FDA Public Health Web Notification: Human tissue processed by Cryolife, Inc.
(You are encouraged to copy and distribute this notification)

August 21, 2002

This provides information about recent actions taken by the Food and Drug Administration (FDA) against Cryolife, Inc. ("Cryolife") of Kennesaw, Georgia. FDA has ordered Cryolife, a human tissue-processing firm, to recall all distributed human allograft tissues, except allograft heart valves, that have been processed by Cryolife since October 3, 2001. This FDA recall order was issued after FDA discovered regulatory violations related to the processing of human tissue by Cryolife, documented fungal and bacterial contamination of Cryolife tissues, and found that Cryolife had not fully implemented adequate corrective actions.

Allograft heart valves processed and supplied by Cryolife have not been included in the FDA recall order. This is because these devices are essential for the correction of congenital cardiac lesions in neonate and pediatric patients and no satisfactory alternative device exists. Under these circumstances, the benefit of these devices outweighs the risk associated with the current manufacturing deficiencies.

Even though FDA has not included allograft heart valves in the FDA recall order for the reason stated above, FDA still has serious concerns regarding the processing and handling of allograft heart valves by Cryolife because patients who receive these devices may be at increased risk for infection. Accordingly, FDA recommends that you consider the following information when determining the appropriate treatment for your patients who have either already received any allograft tissues, including allograft heart valves, processed by Cryolife on or after October 3, 2001, or who have not yet received, but may need to receive an allograft heart valve.

**Background**

FDA has ordered Cryolife to recall distributed human tissue, other than allograft heart valves, processed since October 3, 2001. Under the order, the firm also must withhold from the market all allograft tissue, other than allograft heart valves, processed since October 3, 2001. This Web Notification is alerting you of FDA’s action and is also advising you of certain steps to consider when deciding whether to use Cryolife allograft heart valves. FDA has taken these actions because it has determined that Cryolife cannot ensure that the human tissue it processes for implantation is free from fungal and bacterial contaminants.

Tissue from a donor processed by Cryolife on and after October 3, 2001, has been associated with the November 7, 2001, death of a patient who received a soft tissue implant during reconstructive knee surgery. Additionally, in March 2002, FDA learned that a patient who received a Cryolife allograft heart valve implanted in 2001 developed a fever within two months of the surgery. Cultures of the valve grew Candida Tropicalis and Candida Albicans. FDA learned of a second event that occurred in March 2002 of a patient who also received a Cryolife valve who suffered a cerebrovascular accident and had positive blood cultures for Staphylococcus Epidermidis.

Current federal regulations for human tissue, like that subject to FDA’s recall order, require firms to prepare, validate, and follow written procedures for tissue processing to prevent infectious disease contamination or cross-contamination. Current federal regulations applicable to allograft heart valves also help ensure that appropriate procedures are validated and followed.
During inspections of Cryolife from March 25 through April 12, 2002, FDA found numerous, significant violations of FDA regulations. FDA issued a Warning Letter to Cryolife on June 17, 2002, after determining, among other things, that the firm did not adequately validate its processing and testing methods and did not adequately implement procedures recommended by the Centers for Disease Control and Prevention (CDC), or adequately implement any other appropriate procedures, to ensure that tissue processed by the firm is not contaminated.

After determining that Cryolife failed to take adequate corrective measures to address possible infectious disease contamination of tissue, and after reviewing information provided by the firm in response to FDA’s warnings, FDA issued the present order for retention, recall and/or destruction of allograft tissues other than allograft heart valves, and is issuing this Web Notification to physicians regarding FDA’s recommendations for both allograft heart valves and other allograft tissues. FDA’s concerns described in the order relate specifically to bacterial and fungal contamination of soft tissues, such as cartilage and tendons.

If a bacterial or fungal infection were to occur following tissue implantation, the signs and symptoms usually appear within days to weeks after implantation. Therefore, it is unlikely that patients who have not recently received a tissue implant are likely to be at future risk. However, concerned patients are encouraged to contact their physicians.

**FDA Recommendations**

**A. Allograft tissues (except allograft heart valves) that are subject to the FDA Order for Retention, Recall, and/or Destruction:**

If you are a physician who is caring for a patient who was recently implanted with Cryolife processed tissue, FDA recommends that you:

- Carefully monitor the patient for both fungal and bacterial infections

If you are a surgeon who is considering using Cryolife processed tissue, FDA recommends that you:

- Quarantine all tissue subject to the recall order. Follow the instructions for disposal when received from Cryolife.
- Consider using processed allografts from alternative manufacturers/processors

**B. Cryolife allograft heart valves:**

If you are a physician who is caring for a patient who was recently implanted with a Cryolife allograft heart valve, FDA recommends that you:

- Carefully monitor the patient for both fungal and bacterial infections
- Report all adverse reactions to both FDA and Cryolife
- Inform your patient of FDA’s concerns with Cryolife allograft heart valves and discuss the potentially higher risk for infection

If you are a surgeon who is considering implanting a Cryolife allograft heart valve, FDA recommends that you:
• Consider the information provided in this notification in your evaluation of therapeutic options for potential heart valve recipients
• Consider using processed allografts from alternative manufacturers/processors
• Inform the prospective patient of FDA’s concerns with Cryolife allograft heart valves and discuss the potentially higher risk for infection

**Reporting Adverse Events to FDA**

FDA has different adverse event reporting requirements for allograft heart valves and allograft tissues:

FDA regulates allograft heart valves as medical devices while it regulates other allograft products as tissues. Because FDA considers Cryolife allograft heart valves to be medical devices, hospitals and other user facilities are subject to the mandatory reporting requirements for reporting deaths or serious injuries associated with these devices (see 21 Code of Federal Regulations part 803 for details on reporting certain deaths and serious injuries). On the other hand, because FDA considers the other allograft products subject to the recall order to be tissues, hospitals and other user facilities are not subject to mandatory reporting requirements for these products.

**Reports of Deaths or Serious Injuries associated with allograft heart valves:**

If you become aware of an adverse event that reasonably suggests that a Cryolife allograft heart valve has or may have caused or contributed to a death or serious injury, you should follow the procedures established by your facility for mandatory reporting.

**Reports of any other adverse events or information about contaminated allograft tissues:**

While it is not mandatory to report such events to FDA, if you have reason to believe that you have received contaminated tissue from Cryolife, please be aware that MedWatch, the FDA’s voluntary reporting program, is open to receiving such reports. MedWatch reports are accepted four ways: online at [http://www.accessdata.fda.gov/scripts/medwatch](http://www.accessdata.fda.gov/scripts/medwatch); by telephone at 1-800-FDA-1088; by FAX at 1-800-FDA-0178; or by mail to MedWatch, Food and Drug Administration, HF-2, 5600 Fishers Lane, Rockville, MD 20857.

**Getting More Information**

If you have questions regarding the soft tissue products distributed by Cryolife, please use the Voice Information System – Direct access to a Consumer Safety Officer or Public Affairs Specialist (800-835-4709; 301-827-1800). You also may contact FDA by emailing your questions about biological products to [OCTMA@CBER.FDA.GOV](mailto:OCTMA@CBER.FDA.GOV).

If you have questions regarding allograft heart valves, please contact the Consumer Staff, Center for Devices and Radiological Health, at 301-827-3990 (Press 5 to speak with a staff member).

All of the FDA medical device postmarket safety notifications can be found on the World Wide Web at [http://www.fda.gov/cdrh/safety.html](http://www.fda.gov/cdrh/safety.html). Postmarket safety notifications can also be obtained through email on the day they are released by subscribing to our list server. You may subscribe at [http://list.nih.gov/archives/dev-alert.html](http://list.nih.gov/archives/dev-alert.html). You may also subscribe by sending an email to
listserv@list.nih.gov. In the body of the text, type "SUBSCRIBE DEV-ALERT firstname lastname".