National Aeronautics and Space Administration

EXPLORATION MEDICAL INTEGRATED PRODUCT TEAM (XMIPT)

2024 Aerospace Medical Association Annual Scientific Meeting

Pilot Study of Medications Exposed to Vacuum

Phyllis Friello | 5/8/24

Disclosure Information
93rd Annual Scientific Meeting

I have no financial relationships to disclose.

I will not discuss off-label use and/or investigational use in my presentation

Medications in a Vacuum Pilot Study

Overall, this study is intended to assess the impacts of vacuum exposure on medications and their packaging and to help identify those that maybe most tolerant of such exposures for selection and prioritization in future NASA and Department of Defense (DoD) spacecraft medical kits.

This presentation will present an overview of the two-phase pilot study design, and results summary of the first phase.

Photo credit: https://lms.smu.edu.ph/course/info.php?id=8495

Background & Need

This study is a collaboration between the XMIPT and the Clinical and Operational Space Medicine Innovation Consortium (COSMIC), 59th Medical Wing, Lackland Air Force Base, Texas

- Although most medical kits are and will be stored in a pressurized, climate-controlled environments, there are specific scenarios in which they may become exposed to vacuum.
- For NASA missions, these include the vehicle being brought to vacuum to enable clearance of atmospheric contaminants, and in the airlock (in which kits may be stored) during extravehicular activities.
- For the United States Air Force, large amounts of the aeromedical evacuation and en route patient movement occur on large transport aircraft at high altitudes. Emerging discussions include the use of supersonic, hypersonics, and vertical take-off, vertical-landing rockets for extremely rapid movement of medical supplies and equipment.

COSMIC
CLINICAL & OPERATIONAL SPACE MEDICINE INNOVATION CONSORTIUM
59TH MEDICAL WING, SAN ANTONIO, TEXAS
711TH HUMAN PERFORMANCE WING, DAYTON, OHIO

Pilot Study Phases

NOV 2023 — Phase A Vacuum Exposure
Objective: Testing Package Integrity

Phase A	Arm 1	Arm 2
Rate	1 psi/min	7 psi/min
Packaging	Solids: Manufacturers Fluids: Manufacturers	Solids: Manufacturers Fluids: Manufacturers
Duration	1h Vacuum Exposure	1h Vacuum Exposure
API Testing	None	None
Meds	Solids: 12 medications Fluids: 10 medications (liquids/aerosol, gel)	Solids: 12 medications Fluids: 10 medications (liquids/aerosol, gel)

MAY 2024 — Phase B Vacuum Exposure
Objective: Testing Stability & API

Phase B	Arm 1	Arm 2
Rate	1 psi/min	No exposure
Packaging	Solids: No Packaging Fluids: Manufacturers	Solids: No Packaging Fluids: Manufacturers
Duration	8h Vacuum Exposure	None
API Testing	3 time points	3 time points
Meds	Solids: 12 medications Fluids: 7 medications	Solids: 12 medications Fluids: 7 medications

Medications and Packaging

- Currently, for ISS flights most oral medications are repackaged in resealable zip bags. Specific packaging for exploration medications has yet to be determined.
- In contrast to NASA, the DoD leaves medications in manufactures packaging during transport due to markedly lower restrictions on mass and volume compared to spaceflight.
- The medications and formulations selected were based on those currently being considered for flight on Artemis missions and to expose different formulation types and medications of different vapor pressures.

Photo Credit: NASA

Updated, modular CCATT Medication Box. Photo Credit: US Air Force

Chamber Exposures

Phase A samples were taken to vacuum at the rates of 1 psi/min, and 7 psi/min and held at vacuum for 1hr.

- The rate of 1psi/min was selected as the depress/repress rate to reflect historical rates and to avoid overestimating package failure rates.
- The depress rate of 7psi/min was selected to represent a worst-case contingency depress scenario.
- One hour hold was chosen to mirror the duration of a controlled repress/depress scenario for toxic atmosphere response.

External and internal views of Chamber B-3. KBR facilities, San Antonio, Texas

Medication Selection

Phase A Medications	Phase B Medications
Medication - Fluids	
Epinephrine (EpiPen) 0.3mg	Epinephrine (EpiPen) 0.3mg
Moxifloxacin (Vigamox) 0.5%	Moxifloxacin (Vigamox) 0.5%
Tetracaine Ophthalmic 0.5%	Tetracaine Ophthalmic 0.5%
Dexamethasone 10 mg/ml	Dexamethasone 10 mg/ml
Diphenhydramine 50 mg/mL	Promethazine 25 mg/mL
Oxymetazoline (Afrin) 0.5%	Oxymetazoline (Afrin) 0.5%
Albuterol 90 mcg	Albuterol 90 mcg
Hydrocortisone 1%	Hydrocortisone 1%
Lidocaine Jelly 2%	Lidocaine Jelly 2%
Cyanoacrylate (Dermabond)	Cyanoacrylate (Dermabond)
Medications - Solids	
Clindamycin 300 mg	Clindamycin 300 mg
Cefdinir 300mg	Cefdinir 300mg
Doxycycline 100mg	Doxycycline 100mg
Ondansetron ODT (Zofran) 4mg	Ondansetron ODT (Zofran) 4mg
Pseudoephedrine 120mg	Pseudoephedrine 120mg
Ibuprofen (Motrin) 400mg	Ibuprofen (Motrin) 400mg
Acetaminophen 500mg	Acetaminophen 500mg
Meclizine 25mg	Meclizine 25mg
Diphenhydramine 50mg	Diphenhydramine 50mg
Promethazine 50mg	Promethazine 50mg
Bisacodyl (Dulcolax) 5mg	Bisacodyl (Dulcolax) 5mg
Loperamide HCl Imodium 2mg	Loperamide HCl Imodium 2mg

- Samples are prepared in the NASA JSC Pharmacy and transported to the KBR test chambers for exposure
- Due to availability, Diphenhydramine 50 mg/mL vial was substituted for Promethazine 25 mg/mL vial in Phase A
- Hydrocortisone, Lidocaine and Cyanoacrylate will not undergo API testing in Phase B due to limitations associated with extraction methods

Phase A Test Parameters

Pre & Post Exposure Medication Test Parameters:

- **Visual evaluation of containers and medications for three failure criteria:**
  1. Is the medication package sealed?
  2. Is the medication packaging intact, free from tears, breaks, rips?
  3. Is the interior container seal intact?

- **Sample mass**

10 bottles or packages of each medication were exposed in Arm 1 & Arm 2

Samples in the vacuum chamber

Samples removed from the vacuum chamber

Phase A Results

Visual Observations

- No observed rips, breaks or tears in any of the samples
- Distortions observed in the packages of solid medications

	Medications A1 (1 psi/min)	Medications A2 (7 psi/min)
Bottles collapsed inward	2	1
Inner foil seal ballooned	2	2
Foil of blister pack ballooned	1	1
Bottom of bottle ballooned	6	5

Sample Mass

- Except for Albuterol and Pseudoephedrine, medications had changes in mass less than 0.1 g

	A1 (1 psi/min) average change	A2 (7 psi/min) average change
Solids	0.04 g (SD 0.39)	0.02 g (SD 0.02)
Fluids	0.01 g (SD 0.14)	0.02 g (SD 0.12)
Albuterol	0.46 g (SD 0.01)	0.32 g (SD 0.005)
Pseudoephedrine	0.15 g (SD 0.01)	0.03 g (SD 0.09)

Samples removed from vacuum chamber

Visual Observations

Solids	A1 # of meds affected	A1 meds affected	% of bottles/med	A2 # of meds affected	A2 meds affected	% of bottles/med
Collapsed inward	2	Clindamycin	10	1	Clindamycin	10
		Ondansetron	10			
Inner seal intact, foil seal ballooning	2	Cefdinir	10	2	Loperamide HCl	100
		Ibuprofen	100		Ibuprofen	10
Foil back ballooning	1	Pseudoephedrine	100	1	Pseudoephedrine	10
Bottom evidence of ballooning	6	Doxycycline	100	5	Ibuprofen	10
		Acetaminophen	100		Acetaminophen	100
		Promethazine	100		Meclizine	100
		Diphenhydramine	100		Promethazine	100
		Bisacodyl	100		Bisacodyl	100
		Loperamide	100			
No change	1			4		
Fluids				0		
No change	10			10		

Next Steps - Phase B

Phase A Vacuum exposure for testing package integrity - 11/23

Phase A	Arm 1	Arm 2
Rate	1 psi/min	7 psi/min
Packaging	Manufacturers	Manufacturers
Duration	1 hr. vacuum exposure	1 hr. vacuum exposure
API Testing	None	None
Meds	Fluids (10 medications) (liquids/aerosol, gel)	Fluids (10 medications) (liquids/aerosol, gel)
	Solids (12 medications)	Solids (12 medications)

Phase B Vacuum exposure for API and stability testing - 5/24

Phase B	Arm 1	Arm 2
Rate	1 psi/min	No vacuum exposure
Packaging	No Packaging for solids	No Packaging for solids
	Manufacturers packaging for fluids	Manufacturers packaging for fluids
Duration	8 hr. vacuum exposure	None
API Testing	3 time points	3 time points
Meds	Fluids (7 medications)	Fluids (7 medications)
	Solids (12 medications)	Solids (12 medications)

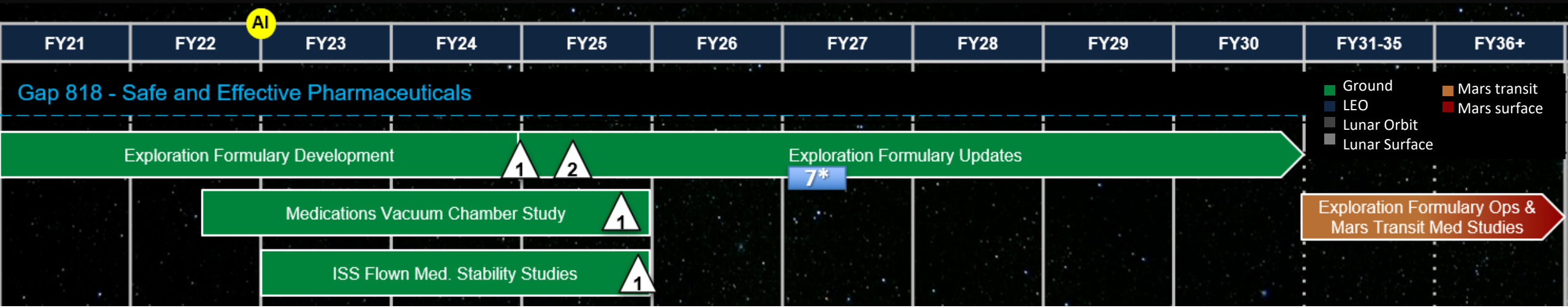
Summary of Key Takeaways

- Effects of vacuum exposure in Phase A included no observations of gross package failures. However, there were reversible changes such as ballooning which were limited to the bottles.

- Phase B will test the physical and chemical stability, including API, color changes and physical breakdown of the selected medications following exposure to vacuum.

BACK-UP

Pharmaceutical Studies



- Overview
  - The shelf lives of most medications are less than the duration of an expected Mars mission
  - Safety and efficacy of medications beyond expiration dates are unknown for most medications
  - The impacts of environmental exposures such as radiation and vacuum on medications and packaging are not fully characterized

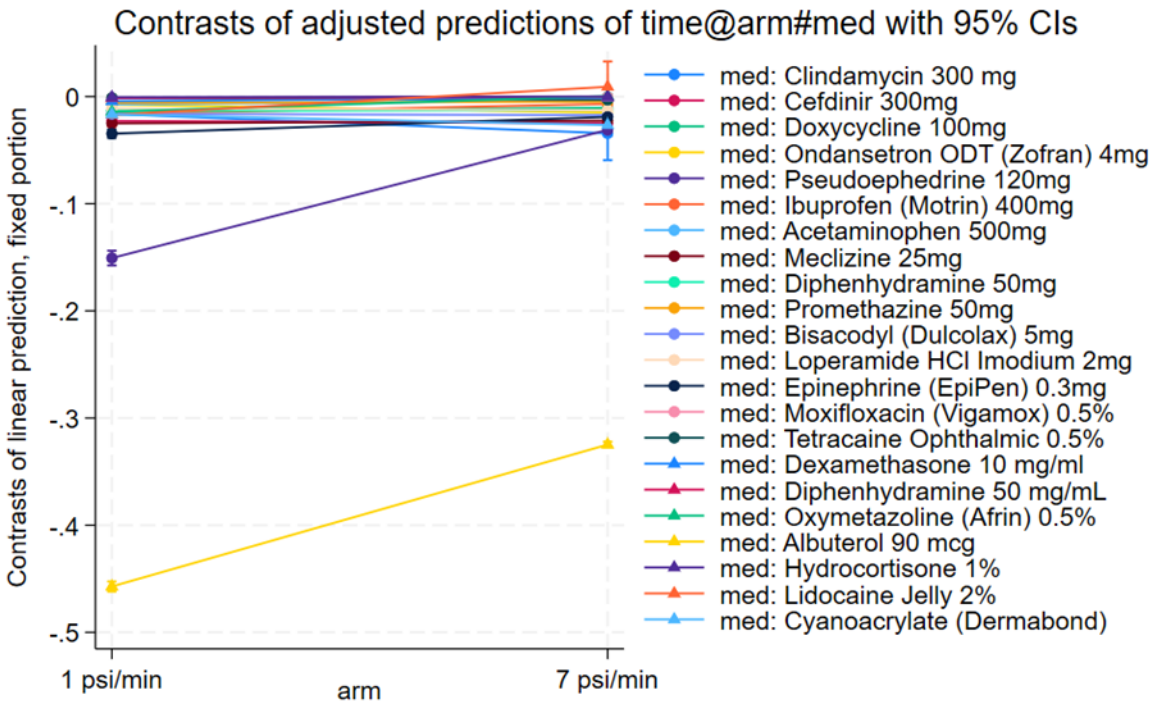
- Key
  - △1 Swim lanes represent data collection activities required to characterize medication stability and efficacy during spaceflight-relevant exposures
  - △2 HRP Deliverable: Exploration Formulary v3.0
  - 7* System prototype demonstration in a space environment

Gap List

1.7	Safe and Effective Pharmaceuticals [3508]	Capability to maintain medication safety and effectiveness over the course of all exploration mission concepts despite increased exposure to environmental stressors.	• Pharm

Phase A Results

Marginal pre to post contrast for each medication and arm



- Based on our prior understanding and analyses of the current experiment, there is a 90% probability that the gross package failure rate is below 19% for each tested medication.