Urgent Product Information
EVICEL® Fibrin Sealant (Human)
All Lots and Product Codes

July 2, 2012

Dear Operating Room Directors, Materials Managers, and Risk Managers:

PLEASE DISTRIBUTE THIS INFORMATION TO ALL STAFF WITHIN YOUR DEPARTMENT WHO USE EVICEL® Fibrin Sealant (Human)

Ethicon and Omrix Biopharmaceuticals would like to make you aware of the risk of fatal adverse events associated with improper spray application technique of EVICEL® Fibrin Sealant (Human). We have received reports of air or gas embolism occurring in association with the use of spray devices employing a pressure regulator to administer EVICEL®. These events appear to be related to the use of the spray device at higher-than-recommended pressures and/or in closer-than-recommended proximity to the tissue surface.

The risk of air or gas embolism is an identified risk for all fibrin sealants utilizing pressurized air or gas to apply the product. A class warning for all fibrin sealants regarding the risk of fatal air or gas embolism was issued in the U.S. on September 22, 2009 - FDA Safety Notification: Risk of Life-Threatening Air or Gas Embolism with the Use of Spray Devices Employing Pressure Regulator to Administer Fibrin Sealants - EVICEL®. http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/ucm219997.htm?utm_campaign=Google2&utm_source=fdaSearch&utm_medium=website&utm_term=evicel%20air%20embolism%20air%20embolism&utm_content=1. On April 11, 2012 the UK Medicines and Healthcare products Regulatory Agency (MHRA) issued a Medical Device Alert - Medical Device Alert: Air or gas-pressurised spray devices for application of sprayable fibrin sealants used for intra-operative haemostasis (MDA/2012/019). http://www.mhra.gov.uk/Publications/SafetyWarnings/MedicalDeviceAlerts/CON149556

To date, there have been no air or gas embolism adverse events reported when the spray application technique is used according to the pressure and distance recommendations stated in the product Instructions for Use (IFU).

We would like to remind you of important instructions for use when utilizing the spray application technique with air or gas pressure regulators. Please note that we are not initiating a product recall, and these occurrences are not related to product quality.

Instructions for Product Use:

• When applying EVICEL® using the spray application technique, the pressure should be within the recommended range as outlined below. Please note the correct parameters for spray application differ for open and laparoscopic procedures:

  o For open surgical procedures utilizing the standard 6 cm yellow flexible tip which comes with the applicator device, the recommended spray application parameters are:

<table>
<thead>
<tr>
<th>Distance</th>
<th>Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-15 cm (4-6 inches)</td>
<td>20-25 psi / 1.4-1.7 bar</td>
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</table>
For laparoscopic surgical procedures utilizing accessory tips the recommended spray application parameters are as follows:

35 cm Black Rigid Tip

<table>
<thead>
<tr>
<th>Distance</th>
<th>Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-10 cm (1.6-4 inches)</td>
<td>15-20 psi / 1.0-1.4 bar</td>
</tr>
<tr>
<td>10-15 cm (4-6 inches)</td>
<td>20-25 psi / 1.4-1.7 bar</td>
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</tbody>
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45 cm Yellow Flexible Tip

<table>
<thead>
<tr>
<th>Distance</th>
<th>Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-15 cm (1.6-6 inches)</td>
<td>20-25 psi / 1.4-1.7 bar</td>
</tr>
</tbody>
</table>

Recommendation for Minimization of Risk of Air or Gas Embolism

- We recommend the use of CO₂ (where possible) as the gas for spray application since it is more soluble in blood and has the potential to reduce the harm associated with gas embolism. **We are not contraindicating the use of air as the product can be used safely with air when the indications for distance and pressure are appropriately observed.**
- Blood pressure, pulse rate, oxygen saturation and end tidal CO₂ should be monitored closely when spraying EVICEL®, because of the possibility of occurrence of air or gas embolism.
- When using accessory tips for laparoscopic surgical procedures with EVICEL®, the instructions for use of the tips should be followed with respect to distance and pressure.

We are asking you to please take the following actions:

- Fill out the enclosed Business Reply Card and return it to the address printed on the card.
- For customers confirming the use of one or more Omrix Pressure Regulators at your facility: after we receive your Business Reply Card, you will receive a follow-up package containing a label and instructions on how to affix the label to the Pressure Regulator(s). This label provides a point-of-use reminder of the proper pressure range for EVICEL®.

Within the next three months, a company representative will visit your facility to ensure receipt of this notification and, in the case of customers using Omrix Pressure Regulators, to ensure receipt and application of the pressure range label to the pressure regulator.

We are here to support you in the safe and efficacious use of this product, and are available to answer any questions that you have. To speak with someone at the company, please contact your sales representative, or call 1-877-ETHICON to speak with a member of our Medical Affairs department.

The United States Food and Drug Administration has been advised of these occurrences.

Thank you for your prompt attention to this matter.

Sincerely,

Christiana Bielinski
Group Director, Quality and Compliance
ETHICON™ Biosurgery

Jeffrey Hammond MD, MPH, FACS
Group Director, Medical Affairs
Ethicon
Urgent Evicel Product Information

Do you understand the contents of this notification? [ ] Yes [ ] No

**Confirmation of Omrix Pressure Regulator**

<table>
<thead>
<tr>
<th>PRODUCT DESCRIPTION</th>
<th>QTY OF OMRIX UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omrix Pressure Regulator</td>
<td></td>
</tr>
</tbody>
</table>

Your timely response to this notification is requested. Please fill out, tear off, and mail this reply card within five (5) business days, even if you do not have the product. Thank you.

Signature ________________________ Title ________________________

Name ________________________ Phone ________________________

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ETHICON, Inc.

Omrix Pressure Regulator

July 2, 2012

Event 4791

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