The ThermaFix process difference

According to available literature, there are two major binding sites for calcium which lead to tissue calcification:

- Tissue phospholipids
- Residual or “unstable” glutaraldehyde molecules

While other tissue treatments may extract or coat one of these two calcium binding sites, only the ThermaFix advanced tissue process extracts both sites.

- Removing unstable glutaraldehyde molecules with proprietary thermal heat treatment reduces calcium binding
- Removes 98% of phospholipids with patented chemical treatment
- Not a reversible binding like other tissue treatments

ThermaFix advanced tissue process.
The only tissue process to extract both major calcium binding sites

<table>
<thead>
<tr>
<th>Process</th>
<th>Magnesium</th>
<th>Phospholipids</th>
<th>Glutaraldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>ThermaFix</td>
<td>Extract</td>
<td>Extract</td>
<td>Extract</td>
</tr>
<tr>
<td>Carpentier-Edwards</td>
<td>Extract</td>
<td>Extract</td>
<td>Extract</td>
</tr>
<tr>
<td>Cupurandol Bioprocess</td>
<td>Extract</td>
<td>Extract</td>
<td>Extract</td>
</tr>
</tbody>
</table>
The ThermaFix process advantage
- An effective tissue treatment targets calcification
- Glutaraldehyde fixation is only the first step in the tissue treatment process
- Glutaraldehyde fixation helps in tissue preservation, sterility, improved biocompatibility and structural stability

Extraction is better than coating
- The ThermaFix advanced tissue process extracts phospholipids and unstable or residual glutaraldehyde molecules
- Other tissue treatments may only coat these calcium binding sites. As a result, their anticalcification effect may be reversible

MECHANISM OF ACTION

Unintended leaflet tissue — in the body
Tissue phospholipids and unstable glutaraldehyde molecules are major calcium binding sites, which lead to tissue calcification.

ThermaFix process Step 1: Unstable glutaraldehyde molecule removal — in the lab
Proprietary thermal treatment removes unstable glutaraldehyde molecules, major calcium binding sites.

ThermaFix process Step 2: Phospholipid removal — in the lab
Patented chemical treatment removes 98% of tissue phospholipids, a major calcium binding site.

Not a reversible binding like other tissue treatments
- Remedial heat treatment reduces calcium binding
- The anticalcification effect may be reversible

Not a reversible binding like other tissue treatments
- Up to 81% reduction in calcium uptake over glutaraldehyde controls in small animal studies.

Durability and tissue treatment
The ThermaFix advanced tissue process is available on the Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis, which is designed with 20-year unparalleled durability data.

ThermaFix advanced tissue process results
- As the only tissue treatment to remove both major calcium binding sites, the proprietary ThermaFix advanced tissue process reduced calcium uptake by up to 81% over glutaraldehyde controls in small animal studies.
- 75% reduction in calcium uptake over controls in juvenile sheep study.

Prepare to change the way you think about tissue treatments
- The only tissue process to remove both major calcium binding sites.
- Up to 81% reduction in calcium uptake over glutaraldehyde controls.
- Not a reversible binding like other tissue treatments.

References:
**The ThermaFix process advantage**

- An effective tissue treatment targets calcification
- Glutaraldehyde fixation is only the first step in the tissue treatment process
- Glutaraldehyde fixation helps in tissue preservation, sterility, improved biocompatibility and structural stability

**Extraction is better than coating**

- The ThermaFix advanced tissue process extracts phospholipids and unstable or residual glutaraldehyde molecules
- Other tissue treatments may only coat these calcium binding sites. As a result, their anticalcification effect may be reversible

**MECHANISM OF ACTION**

**Un-treated leaflet tissue — in the body**

Tissue phospholipids and unstable glutaraldehyde molecules are major calcium binding sites, which lead to tissue calcification.

**ThermaFix process Step 2:**

Phospholipid removal — in the lab

Proprietary thermal treatment removes unstable glutaraldehyde molecules, a major calcium binding site.

**Treated leaflet tissue — in the body**

As the only tissue treatment to extract both major calcium binding sites, the proprietary ThermaFix advanced tissue process reduced calcium uptake by up to 81% over glutaraldehyde controls in small animal studies.¹⁻⁹

**Durability and tissue treatment**

The ThermaFix advanced tissue process is available on the Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis, which is designed with 20-year unparalleled durability data.

**ThermaFix advanced tissue process results**

As the only tissue treatment to extract both major calcium binding sites, the proprietary ThermaFix advanced tissue process reduced calcium uptake by up to 81% over glutaraldehyde controls in small animal studies.¹⁻⁹

**Up to 81% reduction in calcium uptake over glutaraldehyde controls**

**75% reduction in calcium uptake over controls in juvenile sheep study**

**See our mechanism of action at www.edwards.com/thermafix**
The ThermaFix process advantage
- An effective tissue treatment targets calcification
- Glutaraldehyde fixation helps in tissue preservation, sterility, improved biocompatibility and structural stability

Extraction is better than coating
- The ThermaFix advanced tissue process extracts phospholipids and unstable or residual glutaraldehyde molecules
- Other tissue treatments may only coat these calcium binding sites. As a result, their anticalcification effect may be reversible

ThermaFix advanced tissue process results
As the only tissue treatment to extract both major calcium binding sites, the proprietary ThermaFix advanced tissue process reduced calcium uptake by up to 81% over glutaraldehyde controls in small animal studies. 

MECHANISM OF ACTION

Unstable leaflet tissue — in the body
Tissue phospholipids and unstable glutaraldehyde molecules are major calcium binding sites, which lead to tissue calcification.

ThermaFix process Step 1: Unstable glutaraldehyde molecule removal — in the lab
Proprietary thermal treatment removes unstable glutaraldehyde molecules, a major calcium binding site.

ThermaFix process Step 2: Phospholipid removal — in the lab
Patented chemical treatment removes 98% of tissue phospholipids, a major calcium binding site.

Trated leaflet tissue — in the body
As the only tissue treatment to remove both major calcium binding sites, the ThermaFix advanced tissue process reduced calcium uptake by up to 81% over glutaraldehyde controls in small animal studies.

Prepare to change the way you think about tissue treatments

Not a reversible binding like other tissue treatments

Durability and tissue treatment
The ThermaFix advanced tissue process is available on the Carpentier-Edwards PERIMOUNT Pericardial Bioprosthesis, which is designed with 20-year unparalleled durability data.

Animal test results — calcium uptake reduction

Up to 81% reduction in calcium uptake over glutaraldehyde controls

75% reduction in calcium uptake over controls in juvenile sheep study

Breaking the chain of tissue calcification

The only issue process to remove both major calcium binding sites
According to available literature, there are two major binding sites for calcium which lead to tissue calcification.

- Tissue phospholipids
- Residual or "unstable" glutaraldehyde molecules

While other tissue treatments may extract or coat one of these two calcium binding sites, only the ThermaFix advanced tissue process extracts both sites.

**The ThermaFix process difference**

Removing unstable glutaraldehyde molecules with proprietary thermal heat treatment reduces calcium binding.

Removes 98% of phospholipids with patented chemical treatment.

Not a reversible binding like other tissue treatments.
The only tissue process to remove both major calcium binding sites

- Removing unstable glutaraldehyde molecules with proprietary thermal heat treatment reduces calcium binding\(^1\)-\(^6\)
- Removes 98% of phospholipids with patented chemical treatment\(^5\),\(^6\)
- Not a reversible binding like other tissue treatments\(^9\)
- Up to 81% reduction in calcium uptake over glutaraldehyde controls in small animal studies\(^5\)

References:

No clinical data are available which evaluate the long-term impact of the Edwards Lifesciences tissue treatment in patients.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.
See instructions for use for full prescribing information.
Edwards Lifesciences devices placed on the European market meeting the essential requirements referred to in Article 3 of the Medical Device Directive 93/42/EEC bear the CE marking of conformity.
Edwards Lifesciences, Edwards, the stylized E Logo, ThermaFix, and XenologIX are trademarks of Edwards Lifesciences Corporation. Carpenter-Edwards and PERIMOUNT are trademarks of Edwards Lifesciences Corporation and are registered in the U.S. Patent and Trademark office.
©2004 Edwards Lifesciences LLC
All rights reserved. AR00726