



# Intravenous Fluid Mixing in Normal Gravity, Partial Gravity, and Microgravity: Down-Selection of Mixing Methods

*Charles E. Niederhaus  
Glenn Research Center, Cleveland, Ohio*

*Fletcher J. Miller  
National Center for Space Exploration Research, Cleveland, Ohio*

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National Aeronautics and  
Space Administration

Glenn Research Center  
Cleveland, Ohio 44135

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# **Intravenous Fluid Mixing in Normal Gravity, Partial Gravity, and Microgravity: Down-Selection of Mixing Methods**

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National Aeronautics and Space Administration  
Glenn Research Center  
Cleveland, Ohio 44135

Fletcher J. Miller  
National Center for Space Exploration Research  
Glenn Research Center  
Cleveland, Ohio 44135

## **Introduction**

The self-sufficient, long-duration missions envisioned under the Vision for Space Exploration will require development of new methods to handle crew medical care. Medications and intravenous (IV) fluids have been identified as one area needing development in order to determine the proper supplies required, ensure efficacy throughout the mission, and minimize the mass and volume of supplies required. It has been proposed that storing certain medications and solutions as powders or concentrates can both increase the shelf life and reduce the overall mass and volume of the medical supplies. These powders or concentrates would then be mixed in an IV bag with Sterile Water for Injection produced in situ from the potable water supply.

Mixing of fluids is less efficient in microgravity for several reasons:

- The loss of buoyancy effects due to density gradients arising from concentration gradients. Buoyancy increases mixing during injection procedures as well as mixing operations such as impeller mixing and container oscillations typical in ground mixing.
- The motion of granules is different in the system. Dissolution is affected by the local flow past the granule, and dissolution is a significant portion of the overall mixing time. This flow will depend on whether the granule is suspended in the fluid, which depends on the gravity level and flow velocities.
- The minimization or elimination of a free surface between liquid and gas in the container due to gas-liquid separation concerns, which reduces internal fluid motion with many mixing processes.

Molecular diffusion cannot be relied upon to eliminate residual concentration gradients for items that may need immediate use. In a simple Skylab experiment, ordinary tea in a water-filled tube diffused only 1.96 cm in 51.5 hr (ref. 1). Computations done by us have shown that 1 mm granules of high-diffusivity sodium chloride evenly distributed to produce a 0.9% solution would take nearly 40 min to dissolve and diffuse to provide 95% uniformity. Therefore, an efficient, quantifiable mixing method must be developed to allow for safe and timely generation of IV fluid from potable water.

The goal of this project is to develop a method of mixing powders and concentrates with sterile water for potential International Space Station (ISS) and exploration mission use. This document describes the analyses and down-select activities used to identify the IV mixing to be developed that is suitable for ISS and exploration missions. The down-selected method has the potential to work at any gravity level, although the operating parameters may change depending on gravity level. This assessment utilizes reference supported engineering analysis based on seven functional criteria to rank the applicability of eight proposed mixing methods, with a down-select activity identifying the two highest ranked methods that were further studied. The two highest ranked mixing methods were further studied utilizing

theoretical analyses, laboratory experiments, and drop tower experiments to select the preferred method. The chosen method will undergo further development, including reduced-gravity aircraft experiments and computations, in order to fully develop the mixing method and associated operational parameters.

## **Mixing Constraints and Ranking Criteria**

The chosen microgravity mixing method must have several attributes in order to be effective. For one, it must produce timely mixing of the solution. Some of these medications may be required immediately for emergencies, and slow mixing processes could jeopardize the patient. Some simple theoretical and ground studies performed recently at NASA Glenn have shown that it takes vigorous mixing to completely mix typical sodium chloride and glucose solutions within 5 min. For instance, a 1-in. magnetic stirrer bar rotating at 1000 rpm took 30 min to fully mix a 0.9% sodium chloride solution in a 1-L IV bag from crystals. Most other solutions with larger molecules will take longer to mix due to smaller diffusion coefficients. The goal is a method that can mix typical constituents in 15 min or less. The 15-min time limit was self-imposed as an appropriate limit at this early stage of development. The actual hardware parameters can be adjusted at a later stage once a firm time limit criterion is established. At this stage of development, a solution will be considered mixed when the local concentration everywhere is within  $\pm 5\%$  of the final concentration. This compares with the USP (United States Pharmacopeia) 28 standards for premixed solutions of Dextrose Injection and Sodium Chloride Injections that have a tolerance of  $\pm 5\%$  of the stated concentration.

Another constraint is that the method must be sterile to prevent contamination concerns. Any required sterilization procedure requires time and consumables. The number of items that must be sterilized should be minimized. The fittings on the water supply will always require sterilization, but careful design may eliminate other sterilization procedures. A third constraint is that the method should be flexible to handle multiple types of powders and concentrates with different granule sizes and diffusion coefficients. The mixing required for low molecular mass, high-diffusivity NaCl will be quite different than that required for complex, high-molecular mass drugs. A final constraint is the mixing system should have a low equivalent system mass (ESM), a cost-type metric used to evaluate comparable technologies based on mass, volume, power, cooling, and needed manpower. It includes the basic mass of the system and consumables, plus factors associated with power consumed and cooling and volume required. For instance, the factor associated with power takes into consideration the mass of the power generation system required to produce the power plus all associated power distribution systems. This can be accounted for as a kilogram of mass per watt of power required. Heat generated in a closed environment has an associated cost for environmental cooling loops and radiators to dissipate the heat. Volume requirements lead to structural mass and shielding. These factors vary based on the mission and predicted hardware required. ESM is an objective way to compare different technologies while avoiding any analyst prejudice.

Using these aforementioned constraints as a basis, seven evaluation criteria were derived for the initial down-select activity. These criteria are

### **Efficiency**

The ability to mix the powder or concentrate rapidly with minimal power consumption.

### **Sterility**

The ability to maintain the sterility of the system over the mission duration. This includes crew time as well as mass of consumables.

### **Flexibility**

The ability to vary the process to allow mixing various powders and concentrates to the degree required.

### **Equivalent System Mass**

The overall mass required for the system, including consumables.

### **μg Confidence**

The confidence that the mixing method can be successfully adapted to microgravity use.

### **Operations**

Ease of use and amount of crew time needed to complete the operation.

### **Development Ease**

Overall effort needed to successfully adapt method to microgravity for all of the various powders and concentrates needed.

For the analysis exercise of proposed IV fluid mixing methodologies, each criterion was given a score of high (H), medium (M), or low (L) depending on understood engineering principles or the results of small experiments.

## **Mixing Methods Evaluated**

Eight mixing concepts were conceived and considered as possible mixing methods that could function in normal gravity, partial gravity, and microgravity. The mixing times may vary as a function of gravity, but the hardware will function in any gravity level assuming the proper gravity vector orientation. The mixing time for these initial concepts may not necessarily meet the self-imposed constraint of 15-min mixing time.

### **Built-In Recirculation Loop Mixing In-Bag**

A custom IV bag would have a flat semicircular loop built into one end of the bag connected to the main volume. The loop would be placed into a peristaltic-like pump device that would circulate the fluid inside the bag and mix the contents (fig. 1).

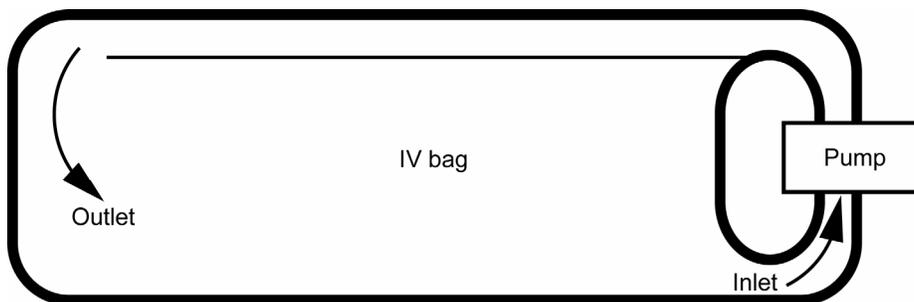


Figure 1.—Built-in recirculation loop mixing.

### Inline Mixer During Filling

The incoming water would be mixed with the concentrate or powder prior to entering the IV bag. For concentrates, a second pump would inject the liquid at the appropriate rate to transfer both the concentrate and water into the IV bag in the same amount of time. An inline mixer similar to those used in 1-g industrial processes that swirls the flow in alternating directions would be incorporated into the bag inlet. A similar method could be used for powders, in that the fluid flows through a chamber containing the powder prior to entering the IV bag. A swirling inlet mixer would further mix the fluid (fig. 2).



Figure 2.—Inline mixing.

### Magnetic Stirrer Bar Mixing in Bag

A magnetic stirrer bar would be placed into the bag, and an external rotating magnet or rotating magnetic field would rotate the bar in bag to produce mixing. This method is similar to mixing in a standard laboratory setting (fig. 3).

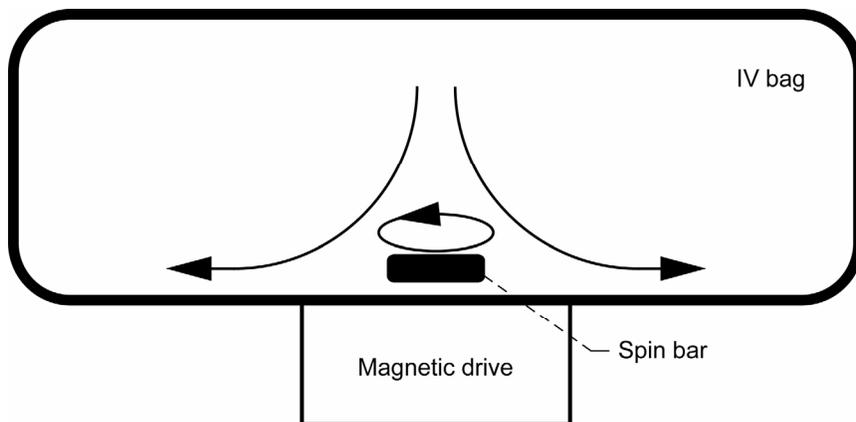


Figure 3.—Magnetic stirrer bar mixing.

### **Stirring Shaft With Impeller Mixing in Bag**

A rotating shaft with impellers would mix the fluid in a manner similar to 1-g applications (fig. 4).

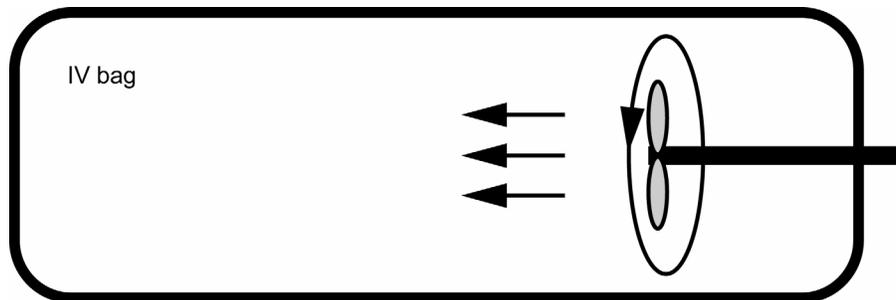


Figure 4.—Stirring shaft mixing.

### **Ultrasonic Vibrating Rod Mixing in Bag**

An ultrasonic vibrating rod would induce cavitation and internal fluid motion to mix the fluid in a manner similar to 1-g applications (fig. 5).

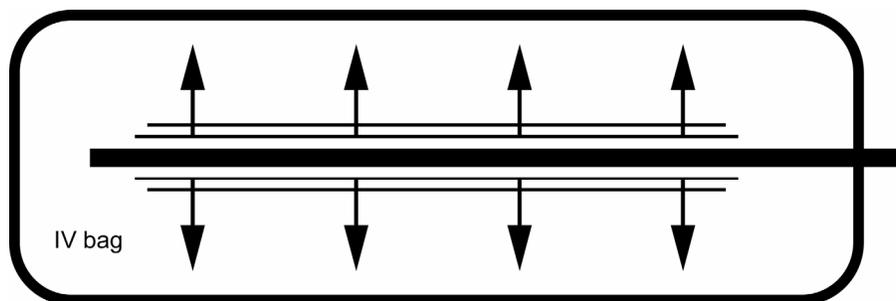


Figure 5.—Ultrasonic vibrating rod mixing.

### **Container Shape-Change Induced Mixing in Bag**

The external surface of the bag would be manipulated in a prescribed motion to produce an internal flow to mix the fluid (fig. 6).

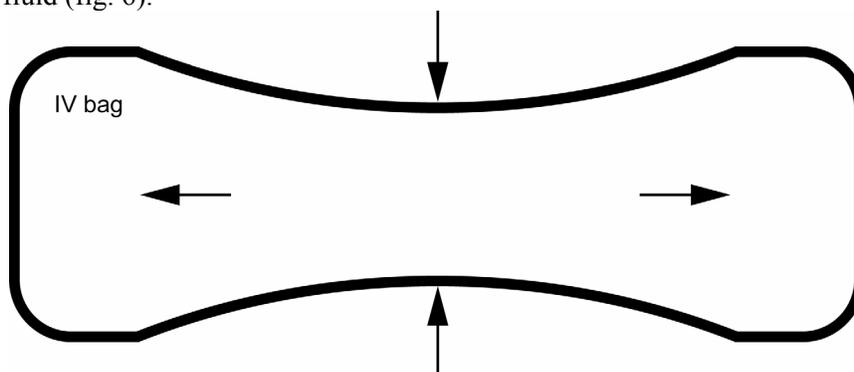


Figure 6.—Container shape-change mixing.

### **Vibrating Wall Induced Mixing in Bag**

One side of the bag would be in contact with a surface that would vibrate at moderate frequency. The surface motion of the bag would induce internal flows to provide the mixing (fig. 7).

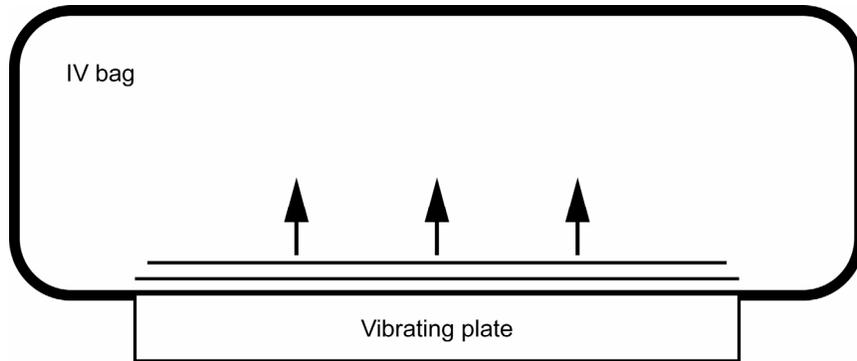


Figure 7.—Vibrating wall mixing.

### **Acoustic Streaming Induced Mixing in Bag**

An ultrasonic transducer in contact with the bag would induce a jet in the fluid from the viscous dissipation of the sound waves. The jet would produce an internal fluid circulation that would provide the mixing (fig. 8).

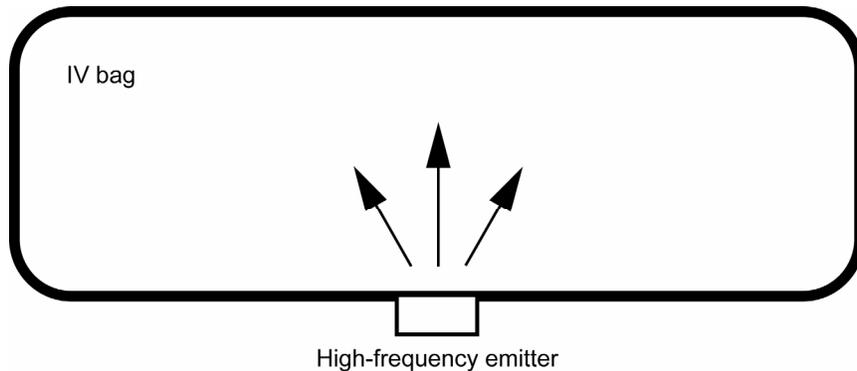


Figure 8.—Acoustic streaming mixing.

### **Evaluations and Down-Selection Process**

Each of the conceived methods was the subject of a research-supported engineering analysis, in that the selection criteria scoring was assigned based on sound engineering judgment supported by literature and technology surveys or small experiments used to verify engineering assessments. The following summarizes the findings regarding each proposed method with the criteria scoring listed in table 1:

TABLE 1.—EVALUATION OF MIXING METHODS ACCORDING TO SELECTION CRITERIA

	Efficiency	Sterility	Flexibility	Equivalent system mass	µg confidence	Operations	Development ease	Unweighted score	Relative ranking
Recirculation loop	H	M	H	H	M	M	M	17	4
Inline mixer	M	H	L	M	L	M	L	12	8
Magnetic stirrer bar	H	H	H	M	H	H	M	19	1
Shaft with impeller	H	M	H	M	H	M	M	17	4
Vibrating rod	M	M	H	M	L	M	L	13	7
Shape change	L	H	H	M	M	M	M	15	6
Vibrating surface	M	H	H	H	H	H	M	19	1
Acoustic streaming	M	H	H	H	H	H	L	18	3

### **Built-In Recirculation Loop Mixing in Bag**

This method is a refinement of the method originally proposed for the Automated Culture Water Assembly (ACWA) program (NASA Johnson Space Center EB/Biomedical System Division). The ACWA concept was to add water to a concentrated solution in a partially filled bag, and then transfer the contents to and from a second bag until fully mixed. The disadvantage was that a second bag would be used, and all of the internal plumbing would be contaminated. The refinement is to build a loop into the end of one bag that could be used with an external peristaltic pump. The fluid will recirculate inside the bag until fully mixed. Relatively large internal fluid velocities could be generated to provide the mixing. Flow velocities and mixing time could be adjusted depending on the chemical being mixed. This method has disadvantages when powders are used. Powder, which could become larger granules after long-term storage, could potentially puncture the bag and tubing when passing through the peristaltic pump. Powder clumping can occur due to humidity, compaction, and chemical reactions, to name a few mechanisms. This clumping is difficult to predict for the wide range of powders that may be stocked. The NASA Biotechnology Cell Science Program flew the Rotating Wall Perfused Vessel (RWPV) to grow cell tissue cultures several times on the shuttle and Mir. In 1998 on Mir, a U.S. astronaut noticed a crystalline blockage in a little-used flexible tube. The blockage was broken up with finger pressure, but in the process the tube was punctured (ref. 2). Filters could be used to prevent the powder from entering the pump section, but the powder would accumulate on the filter and reduce the flow rate. Determining the desired filter characteristics could be problematic given the number of powders that may be flown. If the powders were nonwetting, air in the system will attach to the particles on the filter and further reduce the flow rate.

#### ***Analysis***

While this method promises moderate mixing efficiency, the problems raised by excluded powders from the pump device would be difficult to solve. It would be especially problematic determining how the powders would affect the pump filter performance efficiency in microgravity.

### **Inline Mixer During Filling**

This concept would mix the concentrate or powder while the IV bag is being filled. This method has many advantages when using concentrated liquid, but would not be as effective for powders. With

liquid/liquid mixing, the two liquids would be pumped at the appropriate rate to transfer both liquids into the IV bag in the same amount of time. An inline mixer similar to those used in 1-g industrial processes (ref. 3) would be incorporated into the bag inlet to ensure the mixing was completed before the fluids entered the bag. The mixing could be accomplished relatively quickly. Disadvantages are that the degree of mixing is limited with this method, and the degree of mixing is fixed by the design of the inline mixer. Different mixers would have to be used to change the product uniformity. Also, slugs of gas from the water supply would create pockets of nonuniformity. In addition, a separate apparatus would have to be employed to mix powders. A similar method could be used for powders, in that the fluid flows through the powder prior to entering the IV bag. However, the flow rate would have to be adjusted depending on the properties of the individual powder as well as be adjusted as a function of time to compensate for the change in granule size. The flow rate would be low for powders, and the solution would have relatively low uniformity. Clumping of the powder in long-term storage would be difficult to compensate for.

### ***Analysis***

This method has limited flexibility, and is more suitable for liquid/liquid mixing than the more likely powder mixing. The great number of variables for powder mixing would take significant development to ensure adequate mixing.

## **Magnetic Stirrer Bar Mixing in Bag**

This method is similar to mixing often done in laboratory settings (refs. 4 and 5). A magnetic stirrer bar would be placed into the bag, and an external rotating magnet or rotating magnetic field would move the bar to produce mixing. This method could produce large internal velocities to quickly mix liquids and even difficult powders. The stirrer bar could be sealed inside the bag to ease contamination issues. One disadvantage is the effect of trapped gas in the system. The gas would collect somewhere along the rotation axis of the stirrer bar where the centrifugal forces are minimum. The gas would change the internal fluid velocities developed in microgravity when compared to normal gravity. Short-duration microgravity testing and computational fluid dynamics (CFD) analysis would have to be done to determine the exact reduction in mixing efficiency. One effective solution is a long stirrer bar that extends outside of the bubble region. Another potential disadvantage is that centrifugal force may distribute the granules along the outer edge of the bag. The fluid motion should recirculate the granules towards the center, but seams or dead zones such as corners or outlets could trap the granules. These outer regions are where the fluid velocity is lowest, and the time to dissolve and mix any granules trapped there would increase. A third disadvantage is that the stirrer bar can sometimes break free of the magnetic field if the speed is too high and could potentially drift around inside the bag until it could be recaptured.

### ***Analysis***

This method has good flexibility and is conceptually simple to implement. Some operational issues exist in the proper alignment of the magnetic spinner. Electromagnetic interference (EMI) is also a flight concern with this system.

## **Stirring Shaft With Impeller Mixing in Bag**

Similar to the stir bar above, this method is one of the most efficient in ground-based mixing (ref. 6). A shaft with impeller blades would rotate to produce large internal motion and mix the solution. The speed and mixing time could be changed to accommodate different solutions. Gas in the system would collect on the shaft in microgravity, and the effects would have to be determined. A reusable stirring impeller could be used, but that would require a relatively large bag opening as well as the ability to sterilize and store the impeller. A smaller stirring shaft with impeller could be built into each bag to

eliminate the need for sterilization, but this would increase the storage volume and mass. Storing a bag with relatively moderately sharp edges could be a concern. Folding impellers that open by centrifugal force could be designed to reduce the storage concerns, but increases weight and raises issues of reliability. This method could also have the problem of centrifugal force trapping granules along the outer edge similar to the magnetic stirrer bar method. Finally, unlike the stir bar, this method requires a bag penetration with rotating seal for the shaft.

### ***Analysis***

A reusable stirring shaft would pose serious sterility issues, as well as operator time issues. It would be extremely difficult to remove the stirrer in microgravity without contamination and spillage concerns. A single-use stirrer contained in the bag would have greater mass than a magnetic stirrer bar and both would have puncture concerns.

### **Ultrasonic Vibrating Rod Mixing in Bag**

A common laboratory mixer uses a rod that is vibrated ultrasonically to induce fluid flow, cavitation, and mixing (ref. 7). Typical laboratory rods are 0.5 in. in diameter, and may taper or step down to a smaller diameter. An ultrasonic transducer drives the rod at its resonant frequency to produce a large motion. The rod could either be reusable or single-use contained in each bag. A large portion of the mixing is produced because of the formation and collapse of small gas bubbles in the fluid. It is unclear whether all of the bubbles formed collapse, or if they rise due to buoyancy and increase the mixing in normal gravity. The formation of bubbles is of concern in microgravity, as they may take a long time to collapse or adsorb. Sterilizing reusable rods is a concern, while the additional mass and storage volume for single-use rods would also be a disadvantage. This method also requires a seal where the rod penetrates the bag.

### ***Analysis***

A reusable vibrating rod would pose serious sterility issues, as well as operator time issues. A single-use stirrer contained in the bag would have greater mass than a magnetic stirrer bar. Bubble formation is also a concern.

### **Container Shape-Change Induced Mixing in Bag**

This concept envisions manipulating the bag exterior in such a fashion to produce internal fluid motion to provide mixing. It is similar in concept to part of the experiments in the Cellular Biotechnology Operations Support System: Fluid Dynamics Investigation (CBOSS-FDI) led by Dr. Joshua Zimmerberg and the NASA Biotechnology Cell Science Program (CBOSS-FDI SCR Package). The experiments for CBOSS-FDI were designed to establish a procedure to ensure mixing of injected cells into a culture medium. A large portion of the mixing was obtained by repeated injection and withdrawals, with further mixing provided by a circular hand movement on the surface of the bag. The repeated injection and withdrawal procedure would not be duplicated as it contaminates a second container. The bag manipulation could be done mechanically to minimize astronaut involvement and increase repeatability. This method would produce relatively low shear in the fluid, with a resulting low to very low mixing rate. It is also relatively complex mechanically, with reliability issues.

### *Analysis*

This method is mechanically complex with a low mixing efficiency when compared to other methods.

### **Vibrating Wall Induced Mixing in Bag**

Vibrating surfaces at relatively low frequencies (~1 kHz) can produce steady streams of fluids perpendicular to the surface due to viscous forces at the boundaries (refs. 8 and 9). A flexible surface that oscillates both spatially and temporally in a sinusoidal motion produces flow away from the motion antinodes and towards the nodes. In a closed container, this will result in a series of vortices producing internal motion to mix the solution. This method would produce moderate velocities for mixing the solution. The method would be unobtrusive and thus not have sterility issues.

### *Analysis*

This method provides only a low-to-moderate mixing efficiency, which can be translated in to longer mixing time than other methods. Other disadvantages include adapting the technique to the nonoptimal bag shape and an unknown effect of bubbles in microgravity.

### **Acoustic Streaming Induced Mixing in Bag**

Acoustic streaming is a relatively new technique that is being investigated for industrial applications (refs. 10 and 11). Sound waves propagating through a fluid are attenuated by viscous dissipation, resulting in a pressure gradient that produces fluid motion. The attenuation is greater at higher frequencies, with typical units operating in the 200 kHz to 4 MHz range. Focusing the sound waves also produces greater attenuation and thus higher fluid velocities. Operations in water can commonly produce velocities of ~5 cm/s (ref. 12). This could potentially be an effective, nonintrusive mixing technique. However, coupling the transducer to the IV bag could be problematic. Typically, the transducer is built into the wall of the container. If a simple device were incorporated into the wall of an IV bag, half of the energy would be lost to the outside surface of the transducer. A reusable transducer built into the mixing unit could be used with the bag pressed into the transducer. A coupling gel would be required to increase the coupling efficiency between the transducer and container. The use of a gel would increase the mass requirements and introduce cleanup requirements. Also, it is unclear what coupling efficiency to expect, as development of this technology has focused on transducers built into rigid container walls.

### *Analysis*

This method holds great promise for mixing, but is still in the early development stages. Significant effort would be required to develop it for flight use. Coupling of the transducer to the bag could ultimately remain a problem.

Table 1 summarizes the criteria scoring of each of the mixing methods (high being better). To objectively compare each method, an unweighted score (L = 1, M = 2, and H = 3) was assigned to each criterion. Summing these scores provides the relative ranking of the various methods.

### **Down-Selected Methods**

From the relative rankings determined in this analysis, the two mixing methods chosen for continued investigation were the magnetic stirrer bar and the vibrating wall. A description supporting their selection and describing the next steps in the assessment of these two mixing processes follows.

## **Magnetic stirrer bar mixing in bag**

This method provides large internal velocities to produce efficient mixing, probably second only to the spinning shaft with impeller. In addition, it is relatively lightweight, even if a spinner is included in each bag. A single-use spinner in each bag would greatly reduce any sterilization issues and could be made relatively lightweight to minimize mass. There is also the option of reusing the spinner after the bag is used, which would reduce the mass flown, but increase sterility concerns when placing the spinner in a new bag after sterilization. The method is flexible to allow for quick, gross mixing for those solutions where it is acceptable, and can also provide a very uniform solution if desired. Operationally, the astronaut would only have to attach the bag to the water source, secure the bag, and ensure the spinner is over a highlighted location.

Two microgravity issues will have to be addressed during the development process: bubbles in the system and centrifugal forces on the granules. A third issue, density gradients in the fluid, could be significant at low rotational speeds such that buoyancy forces dominate over centrifugal forces. The location of bubbles in the bag will change in microgravity to a location on the spinner axis but away from the wall. This location will modify the velocity field from normal gravity testing, but should not greatly affect the mixing efficiency. Drop tower experiments, reduced-gravity aircraft flights, and CFD should be sufficient to provide insight into this issue and allow for accurate estimates of mixing time in microgravity.

The motion of the granules to be dissolved will change in microgravity if the granules are large and/or have a large density difference from water. This concerns the early stages of mixing before the granules have dissolved, but could significantly increase the mixing time if not correctly addressed. The relative importance of the centrifugal forces depends on the granule density and size. Most granules will be denser than the water and the centrifugal forces will drive larger granules towards the outside of the bag. In normal gravity the larger granules will fall to the bottom of the bag in locations with low velocity, while fluid forces keep smaller granules circulating. In microgravity, the centrifugal forces will tend to force larger particles towards the outside of the bag if the fluid velocity near the wall is insufficient to keep them circulating. This will only be a problem in dead zones such as corners and outlet fittings, but these areas would be a problem for any mixing method. Proper bag design can minimize these dead zones. Certain commercial IV bags have large pockets at the far corners due to the design of the outlets and the bag hanger. These types of pockets would have no mixing circulation and must be eliminated. Alternating spinner rotation, possibly with multiple spinners, can produce increased shear to enhance mixing and possibly dislodge granules in small dead zones such as bag seams if necessary. Granules of materials lighter than water will also change their motion in microgravity and will require similar analysis, but in general will have fewer problems.

The change in granule location and motion will influence the mixing rate experienced in microgravity. Drop tower experiments, reduced-gravity aircraft flights, and CFD will quantify the microgravity motion of granules. Once the microgravity motion of the particles is understood, the effects on mixing can be determined, and appropriate ground experiments conducted to quantify the effect on mixing time.

The loss of buoyancy effects will not cause any major issues that would prevent microgravity operation. It will provide subtle differences in the concentration field during mixing, and could affect the mixing time. Ground-based microgravity experiments may be difficult to conduct to evaluate this effect. CFD studies will be the main method to quantify the effects on mixing due to reduced buoyancy.

## **Vibrating Wall Induced Mixing in Bag**

This method would provide moderate mixing, would be nonintrusive and would require the least mass of the proposed methods. Bubbles would be driven away from the vibrating surface and have little influence on the mixing. The particles should stay suspended with this method, but there will also be dead zones such as corners that will have to be minimized or eliminated. Special care has to be taken in ground

testing to avoid mixing from gravity-induced motion. Gravity waves can arise on any flexible density interface, such as an air and water interface if bubbles are in the system or the bag and air interface on the upper surface of the bag. These waves can greatly enhance mixing, yet would not arise in microgravity. For instance, simple experiments in an ultrasonic bath provided good mixing as a result of gravity waves on the free surface. Once a film was placed on the surface to damp out the gravity waves, the mixing was greatly reduced. It may prove difficult to generate sufficient internal motion to provide effective mixing. This is especially true for the IV bags, whose geometry makes it difficult to generate mixing due to resonance effects.

Granule location will be different in microgravity, and will influence the initial mixing rate. In normal gravity the granules will be located on the bottom of the bag, away from the vibrating surface. This will result in lower mixing. The granules will be distributed throughout the bag in microgravity and should produce greater mixing. There will be some motion that may cause the granules to collect in low-velocity regions such as corners. Drop tower experiments, reduced-gravity aircraft flights, and CFD will quantify the microgravity motion of granules. Once the microgravity motion of the particles is understood, the effects on mixing can be determined, and appropriate ground experiments conducted to quantify the effect on mixing time.

## **Final Selection**

The two down-selected methods were evaluated over a 1-month period. Experiments were conducted to evaluate mixing performance, and work was done to further refine estimated microgravity performance and operational issues.

Magnetic stirrer bar experiments were set up using a common laboratory stirring plate and stir bars. Both a Schlieren system and a Planar Laser-Induced Fluorescence system were used to qualitatively determine when solutions were fully mixed. Standard size 1- by 3/8-in. stirrer bars spinning at 1000 rpm could mix a 1-L 0.9% saline solution from a liquid NaCl concentrate in under 45 sec. Stirrer bars as small as 30 by 3 mm could still mix a 1-L 0.9% saline solution from NaCl crystals in under 9 min when run at 700 rpm. Initial drop tower experiments were conducted using 1-L bags to determine the effects of bubble migration in microgravity. There were concerns that unwanted bubbles would coalesce and surround the stirrer bar, reducing or eliminating its ability to mix the fluid. Other concerns were with powders and whether the centrifugal forces would force the granules to the perimeter and reduce the dissolution rate. Various bubble sizes, stirring rates, initial bubble orientation, and fluid properties were examined. The first experiments were inconclusive due to the short microgravity period, but no major deficiencies were found. Later aircraft experiments with longer microgravity time were conducted and are under analysis, but preliminary results still find no microgravity operational deficiencies.

Vibrating surface experiments were conducted using an ultrasonic bath apparatus, as well as a laboratory-type shaker table. An IV bag with distilled water and a carefully injected dyed salt concentrate was placed into a filled ultrasonic cleaning bath apparatus. The initial experiments in the ultrasonic bath seemed to indicate efficient mixing of the liquid concentrate. However, these experiments had an internal bubble of ~50 mL, typical of standard commercial IV bags. The internal free surface (gas-liquid interface) would oscillate vigorously under excitation, producing relatively efficient mixing. The waves and resulting mixing are gravity-capillary waves as the result of the Faraday instability. This instability is well known, and is the result of a vertical oscillation of a liquid-free surface in a gravitational field. These types of waves cannot form without a gravity field, and thus this mixing method would not function in microgravity. When experiments were conducted without the bubble, the mixing was indistinguishable from diffusive mixing (extremely slow). No discernable mixing was noticeable after 2 hr in the ultrasonic bath.

Further experiments were conducted with a laboratory vertical shaker table to try to produce better mixing. The IV bag was supported from below in several configurations to oscillation different portions of the lower surface. The frequency of oscillation was varied from 10 up to 200 Hz at the maximum amplitude the shaker was capable of producing. The IV bag was filled with distilled water and a carefully

injected dyed salt concentrate. The bag did not contain a bubble, as this is the desired configuration for safe microgravity operation and to avoid exciting the Faraday Instability that would not exist in microgravity. None of the experiments produced mixing that was noticeably greater than diffusive mixing. Theoretical analysis revealed that the vibrating surface would probably produce mixing times no better than an order of magnitude longer than the stirrer bar.

The magnetic stirrer bar experiments produced significantly greater mixing than any of the vibrating surface configurations. The total mass of the stirring plate and stirrer bars was ~1.2 kg for 100 liters of solution (1 kg stirrer plate plus ~2g/bar) was also less than the vibrating plate apparatus of ~15 kg. Initial drop tower experiments of the magnetic stirrer bar method were not conclusive, but indicated that the worst concerns were not realized. In light of the significantly lighter weight, well-defined operating parameters, and the drastically faster mixing, the magnetic stirrer bar method was chosen as the preferred mixing method for microgravity mixing of IV fluids.

## Conclusions

Eight different methods for mixing IV solution in partial and microgravity were evaluated on their potential effectiveness for Exploration missions. The candidate methods were determined by considering ground-based mixing techniques for large- and laboratory-scale mixing. Unique methods were also considered for this application. The eight methods were evaluated with respect to seven criteria to determine the most promising candidates. Many of the methods have serious issues such as sterility concerns or microgravity limitations that preclude their choice for exploration missions.

Two methods were selected for further work prior to a final selection: magnetic stirrer bar and vibrating surface. The magnetic stirrer bar method provides very efficient mixing with minimal mass requirements. The vibrating surface method provides nonintrusive mixing, but with longer mixing times. Both of the methods have minimal sterilization and clean-up issues. These methods will be worked in parallel until the final down-select. Both of these methods have enough differences in microgravity operation that careful analysis is required to ensure adequate performance.

The two down-selected methods were further developed over a month-long period. The vibrating surface method in the configurations tested proved to be very ineffective in producing mixing of either a liquid concentrate or a powder. The magnetic stirrer bar method has well defined operating procedures, is lightweight, has minimal sterility issues, and proved to be very effective in mixing both liquid concentrates and powders. Initial microgravity experiments on the magnetic stirrer bar were not conclusive, but did not reveal any gross microgravity deficiencies. The decision was made that the magnetic stirring bar method was obviously superior, and chosen as the preferred mixing method. Experiments will continue to refine the method and determine the required operational parameters for microgravity operation.

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<b>14. ABSTRACT</b> The missions envisioned under the Vision for Space Exploration will require development of new methods to handle crew medical care. Medications and intravenous (IV) fluids have been identified as one area needing development. Storing certain medications and solutions as powders or concentrates can both increase the shelf life and reduce the overall mass and volume of medical supplies. The powders or concentrates would then be mixed in an IV bag with Sterile Water for Injection produced in situ from the potable water supply. Fluid handling in microgravity is different than terrestrial settings, and requires special consideration in the design of equipment. This document describes the analyses and down-select activities used to identify the IV mixing method to be developed that is suitable for ISS and exploration missions. The chosen method is compatible with both normal gravity and microgravity, maintains sterility of the solution, and has low mass and power requirements. The method will undergo further development, including reduced gravity aircraft experiments and computations, in order to fully develop the mixing method and associated operational parameters.					
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