Pharmaceutical Stability Risk – Overview and Forward Work

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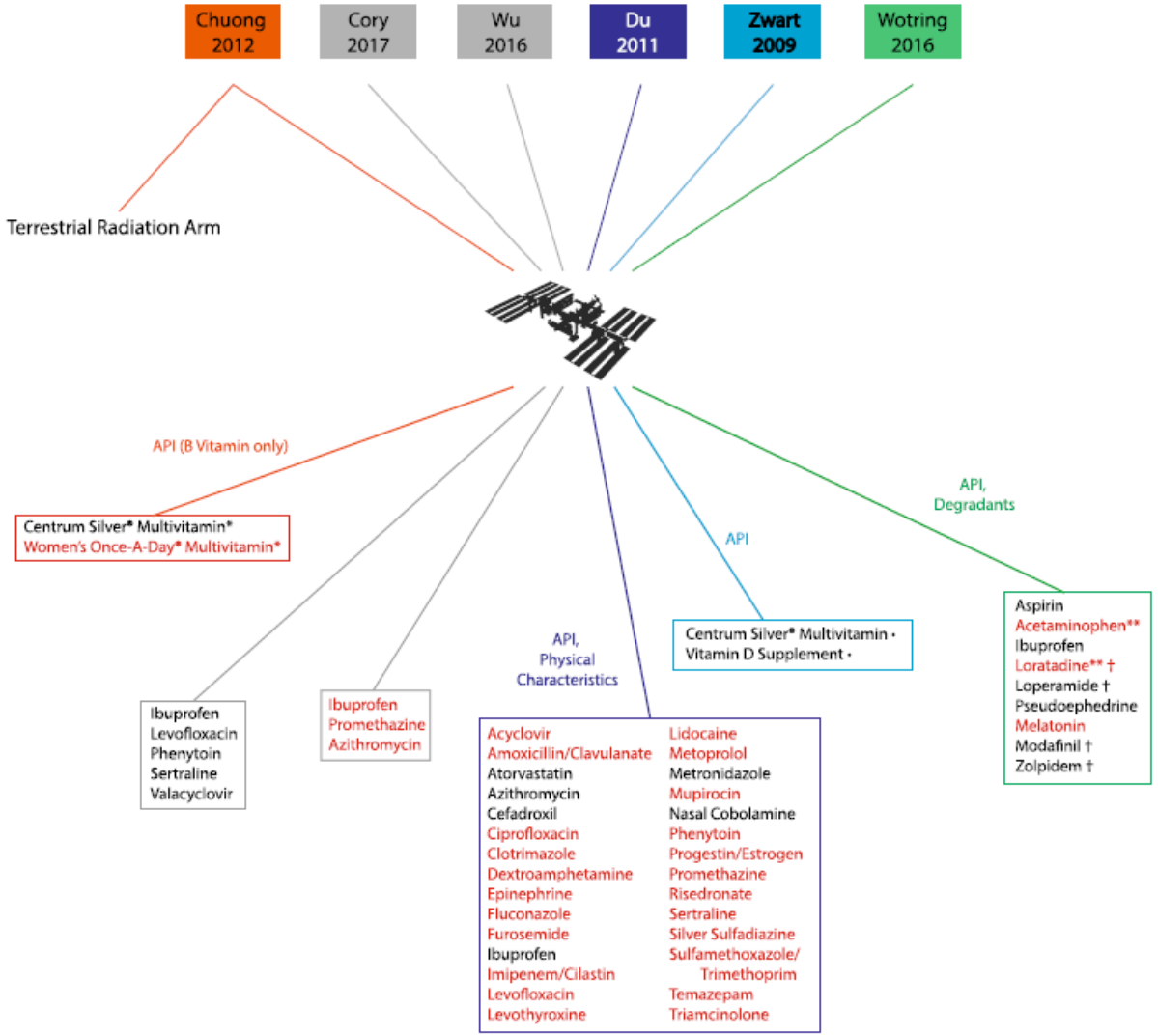
“Expanding the Boundaries of Space Medicine and Technology”

Goal

Provision of a safe and effective medication formulary that treats the conditions that arise in exploration spaceflight

- **Safety/Toxicity/Degradants**
- **Effectiveness/Stability/API (Active Pharmaceutical Ingredient)**
  - USP determines standard for stability
  - Typically API within 10% of specification

Prior Studies



Blue et al. Supplying a Pharmacy for NASA Exploration Spaceflight: Challenges and Current Understanding. *Npj Microgravity.* (2019)5:14.

Risk of Ineffective or Toxic Medications due to Long Term Storage

- Given that there is no current method to sufficiently characterize medication use, drug quality and performance, clinical outcomes, and the impact of a hostile space environment on pharmaceutical stability and potency during long-duration exploration missions, there is a possibility that provision of a safe and effective drug treatment will be significantly limited, impacting crew health and performance.

DRM Categories	Mission Duration	LxC OPS	Risk Disposition	LxC LTH	Risk Disposition
Low Earth Orbit	6 Months	1 x 1	Accepted	1 x 1	Accepted
	1 Year	1 x 1	Accepted	1 x 1	Accepted
Deep Space Sortie	1 Month	1 x 1	Accepted	1 x 1	Accepted
Lunar Visit/ Habitation	1 Year	1 x 1	Accepted	1 x 1	Accepted
Deep Space Journey/ Habitation	1 Year	2 x 2	Accepted	1 x 1	Accepted
Planetary	3 Year	3 x 4	Requires Mitigation	3 x 4	Requires Mitigation

A Particular Challenge for Exploration Missions

- Minimal to no resupply
- Longer mission durations
- Longer exposure to space environment (for both humans and meds)
- Medical conditions more consequential

Three Primary Questions

1. How do we package/store medications?
2. How do we pick which medications study?
3. How are those medications impacted by spaceflight?

Packaging and Storage

- Historically, medications typically repackaged on ground prior to flight for operational reasons (volume, convenience of use)
- Terrestrially, re-packaging invalidates manufacturer's stated shelf life
- In flight, re-packaging may lead to increased exposure to flight environment (radiation, humidity, temperature, CO2, etc.) that accelerates degradation process

- Insert Photo of re-packaged meds

Packaging and Storage

- **Four Options:**
  - Manufacturer's packaging
  - Re-packaging as currently done for ISS
  - Novel packaging/storage strategies (e.g. nitrogen purge, ceramic coating, just-in-time manufacture)
  - Shielding or environmental control chambers

- **Optimize among competing factors:**
  - Preserve API
  - Minimize degradants/toxicity
  - Minimize resource footprint (mass, volume, power, etc.)

- **Understand feasibility:**
  - Technical
  - Operational
  - Economic
  - Regulatory

Exploration Candidate Formulary

1. ExMC Pharmacy Research Prioritized Medication List – 2019
2. Supplement with:
   - Conditions from LOC IV/V Accepted Medical Condition List
   - Condition -> Capability -> Resource tracings from medical system SysML model
3. Final inputs from IMPACT trade space tool results

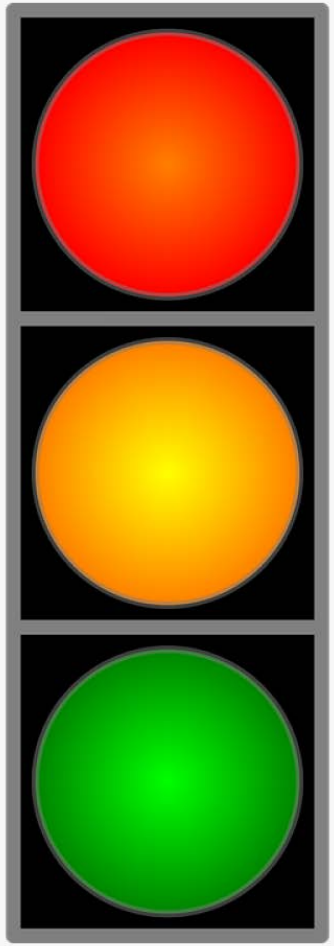
Data gathering for medications on the Exploration Candidate Formulary

- Create Pharmacy Information Database
  - Spaceflight data
  - Analog data (e.g. NSRL)
  - Terrestrial data (e.g. FDA)

Data attributes include:

- Drug Product – generic name
- Strength
- Dosage form
- Therapeutic Classification
- Chemical Structure (API)
- Chemical Class (API)
- API Drug Degradation pathways (chemical reactions)
- API Degradation Products
- API Degradation Product structure (Toxic Y/N)
- Environmental sensitivities (light/UV, temperature, humidity, radiosterilization)
- Shelf-life extension data (terrestrial data, FDA – can include)
- Mass, dimensions of packaging
- Spaceflight usage data (citation or summary)
- Spaceflight stability data (citation or summary)
- Analog environment stability data (citation or summary)
- Spaceflight PK/PD data (citation or summary)
- Analog environment PK/PD data (citation or summary)
- References for above data

Categorize Meds on Exploration Candidate Formulary



- Create systematic, traceable, repeatable process for assigning each medication to a color category
- Further characterize all “yellow” medications
  - Gateway
  - ISS
  - NSRL
  - Accelerated stability
  - FDA data

Flight Study of Medications

- Study “yellow” medications
- Arms for different packaging/storage strategies
- Phased return of samples over time
- Consider other environmental interactions
  - Radiation shielding
  - CO2
  - Temp/humidity

PK/PD, Pharmacogenomics

- **PK/PD**
  - Pharmacokinetics (PK)- body's effects on the drug
  - Pharmacodynamics- drug's effects on the body
  - As physiology changes in flight, the effects of the body on the drug and the drug on the body may change
  - Limited quality and quantity of evidence

- **Pharmacogenetics/Pharmacogenomics**
  - Tailoring of medication choice, dosing, and schedule to individuals' specific –omics profile
  - Currently test individual crewmember susceptibility to sleep/wake meds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EXPLORATION MEDICAL CAPABILITY
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Questions?