Medication Storage and Protection System
Operational Concepts and Requirements

Aerospace Medicine Research Rotation
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Context

Risk

- Risk of Unacceptable Health and Mission Outcomes Due to Limitations of In-flight Medical Capabilities

Gap

ExMC 4.17

- Lack of adequate protection for medications to preserve stability and shelf life in exploration class missions
Medication use on STS and ISS

- Most frequent medical complaints:
  - Space Motion Sickness
  - Headaches
  - Sleep disturbance
  - Back pain
  - Nasal congestion

- ISS CHeCS Medical Kit (2008): 120 medications
  - 54 solid formulations (tablets, capsules)
  - 11 semi-solid formulations (creams, ointments)
  - 34 liquid formulations in bottles
  - 19 liquid injectable formulations
  - 2 inhalers
Medication shelf life
About medication stability

- **Chemical**
  - Chemical integrity and potency of active ingredient

- **Physical**
  - Appearance, dissolution, suspendability

- **Microbiological**
  - Resistance to microbial growth

- **Toxicological**
  - No increase in toxicity
Medications do expire

Stability Profiles of Drug Products Extended beyond Labeled Expiration Dates

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About medication stability

- Some expired medications are ineffective
- Some expired medications are toxic

<table>
<thead>
<tr>
<th>Ineffective</th>
<th>Toxic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin + Clavulanate</td>
<td>Ibuprofen</td>
</tr>
<tr>
<td>Mupirocin</td>
<td>Gabapentin</td>
</tr>
<tr>
<td>Levothyroxin</td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td></td>
</tr>
<tr>
<td>Risedronate</td>
<td></td>
</tr>
<tr>
<td>...</td>
<td></td>
</tr>
</tbody>
</table>
Context

Risk • Risk of Unacceptable Health and Mission Outcomes Due to Limitations of In-flight Medical Capabilities

Gap ExMC 4.17 • Lack of adequate protection for medications to preserve stability and shelf life in exploration class missions

Task • Development of methods/technologies for protecting medications in spaceflight

Deliverable • TRL 6 system to preserve stability and shelf life of medications

Medication Storage and Protection System (MSPS)
Project goals

Identify factors affecting medication stability
↓
Generate operational concepts for MSPS
↓
Write functional requirements for MSPS
↓
Draft verification requirements for MSPS
Factors affecting medication stability

- Water content variation
- Temperature
- Light
- Ionizing radiations?
- Oxygen exposure
- Microbial contamination
- pH
Water content variation

Medication degradation rate

\[ \ln k = \ln A - \frac{E_A}{RT} + B(RH) \]

Critical relative humidity

<table>
<thead>
<tr>
<th>Excipient</th>
<th>CRH at 20°C</th>
<th>CRH at 40°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextrose</td>
<td>100</td>
<td>88</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>80</td>
<td>69</td>
</tr>
<tr>
<td>Sucrose</td>
<td>86</td>
<td>83</td>
</tr>
<tr>
<td>Xylitol</td>
<td>91</td>
<td>73</td>
</tr>
<tr>
<td>Tartaric acid</td>
<td>84.5</td>
<td>78</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>84</td>
<td>82</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Sodium citrate</td>
<td>60.5</td>
<td>78</td>
</tr>
<tr>
<td>Polyethylene glycol (PEG3350)</td>
<td>94</td>
<td>85</td>
</tr>
<tr>
<td>Sodium carboxymethylcellulose</td>
<td>84</td>
<td>84</td>
</tr>
</tbody>
</table>

Environment

Headspace

Acetaminophen
Acetylsalicylic acid
Semi-solids
Liquids
Water content variation

Moisture vapor transmission rate

**Table 5.** Representative Moisture Vapor Transmission Rates (MVTR) for a Number of Pharmaceutical Packages

<table>
<thead>
<tr>
<th>Package</th>
<th>Package Size</th>
<th>MVTR (mg/day), 23°C/75%RH</th>
<th>MVTR (mg/day), 40°C/75%RH</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDPE</td>
<td>40 cm³ bottle¹</td>
<td>0.15</td>
<td>0.70</td>
</tr>
<tr>
<td></td>
<td>60 cm³ bottle</td>
<td>0.262</td>
<td>1.352</td>
</tr>
<tr>
<td></td>
<td>180 cm³ bottle</td>
<td>0.521</td>
<td>2.688</td>
</tr>
<tr>
<td>Polyvinylchloride (PVC) blister (250 μm thick)</td>
<td>23.9 × 9.5 × 8.2 mm capsule</td>
<td>1.187</td>
<td>3.885</td>
</tr>
<tr>
<td></td>
<td>13.3 × 7.5 × 4.4 mm capsule²</td>
<td>0.259</td>
<td></td>
</tr>
<tr>
<td>Polyvinylidene chloride (PVDC) blister (190 μm thick)</td>
<td>23.9 × 9.5 × 8.2 mm capsule</td>
<td>0.230</td>
<td>1.200</td>
</tr>
<tr>
<td>Polychlorotrifluoroethylene (PCTFE), Aclar™ UltRx 2000 blister</td>
<td>23.9 × 9.5 × 8.2 mm capsule</td>
<td>0.028</td>
<td>0.142</td>
</tr>
<tr>
<td></td>
<td>14.5 × 0.3 mm round</td>
<td>0.013</td>
<td>0.100</td>
</tr>
<tr>
<td>Polychlorotrifluoroethylene (PCTFE), Aclar™ UltRx 3000 blister</td>
<td>23.9 × 9.5 × 8.2 mm capsule</td>
<td>0.018</td>
<td>0.103</td>
</tr>
<tr>
<td></td>
<td>14.5 × 0.3 mm round</td>
<td>0.007</td>
<td>0.062</td>
</tr>
<tr>
<td>Polychlorotrifluoroethylene (PCTFE), Aclar™ RX160 blister (305 μm thick)</td>
<td>13.3 × 7.5 × 4.4 mm capsule²</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>Foil-foil cold-formed blister</td>
<td>23.9 × 9.5 × 8.2 mm capsule</td>
<td>0.00067</td>
<td>0.0037</td>
</tr>
<tr>
<td></td>
<td>13.3 × 7.5 × 4.4 mm capsule²</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

The MVTR values were determined using gravimetric changes for each container according to USP24/NF18 at 23°C, and modified accordingly for 40°C.
Water content variation
Temperature

- Definitions:
  
  Cold: <8°C
  Cool: 8-15°C
  Controlled Room Temperature: 15-30°C, mean <25°C

- Some medications have specific requirements
Light

- < 200 nm → Absorbed by air
- 320-350 nm (UV) → Maximal medication sensitivity
- > 800 nm → Heat transfer
- 44% of solid medications in CHeCS are light-sensitive
Ionizing radiations

- Solar Particle Events (SPE)
- Galactic Cosmic Rays (GCR)

Effective shields: water, polyurethane
Oxygen

Fig. 6. Observed degradation as a function of oxygen concentration (formulation A).
Microbial contamination
pH
Solutions on earth

- Packaging
  - Blister packs
  - Amber-coloured containers
- Storage environment
- Repackaging
Current NASA practice

- Medications repackaged in plastic bags
- Stored in Nomex cases within CHeCS
Extending shelf life

- Temperature
- Moisture
- pH
- Oxygen
- Microbes
- Light
- Radiations
Extending shelf life

Moisture
- 1x
  - Relative humidity <40%

Light
- 1-1.25x
  - Complete protection between 200 nm and 800 nm during storage
  - Partial protection between 290 nm and 450 nm during access

Temperature
- 2-4x
  - Mean storage temperature between 8°C and 15°C

pH
- 1x
  - Standard USP packaging requirements

Microbes
- 1-1.25x
  - Protection from oxygen contact

Oxygen
- 1x?
  - Shielding from solar particle events
  - Shielding from galactic cosmic rays

Radiations
Stability assessment

• Non-destructive

• 3 strategies:
  
  Visual inspection
  
  Raman spectroscopy
  
  Near-infrared spectroscopy
Other requirements

- Fast access
  - < 60 seconds (nominal)?
  - < 30 seconds (emergency)?
- Ability to repackage opened medications
- Integration with the Medical Consumables Tracking system
The next steps

- Requirements review
- Design
- Testing
  - Ground verification
  - ISS test run
Beyond MSPS

Mission to Mars

- Shelf life = 2 years
- 4x distribution
- 2.5x shelf life extension

1 year

Mission to Mars

- Shelf life = 2 years
- 4x distribution
- 2.5x shelf life extension

1 year
Thanks

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