ORBIS MICROBUBBLE GENERATOR FREQUENTLY ASKED QUESTIONS

GENERAL USAGE

Is the product reusable?

No. Orbis is a single use / single patient use device.

Is there an expiration date?

Yes. Please check the expiration date on the package.

How is Orbis generated agitate different from manually agitated saline?

The Orbis Microbubble Generator mechanically produces microbubbles as the plunger is pressed, producing highly consistent microbubbles. It also includes a small amount of polysorbate 80 which acts as a surfactant (like mixing saline with blood) to allow for longer duration of the microbubbles.

Eimer et al showed in an animal study of an early version of the device (Eimer et al., *Performance Characteristics of a Novel Echocardiographic Contrast System*; ASE 2022) that the Orbis produced significantly smaller and more consistent microbubble size compared to manually agitated saline. Orbis also demonstrated increased peak echogenicity as measured by grayscale and increased duration of echogenicity compared to manually agitated saline.

What size saline filled syringe should I use with Orbis?

Orbis is designed to work only with a 10ml filled syringe.

What size needle should I use with Orbis?

Orbis is compatible with 20 - 22-gauge needles or intravenous lines.

What happens if I do not inject all 10ml of saline at once?

If you pause after injecting a portion of the 10 ml of saline, you can restart and continue delivering the remainder of the 10 ml of saline through the Orbis.

Can the Orbis be attached to and work with a 3 way stop cock?

Orbis eliminates the need for a 3-way stopcock for agitation but works with any luer lock if one is needed.

What machine settings should be used with Orbis?

Use the machine settings you would normally use for a cardiac bubble study with agitated saline.

What is the size of Orbis microbubble vs. agitated saline microbubbles?

Eimer et al showed in an animal study with an early version of the device (Eimer et al., *Performance Characteristics of a Novel Echocardiographic Contrast System*; ASE 2022) that the Orbis produced smaller and more consistent microbubble size compared to manually agitated saline with a significantly lower incidence of large (>104.7µm) bubbles.

Can Orbis be used in a sterile procedure (e.g. for pericardiocentesis and central venous line control or placement)?

Yes. The Orbis device is provided sterile.

Can Orbis be delivered by the sonographer performing the echo?

Orbis is designed to allow for the sonographer to inject the agitated saline. However, you should follow the policies of your institution.

Can Orbis be used in pediatric patients?

No. Currently Orbis is only indicated for adult patients.

SAFETY

What are the contraindications for Orbis?

There are no known contraindications for Orbis.

What is PS-80 (Polysorbate 80)?

Orbis contains a small amount of Polysorbate 80. Polysorbate 80 (also known as Tween 80 or Ethoxylated Sorbitan Monooleate) is a nonionic surfactant that is commonly used in foods, pharmaceutical preparations, and cosmetics as an emulsifier, dispersant, or stabilizer. It is part of a larger group of polysorbates, which are well characterized chemicals consisting of a common structure of sorbitan or sorbitol, etherified with polyethyoxy (PEG) chains, and esterified with fatty acids. Common polysorbates include: Polysorbate 20, Polysorbate 40, Polysorbate 60, Polysorbate 80, Polysorbate 65, and others.

Is polysorbate safe?

The U.S. FDA has listed a maximum daily exposure (MDE) for polysorbate 80 of 4,680 mg for intravenous injection in the Inactive Ingredients Database (U.S. FDA, 2024). Even with the maximum recommended use of the Orbis device (4 x devices as worst case for injections), the maximum potential exposure polysorbate 80 in the Orbis device more than 500 times less than the MDE. Therefore, the results of the toxicological risk assessment indicate that the maximum total intravenous injection is expected to be of low toxicological risk to a patient.

Do we need to ask patients if they have a known allergy to polysorbate 80?

Yes. While allergies to PS-80 are very rare, you should ask patients if they have a known allergy to it.

Do we need an allergy kit available when use Orbis?

Orbis contains PS-80, a common surfactant that has a very high-margin of safety and allergies are rare. Follow your institution's policies for having allergy kits available.

Is there a potential for an air embolism Orbis microbubbles?

Orbis provides approximately 1mL of air per injection, the same or less as standard of care.

According to IEC 60601-2-24, infusion of air is safe when 1 mL of air is present as a bolus arterially within a 15-minute span. Surfactants are known to decrease the surface tension between the bubble and fluid, which facilitates bubble breakup and reabsorption (Branger and Eckman, 2002). In rats, the reabsorption time of an emboli when pretreated with saline was 14.5 to 23.1 minutes, while in surfactant pretreated rats, was 10.2 to 14.8 minutes (Branger and Eckman, 2002).

In five preclinical porcine studies conducted by ASI, a number of injections with the Orbis devices was conducted with no incidence of air emboli. The studies included upwards of 20 injections of the device with an upwards rate of 1 injection per 3.5 minutes.

Do Orbis microbubbles survive the lungs?

No, Orbis microbubbles do not survive the lungs. Our testing has shown that Orbis' microbubbles are within the same range of size as standard of care, but with a much tighter and smaller distribution.

Additionally, ASI has conducted five preclinical (porcine) studies and confirmed the Orbis microbubbles do not survive the lung. Porcine is the standard model for cardiac studies.