

---

## **2013 Pharmacology Risk Standing Review Panel Status Review**

### **Statement of Task for:**

*The Risk of Clinically Relevant Unpredicted Effects of Medication*

### **Comments to the Human Research Program, Chief Scientist**

---

2013 Pharmacology Risk Standing Review Panel (SRP) Status Review WebEx/teleconference participants:

#### **SRP Members:**

Jurgen Venitz, M.D., Ph.D. (Chair) – Virginia Commonwealth University  
Suresh Mallikaarjun, Ph.D., FCP - Otsuka Pharmaceutical Development & Commercialization, Inc.  
Leon Shargel, Ph.D. – Applied Biopharmaceutics, LLC

#### **National Space Biomedical Research Institute (NSBRI):**

Dorit Donoviel, Ph.D.

#### **NASA Johnson Space Center (JSC):**

David Baumann  
Tina Bayuse, Pharm.D  
Ronita Cromwell, Ph.D.  
Sarah Lumpkins, Ph.D.  
Peter Norsk, M.D.  
Michele Perchonok, Ph.D.  
Mark Shelhamer, Sc.D.  
LaRona Smith, MSN, RN  
Susan Steinberg, Ph.D.  
Virginia Wotring, Ph.D.

#### **NASA Headquarters (HQ):**

Bruce Hather, Ph.D.  
Victor Schneider, M.D.

#### **NASA Research and Education Support Services (NRESS):**

Tiffin Ross-Shepard

---

On December 5, 2013, the Pharmacology Risk SRP, participants from the JSC, HQ, the NSBRI, and NRESS participated in a WebEx/teleconference. The purpose of the call (as stated in the Statement of Task) was to allow the SRP members to:

1. Receive an update by the HRP Chief Scientist or Deputy Chief Scientist on the status of NASA's current and future exploration plans and the impact these will have on the HRP.
  2. Receive an update on any changes within the HRP since the 2012 SRP meeting.
-

3. Receive an update by the Element or Project Scientist(s) on progress since the 2012 SRP meeting.
4. Participate in a discussion with the HRP Chief Scientist, Deputy Chief Scientist, and the Element regarding possible topics to be addressed at the next SRP meeting.

Based on the presentations and the discussion during the WebEx/teleconference, the SRP would like to relay the following information to Dr. Shelhamer, the HRP Chief Scientist.

1. The SRP was very pleased with the progress presented in the pharmacology discipline since the 2012 review.
2. The SRP would specifically like to commend Dr. Wotring for finally getting the in-flight medication use initiative off the ground (Dose Tracker project). This project will attempt to finally address the issue in pharmacology of spaceflight, namely a formal assessment of (currently unknown) medication use by astronauts in-flight.
3. The SRP recommends (*in-vivo*) whole animal pharmacokinetic (PK)/tissue distribution studies in-flight rather than *in-vitro* hepatic drug metabolism studies in-flight in order to elucidate any effects of spaceflight on hepatic drug metabolism. There are many ‘classical’ studies in rats and mice in which the pharmacodynamics (PD) (early literature used the term, ‘pharmacological’) affects were observed in whole animals, including autonomic, central nervous system and motor functions. Most of these methods are non-invasive. Sparse blood sampling can also be performed for PK analyses with the results compared to Earth-side ground-based controls.
4. With respect to drug stability, in addition to the unit dose packaging, the SRP recommends looking into adsorbents for moisture and oxygen that are routinely placed into multi-dose containers of tablets and capsules to provide a longer shelf-life stability.
5. The SRP recommends that Dr. Wotring follow up with the appropriate HRP Elements on the need/use of prospective, terrestrial “thorough QTc” studies (with dense EKG recordings and appropriate negative and positive controls) for relevant medications to assess any risks of drug-induced cardiac arrhythmia, especially for “grandfathered” medications whose risk for QTc prolongation may not have been properly assessed.
6. At the 2014 SRP meeting, the SRP would like to review and discuss in detail (proposed) performance metrics and milestone timelines for the various tasks.