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President’s Message
“Winter Greetings”

Dear Members,

I wish you winter greetings, although winter is a relative term down here in Louisiana. As most of you know, we are the new kids on the block being the newest specialty section within SOT. Not only are we new, but we are emerging, having grown from an initial membership of 100 to currently about 150. Thus, I want to thank all of you for being members of the Clinical and Translational Specialty Section (CTTSS) – without your support we would not have been able to become a specialty section. Our continuation relies on you renewing your membership, so please remember to “tick the box” for CTTSS when you renew your SOT membership this year.

Because this is our last newsletter of the year, I feel the need to mention our important activities – sort of like one of those Christmas cards that you fill with all the news about junior’s accomplishments in karate class, middle school, etc. Most of our activities were centered on the annual SOT meeting.

Don’t forget to register for the 2015 SOT meeting in San Diego, March 22-26.
Submit a Late-Breaking Abstract: January 12, 2015
Early Bird Registration: January 31, 2015
Standard Registration: February 28, 2015
http://www.toxicology.org/AI/MEET/am2015/
Two symposia (“Clinical Evaluation of Emerging Biomarkers of Drug-Induced Liver Injury” and “Somatic Cell Therapy-Paradigms for Investigational New Drug (IND)—Enabling Programs, Scientific and Regulatory Considerations, and Clinical Translation”) were chaired by CTTSS officers and we endorsed two additional symposia/workshops at the meeting. At our reception/business meeting, Dr. Jeff Brent enlightened us about development of antidotes – more details about his presentation are given elsewhere in the newsletter for those of you who could not attend. We presented Dr. Brent with a CTTSS Career Achievement Award. Congratulations also went out to our young members, to Corie Robinson (Graduate Student Travel Award for her poster “Are succinate and diglycolic acid taken up into human kidney proximal tubule cells by the same sodium dicarboxylate transporters?” and to Mitchell McGill PhD (Postdoctoral Fellows Travel Award) for his poster “Serum biomarkers of mitochondrial damage in survivors and non-survivors of acetaminophen-induced acute liver failure: implications for the mechanism of hepatotoxicity in humans.” We expect to have another interesting meeting in San Diego this March, because we again have two symposia that are being presented by CTTSS members (see details elsewhere). Our reception/business meeting will be Wednesday evening (March 25) from 6 to 7:30, so please mark it on your calendars – details on our invited speaker will be coming in the February newsletter. Also, please note that the awards deadline for the Graduate Student and Postdoctoral Travel Awards to attend the SOT meeting is coming up very soon (December 31, 2014). We encourage applications from members and their trainees – details on the applications are on our webpage on the SOT website. Note that the application process is very easy, just a copy of your abstract and a letter from the mentor (who has to be a CTTSS member).

Because we are still establishing ourselves as a specialty section, I want to encourage you to tell me (kmcmar@lsuhsc.edu) what you would like for this section to do for you. What activities would you like us to undertake? Some of the ideas we have been pondering include presenting a CTTSS-relevant webinar or webinar series – I encourage you to send us some ideas of topics. Another lucrative activity for specialty sections is to officially sponsor a CCT (Contemporary Concepts in Toxicology) meeting. These tend to be one or two-day meetings on a focused topic, so are ideal for a small group like ours to sponsor. Details are provided on the SOT website, but SOT does provide seed money to help in the planning and will share the profits (hopefully it is profitable).
Ideas for such meetings are welcome – I promise you won’t have to organize it unless you want to. Lastly consider putting together a symposium for the annual meeting – despite our track record these past two years, you do not have to be an officer to organize one!

I have a couple of end-of-the-year reminders, beyond renewing your membership. We will need to elect new officers for next year – specifically a new Vice President-Elect, a Councilor, a Postdoctoral representative and a Graduate Student representative. If you would like to nominate someone for one of these positions (or volunteer yourself!), please send me the information (kmcmar@lsuhsc.edu). We will need to get their biographical information to SOT early in January, so let me know by the end of December. Secondly, it is the time of the year to think about lowering your taxes – there is nothing easier than making a tax-deductible donation to CTTSS (through SOT). Although we do not have an endowment fund, the policy of CTTSS is that any money that is donated to the section will be used strictly for awards. Be sure to indicate if you do send money to SOT, that you want it dedicated to CTTSS and for their awards. They take credit cards, FYI.

Thank you for your attention – looking forward to seeing you in San Diego. Best wishes to all for the upcoming year.

Sincerely,
Kenneth McMartin

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**Notes from the 2014 CTTSS meeting/lecture**

Hope you remember the excellent chance to meet fellow members, our business meeting run by Allister Vale, our CTTSS President for 2013-2014. Dr. Jeffrey Brent received the Career Achievement Award and presented a great talk on “Translational Antidote Research: a Bedside to Bench Tale” (transcript below). The Graduate Student Travel Awards was presented to Corie Robinson from Louisiana State University Health Sciences Center. The Postdoctoral Fellow Travel Award was presented to Mitchell McGill from the University of Kansas Medical Center Congratulations to both!

*Allister Vale and Corie Robinson*

*Allister Vale and Mitchell McGill*
“Translational Antidote Research: a Bedside to Bench Tale”
Jeffrey Brent, MD, PhD, FAACT, FACMT

It is an honor to give this presentation associated with my receipt of the Career Achievement Award by this Section. I particularly wish to offer my gratitude to Dr. Vale for his excellent leadership of this important section of the Society.

The development of new antidotes may sometimes proceed in a counterintuitive fashion. Usually the evolution of a new agent is governed by a fundamental paradigm starting with an observation, or a series of observations, leading to a hypothesis about the potential utility of the antidote, which then in an orderly fashion leads to hypothesis testing studies, preclinical and clinical safety evaluations and clinical efficacy trials. If we look at the development of fomepizole (4-methyl pyrazole, 4-MP), however, an interesting tale emerges demonstrating that this theoretical paradigm does not always apply.

Much of the early work on the development of fomepizole can be traced to studies at the Karolinska Institute where Hugo Theorell brought attention to 4-MP when he reported on the studies of von Wartburg showing that this molecule was an effective inhibitor of alcohol dehydrogenase (ADH) at submicromolar concentrations \textit{in vitro}. Studies in rats by David Lester et al (1968) at Rutgers University demonstrated that 4-MP and other 4-substituted pyrazoles, inhibited ethanol oxidation \textit{in vivo}. Simultaneously, Theorell et al (1969) reviewed the effects of a number of heterocyclic compounds on the enzymatic activity of hepatic ADH and noted that of 31 compounds tested, 4-MP had the lowest inhibitory constant, reported to be 0.08 micromolar. This represents approximately 8,000 times greater binding affinity of 4-MP for human ADH than for ethanol.

The following year the first published administration of 4-MP in humans was reported by Blomstrand and Theorell (1970) who demonstrated that doses up to 10 mg/kg administered intravenously to 7 human volunteers, two of whom were alcoholic, had a dose-dependent inhibitory effect on ethanol oxidation. At the 10 mg/kg dose there was an approximately 50% inhibition of the rate of ethanol metabolism. In 1973, Blomstrand and Kager demonstrated that in eight volunteers an intravenous dose of 180 mg (approximately 2.6 mg/kg) of 4-MP prevented the inhibition of fatty acid oxidation by ethanol. Bjorkhem et al (1975) from the Karolinska Group published prior work on the development of a mass spectroscopy technique for the analytical determination of 4-MP in serum and demonstrated that this can be done following the intravenous administration of 4-MP to one subject and subsequent collection of serum.

It is important to note that during this time period of human experimentation there were no published safety studies providing reassurance that major adverse effects would be unlikely to occur with 4-MP administration. However, published papers during this time period from Karolinska make reference to unpublished animal studies in rats and dogs reportedly showing an absence of significant toxicity. It was not until 1974, however, that the first published toxicity study, described as a long-term study but actually involved 12-week oral administration in rats and therefore is best characterized as a sub-chronic study, reported on the safety of 4-MP as evidenced by data on complete blood counts, serum chemistries, and histopathology (Kager, 1974).

The potential of 4-MP as an antidote for methanol poisoning was realized by McMartin,
first studying under Tephly at the University of Iowa and then subsequently as a postdoctoral fellow at Karolinska. The McMartin studies form the basis for our understanding of the use of 4-MP as an antidote for the clinical management of methanol toxicity. These studies were done in monkeys and validated that model as a good mimic for human methanol poisoning. McMartin and colleagues demonstrated that the acidosis and toxicity following methanol administration were the result of it being metabolized to formic acid, and that a dose of 15 mg 4-MP/kg, or greater, inhibited methanol metabolism and thereby prevented both the development of metabolic acidosis and toxicity. These doses were associated with plasma 4-MP concentrations of \( \geq 9 \) micromolar (\( \mu \text{M} \)). While the studies of McMartin were underway, Clay and Murphy, were doing similar studies showing that 4-MP inhibits the metabolism and toxicity of ethylene glycol.

Although there was extremely limited human experience with the administration of 4-MP, the first published clinical use of this antidote was by Lindros et al (1981) from Finland. They took note of the potential severe manifestations of disulfiram-alcohol interactions, which had been reported to cause respiratory depression, cardiac dysrhythmias, myocardial infarction, acute congestive heart failure, alterations of consciousness and seizures. At the time of their publication there had already been 20 disulfiram-related deaths reported, 13 of which involved excessive doses. They therefore undertook an evaluation of the utility of 4-MP in the treatment of these reactions.

In the course of doing so, they reported its clinical use in a 36-year-old male who presented to the University Hospital in Helsinki with flushing, tachycardia, nausea, emesis and chest pain. He was a chronic alcoholic with a history of relapsing pancreatitis, and despite his young age, was diagnosed with ischemic cardiovascular disease requiring nitroglycerine. A day prior to admission his wife had secretly given him disulfiram. The following morning he drank two bottles of red wine causing him to present with flushing, tachycardia, and chest pains. While being monitored, blood samples were drawn for ethanol and acetaldehyde determinations at three-minute intervals, a dose of 7 mg/kg of 4-MP was given intravenously, and these parameters were followed for the subsequent three hours. During that time period, the intensity of his flushing markedly reduced and ST-depressions on his electrocardiogram resolved. Within 30 minutes of receiving the 4-MP his tachycardia normalized and, importantly, his blood acetaldehyde concentration, which was constant at 60-70 \( \mu \text{M} \) for the 9 minutes prior to the dose of 4-MP, dropped to <10 three minutes later.

Recognizing the potential for 4-MP in the treatment of these reactions Lindros et al studied 4 human volunteers given 0.2 grams/kg of ethanol followed by a dose of the aldehyde dehydrogenase inhibitor calcium carbimide. Thirty minutes after the ethanol infusion, but prior to the calcium carbimide, an unspecified dose of 4-MP or saline was given intravenously and blood acetaldehyde and ethanol concentrations were sequentially determined using headspace chromatography. It should be noted that despite the small dose of ethanol given, corresponding to approximately 150 ccs of red wine, subjects exhibited facial flushing and tachycardia.
associated with elevations of blood acetaldehyde concentrations up to the range of 70-80 µM. However, in those individuals given 4-MP, the concentration of acetaldehyde rapidly fell to 5-7 µM post-administration.

The first reported clinical use of 4-MP in the treatment of toxic alcohol or glycol poisoning was published in 1986 when Baud et al (1986), from the toxicology unit in Paris, described their use of oral 4MP in three individuals using a loading dose of 15 mg/kg, followed by 5 mg/kg twelve hours later and 10 mg/kg every 12 hours subsequently. This regimen caused a drop in plasma oxalate concentrations, reduction of urine oxalate excretion, preservation of renal function, and resolution of metabolic acidosis. However, it was not until 1988 that Jacobsen et al, working in McMartin's laboratory, published the first major human safety study, using ascending 4-MP doses. They showed that subjects given up to 100 mg/kg, and generating 4-MP plasma concentrations of nearly 1,500 µM, tolerated the drug without significant adverse effects.

Those studies lead to the development of an Investigational Drug Application to the U.S. Food and Drug Association and subsequent funding by that agency for a prospective study on the use of 4-MP in the treatment of ethylene glycol and methanol poisoning. The subsequent study was a multi-center clinical trial by a group constituted as the Methyl-Pyrazole for Toxic Alcohols Study Group (The META Study) in which it was demonstrated that fomepizole treatment was associated with a rapid decline in plasma glycolate concentrations following ethylene glycol poisoning and that was accompanied by a normalization of arterial pH. (Brent et al, 1999) Patients who had normal renal function at the time that fomepizole were administered maintained their renal function without abnormality. However, the uncertainty of the efficacy of this antidote at the time the trial was initiated caused us to use a series of triggers (renal dysfunction, significant metabolic acidosis, serum ethylene glycol concentrations > 50 mg/dl) for simultaneous hemodialysis.

At approximately the same time as the publication of the META trial results on ethylene glycol toxicity the Paris Group presented their retrospective experience (Boron et al, 1999) and reported similar results. However, the French investigators did not rely on hemodialysis as an adjunctive therapy, which we know today is an unnecessary treatment in most cases if renal function is preserved.

Subsequently, the META Trial results on methanol toxicity were published demonstrating fomepizole’s efficacy in the treatment of this poisoning. (Brent et al, 2001) With fomepizole administration plasma formic acid concentrations rapidly normalized and patients tended to survive unless they were in extremis at the time of presentation. At about the same time the French Group reported their experience in the treatment of methanol poisoning with fomepizole (Megarbane et al, 2001) and demonstrated similar results. One challenge in the treatment of methanol poisoning that was noted in the META Trial was that once its metabolism is inhibited by fomepizole methanol has a half-life of approximately 54 hours because, unlike ethylene glycol, it does not have major alternate routes of clearance. Thus, while ethylene glycol toxicity can
generally be treated with fomepizole in the absence of hemodialysis, except in cases of extreme metabolic derangements or renal failure, the same cannot be said about methanol poisoning.

There has only been one controlled clinical trial comparing ethanol treatment to fomepizole and that was in the veterinary literature, where a randomized clinical trial was done in dogs following ethylene glycol poisoning. (Grauer, 1987) That study showed that while both ethanol and fomepizole attenuated the metabolic acidosis and were efficacious in preventing nephrotoxicity, ethanol was associated with severely increased central nervous system depression. A similar retrospective clinical experience in humans was reported by Lepik et al (2009), which found a markedly lower incidence of adverse reactions in patients treated with fomepizole than those treated with ethanol. Ethanol treated patients were reported to develop coma, agitation (which could be extreme), cardiovascular toxicity and potentially life threatening respiratory depression and hypotension at a greater frequency than seen with fomepizole.

Although there are no controlled clinical trials in humans comparing ethanol and fomepizole, a multi-center retrospective study has identified that in those patients with methanol toxicity who are sick enough to develop compensatory hyperventilation, there was a significantly greater mortality in those patients treated with ethanol compared to fomepizole. (Paasma, 2012)

Future research on fomepizole as an antidote should revolve around assessing its utility as an oral agent, thus making the treatment of most cases of ethylene glycol or methanol poisoning, until recently diseases that required treatment in intensive care units, amenable to outpatient management.

2015 Award Information
A reminder that we have two Travel Awards available one for Graduate students and one for Post-doctoral fellows to help them present their abstract at SOT 2015.

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<tr>
<th>Award Title</th>
<th>Clinical and Translational Toxicology SS Graduate Students Travel Award</th>
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<td>Award Description</td>
<td>Current graduate students attending the SOT Annual Meeting are encouraged to compete for the Clinical and Translational Toxicology Specialty Section (CTTSS) Graduate Students Travel Award. Submission requirements are:</td>
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<td>1. An abstract must have been submitted and accepted for the upcoming SOT Annual Meeting with the graduate student as the presenting author;</td>
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<td>2. A letter must be received from a mentor who is a CTTSS member outlining the student's role in the research;</td>
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<td>3. Recipients of this award will not accept travel awards from any other Specialty Section for the SOT Annual Meeting;</td>
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<td>4. The awardee will receive a monetary prize of $300 and recognition plaque;</td>
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<td>5. A graduate student can only win the CTTSS Graduate Students Travel Award once.</td>
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<td>A copy of the accepted abstract and a statement from the graduate student's mentor must be sent as an electronic file attachment (Word or pdf) to Kenneth McMartin no later than December 31. The awardee will be notified by February 1.</td>
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### Award Title

**Clinical and Translational Toxicology SS Postdoctoral Fellows Travel Award**

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<th>Award Description</th>
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<td>Current postdoctoral (postdoctoral fellow/researcher; fellow in clinical/medical toxicology) fellows attending the SOT Annual Meeting are encouraged to compete for the Clinical and Translational Toxicology Specialty Section (CTTSS) Postdoctoral Fellows Travel Award. Submission requirements are:</td>
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<tr>
<td>1. An abstract must have been submitted and accepted for the upcoming SOT Annual Meeting with the postdoctoral fellow as the presenting author;</td>
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<tr>
<td>2. A letter must be received from a mentor who is a CTTSS member outlining the fellow's role in the research;</td>
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<tr>
<td>3. Recipients of this award will not accept travel awards from any other Specialty Section for the 2014 SOT Annual Meeting;</td>
</tr>
<tr>
<td>4. The awardee will receive a monetary prize of $300 and recognition plaque;</td>
</tr>
<tr>
<td>5. A postdoctoral fellow can only win the CTTSS Postdoctoral Fellows Travel Award Award once.</td>
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</table>

A copy of the accepted abstract and a statement from the graduate student's mentor must be sent as an electronic file attachment (Word or pdf) to Kenneth McMartin no later than **December 31**. The awardee will be notified by February 1.

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Dr. Vishal Vaidya received his PhD in Toxicology from the University of Louisiana in 2003 and completed his postdoctoral fellowship in nephrology from Brigham and Women’s Hospital in 2007. As an Assistant professor at Harvard, Vishal has faculty appointments at Brigham and Women’s Hospital where he directs the Laboratory of Kidney Toxicology and Regeneration; at Harvard Medical School where he heads the Systems Toxicology program within the Harvard Program in Therapeutic Sciences; at Harvard School of Public Health where he directs a 5-credit course on Principles of Toxicology-Molecular and Translational Toxicology every Fall (EH504); and at Harvard Clinical and Translational Science Center (Harvard Catalyst) where he directs the course “Understanding Biomarker Science: From Molecules to Images”.

Vishal’s laboratory uses cellular systems, mouse models, as well as human biospecimens, and applies methodologies at the interface of cell and molecular biology, systems toxicology, and translational science in understanding kidney disease. Vishal’s work, supported by an NIH/NIEHS Pathway to Independence grant, in
collaboration with the Predictive Safety Testing Consortium, led to the first kidney toxicity biomarker (Kidney Injury Molecule-1) qualified by the US-FDA and the European Medicines Agency in 2008. In 2011, Vishal won the NIH/NIEHS Outstanding New Environmental Scientist (ONES) award. The ONES-funded project not only led to the identification of urinary fibrinogen as a translational biomarker for early detection of kidney damage but also demonstrated the therapeutic potential of fibrinogen-derived BB15-42 peptide in kidney injury. In 2013, Vishal was selected as one of six North American scientists to win the Innovation in Regulatory Science Award from the Burroughs Wellcome Fund. The goal of this project is to develop a high-throughput predictive kidney toxicity method by using tools and technologies at the forefront of quantitative systems pharmacology. Advancing their translational biomarker discovery work Vishal’s laboratory has recently identified a panel of urinary miRNAs as sensitive and mechanistic indicators of kidney injury in humans.

In recognition of the seminal scientific contributions that Vishal’s laboratory has made to advance toxicological science over the last 5-7 years, Vishal received the Leading Edge in Basic Science Award at the annual Society of Toxicology (SOT) meeting in March 2014 and he is also the recipient of the Achievement Award to be given at the SOT 2015 annual meeting in San Diego, CA.

Dr. Vaidya has been a member of the Society since 1999. During this time he has served as a member of the CRAD Committee (2006–2009) and Continuing Education Committee (2011–2014). He has also served as Councilor to the SOT Northeast Regional Chapter (2010-2012).

A new innovative in vitro method based on the CULTEX Radial Flow System (RFS) to assess acute pulmonary toxicity of fine dusts and nanoparticles

Dirk Steinritz and Horst Thiermann, Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany.

The ongoing industrial development in emerging industrialized countries has resulted in significant air pollution that is linked to a plethora of health risks and diseases. Moreover, new everyday products with potential toxic properties (e.g. nanoparticle containing sprays) have found their way into all areas of modern life and industry. Inhalation is the main exposure route with regard to airborne particles (i.e. gases and aerosols based on dusts or liquids). Some 12,000 liters of air pass the lungs per day which may result in a pulmonary exposure to up to 25 million particles per hour. Beside chronic exposure to harmful chemicals, even a single exposure is sometimes sufficient to cause severe health effects with an unfavorable prognosis.

The incidence of pulmonary maladies has increased dramatically over the last decades. Unfortunately, for a wide range of compounds knowledge about the toxic properties is lacking or even missing with regard to lung toxicity. Thus, studies resulting in a profound toxicological risk assessment are needed to minimize the health hazards emanating from such compounds.

Human in vivo data with regard to acute lung toxicity, which in theory should provide the best data available, are rare or missing. Even if such data are available they are usually limited in their evidence. Either the exposed
population is too small for a profound toxicological risk assessment, the exposure conditions (i.e. exposure dose over time) are unknown, or exposed persons suffer from pre-existing illnesses that might aggravate an additional exposure towards chemical compounds.

To fill this gap, adverse biological effects of inhalable substances are explored in animal experiments. However, significant interspecies differences might occur making a translation of in vivo animal data to the human situation at least challenging or in the worst case even impossible.

Moreover, the use of laboratory animals is under critical observation: Ethical constraints and economic feasibility demand alternative methods for replacing animal experiments according to the “3R” (Replacement, Reduction, Refinement of animal experiments) principles described by Russel and Burch in 1959. In many countries, these 3R are now explicit in legislation governing animal use. Thus, reliable non-animal methods, such as in vitro models, have to be developed to fill this gap.

In vitro models show several advantages compared to animal models: (1) Advanced in vitro models are based on human cells thus avoiding interspecies differences; (2) cell culture models are suitable to investigate dose-response relationships and pathomechanisms with a clear assignment of the toxic effects to a specific cell type; (3) the use of well-established cell lines (e.g. A549 cells) can minimize inter-individual effects (that will occur in animal models) as these cell lines are commercial available, well characterized and stable in culture over a large number of cell passages.

However, toxicological studies performed so far usually use submerse exposure conditions which represent a non-physiological situation. Therefore, advanced exposure methods were developed that allow a direct exposure of human lung epithelial cells at the air liquid interface (ALI) mimicking the physiological alveolar conditions more closely. The commercial available Cultex Radial Flow System (RFS) used in our studies realizes the exposure of cultivated cells to airborne particles of defined size under physiological conditions. In brief, the complete setup consists of four functional units (Fig. 1):

![Fig 1: Complete setup of the commercial available Cultex Radial Flow System with (A) particle generation unit, (B) test aerosol unit, (C) temperature control unit and (D) pure air control unit.](image)

The particle generation unit (Cultex Dust Generator (DG) according to Wright (A), two Cultex RFS modules with one module for exposure experiments with the test aerosols (B)
and one module for the pure air controls (D) and the temperature control module (C) to ensure 37 °C in both RFS units.

Compounds to be tested were pressed using a substance-specific procedure using a specifically developed hydraulic press. Afterwards, particles were generated in the particle generation unit by scraping with predefined parameters (rotation speed 800 U/min, airflow 8 L/min). Synthetic air was used as carrier gas for generating the test aerosols (B) and for the pure air controls (D).

Using this setup we examined different substances to evaluate whether they reveal toxic characteristics. Two compounds are exemplary presented here:

Lactose monohydrate was expected to have no or only very little effect in our test system, as this substance is routinely used as pharmaceutical vehicle with practically no known acute toxicity in healthy adults. Our results (Fig. 2) confirmed the expectations: At no point in time a significant decrease of cell viability in reference to the pure air controls (100 %) was observable.

Copper(II)sulfate showed the highest toxicity of all tested substances in our experiments. Already a 15 min exposure led to a substantial decrease of cell viability to approximately 20% that further declined in a time-dependent manner (Fig. 2). This is in line with in vivo data that revealed acute inflammatory responses in the rat lung already after exposure to 5 µg CuSO₄.

![Fig 2: Cell viability at 24h after 15, 30 or 60 min exposure to lactulose (white boxes) or copper(II)sulfate (grey circles). Data from 9 individual experiments are presented, error bars indicate SD and * indicate significant differences to pure air controls (100 % cell viability) with p < 0.05.](image)

In general, our in vitro data were in very good agreement with existing in vivo data underlining the general applicability of the Cultex RFS method to assess pulmonary toxicity (for further details see Steinritz et al., 2013 - Chem Biol Interact). Nevertheless, the presented method requires the compressibility of the test compound and reliable particle generation in the dust generator. Our results are encouraging and future work is planned to improve reproducibility, to consolidate the results so far and to develop a statistical data interpretation procedure that can be used to translate the in vitro results to the human situation.
Important CTTSS dates for 2015 SOT Annual Meeting:
San Diego, CA
March 22-26 2015

CTTSS Reception/business meeting:
Wednesday, March 25 at 6:00 to 7:30pm

CTTSS Sponsored Symposia:
Local and Systemic Toxicity from Cobalt and Chromium-Containing Hip Prostheses: Tuesday, March 24, at 9:00 am to 11:45 am
New Developments in the Management of Nerve Agent Poisoning, Tuesday, March 24, at 1:30 pm to 4:15 pm

CTTSS Officers:
President: Ken McMartin
Vice President: Horst Thiermann
Vice President-Elect: Jiri Aubrecht
Secretary-Treasurer: Tao Wang
Three Councilors: Charles Lindamood III, Allister Vale and Richard Wang
Postdoctoral Representative: Tracie Baker
Student Representative: Michelle Carroll Turpin