1. Approve minutes from April 7, 2015 monthly meeting.
Available at: http://www.sra.org/sites/default/files/u35/Minutes_04-07-15.pdf (All)
The minutes of the April meeting were approved.

2. Update on 2015 DRSG Teleseminar planning (Allen and all)
Four teleseminars have been confirmed:
   - June: Dale Hattis on population-based data on inter-individual variability
   - July: Bernard Goldstein on fracking
   - September: Rosalind Wright on dose-response of psychosocial stressors
   - October: Dan Krewski on Joint Model for Excess and Deficiency on copper

Kan will send some template emails he previously used to announce the teleseminar and to ask for abstracts.

Patty mentioned that the information on the planned teleseminars can be placed on the “What’s New” section of the SRA website.

3. Update on student award submission elicitation (Sarah and all)
Sarah has sent the announcement to her UCLA contacts, and other universities, such as John Hopkins (the Center for Alternatives to Animal Testing), Harvard and Yale, also to AAAS and other specialty groups. The feedback has been very positive. Sarah will send a reminder to the DRSG list.

4. Treasury report (Julia)
The most recent financial statement shows total expenses of $3,713.18 for last year’s SRA Annual Meeting and an ending balance of $7,385.02.

An annual income is provided by SRA: $500 for the mixer, and $500 for the student award. The rest of the annual income comes from dues.
The benchmark dose modelling workshop through which funds were generated in previous years will not be held this year. However, the categorical regression workshop is planned at the SRA Annual Meeting instead.

5. Discuss symposium topics for SRA 2015 (All).

a. Peg Coleman: Joint DRSG and MRASG Round Table Symposium:
For abstract, see April meeting minutes. Peg further developed the idea with MRASG but they said that they do not have the budget to support the symposium
Session 1 on innate immune interaction and on low dose interactions: confirmed speakers from
   - NIH
   - University of Maryland-Baltimore (Mark Shirtliff),
   - Massachusetts General Hospital in Boston (Ramnik Xavier), and the
   - National Cancer Institute in Bethesda.

Session 2: panel discussion
Only 2 non-member registrations for session 2 needed and 4 for session 1
Expected expenses: for speakers travelling from Washington area the train ticket costs around $20, airfare for speaker coming from Boston is expected to cost around $250. See if it is possible to schedule speaker coming from Boston for a timeslot that enables him to come and return in one day.
Panellists would come from DC area.
Max. expenses: six one day registrations to be waived plus travel. A one-day registration was $250 last year.

No individual abstracts are needed from panellists; one abstract is needed for whole panel.

Julie highlighted that it would be important to agree on whom to assign funds as soon as possible.

b. Allen Davis and Jeff Gift: Symposium on model uncertainty
The initially proposed symposium on “Approaches to addressing uncertainty and variability in dose-response analyses in chemical risk assessments” was split, and half of the proposed talks was assigned to this symposium on model uncertainty. Confirmed speakers:

- Kan on model averaging,
- Leonid Kopylev on benchmark dose estimation,
- Matt Wheeler on semi-parametric dose response modelling and
- Woody Setzer on a flexible parametric model to fit continuous data. Wout Slob from RIVM, NL, was very interested in participating but he realized that due to time constraints he will not be able to contribute at this point.

See appendix 1 for more information.

c. Allen Davis and Jeff Gift: Symposium on probabilistic approaches
Four speakers confirmed:

- Weihsueh on basic practices of probabilistic dose response modelling;
- Dale Hattis on uncertainty factors related to interindividual variability;
- Bill Mendez will deliver the presentation that he puts together with Bruce Allen. They develop an approach for the assessment of arsenic exposures from multiple epidemiological studies.
- Ingrid Druwe on combining results of multiple high throughput screening data

See appendix 2 for more detailed information.

No money needed for both symposia

d. Michelle Deveau and Julia Pletz: Joint DRSG and OHSSG symposium
Five confirmed speakers, and potentially one more speaker:

- Michelle will speak on incorporation of chemical-specific data in dose–response assessments,
- Mike Jayjock on accounting for atypical exposure durations and patterns
- Scott Dotson on the NIOSH cumulative risk project
- Kannan Krishnan on PBPK modelling
- Ester Lovsins Barle on a comparison of carry-over limit and occupational exposure limit calculations

Trying to set it up as 2 sessions

Adam Finkel who was invited to speak on low dose-linear dose-response assessment said that he has already committed to other talks at SRA. So, this topic would have to be covered by another person.

Prof. Calabrese from the University of Massachusetts, Amherst recently sent an email to Kan with regard to his opinion on linear no threshold dose-response.

Mike mentioned that Paul, Adam Finkel, Ken Bogan and himself have been speaking on low dose response relationships. Prof. Calabrese has a strong opinion on the topic so if he speaks at a symposium, a counterpart opinion would be needed, such as an agency’s perspective.

Resha added that it is important to distinguish between low dose-non linear dose response relationship and threshold/non-threshold considerations – both are completely different topics that should be assessed separated from each other.

Weihsueh seconded Resha’s opinion that such a session would need to be strongly structured and well defined.
Funds needed:
Mike Jayjock will travel to DC on his personal expense. DRSG funding would be needed for his parking ticket ($20-30).

e. Paul Schlosser and Mike Musso: Symposium on uncertainty factors

f. Sara Henry: Symposium on tobacco

No DRSG funds will be needed.

Additional symposium proposed by Weihsueh Chiu on harmonising risk assessment for cancer and non-cancer endpoints
Funding through DRSG would be necessary. Cost-benefit topics will be discussed which is why a co-sponsorship by the Economics and Benefits Analysis Specialty Group is intended.

Speakers:
- Betty Meek
- Weihsueh Chiu
- 2 Environ associates
- J. Rodricks

Overall, one person can contribute to two sessions. It is possible for an invited speaker to propose another topic or participate in a panel discussion as panellist or two s/he can propose two talks.

6. Brief update on the new email list (Kan)
Officially, the list of Indiana University is now used. Two unsubscribed to first email and four bounced back.

7. Other items?
None.
**APPENDIX 1**

**Symposium Title:** Approaches to addressing model uncertainty in dose-response analyses in chemical risk assessments  

**Co-Chairs:** J. Allen Davis and Jeff Gift

**Abstract:** Benchmark dose (BMD) modeling has become the standard for estimation of points of departure (POD) in chemical risk assessments, and the U.S. EPA has led the advance of these methods through the release of its Benchmark Dose Software. However, the field of dose-response modeling has continued to advance and the EPA has been encouraged to keep up with current issues. Of particular interest is the issue of model uncertainty, and the appropriate methods with which to address and reduce this uncertainty. In EPA’s BMDS, a suite of parametric models is fit against a dataset, and a single model is selected based on a comparison of model fits, often irrespective of biological considerations. This approach has been criticized as not adequately accounting for model uncertainty or biological considerations. Model averaging is one approach to addressing these issues, and the EPA has developed Bayesian methods that allow for the calculation of weighted BMD estimates that incorporate prior (biological information) and post (model fit) considerations. Alternative approaches for addressing model uncertainty involve the use of a single sufficiently flexible non-parametric, semi-parametric, or parametric model capable of covering a wide set of possible dose-response shapes. When informative biological data are lacking, these flexible model methods offer a simpler, unambiguous approach that obviates the need for selecting a single best model, or averaging the results of multiple models. The objective of this symposium is to discuss recent advances in dose-response methodologies as they relate to characterizing the risk to human health from exposure to exogenous chemical agents.

Model averaging – Kan Shao  
Non-parametric Bayesian approach to benchmark dose estimation – Leonid Kopylev, Maria Spassova, John Fox, Paul White  
Semi-parametric dose response modeling – Matthew Wheeler  
Use of a flexible parametric model to fit continuous data – Woody Setzer, Wout Slob

*Disclaimer: The views expressed in the proposal are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.*

**APPENDIX 2**

**Symposium Title:** Probabilistic approaches to dose-response analyses in chemical risk assessments  

**Co-Chairs:** J. Allen Davis and Jeff Gift

**Abstract:** In recent years, probabilistic approaches have been recommended for use in dose-response assessments in order to reduce various uncertainties in modeling or assessment decisions, to incorporate population-level variability data into modeling schemes, and to aid in the conduct of meta-analytic dose and hazard analyses. In order to step away from derivation of reference values based on a single point-of-departure, probabilistic methods can be used to express adjustment/uncertainty factors as distributions, and to quantify protection goals in terms of both incidence and magnitude. The recently developed WHO/IPCS framework will be discussed in this context. There is also uncertainty in how different individuals may react to exposure to toxic chemicals, and thus, probabilistic methods that incorporate interindividual variability into dose-response analyses should be considered and will be discussed. Probabilistic approaches can also reduce the uncertainty surrounding the selection of single datasets to on which to base dose-response analyses. EPA has developed Bayesian meta-regression methods that combine the results of multiple studies into one probabilistic risk analysis, thereby incorporating information from multiple...
datasets into the estimation of a single dose-response curve. Lastly, Bayesian data integration methods can be used to combine evidence from multiple high throughput screening assays to bolster hazard identification and to calculate risk-specific concentrations. The objective of this symposium is to discuss recent advances in probabilistic dose-response methodologies as they relate to characterizing the risk to human health from exposure to exogenous chemical agents.

Probabilistic dose response modeling – basic practices and WHO/IPCS guidance – Weihsueh Chiu
Probabilistic approaches to incorporate interindividual data into dose response analyses – Dale Hattis
Bayesian meta-regression techniques for combining multiple epidemiological studies – Bruce Allen, Bill Mendez
Bayesian evidence integration of high throughput screening data – Ingrid Druwe

Disclaimer: The views expressed in the proposal are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.

APPENDIX 3

SRA 2015 Symposium Proposal: Dose–response for occupational and environmental chemical exposures

Co-chairs: Michelle Deveau, University of Ottawa; Julia Pletz, Novartis
Specialty groups: Dose Response; Occupational Health and Safety; Multi-disciplinary track

Draft symposium abstract; please feel free to provide suggestions:

Dose–response analysis is a major element of the development and application of occupational and environmental exposure limits. Risk analyses for occupational and environmental exposures are often performed by different organizations and practitioners, usually without accounting for the potential of accumulation from both sources of exposures. Although the broad dose–response processes are similar between exposure scenarios, many differences also exist. The goal of this symposium is to describe various facets of dose–response analysis for occupational chemical exposures, while highlighting the similarities and differences from assessments performed for general populations. Methods of encouraging linkages and collaboration between the two groups of practitioners—both existing and proposed for the future—will be explored as a means of facilitating more holistic and consistent processes in risk assessments.

Confirmed speakers:

1. Incorporation of chemical-specific data in dose–response assessments for occupational and environmental exposure limits – Michelle Deveau, University of Ottawa
2. Accounting for atypical exposure durations and patterns – Mike Jayjock, Jayjock Associates, LLC; Tom Armstrong, TWABHR Occupational Hygiene Consulting LLC
3. Update on NIOSH cumulative risk project – Scott Dotson, NIOSH
4. PBPK modelling of occupational exposures (specific topic yet to be confirmed) – Kannan Krishnan, Université de Montréal

Other potential presentations (to be confirmed):

1. Low-dose linear dose–response assessment – Michelle emailed Adam Finkel (University of Pennsylvania)
2. Adequacy of existing OSHA Pb standards for protection of military firing range personnel – Michelle emailed Tricia Underwood (Office of the Secretary of Defense)
3. Potential conflicts in applicable legislation—a case study of OSHA standards and EPA guidance on vapour intrusion in the workplace – Michelle emailed Tricia Underwood (Office of the Secretary of Defense)

4. Comparison of methods for calculation of carry-over limits and their values with occupational exposure limits – Julia asked Ester Lovsin Barle, Novartis

5. If we’re missing presentations, Michelle can ask Bette Meek for a suggestion for a related MOA topic, or we can hold a panel discussion

**Keywords:** dose–response assessment, occupational exposure limits

**APPENDIX 4**

**Joint Dose-Response Specialty Group and Microbial Risk Analysis Specialty Group Symposium**

**Society for Risk Analysis (SRA) Annual Meeting, Arlington, VA**

**Dec 7-9, 2015 at the Crystal Gateway Marriott**

**SRA Theme:** Empires of Risk Analysis: Science, Policy, and Innovation

**Proposed Symposium Title:** Exploring Influences of the Microbiota on Innate Immunity and Microbial Dose-Response Relationships

Microbiologists, immunologists, and other scientists recognize that innate immune defenses protect against low doses of many pathogens as the first line of defense, and that high doses of pathogens overwhelm the innate immune system and activate additional adaptive immune defenses. However, dose-response models commonly used in microbial risk assessment do not explicitly account for innate immunity, and many risk assessment teams adopt simplifications of microbial dose-response relationships as policy decisions. For example, in the absence of definitive scientific data to predict human responses in the low-dose region for many pathogens, common simplifications include the use of models with low-dose linearity and independent action assumptions, rather than acknowledging more complex dose-dependencies. These policy choices can bias simulation results and overpredict disease, especially for less virulent pathogens that exhibit sublinear low-dose behavior or thresholds for illness. A major innovation in microbiology that impacts prediction of the outcomes of innate immune interactions in the low-dose region is the culture-independent nucleic acid based methods evolving in the Human Microbiome Project ([https://commonfund.nih.gov/hmp/](https://commonfund.nih.gov/hmp/)). Recent results of microbiome studies are transforming our knowledge of the diverse indigenous microbiota residing in specific niches of our bodies. Medical microbiology text books now acknowledge ‘colonization resistance’ as a dose-dependent interaction of microbiomes that protect hosts from low levels of pathogens ingested, inhaled, or contacting the skin or mucosal surfaces.

Subject matter experts will present data on the microbiota as an innate defense mechanism and its impact on dose-response relationships for microbial pathogens.

**Session 1 Co-chairs:** Peg Coleman, CSC, and Karin Hoelzer, The Pew Charitable Trusts

Subject Matter Experts (SMEs) in Innate Immune Interactions with Microbiota and Pathogens

- Emmanuel Mongodin, U MD School of Medicine, Baltimore, on the microbiota (nasal, oral, GI), community genomics, and colonization resistance
• Mark Shirtliff, U MD School Medicine, Baltimore, on *Staphylococcus aureus* nasal carriage and innate immunity

• Gloria Solano-Aguilar, USDA ARS, on GI microbiota of children, adults, and elderly adults in health and disease

In session 2 of this invited symposium, subject matter experts on the human microbiota in health and disease will join risk practitioners and regulators in posing and discussing researchable questions and approaches to advance microbial dose-response studies to account for the presence and absence or compromise of the indigenous microbiota. The strengths and limitations of the culture-based and culture independent methods for microbial prevalence and abundance will be considered for both exposure and dose-response assessments. Available dose-response datasets will be identified that illustrate ‘colonization resistance’, the dose-dependent interaction of microbiomes that protect hosts from low levels of pathogens ingested, inhaled, or contacting the skin or mucosal surfaces. Diverse pathogens and model systems will be considered for future experimental work in human and animal models (*in vivo* and *in vitro*). As NextGen chemical risk assessment is evolving with expanding knowledge of computational toxicology, so evolution of NextGen microbial risk assessment incorporate scientific innovations that advance our knowledge of human microbiomes in health and disease. Panelists and the audience will consider some test cases to develop more biologically relevant models for prediction of the likelihood and severity of diseases of the respiratory, skin, and gastrointestinal systems from low dose exposures to pathogens in the midst of diverse and abundant populations of human microbiota.

**Session 2 Co-chairs for Round Table Panel Discussion:** Peg Coleman, CSC, and Isabel Walls, USDA NIFA

Panelists (including invited speakers from Session 1)

• Amanda Payne-Virostko, Navy, Dahlgren, VA; experimental systems for GI microbiota

• Kerry Dearfield, USDA FSIS; IRAC and microbial risk

• Chris Elkins, FDA CFSAN; microbiota science and microbial risk

• Gene McClellan, ARA, Inc., Arlington; biothreat risk, time- and dose-dependency models of tularemia in GI and respiratory tract