meeting in San Diego.
DTSS Financial Report:

The net DTSS assets as of August 2014 are $14,096. This amount includes our budget after clearing all expenses from the 2014 Annual meeting. The balance still includes $5000 received from Battelle in 2013 for the Battelle Research Student Awards. The cost of the DTSS reception and Officer’s meeting at the 2014 Annual Meeting was $3,608.52. The cost of the 2014 awards and plaques was $1086.02.

The May 2014 summary is included to show DTSS’s annual meeting expenses.
DTSS awards given out at the DTSS Reception at the 2014 SOT Annual Meeting in Phoenix, AZ:


The Sinclair Student Award was given to Shuxi Qiao (University of Arizona, Tucson, AZ) for the work: “Repurposing the aminophenol-antimalarial amodiaquine for autophagy-directed anti-melanoma intervention.”

The Stratacor Post Doctoral Award went to Satya Achanta (Yale University School of Medicine, New Haven, CT) for the work: “TRPA1 inhibitors counteract inflammation and edema in a mouse model of CS tear gas agent-induced cutaneous injury,.”

Please, visit the Dermal Toxicology Specialty Section website for information about awards available for 2015:

• Dermal Toxicology Specialty Section Annual “Paper of the Year” Award
• Dermal Toxicology Specialty Section Sinclair Student Award
• Dermal Toxicology Specialty Section Battelle Student Research Award
• Dermal Toxicology Specialty Section Stratacor Post Doctoral Award

Further information can be obtained from DTSS Councilor, Adrienne Black, and to whom applications for all awards should be sent (adrienne159@gmail.com). The deadline for all applications is January 31, 2015.

In addition, a Kindle Fire HD was awarded as a door prize from contact information submitted during the 2014 Student-Postdoc Mixer. This prize was sponsored by MB Research Labs.
Recent DTSS Member Publications

The following is a list of publications self-reported by DTSS members that were published in 2014:


Please forward this newsletter to your colleagues that might be interested in becoming a member of DTSS!
Pictures from 2014 DTSS Reception

George DeGeorge (Past DTSS President)
Jill Harvilchuck (DTSS Secretary/Treasurer)
Mike Babin (DTSS Councilor)

Stratacor Post Doctoral Award

Satya Achanta
Bill Reifenrath (Past DTSS President)
George DeGeorge (MB Research Labs) presenting a Kindle Fire HD as a door prize) to Anand Ravindran

Wally Hayes
Jim Riviere (Past DTSS President)