

UNCLASSIFIED

AD NUMBER
ADB192333
NEW LIMITATION CHANGE
TO Approved for public release, distribution unlimited
FROM Distribution authorized to DoD only; Proprietary Info.; 14 Dec 89. Other requests shall be referred to Commander, US Army Medical Research and Development Command, Attn: MCMR-RMI-S, Fort Detrick, Frederick, MD 21701-5012.
AUTHORITY
USAMRMC ltr., 21 Apr 97

THIS PAGE IS UNCLASSIFIED

AD-B192 333

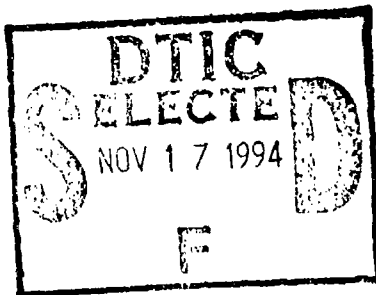


SRI-Org-94-768-7654

L
O

Project 7654-X

**MICROENCAPSULATION OF DRUGS IN THE MICROGRAVITY ENVIRONMENT
OF THE UNITED STATES SPACE SHUTTLE**



Midterm Report

Thomas R. Tice
Richard J. Holl

October 3, 1994

Supported by:

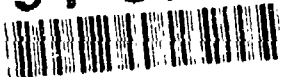
U.S. Army Medical Research and Materiel
Command, Fort Detrick, Frederick, MD
21702-5012

Contract DAMD17-92-C-2011

NOTICE

auth
Distribution limited to DOD Components only (~~to include DOD Contractors~~): Proprietary Information, December 14, 1989. Other requests must be referred to Commander, US Army Medical Research and Development Command, ATTN: MCMR-RMI-S, Fort Detrick, Frederick, Maryland 21701-5012.

94-35479



288

SOUTHERN RESEARCH INSTITUTE
2000 Ninth Avenue South
Birmingham, Alabama 35205

94 11 10 07 4

REPORT DOCUMENTATION PAGE

FORM 100-100
MAY 1962 EDITION
GSA GEN. REG. NO. 27

3 Oct 94

Midterm 5/4/92 - 10/3/94

Microencapsulation of Drugs in the Microgravity
Environment of the United States Space Shuttle

DAMD17-92-C-2011

Thomas R. Tice
Richard J. Holl

Southern Research Institute
2000 Ninth Avenue South
P.O. Box 55305
Birmingham, AL 35205-5305

U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, MD 21702-5012

~~Limited - Proprietary Information, December 14, 1989~~

DTIC QUALITY ASSURANCE 5

Microencapsulation, Controlled-release, Space Shuttle
Antibiotics, Drug Development

Unclassified

Unclassified

Unclassified

N/A

N/A

Unclassified

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

_____ Where copyrighted material is quoted, permission has been obtained to use such material.

_____ Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

X Citation of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of the organizations.

_____ In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

_____ For the protection of human subjects, the investigator(s) have adhered to policies of applicable Federal Law 45CFR46.

_____ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

James R. Lio

10/5/94

PI Signature

Date

Approved for	
NIH	✓
DA	✓
USDA	✓
Justice	✓
By _____	
Distribution _____	
Availability Codes	
Dist	Availability or Special
E-4	

TABLE OF CONTENTS

I.	INTRODUCTION	1
II.	BACKGROUND	4
III.	PURPOSE	6
IV.	METHODS OF APPROACH	6
V.	DESCRIPTION OF WORK	7
	A. General Design and Fabrication	7
	B. Design and Fabrication of MIS Hardware Systems	13
	C. Containment Levels for MIS-B.	19
VI.	CONCLUSIONS	23
VII.	REFERENCES	24

MICROENCAPSULATION OF DRUGS IN THE MICROGRAVITY ENVIRONMENT OF THE UNITED STATES SPACE SHUTTLE

I. INTRODUCTION

The United States Army Institute of Dental Research (USAIDR) has contracted Southern Research Institute (Southern Research) to design and construct an experiment to test the feasibility of making pharmaceutical microspheres in space. The MIS-B experiment will occur on the middeck of the United States Space Shuttle and the MIS-B hardware will occupy the space of two standard middeck lockers.

MIS-B is a continuation of the MIS-A. MIS-A flew aboard Discovery, STS-53, on December 2, 1992. The MIS-B experiments will use the results obtained from the MIS-A experiments to improve the operation of the hardware to enable a larger yield of space-produced microspheres. With a larger amount of space-produced microspheres, more critical examinations of the differences between space- and earth-produced microspheres can be made.

More specifically, the objective of the MIS-B experiment is to demonstrate the feasibility of producing pharmaceutical microspheres in a microgravity environment. To meet this objective, a drug, ampicillin anhydrate, will be microencapsulated in space. By choosing this drug, a direct comparison between earth- and space-produced microspheres can be performed. Ampicillin anhydrate microspheres have been made on earth. In addition, we have shown from the results of MIS-A that the manufacturing microspheres in the microgravity environment of space can improve the quality of the microspheres.

Knowledge gained by this research will indicate whether pharmaceuticals which previously could not be microencapsulated on earth due to solvent incompatibilities or diffusional dilution could be easily microencapsulated in space. Microencapsulation would enable these drugs to be administered in a controlled-release fashion which could increase their therapeutic value. Research conducted at the U.S. Army Institute for Dental Research (USAIDR) indicate that antibiotics microencapsulated in poly(DL-lactide-co-glycolide) have been shown to control wound infections in vivo following a single application directly to the wound. Consequently, controlled-release antibiotic microspheres could have great utility in treating wounds caused during battle.

Below is a list of the specific tasks necessary to complete this contract. The status of these tasks are summarized as well.

- | | |
|---------|---|
| Task 1: | The literature search started under the initial contract will be continued. With the incorporation of new systems into the experimental hardware, more references describing the current knowledge of these systems will be required. |
| Status: | On-going. Literature searches are being conducted to determine whether helium leak testing can be used to test structural and seal integrity. Using helium leak testing has the potential of simplifying the structural and seal integrity tests. |

Task 2: Improvement of the microencapsulation hardware.

Status: Completed. Improvements to the MIS-B hardware include:

- Integrating the plumbing system into a compact unit containing all the components
- Designing each hardening chamber to possess individual primary and secondary containment systems
- Constructing the hardening chamber from aluminum
- Designing a control circuit expressly for MIS-B which replaces the programmable logic controller used in MIS-A
- Redesigning the outer cover and control panel
- Incorporating active cooling into MIS-B
- Incorporating a fan and duct system in each hardening chamber to improve air circulation
- Using a mixture of helium and nitrogen as the backfilling gas to provide both inerting of the hardening chambers and a method of leak detection superior to that use on MIS-A
- Coating the inside surface of the hardening chambers with a fluorosilicone compound to prevent the polymer/drug suspension droplets from adhering to the surface
- Removing the video recording system and fiber optic lighting system
- Removing the electrostatic containment system
- Switching polymer solvent from methylene chloride to ethyl acetate and, as a result, changing the adsorbent from type A molecular sieves to silica gel
- Reducing the x-axis dimension by 0.875 in. to bring MIS-B in compliance for payload envelope
- Reducing the weight to bring MIS-B in compliance for payload weight
- Increasing the number of experiments in MIS-B from two to four
- Increasing the concentration of poly(dl-lactide-co-glycolide) in the polymer/drug suspension from 5.0 wt % to 7.5 wt %

- Task 3: Characterization of the polymer used in the space-produced microspheres.
- Status: The project has not progressed to this point. We anticipate that characterization of the polymer used in the experiments will be performed after the NASA-required safety tests of the MIS-B hardware.
- Task 4: Selection of drug to be microencapsulated in microgravity.
- Status: More than likely, the drug to be microencapsulated will be ampicillin anhydrate, the same drug used in MIS-A. In the next quarter of this research program, we will confirm the selection of ampicillin anhydrate as the drug to be microencapsulated with Dr. Jean Setterstrom.
- Task 5: Equipment review and fabrication.
- Status: In progress. The MIS-B hardware fabrication is nearly completed. We will perform the final assembly and functionality testing of the hardware in the next quarter of this research program. The hardware is scheduled to be placed under configuration control after the hardware functionality test. This test is scheduled for the week of September 26, 1994.
- Task 6: Safety reviews and flight certification.
- Status: The project has not progressed to this point. A Phase 0/1 Safety Review is scheduled for October 27, 1994, at Johnson Space Center.
- Task 7: Flights and flight debriefings.
- Status: The project has not progressed to this point.
- Task 8: Analysis of space-made microspheres.
- Status: The project has not progressed to this point.

To summarize the results obtained in the first half of the research program:

During the first half of the research program, we have changed the design of the MIS-B hardware and software to incorporate the results obtained from MIS-A. These design changes are listed above. Some of the important changes to the design bring MIS-B in compliance with NASA specifications with regard to payload envelop and weight. In addition, the safety review process of MIS-A gave us important insight as to how to redesign MIS-B to accommodate NASA safety concerns. A description of these modifications are summarized later in this report.

MIS-B has been granted tentative manifestation aboard Mission STS-70 pending final safety certification by NASA. STS-70 is scheduled for launch on June 27, 1995. We expect to receive final safety certification of the MIS-B by NASA by February, 1995.

We participated in numerous meetings with the MIS-B integration team from the U.S. Air Force, Aerospace Corporation, Dynetics, Inc., Muniz Engineering, and SAIC, with the appropriate NASA personnel. These meetings were part of the process of redesigning MIS-B with as many appropriate inputs from NASA personnel and other members of the integration team and of introducing MIS into the NASA payload integration and manifestation procedure.

We performed additional experiments on the operation of the MIS-B hardware to confirm that the polymer concentration can be increased while maintaining the same core-loading of drug as was used in MIS-A. By increasing the polymer concentration, a higher yield of microspheres is possible and less solvent adsorbent is needed. These experiments indicated that the polymer concentration can be increased to 7.5 wt % when ethyl acetate is used as the solvent. In MIS-A, methylene chloride was used as the polymer solvent. Because of the low boiling point of methylene chloride, a lower concentration of polymer had to be used. And, a fast spray rate off of the ultrasonic nozzle was required to prevent the polymer from precipitating on the nozzle tip. By using ethyl acetate as the polymer solvent, a slower spray rate and a higher polymer concentration are possible due to the higher boiling point of ethyl acetate compared to methylene chloride.

Finally, on May 12, 1994, we briefed the Space Test Program (STP) DoD Space Experiment Review Board. Along with discussing the military relevancy and need for space flight issues at this briefing, we also presented the latest engineering drawings. We achieved a ranking of 25 out of 45 test programs. However, eight of the programs ranked above MIS-B do not have full funding. Therefore, our ranking is conceivably higher. Also, the programs reviewed represent all test programs in STP including free-flyers as well as those using the Space Shuttle as a launch platform.

II. BACKGROUND

Microencapsulated drugs (antibiotics) capable of providing precise and predictable sustained drug release rates have been of interest to the Department of Defense. Through the microencapsulation of these pharmaceuticals, more effective and efficient treatment of a variety of casualty situations can be achieved.

Research and development of microencapsulated antibiotics are in progress at USAIDR in collaboration with Southern Research. Antibiotics microencapsulated in poly(DL-lactide-co-glycolide) have been shown to control wound infections in vivo following a single application directly to the wound. Consequently, controlled-release antibiotic microspheres should have great utility in treating wounds caused during battle.

Controlled drug delivery offers profound advantages over conventional dosing. It assures patient compliance and simplifies the dosing regimen by requiring only a single dose for long-term therapy. These characteristics can be seen to be of considerable value in situations where mass casualty may occur. Other advantages of controlled drug delivery include more effective utilization of drugs with short half-lives, reduction of toxic side effects by maintaining the drug concentration within therapeutic values, and drug conservation through a more effective dosing regimen. Microencapsulation can also improve the stability of some drugs allowing for longer shelf-life. Lastly, microencapsulation technology provides a way of delivering new proteins and peptides produced from the emerging biotechnology industry. Presently these types of drugs, can not be delivered in a controlled-release fashion by conventional methods (oral administration).

Certain drugs, however, can not be microencapsulated satisfactorily on earth using current microencapsulation technology. To manufacture microspheres on earth, for example, emulsion-based or spray-drying technologies are often used. Although these processes have been used to microencapsulate drugs, both of these technologies have processing requirements which limit their usefulness. More specifically, emulsion-based processes require an organic solvent that dissolves the polymeric wall material. This organic solvent must be immiscible in water to form an oil-in-water emulsion. This organic solvent must also be nontoxic and compatible with the drug. Once a suitable organic solvent is found, emulsion-based microencapsulation may still be difficult to perform because the drug may leach into the water phase (processing medium) of the emulsion before the microspheres are formed.

Spray-drying technology uses air as the processing medium. As a result, drug is not lost to the processing medium (air) during the formation of the microsphere. However, there is only a limited amount of time available to form and dry the microspheres before they collide with each other or the process equipment. As a result, the solvent must be quickly removed from the forming microspheres. This process often results in poor-quality microspheres because the quick removal of solvent causes the formation of irregular-shaped microspheres with poor surfaces and numerous interior voids.

Microsphere manufacturing in microgravity will eliminate the need for a liquid process medium (water) as is necessary in emulsion-based microencapsulation. Consequently, more solvents would be available to dissolve the wall polymer because the requirement of immiscibility in water would be eliminated. In addition, drug loss to the processing medium (air) is eliminated as with spray-drying. However, by being able to slowly remove the solvent from the forming microspheres in space, the microspheres should be highly spherical with high-quality surfaces -- a result impossible to achieve with earth-based spray-drying.

It is anticipated that data obtained from the MIS-B experiment will significantly enhance microencapsulation technology. And, it may provide added direction for the development of novel encapsulation methods for medical and non-medical products.

III. PURPOSE

The goal of this contract is to design and construct a device that can make pharmaceutical microspheres in space. The device fits in the space usually occupied by two middeck lockers aboard the United State Space Shuttle. Four experiments are incorporated into the MIS-B hardware. Once in the microgravity environment of space, three experiments test whether pharmaceutical microspheres can be made by using an ultrasonic spray nozzle to spray a polymer/drug/solvent mixture into a cylinder with subsequent solvent removal. The fourth experiment is similar to the other except that no drug will be incorporated into the polymer solution.

The design of MIS-B depends heavily on the design of MIS-A, on the experience obtained by the MIS-A integration team during the NASA safety review process for MIS-A, and on the results obtained from the successful operation of MIS-A on-orbit during STS-53. All of these factors were considered by the MIS-B design team to insure that MIS-B would be a significantly improved experiment in terms of space-made microsphere yield, of compliance to NASA specifications for hardware manifested in the Shuttle mid-deck, and of fabrication and assembly.

IV. METHODS OF APPROACH

Four experiments are incorporated into MIS-B. Once in the microgravity of space, the experiments will produce pharmaceutical microspheres by using an ultrasonic spray nozzle to spray fluid into a cylinder with subsequent solvent removal. The difference between the four experiments is that one of them will not use the polymer/drug suspension employed in the other three. That is, the fourth experiment will spray only polymer solution. From this fourth experiment, we will have control microspheres without microencapsulated drug to which comparisons can be made. The other three experiments will spray the same polymer/drug suspension to determine the reproducibility of the microencapsulation process, to increase the potential yield, and to have redundancy in the mission in case one of the experiments has operational problems.

All the experiments use ultrasonic spray nozzles to introduce microdroplets of polymer/drug/solvent or polymer/solvent mixtures into the hardening chambers. In microgravity, the microdroplets will float and, upon slow solvent removal, harden into microspheres. The polymer/drug/solvent mixture consists of poly(DL-lactide-co-glycolide) (polymer), ampicillin anhydrate (drug), and ethyl acetate (solvent). The polymer/solvent mixture contains only poly(DL-lactide-co-glycolide) and ethyl acetate.

The four experiments will be performed in groups of two. Each group of two experiments will run simultaneously for about 1¼ hours. After they are completed, the other group of two experiments will run simultaneously for the same duration. The total experimental operational time for MIS-B is about 2½ hours. We have requested minimum activity of the Shuttle during the MIS-B experimental operations. This will provide enough time to spray the experimental mixtures into the hardening chambers and establish a stable condition.

During the solvent removal period, we have requested minimal operation of the Space Shuttle to prevent accelerations which could adversely affect the formation of the microspheres. These accelerations are typically caused by thruster firings performed to maintain orbital integrity. By

keeping the Shuttle in a minimal activity operation, a microspheres will stay approximately in the center of the hardening chambers and not collide with the chamber walls.

After the Space Shuttle lands, we will remove the microsphere product from the four hardening chambers of the MIS-B experiment. We will then analyze the structure and drug-releasing characteristics of these microspheres. Because ampicillin anhydrate microspheres have been made on earth, the release properties of the earth-processed and space-processed microspheres along with other properties of the microspheres can be directly compared. By comparing the two differently processed microspheres, we will be able to determine if the space-processed microspheres have improved or unique properties.

V. DESCRIPTION OF WORK

Major modifications to the design of the MIS-B hardware were needed from the design of MIS-A. The modifications involved correcting the causes of variances to NASA specifications needed for MIS-A, improving the containment design, eliminating unnecessary subsystems that were incorporated in MIS-A, and redesigning the plumbing system of MIS-A. We also modified the MIS-B hardware in other ways that we determined would increase the probability of a successful mission. These modifications will make the safety review process of MIS-B easier, make the prelaunch ground operations easier, improve the seal integrity of the primary and secondary containment systems, improve the operation of MIS-B, and increase the yield of microspheres compared to MIS-A. Modifications which affect the MIS-B hardware as a whole are discussed first. Modifications concerning the separate systems of the MIS-B hardware are discussed afterward.

A. General Design and Fabrication

Two general design considerations were used in the design of MIS-B. First, MIS-A had exceedances to NASA middeck payload specifications in terms of weight, payload envelop, and electromagnetic interference. We examined these exceedances in MIS-A and corrected them in the design of MIS-B. Second, the yield of space-made microspheres was poor in MIS-A. In examining the results obtained from MIS-A, we modified the microencapsulation process in MIS-B with the goal of improving the yield of space-made microspheres.

1. Addressing the MIS-A Exceedances

Weight.

One of the first items which needed to be addressed in the design of MIS-B was the exceedances to NASA middeck payload specifications in both weight and payload envelop present in MIS-A. MIS-A exceeded the NASA weight specification by 22 lbs. (142 lbs. actual vs. 120 lbs. required). Therefore, we decided to address the weight problem first.

We accomplished weight reduction in the design of MIS-B by using both the elimination of unnecessary subsystems incorporated into MIS-A and by better design of the custom fabricated hardware such as structural supports and mounting brackets.

After reviewing the videotape from MIS-A, we have decided that the data obtained from the videotape was not worth the cost in terms of electrical power, weight, and volume of incorporating the video recording system into the hardware. As a result, we decided to eliminate the video recording system into the MIS-B hardware. With the additional electrical power, weight, and volume available from removing the video recording system, more modifications to the MIS-B hardware can be accommodated. In addition, the video recording system (video cassette recorder, 2 cameras, and lamps) consumed the most electrical power of any component in MIS-A. By removing the video recording system, less power will be consumed by MIS-B.

Because of the spray dynamics generated by the ultrasonic spray nozzle, the electrostatic containment system on MIS-A was not strong enough to repel the charged microdroplets back towards the center of the hardening cylinder. As a result, the microdroplets collided with the nylon mesh in the hardening cylinders of MIS-A separating the molecular sieves from the drying area. This was the major reason for the poor yield of space-made microspheres in MIS-A.

Two phenomena are primarily responsible for the low yield of space-produced microspheres in MIS-A. These two phenomena are the forcing of the polymer/drug suspension to the walls of the hardening cylinder by the spray dynamics and the wettability of nylon for the polymer/drug suspension. Because of the strength of these two phenomena, the electrostatic containment field in one of the hardening cylinders was not strong enough to keep the polymer/drug suspension droplets away from the nylon mesh. Although electrostatic containment may prove in the future a valuable method of controlling the polymer/drug suspension spray in microgravity, we believe that electrostatic containment should be eliminated from the MIS-B hardware. Other modifications to the hardware can be made to provide the necessary means of controlling the polymer/drug suspension spray and increasing yields. These modifications can include increasing the volume of the hardening chamber, constructing the hardening cylinder from material nonwetable to the polymer/drug suspension, and finding a method to move the polymer/drug suspension spray away from the ultrasonic spray nozzle.

The subsystems of MIS-A that we determined were unnecessary in MIS-B were:

- Video recording system
- Fiber optic lighting system
- Programmable logic controller (replaced with a custom-designed, hardwired control circuit)
- Electrostatic containment system

With the elimination of these subsystems, a significant weight reduction was possible with MIS-B. In addition to these subsystem eliminations, we chose a different design team for MIS-B than was used for MIS-A. This new design team at Dynetics, Inc., had access to the latest computer-aided design programs. This enabled the design of the custom-fabricated hardware to be precisely controlled so that the minimum weight possible for structurally sound hardware could be realized. In addition, detailed layout of the MIS-B components with the computer could be performed insuring full utilization of the payload envelope available to MIS-B.

Because of these reasons and to increase the redundancy built into the experiment, we decided to increase the number of experiments from two on MIS-A to four on MIS-B. Three of the experiments would be identical - the spraying of a polymer/drug suspension. The fourth would be a control experiment in which only the polymer solution was sprayed.

Payload Envelop

MIS-A exceed NASA middeck payload specifications for payload envelop. The x-axis dimension for MIS-A was 0.875 in. too long. (Note: The x-axis for middeck payloads is oriented from the wire trays onto which the payloads are mounted into the middeck common area.)

Because of the changes to the control system and the incorporation of active cooling into the MIS-B hardware, the outer cover and control panel were redesigned. During this redesign, we took advantage of the opportunity to shortened the x-axis length of the outer cover to conform to NASA specifications for middeck experiments. We used the outer cover from the MIS-A backup model for MIS-B. To accommodate the design changes, we cut the front panel off the MIS-A outer cover and removed enough of the side panels to achieve the 0.875 in. length reduction in the x-axis. Then, we welded a new, redesigned front panel onto the shortened side panels. Incorporated into the new front panel are inlet and outlet ports for the active cooling and a new, redesigned control panel.

The new control panel attaches in a deeper well on the front panel of the outer cover. On MIS-A, the locking toggle switches protruded past the edge of the front panel. Although this did not present a safety concern to NASA, we decided for MIS-B to deepen the well in which the control panel is located to totally contain the locking toggle switches. Besides the main power fuse, the main power switch, and the experimental start switch, the new control panel contains more indicator lamps to display the operating status of the four experiments, an additional locking switch to activate the active cooling system, and an additional fuse for the active cooling power circuit.

Electromagnetic Interference

MIS-A needed a variance because of exceedances to NASA payload specifications for conducted electromagnetic interference. Electromagnetic interference generated by MIS-B should be less than that generated by MIS-A. This is because the main sources of electromagnetic interference are power converters and video equipment. We have removed the video equipment and the electrostatic containment system which possessed a power converter from MIS-B. The only sources of electromagnetic interference on MIS-B will be the ultrasonic spray nozzle power supplies and the main power converters. In addition, we have kept the main power circuitry that was used in MIS-A. Therefore, MIS-B should have less than or equal to the amount of electromagnetic interference generated in MIS-A. If necessary, a variance for MIS-B similar to that granted to MIS-A to exceedances in conducted electromagnetic interference will be obtained.

2. Active Cooling

MIS-B will operate for a longer period of time on-orbit than did MIS-A. Although we are reducing the power consumption of the hardware by eliminating the video recording system, MIS-B

may still generate an unacceptable amount of heat during operation due to the longer operating time. Therefore, we designed MIS-B with active cooling.

During the operation of MIS-A on-orbit, the temperature inside the hardening cylinders reached almost 30 °C after 4 h. Although 30 °C was acceptable for the operation of MIS-A, this temperature is the upper limit of what is tolerable in the experiment. MIS-B hardware will be operating for a shorter time period (2 ½ h); however, two of the ultrasonic spray nozzles and the syringe pumps will be operating for the entire operating time of MIS-B as opposed to only 5 min for MIS-A. Active cooling of the MIS-B hardware may be essential to prevent operating temperatures from exceeding 30 °C.

Active cooling involves the use of a fan to cool the operating hardware. In microgravity, convective cooling does not occur because the density difference between hot and cold air is not present. Therefore, hot air from around operating equipment in microgravity will not rise and be replaced with cooler air. In equipment without active cooling systems, heat generated by operating equipment must be dumped passively. Passive cooling occurs by the conduction of heat from the hot metal components of the operating equipment to cooler metal parts of the Shuttle. For low heat loads, passive cooling is adequate. But, for continuously operating equipment, heat loads may overwhelm the heat conduction capacity. Therefore, fans are used to generate convective air currents which allow for heat to be dumped convectively.

3. Polymer Solvent Change

In MIS-A, we used methylene chloride as the solvent for the polymer. Methylene chloride is an excellent solvent for poly(dl-lactide-co-glycolide). However, methylene chloride is somewhat toxic. Therefore, we have decided to switch the polymer solvent from methylene chloride to ethyl acetate. Ethyl acetate is less toxic than methylene chloride and, therefore, a more readily accepted pharmaceutical solvent. However, ethyl acetate is flammable whereas methylene chloride is not.

An added benefit of switching to ethyl acetate is that ethyl acetate has a much higher boiling point. This effects both safety and operational issues associated with MIS-B. With regards to safety, less pressure will build up inside the primary and secondary containment systems of MIS-B because ethyl acetate will not vaporize as readily as methylene chloride at the maximum design temperature for MIS-B under a credible, two-fault scenario.

With regards to operational issues, a polymer/drug suspension made with ethyl acetate can be sprayed through an ultrasonic spray nozzle at a much slower rate than a similar polymer/drug suspension made with methylene chloride. This is because the ultrasonic spray nozzle heats up when operating. When methylene chloride is used as the polymer/drug solvent, some of it is vaporized at the nozzle tip. This requires that the flowrate of polymer/drug suspension through the nozzle be fast enough to compensate for this vaporization and to keep the nozzle tip cool. In addition, the polymer concentration can not be too high because the viscosity of the fluid being sprayed through an ultrasonic spray nozzle has a direct effect on the spraying efficiency. As a result, polymer concentrations in methylene chloride had to be kept low so that the viscosity increase associated with the vaporization of a portion of the methylene chloride solvent would not adversely affect spraying efficiency.

Because ethyl acetate will not vaporize as readily as methylene chloride, the flowrate of polymer/drug suspension made with ethyl acetate through the ultrasonic spray nozzle can be much slower than that needed if methylene chloride is used as the solvent. In addition, higher polymer concentrations are possible for the same reason. These two effects, slower spraying rate and higher polymer concentrations, are what we have determined to be important in increasing the yield of space-made microspheres. A slower spraying rate will allow for a better utilization of the drying volume available in the hardening chamber. A higher polymer concentration will allow for more polymer and drug to be incorporated into the amount of solvent which can be accommodated inside the payload envelop volume that NASA has given for MIS-B.

In switching from methylene chloride to ethyl acetate, we found that the solvent adsorbent needed to be changed. Ethyl acetate is not efficiently adsorbed into type A molecular sieves which were used in MIS-A. After testing many different types of adsorbents, we found that silica gel performed the best. We will use the silica gel in the form of 8 - 12 mesh beads.

4. Plumbing System

We have also designed new syringe pumps for the MIS-B hardware. Because of the syringe pump modifications necessitated by different operating parameters for MIS-B as opposed to MIS-A, we have redesigned syringe pumps and made substantial improvements to the pump design. The operating parameters for MIS-B involve spraying only half the polymer/drug suspension per hardening chamber and spraying at a much slower flowrate. The new design incorporates many of the same features found in the syringe pumps used in MIS-A. However, the new pump will be lighter, possess simpler construction, and incorporate a more efficient stir motor. The new pump design will also incorporate modifications to address concerns raised by NASA regarding the MIS-A pump design. In addition, each pump is integrated into its respective hardening cylinder structure. That is, all of the components are mounted on a common manifold block. Holes are drilled through the manifold block to connect the components together. And, the components are arranged to provide for the shortest pathlength between them. The components connected to the manifold block are the syringe pump, the mixing motor, the solenoid valve, the safety by-pass, and the ultrasonic spray nozzle. The complete plumbing unit is mounted directly on the top part of the hardening chamber.

5. Hardening Chamber Air Recirculation

To improve the circulation of the polymer/drug suspension droplets sprayed into the hardening chamber, we installed a piezoelectric fan inside the hardening chamber. The fan is situated at the bottom of the hardening chamber and directs a gas stream into a duct. The duct is situated on the side of the hardening chamber interior and ends at the ultrasonic spray nozzle. The flowrate generated by the fan is very slow; we anticipate only a small number of complete turnovers of backfilling gas in the hardening chamber.

The purpose for installing the piezoelectric fan in the hardening chamber is to help disperse the polymer/drug suspension droplets more evenly throughout the hardening chamber volume. A major problem with MIS-A was that the polymer/drug suspension droplets were not adequately dispersed throughout the available hardening chamber volume. As a result, microsphere yields were low. With the piezoelectric fan and other design modifications incorporated into MIS-B, we hope to improve the yield of microspheres with MIS-B.

6. Primary and Secondary Containment Systems

In the process of designing the primary and secondary containment systems for MIS-B, we found that the original MIS-B design of the containment systems would be too difficult to incorporate structurally into the MIS-B hardware. We modified the containment system design to alleviate this problem. The new design of the primary and secondary containment systems involves using separate primary and secondary containments for each hardening chamber.

Each hardening cylinder will have its own primary and secondary containment system. By designing each hardening cylinder with its own primary and secondary containment system, smaller containment volumes result. With smaller containment volumes, less pressure can buildup under maximum design conditions. In addition, we found that the individual containment systems could be packed into a tighter volume.

The primary containment involves the hardening chamber and the plumbing system. This is similar in design to the primary containment system for MIS-A. The secondary containment involves a cylindrical sleeve which fits over the bottom part of the hardening chamber and a cover which fits over the top part of the hardening chamber and the plumbing system.

In addition, we constructed the hardening chamber from aluminum. This is different from MIS-A in which the hardening cylinder was constructed from Nylon. Using aluminum allowed for a stronger, lighter hardening chamber for MIS-B.

After examining the MIS-A hardware post-flight, we found most of the polymer/drug suspension dried on the nylon mesh. In addition, we found that the nylon mesh had a continuous film of polymer/drug suspension for only about 4" down the hardening cylinder. As the axial distance increased down the hardening cylinder away from the ultrasonic spray nozzle, we found less and less polymer/drug suspension dried on the nylon mesh. By modifying the inside surfaces of the MIS-B hardening chamber to make them nonwetable to the polymer/drug suspension, we believe that increased yields of space-produced microsphere will result. We found that a nonwetable surface for the polymer/drug suspension could be formed by coating the inside surface of the hardening chamber, the air ducts, and the adsorbent container with a fluorosilicone coating (Dow Corning 94-003 Dispersion Coating).

7. Control System

Because the operation of MIS-B will be inherently simpler than the operation of MIS-A, the control system for MIS-B may not need to be as complicated as for MIS-A. That is, we eliminated the computer used to control MIS-A and replaced it with a hardwired control circuit. By hardwiring the control circuit in MIS-B, less electrical power and volume will be needed compared to the computer used in MIS-A. In addition, the layout of the control panel components (switches, indicator lamps, receptacles, etc.) will be optimized for space.

8. Backfilling Gas Mixture

A mixture of helium and nitrogen will be used to backfill the primary and secondary containment systems. By incorporating helium into the backfilling gas, a helium leak detector can be used to locate and quantify leaks in the containment systems. This would allow for a faster and more accurate structural and seal integrity tests to be performed during hardware verification and during the prelaunch ground operations. Structural and seal integrity for MIS-A was performed using pressure decay. Pressure decay tests take a long period of time to perform and are extremely vulnerable to changes in temperature. Using a helium leak detector would speed up the verification tests without sacrificing accuracy.

The composition of the helium/nitrogen backfilling gas has not been determined. The amount of helium incorporated into the backfilling gas will be dependent on the accuracy of the detectors. Once the specifications associated with the helium leak detectors are known, it is the optimum amount of helium to incorporate into the backfilling gas can be calculated.

B. Design and Fabrication of MIS-B Hardware Systems

The section below is divided into six sections. Each section describes the progress made with the design and fabrication of each system of the MIS-B hardware. The systems of the MIS-B hardware were designed with flexibility to accommodate future experimental design changes. The systems for the MIS-B hardware are:

- Control Subsystem
- Active-cooling Subsystem
- Ultrasonic Spray Nozzle Subsystem
- Pumping Subsystem
- Hardening Chamber Subsystem
- Electrical Subsystem

We designed the MIS-B hardware with three levels of containment to satisfy NASA safety requirements. The first level of containment comprises the hardening chambers and the pumping system for the polymer/drug/solvent mixture. The second level of containment is an aluminum box which completely encloses the first level of containment, that is, the hardening chambers and the pumping system. This second-level containment also contains the cameras of the video system and the ultrasonic spray nozzles. The third level of containment is another aluminum box which completely encloses the first and second level of containment along with the remaining components of the MIS-B hardware. Located on this outer containment box are the switches and indicator lights required for operation of the MIS-B hardware.

1. Control Subsystem

The control subsystem is used to sequence the various components of the MIS-B subsystems and the four experiments contained within MIS-B. The control subsystem consists of the following components.

- Control Panel
- Microstep Motor Indexers (4)
- Control Boards (2)

Control Panel

The control panel for MIS-B is located on the front panel of the MIS-B outer cover. On the control panel are three switches, four 5-A fuse holders (two active, two spares), one power cable connector, one temperature monitor display, and seven indicator lamps.

One of the three switches activates the active-cooling subsystem. The other two operate the MIS-B experiments. One of these two switches is the main power switch; it is a locking switch. The other switch is a push-button switch which will provide an impulse signal to a latch on Control Board 1. The impulse signal will also cause a "go" command to be sent to the microstep motor indexers which initiates the program resident in non-volatile memory devices on the indexers. In summary, the switches have the following functions.

- Active-cooling Switch - Activates the active-cooling subsystem independent of the main power switch. The switch is a locking switch.
- Main Power Switch - Activates main power to MIS-B. Components that will be powered-up at this time will include the dc-to-dc power converters, the power indicator lamp, the microstep motor indexers, and the control boards. The switch is a locking switch.
- Experiment Start Switch - Provides an impulse signal to initiate the indexers. The switch is a push-button.

The fusing for MIS-B consists of four fuses - two active and two spares. One set of active/backup fuses is used in the main power circuit. The other set is used in the active-cooling subsystem circuit.

Microstep Motor Indexers and Control Boards

The MIS-B control electronics subsystem governs the timing and implementation of the processes involved in the operation of MIS-B. The central components of the system consist of two control boards and four indexers. The control boards were designed and developed by Dynetic, Inc., and the indexers were purchased from Technology 80, Inc. Both the control boards and indexer work

together to control the operation of MIS-B. However, the control program resides in non-volatile memory on the indexer boards.

The control boards are 5.75-in by 5.25-in, double-sided, printed circuit cards. These cards each house 14 integrated circuits, two DIP switches, two momentary switches, and five multi-pin connectors. Various resistors, diodes, and capacitors are also located on the cards. The indexers are 3.0-in by 2.75-in by 1.20-in modules in which is mounted a single printed circuit card for three indexers or two printed circuit cards for the fourth. The second printed circuit card on the fourth indexer provides RS-232 interfacing with a personal computer. The program code used by these indexers is stored in non-volatile memory devices; therefore, no batteries are required by the indexers. In fact, no batteries are required for any component of the MIS-B control electronics.

The control boards govern the actuation of many of the events in the operation of MIS-B. They also provide drive currents for certain events governed by the indexers. The control boards accept the Experiment Run Switch command and control the operation of the run indicator lamp on the control panel, the ultrasonic power supplies, and the solenoid valves. The indexers primarily govern the operation of the stepper-motors found the syringe pumps of MIS-B. They also control the operation of the piezoelectric recirculation fans, the ultrasonic power supply relays, the mixing motors, and the experiment-complete indicator lamps.

Although we are using the same stepper motors that we used in MIS-A, we are changing to the microstep motor drivers to produce a smoother, more controllable motion to the syringe pump. This, in turn, will produce a more uniform spray from the ultrasonic spray nozzles.

2 Active-cooling Subsystem

Although we did not use active cooling in MIS-A, we are incorporating an active-cooling subsystem into MIS-B. This is because we will be operating the ultrasonic spray nozzle and pumping subsystems for a much longer period of time in MIS-B than in MIS-A. From the results of the MIS-A flight aboard STS-53, we found that the internal temperature increased to about 30 °C during the initial operation and, then, decreased. Because of the longer operating period of the spray nozzles and pumps in MIS-B, an active-cooling subsystem would be necessary to maintain a constant internal temperature.

The active-cooling subsystem consists of an inlet port, an outlet port, and a fan. The fan is a conventional turbine cooling fan. The circuitry for the active-cooling subsystem is independent from the MIS-B experiment circuitry and has its own fusing. The inlet and outlet ports is located on the front panel of the MIS-B outer cover. Middeck air will be pulled into MIS-B and circulate inside the outer cover. Then, the air will be exhausted into the middeck. No air exchange will occur inside the secondary or primary containment levels.

Because most of the electronic components are located between the outer cover and the secondary containment level, most of the heat generation will occur in this volume. Therefore, most of the heat load generated by MIS-B can be dissipated by circulating middeck air through this volume.

The active-cooling subsystem can be activated independently of the main power to the MIS-B experiments as long as the MIS-B power cable is connected the Shuttle power bus. Activation of the active-cooling subsystem is accomplished by a switch located on the MIS-B control panel (see Section V.B.1 - Control Subsystem).

3. Ultrasonic Spray Nozzle Subsystem

The ultrasonic spray nozzle subsystem used in MIS-B are the same as used in MIS-A except that two subsystems are used in MIS-B.

Each of the four experiments has a dedicated ultrasonic spray nozzle. The ultrasonic spray nozzle takes the stream of polymer/drug suspension supplied by the pumping system and sprays small diameter droplets into the hardening chamber. The spray nozzle operation is similar to an acoustical speaker. That is, an ultrasonic frequency signal is generated by the ultrasonic power supply. This signal drives the piezoelectric crystal inside the body of the spray nozzle. This, in turn, vibrates a titanium nozzle through which the polymer/drug suspension flows. The nozzle is designed to have a resonance point for the ultrasonic frequency signal at its end. As a result, fluid flowing over the end of the nozzle is vibrated. If this vibration is strong enough, the fluid is sheared into droplets and propelled off the nozzle end. However, the linear velocity at which the droplets are propelled is much slower than for conventional two-fluid or rotary-head spray nozzles. The low velocity spray makes the ultrasonic spray nozzle ideal for microgravity applications.

The ultrasonic spray nozzle subsystem is custom-designed so that two ultrasonic spray nozzles are powered from one ultrasonic spray nozzle power supply. Therefore, two ultrasonic spray nozzle power supplies are used in MIS-B. Both ultrasonic spray nozzle power supplies are located on the electronic tray. A relay is used to switch the operation of the power supply from one ultrasonic spray nozzle to the other. Each power supply has its own relay. The operation of these relays is controlled by the control subsystem. Coaxial cables connect the power supplies to the ultrasonic spray nozzles. Coaxial passthroughs are used to maintain containment of the secondary containment level.

Ultrasonic spray nozzles were chosen for the MIS-B experiment because they can produce a fine spray of 40- to 50- μm microdroplets. Additionally, the spray produced by these nozzles has low initial velocity. Because of this low initial velocity, the microdroplets produced by these ultrasonic spray nozzles have stopping distances at normal air pressure within the size constraints of the hardening chambers.

The ultrasonic spray nozzles were purchased from Sono-tek Corporation (Poughkeepsie, NY). Sono-tek agreed to modify their commercial spray nozzle system so that their nozzles could be more easily adapted to the MIS-B hardware. These modifications reduced the power requirements, the volume, and the weight of the ultrasonic spray nozzle system. These modifications included changing of the power source requirements from 120 Vac to 28 Vdc so that the spray nozzles could be powered directly from the Shuttle power supply. And, a second spray nozzle control module was added to the power supply so that one power source could power both spray nozzles.

By examining the spray pattern produced by the ultrasonic spray nozzle, we were able to determine the average axial and radial velocity of microdroplets of the polymer/drug/solvent mixture off the ultrasonic nozzle tip. For a 50- μm microdroplet, we calculated that the average radial velocity off the ultrasonic spray nozzle tip was about 0.07 cm/sec. At this average radial velocity, the

microdroplet will stop moving due to air resistance in less than 1 cm. For 50- μ m microdroplets, the diffusional velocity is extremely small.

The calculated average axial velocity for a 50- μ m microdroplet is about 0.20 cm/sec. At this average axial velocity, the microdroplets will stop moving due to air resistance in about 3 cm. In practice, the ultrasonic spray nozzle imparts a wide range of axial velocities to the microdroplets. And, convective air currents generated by the microdroplet spray will increase the average stopping distance of the microdroplets. However, in the spraying experiments, we did not measure a spraying distance greater than 16 cm. Therefore, the length of the hardening chamber is sufficient to accommodate the average stopping distance of most, if not all, of the microdroplets sprayed through the ultrasonic spray nozzle.

4. Pumping Subsystem

The pumping subsystem is used to deliver the polymer/drug suspension to the ultrasonic spray nozzles. Each experiment has a complete pumping subsystem for a total of four pumping subsystems in MIS-B. The subsystem consists of a custom-built syringe pump with a built-in agitator. Because we have custom-designed the pump manifold, no plumbing fittings (tees, elbows, etc.) are needed. All of the plumbing is internal to the pump manifold. Therefore, the probability of leaks occurring in the pumping subsystem is greatly reduced. The rest of the subsystem consists of a solenoid valve controlled by the control subsystem, inlet and outlet ports, and a safety bypass. All of these other components are fitted onto the pump manifold.

The plunger in the syringe pump is advanced by a stepper motor. The stepper motor is controlled by microstep motor driver of the control subsystem. Polymer/drug suspension is charged into the syringe pump during the preflight ground operations. The pumping system delivers polymer/drug suspension to the ultrasonic spray nozzle located at one end of the hardening chamber. In case the solenoid valve does not open or the ultrasonic spray nozzle becomes clogged, a relief valve located in the safety bypass opens and allows polymer/drug suspension to bypass the solenoid valve and the ultrasonic spray nozzle. The outlet for the safety bypass is in the hardening chamber. This bypass prevents a breach of primary containment in the case of a solenoid valve failure or a plumbing clog.

5. Hardening Chamber Subsystem

Each experiment has a dedicated hardening chamber subsystem. The hardening chamber is constructed from 6061-T6 aluminum. The inside surface of the hardening chamber is coated with a fluorosilicone coating (Dow Corning Type 94-003 Dispersion Coating). This coating prevents the polymer/drug droplets from sticking to the inside surface of the hardening chamber.

The hardening chamber is constructed as a cylinder which is closed at one end. The open end is attached to a mounting flange. Also attached to this mounting flange is a container for the solvent absorbent. A silica gel absorbent is used to absorb the solvent for the polymer/drug suspension.

A piezoelectric fan is located in bottom part of the hardening chamber at the end opposite the ultrasonic spray nozzle. The fan provides circulation of the polymer/drug suspension spray. This prevents the accumulation of polymer/drug droplets in front of the ultrasonic spray nozzle and moves the droplets throughout the working volume of the hardening chamber. A major problem in MIS-A was that the polymer/drug droplets did not travel down the length of the hardening chamber. The circulation fan should prevent this problem from occurring in MIS-B.

Associated with the piezoelectric fan is a circulation conduit that is located along the side of the bottom part of the hardening chamber. At one end of the circulation conduit is the piezoelectric fan. The other end terminates near the ultrasonic spray nozzle. Sealed pass-throughs on the hardening chamber mounting flange provide electrical connections to the piezoelectric fan. To prevent ground looping, the piezoelectric fan and its driver board are isolated from the MIS-B chassis. We found that current leaked through the mounting hardware that we were going use. We modified the mounting hardware for the piezoelectric fan and driver board to electrically isolate these components by using Nylon instead of aluminum or steel as the material of construction. The electrical connections for the piezoelectric fan are then ganged with the other electrical connections for the motors and valves inside the secondary containment through another sealed pass-through on the bottom part of the secondary containment.

6. Electrical Subsystem

The electrical subsystem contains the wiring harness, the power supplies, and other electronic components. These electronic components are needed to condition the electrical power from the Shuttle power bus and to shield the Shuttle from electromagnetic interference generated by MIS-B.

The electrical leads for the wiring harness are all 22-gauge with Teflon® insulation rated to 200 °C. Two dc-to-dc power supplies are necessary to convert the 28 Vdc power from the Shuttle power bus to 12 Vdc and 5 Vdc. These voltages are needed to power the some of the components of MIS-B.

Because of the ultrasonic power supplies and the dc-to-dc power supplies, MIS-B will probably generate unacceptable levels of conducted electromagnetic interference. Conducted electromagnetic interference is that interference which is conducted through the power leads of MIS-B into the Shuttle power bus. To reduce the conducted electromagnetic interference to acceptable levels, three strategies are used. First, capacitors are connected across the three power leads for MIS-B. Across the ground-to-power and the ground-to-return leads, 0.1 μ F capacitors are used. Across the power-to-return leads, a 1.0 μ F capacitor is used. Second, the power and return leads are counterwound around to toroidal iron core. This causes some of the interference to destructively combine and to cancel each other. Third, the power and return leads are connected to an radio frequency interference filter.

To enable MIS-B to be disassembled easily, we incorporated in-line connector in all wiring harness trunks that connect different subsections of MIS-B. For example, in-line connectors are present in the two wiring harness trunks from the control panel to the electronics board. They are present in the wiring harness trunks which connect the electronics board to the individual experiments. Finally, they are present inside the secondary containment to enable easy removal of the secondary containment box.

C. Containment Levels for MIS-B

1. Overview

Due to the potential toxicity and flammability of the solvent (ethyl acetate) used in the experiments, the MIS-B payload hardware has been designed with double chemical containment. With the amount of ethyl acetate used in the MIS-B experiment (about 20 mL/experiment, 4 experiments), a Level 1 toxicity has been indicated by Dr. Martin S. Coleman/SD4 as the most probable assignment.

The containment levels have been designated primary and secondary. Four primary containment levels are present in MIS-B. Each primary containment level consists of a hardening chamber, an ultrasonic spray nozzle, and a pumping subsystem. The four hardening chambers, the four ultrasonic spray nozzles, and the four pumping subsystems which comprise the primary containment levels are not connected.

Four secondary containment levels are present in MIS-B. Each secondary containment level consists of a top housing which surrounds a hardening chamber and a bottom housing which encloses the pumping subsystem and the ultrasonic spray nozzle. The four secondary containment levels are not connected.

Electrical service to the components of the hardening chamber and pumping subsystems is accomplished by using appropriate bulk-head passthroughs.

2. Primary Containment Level

The primary containment level is essentially the volume in which the actual experiments are performed. Because of the presence of ethyl acetate in the experiments, it is necessary to seal this level. The three components of each primary containment level are the hardening chamber, the ultrasonic spray nozzle, and pumping subsystem.

Hardening Chamber

The hardening chamber is a cylinder with a welded endpiece on one end and the other end open. The open end has a face plate so that the hardening chamber can be attached to the mounting flange. A hemispherical endpiece is welded to the other end of the cylinder. The hardening chamber cylinder body, endpiece, and face plate are constructed from 6061-T6 aluminum.

The hardening chamber cylinder body has dimensions of 10.913 in. length and 6.480 in. inside diameter. It is constructed from 0.125-in. thick aluminum. The hemispherical endpiece has a radius of 10.310 in. and is also 0.125-in. thick. This makes the total length of the hardening chamber 11.715 in. A locator hole is situated in the center of the endpiece to provide a positive fit into the hardening chamber support bracket located in the secondary containment top cylinder. The endpiece also has three feet to provide additional support for the hardening chamber to the secondary containment top cylinder.

The hardening chamber face plate is welded to the open end of the hardening chamber cylinder body. It is designed so that the mounting holes are to the inside of the cylinder body. Twelve helicoil inserts are located in the face plate for bolting the face plate and, subsequently, the hardening chamber to the mounting flange. An O-ring groove is cut in the face plate to accept an ethylene-propylene-diene monomer (EPDM) O-ring. The EPDM O-ring provides chemical seal integrity between the hardening chamber face plate and the mounting flange.

Silica gel is used to absorb the polymer solvent during the experiment. The silica gel is in the form of 3-mm beads. It is obtained from Aldrich Chemical Company, Inc. (Catalog No. 25,562-9). During the experiments, the silica gel beads are contained within a housing attached to the bottom side of the mounting flange. Therefore, the silica gel bead housing will protrude into the hardening chamber cylinder body. The silica gel bead housing has a volume of about 15 cubic inches. This volume is sufficient to hold almost 200 g of silica gel beads.

The silica gel bead housing is in the form of an annulus situated around the ultrasonic spray nozzle. In fact, the housing provides additional support to the ultrasonic spray nozzle. Because of the support given to the ultrasonic spray nozzle, the housing has two O-ring grooves that accept EPDM O-rings. The O-rings maintain primary containment. One EPDM O-ring provides a seal for the ultrasonic spray nozzle. The other EPDM O-ring provides a seal between the inside edge housing and the mounting flange. The outside edge of the housing does not need an O-ring to maintain primary containment. The hardening chamber face plate O-ring serves this purpose.

Pumping Subsystem

The pumping subsystem is other integral part of the primary containment level. It consists of a syringe pump, a pump housing, a solenoid valve, an ultrasonic spray nozzle, and a safety bypass. All five components of the pumping subsystem are contained in or attached to the pump housing. The pump housing is constructed from 6061-T6 aluminum. It is rectangular block with dimensions of 2.800 in. in length, 2.065 in. in width, and 2.250 in. in height.

The pump housing is a manifold to which the stepper motor for the syringe pump is attached. The body of the syringe pump is incorporated into the pump housing. Inlet and outlet ports for charging the syringe pump with polymer/drug suspension are tapped into the pump housing and connect to the syringe pump body. The syringe pump outlet is tapped through the pump housing and leads to the solenoid valve. At the outlet of the solenoid valve, another hole is tapped which leads to the ultrasonic spray nozzle. The ultrasonic spray nozzle inlet tube is press-fit into this hole. The syringe pump outlet also branches to the safety relief valve.

The safety relief valve is preset to open once TDB psig of pressure is generated by the syringe pump. Once the safety relief valve opens, the polymer/drug suspension bypasses the ultrasonic spray nozzle and the solenoid valve and feeds directly to the hardening chamber. Therefore, no breach of primary containment can occur if the solenoid valve fails to open or a clog occurs in the plumbing lines to the ultrasonic spray nozzle.

3. Secondary Containment Level

There are two components of the secondary containment level: a cylindrical housing which surrounds the hardening chamber and a housing which encloses the pumping subsystem and ultrasonic spray nozzle. Both secondary containment level housings attach to the mounting flange.

Each primary containment level has a dedicated secondary containment level. Therefore, there are four secondary containment levels. The primary and secondary containment levels for two experiments are mated together on one mounting flange for structural integrity. The mounting flange is then attached to suitable structural supports inside the outer cover.

The cylindrical housing which surrounds the hardening chamber is constructed from 6061-T6 aluminum. The cylinder body is 11.038 in. in length and has a 7.300 in. inside diameter. Similar to the hardening chamber, the secondary containment has a face plate and an endpiece welded to opposite ends of the cylinder body. Both the face plate and endpiece are constructed from 6061-T6 aluminum. The face plate has twelve helicoil inserts for bolting it to the mounting flange. However, the face plate is designed so that its mounting holes are on the outside of the cylinder body as opposed to the hardening chamber face plate. An O-ring groove is cut into the face plate which can accept an EPDM O-ring. This provides chemical containment for the secondary containment level.

The endpiece is shaped from 0.78-in aluminum circular plate. Its thickness is no less than 0.10 in. The outer axial edge of the plate is rounded to a 1.312-in radius. Situated in the middle of the endpiece is a locator tab. The locator tab fits into the locator hole situated on the outside surface of the hardening chamber endpiece. An inlet port for backfilling the secondary containment level is also located on the endpiece.

For the bottom part of the secondary containment level, a rectangular housing is used. The housing is 6.50 in. in length and 7.50 in. in width. The housing is constructed from 6061-T6 aluminum and was manufactured by Zero Enclosures (North Salt Lake, Utah). The housing is welded to flange so that it can be attached to the mounting flange. The housing flange has 22 mounting holes for attaching the housing to the mounting flange. An O-ring groove is cut into the housing flange. Chemical containment is achieved when an EPDM O-ring is placed in the groove and the housing is bolted to the mounting flange.

4. Mounting Flange

The mounting flange is an integral part of both the primary and secondary containment levels. The mounting flange is the point of attachment for the hardening chamber cylinder body, the silica gel bead housing, and the secondary containment level cylinder on one side and the pumping subsystem and the secondary containment level top housing on the other.

The mounting flange is constructed from 6061-T6 aluminum plate that is 0.50 in. thick. It is 8.13 in. in width and 16.50 in. in length. These dimensions of the mounting flange provide sufficient area for attaching the complete primary and secondary containment levels for two experiments. The mounting flange is designed in this manner to provide additional structural support for the primary and secondary containment levels. It also reduces the volume requirements for structural supports in the MIS-B hardware compared to separate mounting flanges for each experiment. Finally,

preflight ground operations will be easier by having two experiments mated through the mounting flange than if all four experiments were mated together.

5. Outer Cover/Mounting Panel

The outer cover/mounting panel provides debris containment for the rest of the components of the MIS-B payload. It is not sealed. The mounting panel completes the enclosure and provides a structural support for the electronics tray and the secondary containment level. The mounting panel is bolted to a NASA-supplied double adapter plate at the four corner bolt locations.

Located on the front panel of the outer cover are the inlet and outlet ports for the active-cooling subsystem and the control panel. Also located on the front panel is the control panel for MIS-B. The receptacle for the 28 Vdc power cable is located on the control panel along with the switches and indicator lamps for the MIS-B experiments.

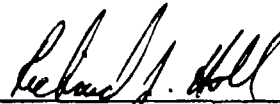
The outer cover for the MIS-A backup model was used to construct the outer cover for MIS-B. The MIS-A outer cover was modified to accommodate the active-cooling subsystem and the new control panel. The length of the MIS-A outer cover was also reduced by 0.875 in. to be in compliance with NASA's payload envelope restrictions for middeck payloads. MIS-A needed a variance to the middeck payload envelope restrictions to become flight-certified. MIS-B will not need this variance.

The payload envelope dimensions for MIS-B are 19.43 in. x-axis, 18.00 in. y-axis, and 21.75 in. z-axis (coordinate system per NSTS 21000-IDD-MDK). These payload envelope dimensions do not include the NASA-supplied double adapter plate and payload mounting panels. Both the outer cover and MIS-B mounting panel are constructed from 6061-T6 aluminum. The MIS-B mounting panel is 0.50 in. thick. To reduce the weight of the MIS-B mounting panel, half the thickness of the panel has been removed in areas deemed insignificant for structural integrity. Four areas were identified and the panel thinned in these locations.

VI. CONCLUSIONS

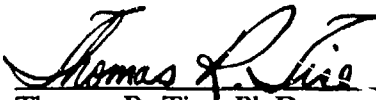
We completed the construction of the MIS-B flight-ready model.

Submitted by:



Richard J. Holl, Ph.D.
Research Engineer

Approved by:



Thomas R. Tice, Ph.D.
Head, Controlled Release Division

SRI-Org-94-768-7654

October 3, 1994

Project 7654-X

NB: H597

(1:4::10:2) kbm

VII. REFERENCES

1. Microcapsules in Space. Payload Integration Plan. NSTS 21216. NASA, Johnson Space Center, Houston, TX. February, 1992.
2. Flight Operation Support Annex. Microcapsules in Space. NSTS 21216, Annex 3. NASA, Johnson Space Center, Houston, TX. January, 1992.



DEPARTMENT OF THE ARMY

US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
FORT DETRICK, MARYLAND 21702-5012

REPLY TO
ATTENTION OF:

MCMR-RMI-S (70-1y)

21 Apr 97

MEMORANDUM FOR Administrator, Defense Technical Information
Center, ATTN: DTIC-OCP, Fort Belvoir,
VA 22060-6218

SUBJECT: Request Change in Distribution Statement

1. The U.S. Army Medical Research and Materiel Command has reexamined the need for the limitation assigned to technical reports written for Contract Number DAMD17-92-C-2011. Request the limited distribution statement for Accession Document Number ADB192333 be changed to "Approved for public release; distribution unlimited." This report should be released to the National Technical Information Service.

2. Point of contact for this request is Ms. Judy Pawlus at DSN 343-7322.

FOR THE COMMANDER:

Gary R. Gilbert
for GARY R. GILBERT
Colonel, MS
Deputy Chief of Staff for
Information Management

Completed
1-10-00
B.W.