

**Proposal for Contemporary Concepts in Toxicology Workshop**  
**March 10, 2018**  
**San Antonio, TX**

**Organizing Committee**

Florence G. Burleson, PhD, Chair, Burleson Research Technologies Inc., Morrisville, NC  
Kenneth L. Hastings, MPH, DrPH, Chair, Hastings Toxicology Consulting LLC, Mount Airy, MD  
John DeSesso, PhD, ATS, Exponent Inc., Alexandria, VA  
Rosalie Elespuru, PhD, US Food and Drug Administration, Silver Spring, MD  
John "Jack" R Fowle, III, PhD, DABT, Science To Inform LLC, Pittsboro, NC  
Holly M. Holmes, MD, MS, AGSF, University of Texas Health Science Center Houston, TX  
Mary Jeanne Kallman, PhD, DSP, Kallman Preclinical Consulting, Greenfield, IN  
S. W. Johnny Lau, PhD, US Food and Drug Administration, Center for Drug Evaluation and Research, Silver Spring, MD  
Donna L. Mendrick, PhD, US Food and Drug Administration, National Center for Toxicological Research, Silver Spring, MD  
Sharmilee P. Sawant, PhD, DABT, Halyard Health, Alpharetta, GA  
Charles E. Wood, DVM, PhD, DACVP, US Environmental Protection Agency, Research Triangle Park, NC

1. *Conference title:*

***Toxicological Concerns in Older Adults, a Neglected Majority***

2. *Type of CCT:*

**One day on site, on Saturday March 10 (day prior to Annual Meeting).**

Two centers located in the San Antonio/Austin area (San Antonio VA hospital and UT Medical School in Austin TX) have large aging and geriatric research programs that will provide a good opportunity to invite local speakers with the required expertise. In addition, Houston (neighboring city) has several established medical schools, including Baylor College of Medicine, University of Texas Health Science Centre, and Texas A&M University School of Medicine, that can provide an additional pool of qualified local speakers. The selected meeting location will attract trainees and scientists from these institutions, and increase the numbers of attendees. The access to local clinical speakers and other scientists is expected to encourage dialogue between clinicians and toxicologists, one of the desired outcomes of this conference.

3. *Importance of the scientific topic and its relevance to toxicology.*

**IMPORTANCE (max. 350 words):** The older adult population is growing faster than the total population in practically all regions of the world—and the difference in growth rates is accelerating. The proportion of older adults is projected to more than double worldwide over the next half century. At the global level, 1 in every 12 individuals was at least 60 years of age in

1950. By the year 2050, more than 1 in every 5 persons is projected to be aged 60 or over. Despite this increase, few issues in toxicological science associated with the aging process have been addressed, and the older adults remain largely unrecognized as a sensitive or vulnerable population. Older adults have uniquely increased susceptibilities to pharmaceuticals and environmental toxicants. While individual symposia have addressed selected topics associated with the complexities of the aging process, a CCT that addresses the toxicities and increased susceptibilities associated with the aging process is both timely and novel.

This workshop will address the following critical needs for older adults:

- 1) Discuss current knowledge of the aging process and susceptibilities resulting in toxicities that are elevated in this population.
- 2) Summarize the most common toxic outcomes related to aging and the physiological systems involved
- 3) Provide an appreciation of the distinct challenges associated with research and clinical trial efforts in this area.
- 4) Encourage dialogue between clinicians and toxicologists to enhance information exchange and collaboration.

#### RELEVANCE TO TOXICOLOGY:

Although considerable effort has been spent addressing the biological aspects of aging, including genetics and pharmacology, toxicological effects specific to older populations have been understudied. The primary goal of this workshop is to increase understanding of the changes associated with the aging process and discuss ways in which these changes may influence toxicity outcomes. The discussions will have potential impact on the development of toxicological assessments, the drug development process, and clinical practice.

4. *Similar themed conferences sponsored by SOT or through other societies that have been held within the last three years or are pending.*

Two searches were performed.

- a) <http://info-centre.jenage.de/ageing/meetings-calendar.html>. Returned a list of 551 meetings occurring between 2010 and 2021
- b) Search of “aging” and “toxicity”

There have been many conferences discussing aging in recent years but none related to specific issues with toxicology. Most were focused on societal issues (e.g., aging policies), the biology of aging, and ameliorating aging by learning about its pathways and specific diseases. Examples some such meetings include:

#### Examples of Past Meetings:

##### **Interventions in Aging**

February 02-05, 2015; Cancun, Mexico

<https://www.fusion-conferences.com/conference20.php>

“A plethora of genetic, dietary and pharmacological interventions can extend healthy lifespan in laboratory animals, and can delay or ameliorate diverse aging-related diseases. Many of the signaling pathways involved are evolutionarily conserved, and are starting to be implicated in human aging. This raises the intriguing possibility of performing preventative medicine against the chronic diseases of our time by targeting the main risk factor for all of them, namely aging. Two important current challenges in the field are (1) to understand the downstream pathways by which longevity interventions combat age-related loss of function and pathology, and (2) to translate the findings into the extension of human healthspan.” There is no duplication of our proposal.

### **Ageing and Degeneration: A Physiological Perspective**

April 10-11, 2015; Edinburgh, UK

<http://www.physoc.org/ageingtopic/>

This two day meeting dealt with understanding aging at a mechanistic level and how it impacts body and brain. Talks included aging and physical activity, exercise and brain health, limitation of skeletal muscle oxygen supply. There is no obvious overlap with our program.

### **Mechanisms of Aging. Cold Spring Harbor Laboratory**

September 26-30, 2016; Cold Spring Harbor, NY

<https://meetings.cshl.edu/meetings.aspx?meet=AGING&year=16>

“The meeting will explore the regulation and function of genes and processes that are now known or suspected to control cellular and/or organismic aging.” Topics included “longevity genes, DNA repair, inflammation, epigenetics, metabolism (intracellular communication/microbiome) and interventions (nutrition/pharmacology). Their agenda does not appear to address toxicity issues related to aging.

### **Geriatrics and Gerontology-2016. (BIT’s 4<sup>th</sup> Annual World Congress)**

November 18-20, 2016; Kaohsiung, Taiwan

<http://www.bitcongress.com/WCGG2016/default.asp>

This meeting had a robust scientific program covering areas such “Frontiers in Aging Research,” “Nutrition and Health in an Ageing Population,” and “Geriatric Medicine.” The latter covered areas such as Nutrition and Health in the Aging Population and Advances in Alzheimer and Parkinson’s Disease Research and Therapeutics, but does not duplicate our program.

### **Aging in America. American Society of Aging 2017 Conference**

<http://asaging.org/sites/default/files/files/2017-AiA-Final-Program.pdf>

March 20-24, 2017; Chicago, IL.

This meeting described advocacy, mental health and aging policies, senior poverty, etc. There was no overlap apparent and even search of the 184 page program for “toxicology” had no hits.

Examples of future meetings:

**2017 American Aging Association Annual Meeting (46<sup>th</sup> AGE Conference)**

June 9-12, 2017; Brooklyn, NY

<http://www.americanagingassociation.org/meeting/program>;

<http://asaging.org/sites/default/files/files/2017-AiA-Final-Program.pdf>

This meeting will discuss the mechanisms of aging (e.g., cell senescence, pathways associated with human longevity) with no apparent overlap with our program.

**2<sup>nd</sup> International Conference on Aging & Gerontology**

June 26-27, 2017; San Diego, CA

<http://aging.conferenceseries.com/events-list/aging-and-disorders>

Age-related diseases will be discussed such as movement disorder and hearing impairment. There is no apparent duplication of our meeting.

**Biology of Aging. Gordon Research Conference**

July 9-14, 2017; Les Diablerets, Switzerland

<https://www.grc.org/programs.aspx?id=13715>

The theme will be "Integrative Biology of Aging: New Insights from Molecules to Systems." "Recent studies from diverse model organisms, such as worms, flies, and mice, have demonstrated that systemic interplay between multiple tissues and organs regulates aging and longevity.... Our major objective is to capture this new wave of the "integrative biology of aging", and further stimulate our thoughts and efforts to translate our knowledge into the development of effective interventions to achieve "productive aging." There seems to be no overlap with our meeting.

**American College of Toxicology**

November 5-8, 2017; Palm Springs, CA

Part of the program will include a symposium entitled "Aging, Drugs, and Immunity". The talks include PK/PD, polypharmacy, immunesenescence, and regulatory aspects. Although there may be slight overlap in content (PK/PD and polypharmacy), the session is drug and therapeutics focused, with different speakers.

5. *Brief outline of structure of the conference.*

**8:30 – 8:45 AM**

**GREETING:** *Florence G. Burlison, PhD, Burlison Research Technologies Inc., Morrisville, NC*

Participants will be welcomed to the meeting with a brief overview of conference objectives and presentations.

**8:45 AM– 9:45 AM**

**KEYNOTE LECTURE: Toxicology of Aging.**

*Proposed Speaker:* Dr. Norman Sharpless (University of North Carolina, Chapel Hill, NC)  
Aging is accompanied by a global susceptibility for a number of different diseases and functional decline that cannot be readily assessed by the currently available approaches. However, the mechanisms that drive this susceptibility, disability and toxic reactions in older adults is poorly understood. The plenary talk will discuss chronological vs. biological aging and how genetic, epigenetic, and environmental factors affect susceptibility to adverse effects.

**9:45 AM – 1:00 PM**

**SESSION I: Changes Associated with Aging and Toxicological Concerns**

*Co-Chairs:*

*Kenneth L. Hastings, MPH, DrPH, Hastings Toxicology Consulting LLC, Mount Airy, MD  
Holly M. Holmes, MD, MS, AGSF, University of Texas Health Science Center Houston, TX*

This session will include five 30-minute presentations about the changes associated with aging and the toxicological outcomes associated with these changes in older adults. At the end of the session there will be a 30 minute panel discussion with audience participation.

**(1) 9:45 AM – 10:15 AM**

**Diseases in Older Adults: Toxicological Consequences**

Proposed Speaker: George Taffet, MD from Baylor College of Medicine

<https://www.bcm.edu/people/view/george-taffet-m-d/b180da60-ffed-11e2-be68-080027880ca6>

Many diseases of aging are the consequence of normal physiologic changes with aging or the result of aberrant processes that can occur with increasing age. Among diseases of aging (such as: neoplastic, cardiovascular, renal, metabolic), several will be selected and the presentation will focus on how aging contributes to toxicities seen in older adults. The impact of decreased physiologic reserve in diseases of aging will be discussed as a mechanism for the difficulty maintaining homeostasis when a toxicological threat occurs.

**(2) 10:15 AM – 10:45 AM**

**The Aging Immune System Modulating Susceptibilities to Chemicals and Drugs**

Proposed Speaker: Jorg Goronzy, MD, Stanford School of Medicine, Palo Alto, CA.

This presentation will review immune system changes associated with aging that impact toxic outcomes. Immune decline can lead to increased susceptibility to air pollution, toxic chemicals, many cancers, and changes in innate immune responses with age can result in tissue damage and autoimmune syndromes such as rheumatoid arthritis.

**AM Session Break: 10:45 AM– 11:00 AM**

**(3) 11:00 AM – 11:30 AM**

**Physiological Changes Associated with Aging – Impact on Xenobiotic Susceptibility**

Proposed Speaker: S.W. Johnny Lau, RPh, PhD, DABCP, US FDA.

This presentation will discuss the changes in pharmacokinetics and pharmacodynamics due to aging. It will help attendees understand and address the potential interactions between xenobiotic exposures and aging to produce adverse health effects in older adults.

**(4) 11:30 AM – 12:00 PM**

**Polypharmacy**

Proposed Speaker: Holly M. Holmes, MD, MS, AGSF, The University of Texas Health Science Center, Houston, TX

Due to the accumulation of multiple age-related conditions and comorbidities, older adults require more medications to manage multiple conditions. Although older adults are at higher risk for chronic disease and therefore have a potentially higher benefit from therapies to treat such conditions, they are also at greater risk of toxicities. Unfortunately, benefits are finite but potential toxicities of multiple therapies can be additive or even multiplicative. In this presentation, the consequences of polypharmacy will be discussed, including the impact on risk for drug-related toxicities and adverse drug events.

**(5) 12:00 PM – 12:30 PM**

**Aging and Increased Susceptibility to Environmental Toxicants**

Proposed Speaker: Wayne Cascio, MD, U.S. Environmental Protection Agency, Research Triangle Park, NC)

This presentation will discuss how air pollution and other environmental factors can disproportionately affect cardiovascular health in older adults. This talk will highlight biological mechanisms of susceptibility specific to this population and public health strategies to mitigate these risks.

**12:30 PM – 1:00 PM**

**Focused Panel Discussion with Audience Participation**

Co-Chairs:

*Charles Wood, Charles E. Wood, DVM, PhD, DACVP, US EPA, RTP, NC*

*John "Jack" R Fowle, III, PhD, DABT, Science To Inform LLC, Pittsboro, NC*

- How do we better recognize age-related susceptibilities in older adults?

- How do we evaluate risk in older adults?
- How do we mitigate such risks in older adults?
- How do we determine the need for significant alteration in combinations of drugs in older adults, e.g. to alter doses or combinations of pharmaceuticals.

**1:00 PM – 2:30 PM**

**LUNCH AND POSTER SESSION**

90 minute poster session and lunch

**2:30 PM – 3:30 PM**

**SESSION II: Evaluation and Consequences of Increased Susceptibilities in Older Adults**

*Co-Chairs:*

*Donna L. Mendrick, PhD, US FDA, National Center for Toxicological Research, Silver Spring, MD*

*Rosalie Elespuru, PhD, US Food and Drug Administration, Silver Spring, MD*

This session will consist of two 25 minute presentations, with 5 minutes Q&A each. The first presentation will discuss challenges in clinical trials in older adults and the second presentation will address the use of nonclinical models of aging to improve the prediction of drug-related adverse events in older adults.

**(1) 2:30 PM – 3:00 PM**

**Clinical Experience in the Aging Population**

Proposed Speaker: Louise McCullough, MD, PhD, University of Texas Health Science Center, Houston, TX

<https://med.uth.edu/neurology/faculty/louise-d-mccullough/>

Older adults have been vastly underrepresented in clinical trials. As a result, little evidence-based data exist to guide their course of treatment. Alternative trial designs and expanded research evaluations are necessary to evaluate therapeutics in this population. This session will focus on clinical trials in older adults for therapeutics designed for the aging population. (25-minute presentation and 5 minutes Q&A)

**(2) 3:00 PM – 3:30 PM**

**Nonclinical Models to Study Aging and Intervention/Prevention**

Proposed Speaker: Caleb E. Finch, PhD, University of Southern California, Davis, School of Gerontology

<http://gero.usc.edu/faculty/finch/>

This presentation will discuss how nonclinical animal models are employed to study the biology of aging and how environmental toxicants, including air pollution, can affect aging and how aging increases susceptibility to airborne pollution. It will include discussion of basic mechanisms of aging, with a focus on inflammation and nutritional

influences. This will be placed in the context of evolution of the human lifespan with reference to diseases of aging, especially Alzheimer disease.

**3:30 PM – 5:15 PM**

**SESSION III: Future Directions in Aging Research Related to Toxicology**

*Co-Chairs:*

*S. W. Johnny Lau, PhD, US Food and Drug Administration, Center for Drug Evaluation and Research, Silver Spring, MD*

*Sharmilee P. Sawant, PhD, DABT, Halyard Health, Alpharetta, GA*

This session will include two 30-minute presentations, a 15 minute break, and an additional 30 minutes for Panel Discussion and Q&A. The first presentation will discuss new testing paradigms for assessing effects on aging. The second presentation will discuss toxicities, and challenges and future directions in aging research. The last 30 minutes of this session will provide a forum for panel discussion with audience participation.

**(1) 3:30 PM – 4:00 PM**

**Modulation of Human Aging and Pharmacologic Interventions**

Proposed Speaker: Warren Ladiges (Department of Comparative Medicine, University of Washington, Seattle, WA

<http://depts.washington.edu/compmed/directory/faculty/ladiges.htm>

Testing drugs for anti-aging effects has historically been conducted in mouse life-span studies, but are costly and time consuming, and more importantly, difficult to recapitulate in humans. In addition, life-span studies in mice are not well suited to testing chemical or drug combinations that target multiple factors involved in aging. Additional paradigms for testing therapeutics/chemicals aging effects will be discussed.

**PM Session Break: 4:00 PM – 4:15 PM**

**(2) 4:15 PM – 4:45PM**

**Mitochondrial Dysfunction and Aging: Challenges and Future Directions**

Proposed Speaker: Luigi Ferrucci, MD, PhD, NIH, Baltimore

<https://irp.nih.gov/pi/luigi-ferrucci>

Aging is accompanied by increased susceptibility for a number of different diseases. The emerging importance of mitochondrial physiology at the interface of aging and diseases suggests that mitochondrial dysfunction may be the shared mechanism by which the risk of developing chronic disease and multimorbidity increases as we age. This inter-relationship can be further complicated by the fact that many diseases, drugs, or environmental toxicants may exacerbate mitochondrial damage, thus triggering a downward vicious cycle. This has important clinical implications and will require

technological advances and extensive collaboration between basic scientists, epidemiologists and clinicians for the development of new intervention strategies.

**4:45 PM – 5:15 PM**

**Focused Panel Discussion with Audience Participation**

*Co-Chairs:*

*John DeSesso, PhD, ATS, Exponent Inc., Alexandria, VA*

*Mary Jeanne Kallman, PhD, DSP, Kallman Preclinical Consulting, Greenfield, IN*

Proposed discussion topics:

- Priorities for future research and a better appreciation of older adults as a specific population
- How to ameliorate or interfere with age-related toxicities
- How do we focus clinical trials on the aging population?
- Applications to the regulatory environment and clinic

**CLOSING REMARKS: 5:15 PM – 5:30 PM**

*Florence G. Burtleson, PhD*

6. *Identify the potential interest level of and impact for various research sectors (ex. industry, government, academic, international...). Explain how this interest and impact was determined (e.g., based on previous related conferences, number of attendees at related symposia, number of articles recently published on topic, related scientific societies, etc.) [Expectation is a minimum of 100 attendees]?*

Interest is expected from all sectors including academia, industry, and government. As for the recently conducted Metabolic Syndrome CCT (March 2017), the timing and venue will encourage attendance by scientists who are already planning to attend the Annual Meeting, as well as some who have a special interest in the topic. Two centers that study aging and geriatrics are located in the San Antonio/Austin area and will provide a good opportunity to attract more participation (including researchers and students) from San Antonio VA hospital and UT Medical School in Austin TX. In addition, Houston (neighboring city) has 3 well-established medical schools that could provide additional attendees with interest in the topic.

If the workshop is offered in conjunction with the SOT Annual Meeting, 100-150 attendees are expected. This workshop would provide a format to bring all of these scientists together for discussion and to further collaborative efforts. In addition to the formal presentations from invited speakers, the lunch poster session is designed to attract trainees and to provide additional opportunities to provide participating scientists the opportunity to showcase their work. An Open Forum Session at the end of the meeting will encourage audience participation and allow further interaction.

7. List the expected outcomes of the conference and new opportunities the conference is expected to create (e.g., what new scientific and/or multidisciplinary interactions will be fostered) [max. 350 words].

This workshop will address the following critical needs for older adults:

- a) Provide a forum to discuss current knowledge of the aging process and susceptibilities resulting in toxicities that are elevated in this population.
- b) Summarize the most common toxic outcomes related to aging and the physiological systems involved for a better understanding of the toxicology of aging
- c) Provide an appreciation of the distinct challenges associated with research efforts in this area.
- d) Encourage dialogue between clinicians and toxicologists to better inform and collaborate.
- e) Publish a manuscript to focus attention on age-related toxic outcomes in older adults.

8. List potential meeting sponsors

Pharmaceutical companies: Abbott Labs, Amgen, Astellas, AZ, Baxter, Biogen, BI, Eisai, Eli Lilly, Genentech, J&J, Merck, Novartis, Pfizer/\$2,500\*, Gilead, Quintiles and Takeda. Additionally pharmaceutical companies that have drugs targeting older adults diseases could also be identified and be willing to contribute

CROs: Charles River, Jackson Labs, Taconic, BRT/\$2,000\*, MPI

Government: NIEHS, FDA, EPA, National Institute on Aging

There may be additional interest from complementary societies such as: HESI, AARP Foundation, PhRMA, American Society on Aging, American Society for Pharmacology and Experimental Therapeutics, American Society for Clinical Pharmacology and Therapeutics, American College of Clinical Pharmacology, The Gerontological Society of America, The American Geriatrics Society, American Chemistry Council, American Public Health Association, and existing SLC societies.

*\*Confirmed meeting sponsor and amount.*

### **Financial Statement**

*Note that the SOT will assume the liabilities for the conference, as well as the liability for financing of the conference. In planning the conference, the goal should be to recover funds (break even) based on registration fees and additional funding from external sources.*

A proposed budget is provided as a separate file. Based on these calculations, with a projected attendance of 119 (including speakers/organizers and staff), the SOT funds would be recovered.