



Medication Storage and Protection System Operational Concepts and Requirements

Aerospace Medicine Research Rotation

Final presentation

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Exploration Medical Capability

NASA Human Research Program

Context

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

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

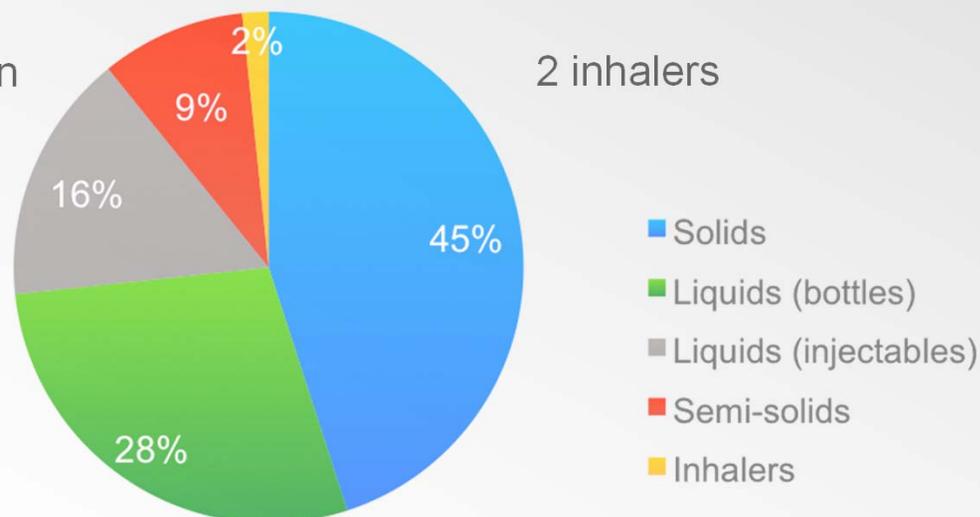
54 solid formulations (tablets, capsules)

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

Ineffective	Toxic
Amoxicillin + Clavulanate Mupirocin Levothyroxin Epinephrine Risedronate ...	Ibuprofen Gabapentin ...

Context

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

Acetaminophen
Acetylsalicylic acid

Semi-solids
Liquids

Water content variation

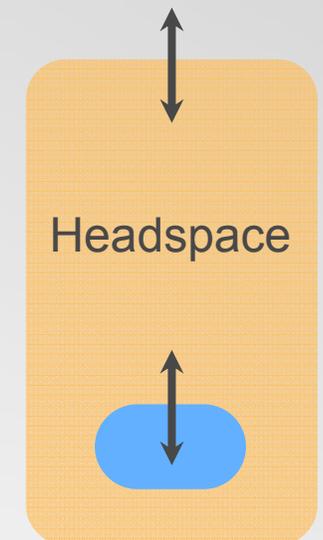
Medication degradation rate $\ln k = \ln A - \frac{E_a}{RT} + B(\text{RH})$

Critical relative humidity

Table 1. Critical Relative Humidity (CRH) Values for Representative Excipients¹¹

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

Environment



Acetaminophen
Acetylsalicylic acid

Semi-solids
Liquids

Water content variation

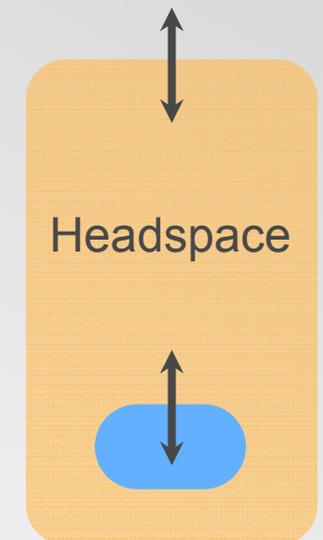
Moisture vapor transmission rate

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

Package	Package Size	MVTR (mg/day), 23°C/75%RH	MVTR (mg/day), 40°C/75%RH
HDPE	40 cm ³ bottle ¹	0.15	0.70
	60 cm ³ bottle	0.262	1.352
	180 cm ³ bottle	0.521	2.688
Polyvinylchloride (PVC) blister (250 μm thick)	23.9 × 9.5 × 8.2 mm capsule	1.187	3.885
	13.3 × 7.5 × 4.4 mm capsule ²	0.259	
Polyvinylidene chloride (PVDC) blister (190 μm thick)	23.9 × 9.5 × 8.2 mm capsule	0.230	1.200
Polychlorotrifluoroethylene (PCTFE), Aclar™ UltRx 2000 blister	23.9 × 9.5 × 8.2 mm capsule	0.028	0.142
	14.5 × 0.3 mm round	0.013	0.100
Polychlorotrifluoroethylene (PCTFE), Aclar™ UltRx 3000 blister	23.9 × 9.5 × 8.2 mm capsule	0.018	0.103
	14.5 × 0.3 mm round	0.007	0.062
Polychlorotrifluoroethylene (PCTFE), Aclar™ RX160 blister (305 μm thick)	13.3 × 7.5 × 4.4 mm capsule ²	0.008	
Foil-foil cold-formed blister	23.9 × 9.5 × 8.2 mm capsule	0.00067	0.0037
	13.3 × 7.5 × 4.4 mm capsule ²	0.001	

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

Environment



Water content variation

Acetaminophen
Acetylsalicylic acid

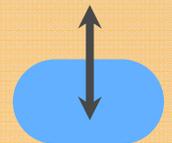
Semi-solids
Liquids



Environment



Headspace



Temperature

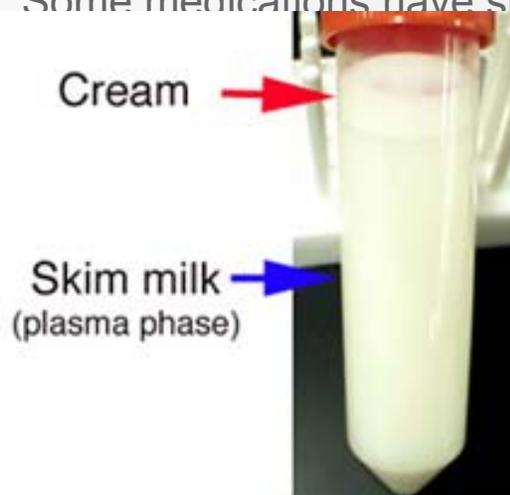
- Definitions:

Cold: $<8^{\circ}\text{C}$

Cool: $8-15^{\circ}\text{C}$

Controlled Room Temperature: $15-30^{\circ}\text{C}$, mean $<25^{\circ}\text{C}$

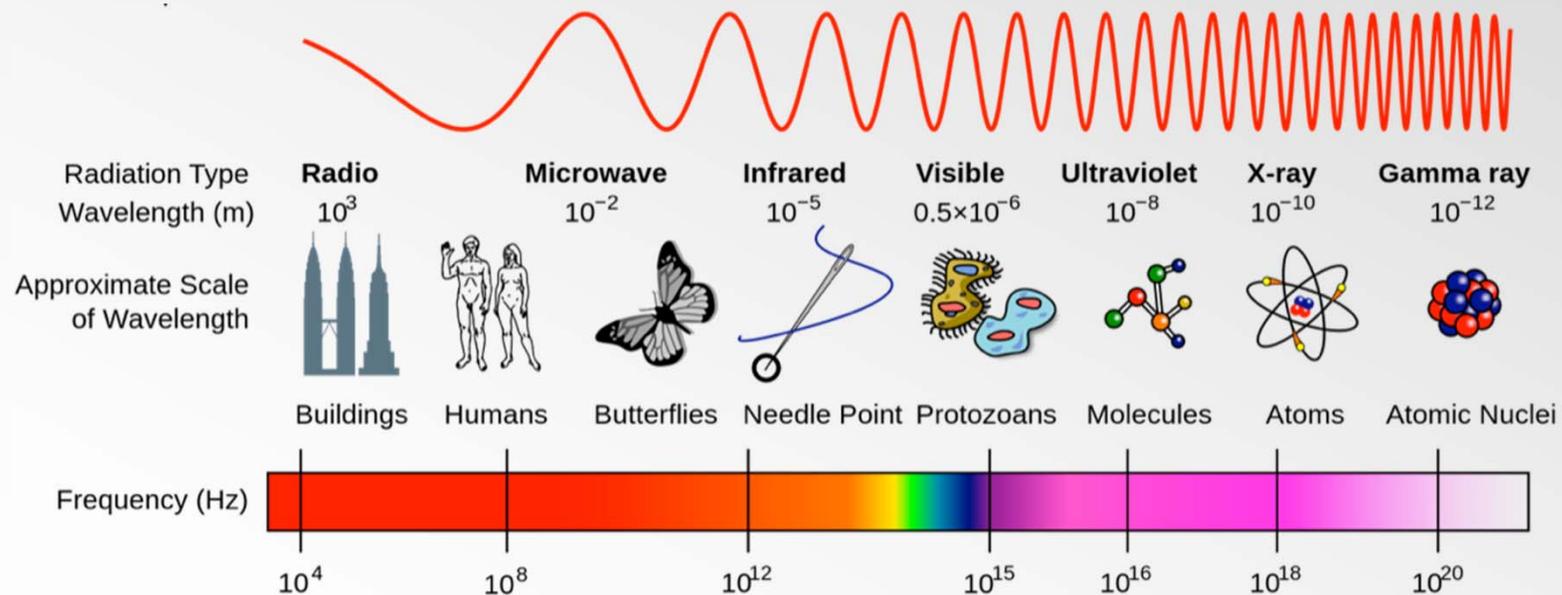
- Some medications have specific requirements



Morphine
 Promethazine
 Omeprazole
 Temazepam
 TMP-SMX
 Ciprofloxacin

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

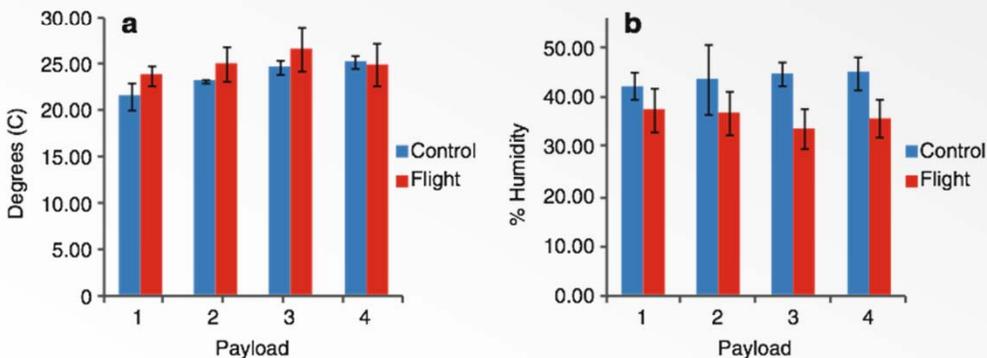


Fig. 6. Comparison of mean temperature (a) and relative humidity (b) conditions between ground and spaceflight

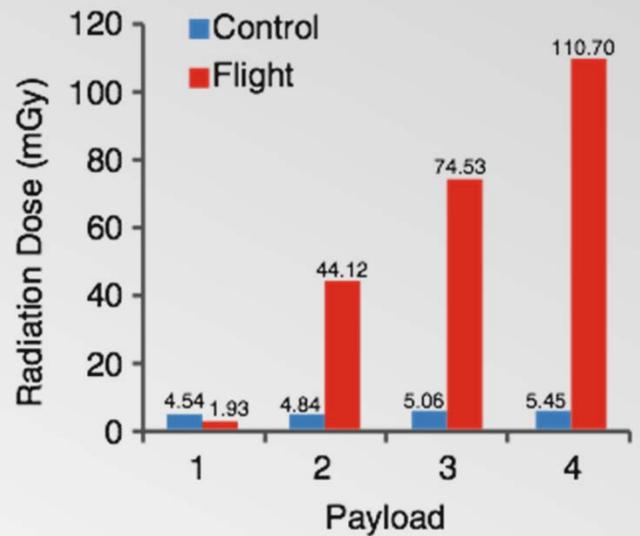
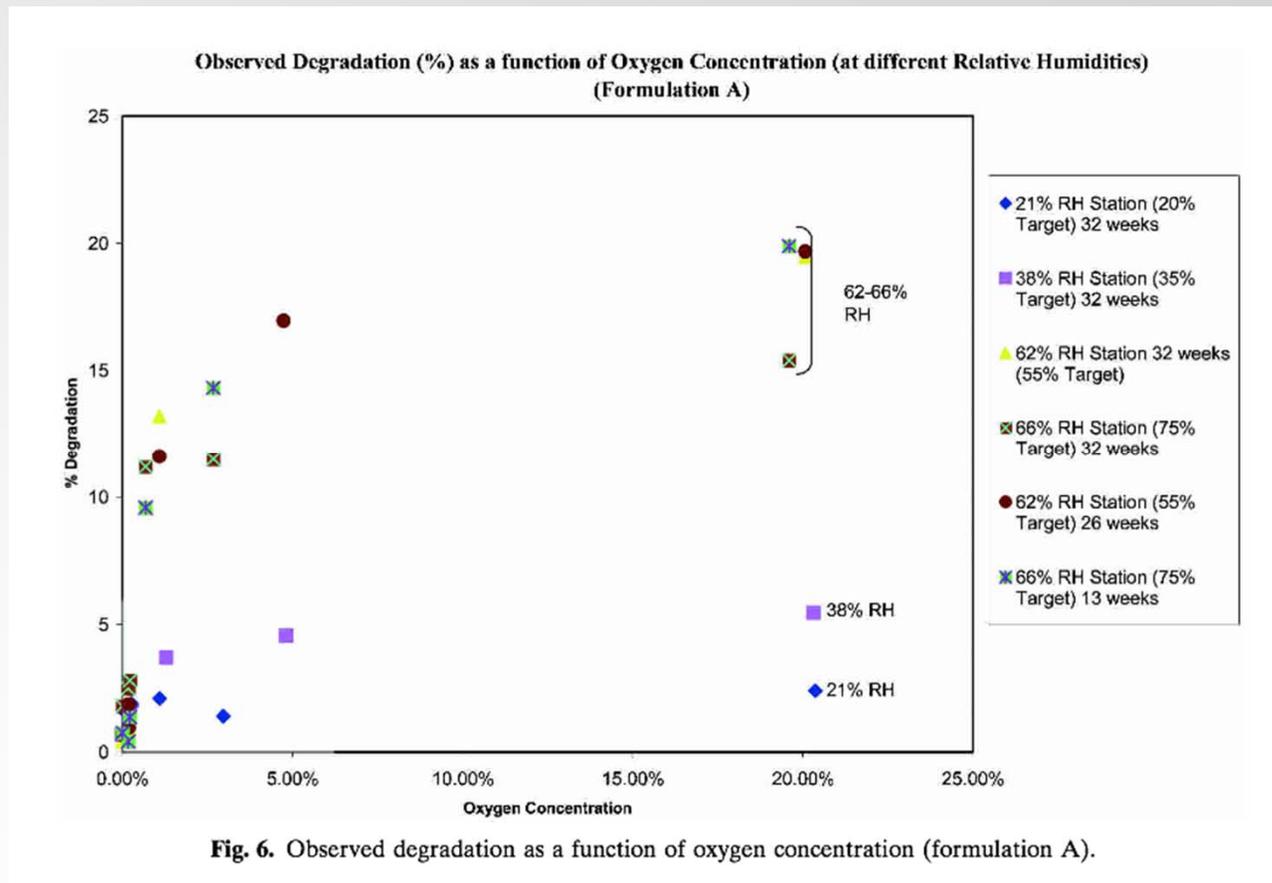


Fig. 7. Comparison of cumulative radiation dose between ground and spaceflight

Oxygen



Microbial contamination



pH



Solutions on earth

- Packaging

 - Blister packs

 - Amber-coloured containers

- Storage environment

- Repackaging

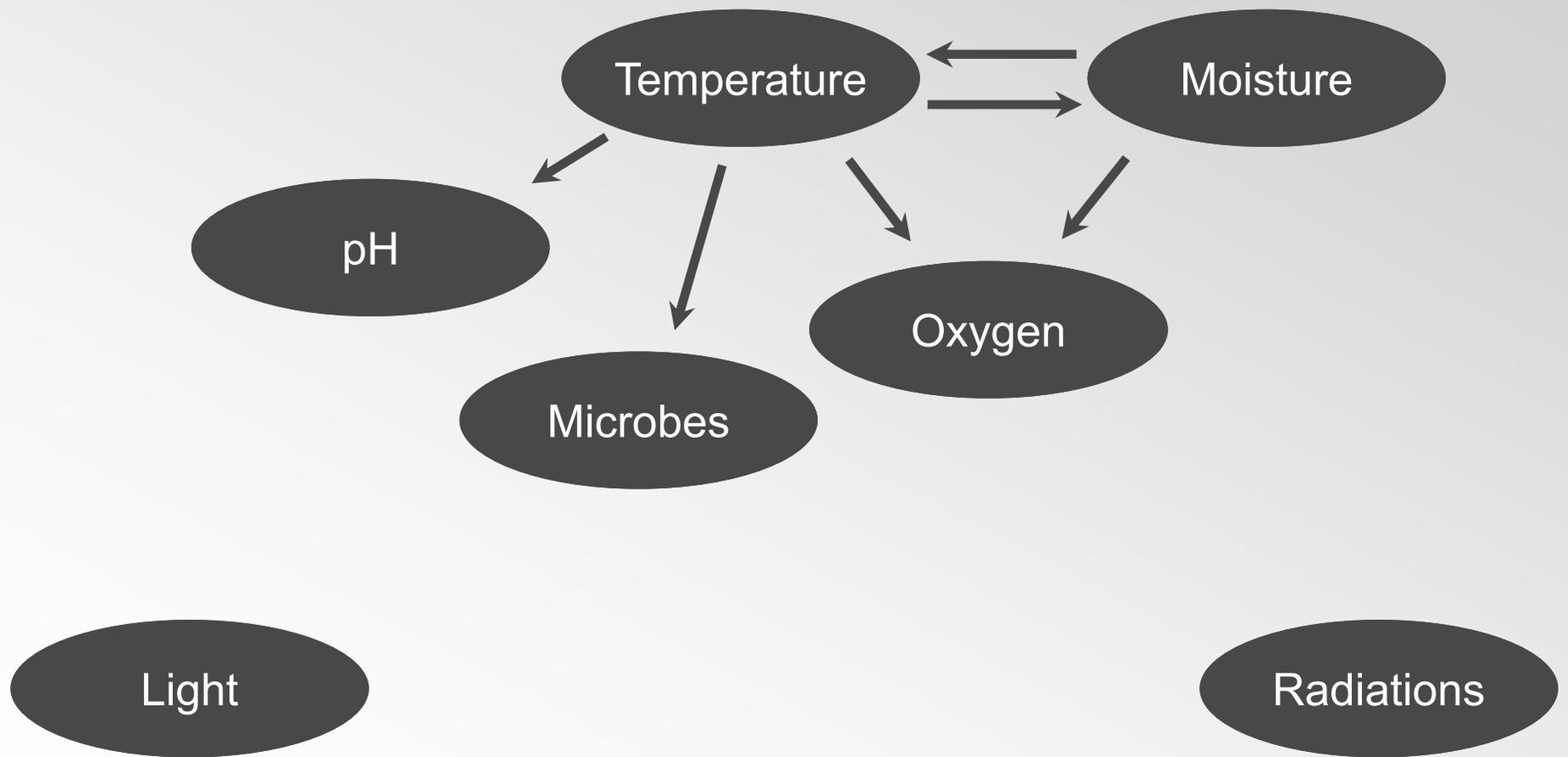


Current NASA practice

- Medications repackaged in plastic bags
- Stored in Nomex cases within CHeCS



Extending shelf life



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

Microbes

1x
Standard USP packaging requirements

Oxygen

1-1.25x
Protection from oxygen contact

Radiations

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

Stability assessment

- Non-destructive

- 3 strategies:

Visual inspection

Raman spectroscopy

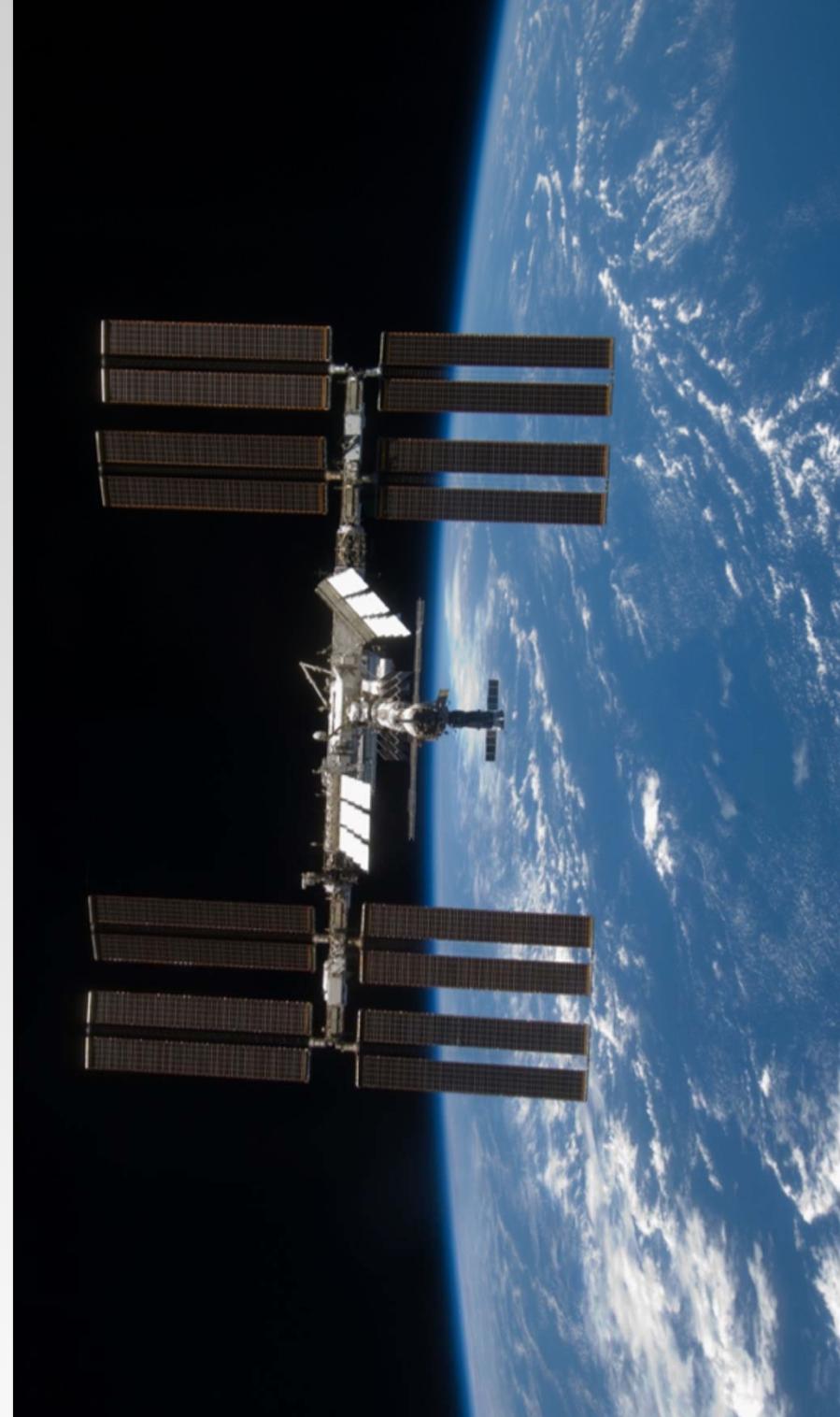
Near-infrared spectroscopy

Other requirements

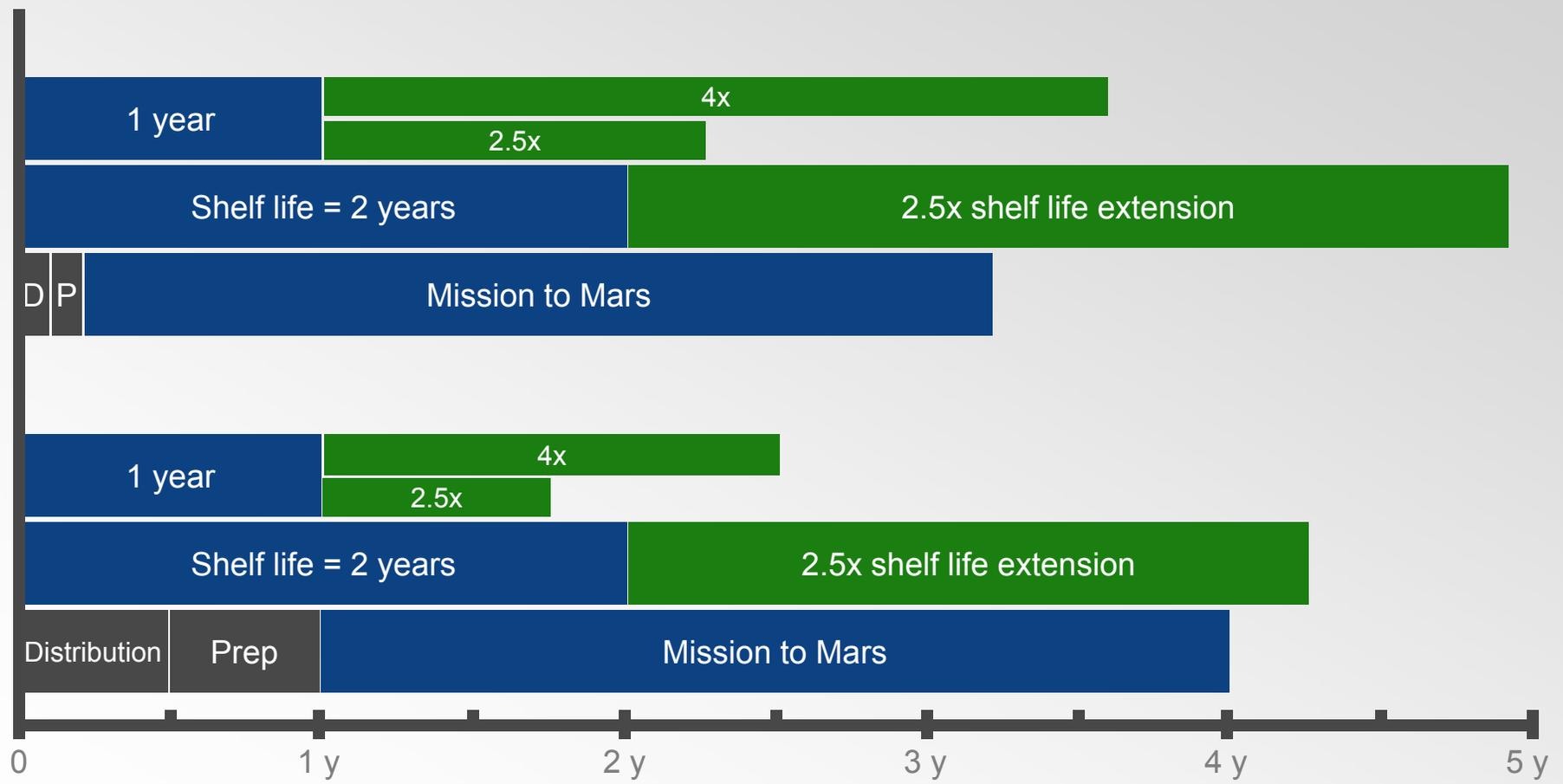
- Fast access
 - < 60 seconds (nominal)?
 - < 30 seconds (emergency)?
- Ability to repackage opened medications
- Integration with the Medical Consumables Tracking system

The next steps

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



Beyond MSPS



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