

energy coagulation or scalpel. Such conditions, if not minimized can result in post operative tenderness and pain, visceral organ entrapment, organ necrosis and risk of morbidity in selected patients.

Studies conducted at both the University of Arizona and Washington University Medical Center explored a novel Omega 3 gel coating, developed exclusively by Atrium, on a Prolite Ultra™ lightweight mesh construction. The purpose of these studies was to evaluate the bio-absorbable oil (BAO) coating's chemical and biomechanical response between surgically dissected abdominal wall tissue as applied by Atrium to the lightweight mesh construction. It was also an objective of these experimental studies to investigate the coating chemistry's effect on scar-like connective tissue formation, cellular remodeling and healing in comparison to bare polymer mesh and bare polymer PTFE films in the same tissue injury model.

It was observed that the Omega 3 gel coating reduced the inflammatory response involved in cellular remodeling and soft tissue healing following surgical tissue dissection. It was also observed that the tenacity and amount of dense tissue attachment, if present at all, was always found to be moderate to significantly reduced, with a more natural, less contracting healing response. The observed effect of the BAO coating was an overall reduction in diffuse tissue attachment or scarring at all time points. Cellular remodeling, new peritoneum formation and mesh incorporation was observed to experience "little to none" adjacent visceral organ involvement.

These observations were in contrast to the bare polymer polypropylene mesh implants and select bare polymer PTFE film materials, whereby dense tissue attachment or scarring was observed, even with use of inert, lightweight Prolite Ultra™ mesh. Any observed visceral organ involvement with the Omega 3 coated samples, which typically originate from the borders of the surgically injured tissue site, were observed to be minimal, insignificant and not permanently anchored as was consistently observed with the bare polymer mesh and some PTFE film explants in this study. The dense tissue attachment involved with the bare polymer mesh explants are characteristic of those tightly

anchored, and highly contracted connective tissue formations, frequently seen in man, months and years after a primary abdominal wall surgical intervention with uncoated synthetic materials.

Omega 3 gel coatings as developed by Atrium, have demonstrated both experimentally and clinically in man, a measurable reduction in tissue attachment, as determined by histological examination of both animal and human explants (Preclinical studies and data on file at Atrium). Early patient follow up with the company's first 134 patient series indicated all patients tolerated the Omega 3 coated gel mesh very well, without any unusual reported complications, or any unusual pain, symptoms or clinical conditions which would indicate an undesirable healing, inflammatory or connective tissue event.\* Longer term post-operative tissue attachment conditions will continue to be monitored and presented for future peer review in time.



\*Data on file at Atrium Medical Corporation.

European Hernia Society Meeting, Turin, Italy, 12/2005 – Abstract Presentation. *Comparison of a Novel Lipid-Based, Bioabsorbable Barrier Mesh to Commercially Available Meshes for Intraperitoneal Placement in Ventral Hernia Repair.* Brent D. Matthews, MD; Washington University School of Medicine, St. Louis, Missouri.

International Hernia Society Meeting, Boston, MA, USA 6/2006, European Association of Endoscopic Surgery Meeting, Berlin, Germany 11/2006 – Abstract Presentation. *Initial Results with the Intra-abdominal Placement of a Biologically-derived, Lipid-based, Bioabsorbable Barrier Mesh.* Richard Pierce, MD, Washington University School of Medicine, St. Louis, Missouri.

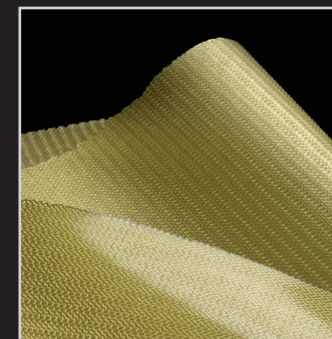


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## Frequently Asked Questions Regarding Atrium's Omega 3 Coated Mesh Products

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## QUESTION 1

**How reliable is the data supporting the use of Omega 3 gel coatings to minimize visceral organ attachment?** (Anyone can design a clinical evaluation or study to reflect the outcome they are looking for.)

Atrium would agree that too many specialty mesh products have inundated the market without genuine scientific support, histological peer review and/or clinical guidelines. Atrium endeavored to provide science to solutions, by investigating use of a known safe, Omega 3 biological chemistry first developed for its drug eluting coronary stent project. It was found early on that a proprietary blend of pharmaceutical grade, contaminant free fish oil could be processed into a thin, uniform bioabsorbable film coating on numerous implantable materials, including lightweight hernia mesh.

Today's C-QUR™ Omega 3 gel coated mesh products are the result of many years of research, processing developments and implant testing in both small animal, large animal and humans, prior to commercial availability.

The first 3 pre-clinical models were performed by an independent pathology lab at the University of Arizona and were focused on determining the viability of using Omega 3 chemistry as a means to minimize or reduce the typical foreign body reaction currently seen with synthetic reinforcement mesh and microporous polymer films. We discovered that by use of a unique Omega 3 gel coating developed at Atrium, the bioabsorbable complex provided minimal to no visceral organ attachment as the coated mesh incorporated with tissue when placed along the abdominal wall. Clinical pathology revealed a smooth, confluent layer of tissue or neoperitoneum along the visceral surface. We also found by lightly coating the individual knitted filaments, we determined a way to balance the ingrowth and minimalization of the visceral organ attachment from one side to the other. The result is a preferred, lightweight knitted structure that becomes firmly incorporated even when fully encapsulated with the Omega 3 gel coating. Several challenging tissue defect models in animals demonstrated consistent cellular response with the impregnated lightweight mesh. This data was used for our

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U.S. FDA 510(K) submission and premarket notification clearance.

Atrium further conducted a pre-clinical rabbit study to better understand how C-QUR™ mesh would compare to the performance of other competitive mesh products. Histology and cell response were also evaluated at the same independent lab. These results were presented at the International Hernia Seminar meeting in Boston, Massachusetts in June 2006. This study revealed that the biological Omega 3 coated C-QUR™ mesh provides equivalent reduction in visceral organ attachment formation as laminated PTFE film products, with less gross and histological inflammatory response. The C-QUR™ mesh was also found to be firmly and uniformly anchored to the abdominal wall tissue, during and after Omega 3 coating absorption.

As part of the company's new technology quality system, Atrium conducted a 9 month market evaluation with over 35 physicians across the US, whereby both C-QUR™ mesh and C-QUR Edge™ products were utilized in both open surgical and laparoscopic hernia repairs. The market evaluation was conducted in 134 patients, to determine C-QUR™ mesh and C-QUR Edge™ handling characteristics, product performance, preferred shape, size and configurations. Each case was documented with an in-depth questionnaire, including office follow-up evaluations with these patients of approximately 6 months.

This detailed pre-clinical and market evaluation process provided invaluable clinical experience and important design, configuration, size and package information. In fact, such clinical experience allowed the company to make subtle improvements in its film liner and pouch packaging for ease of use, box size, mesh geometry and edge reinforcement dimensions for more challenging laparoscopic and open surgery soft tissue repairs. No other commercially available coated mesh product that we know of has undergone as much pre-clinical testing and clinical follow-up experience prior to commercial availability as C-QUR™ Mesh and C-QUR Edge™ products. Atrium's C-QUR™ Mesh family of products are the first of a series of many exciting new bioabsorbable oil (BAO) coated medical devices. C-QUR Edge™ was found to satisfy the physician's unmet need for a rein-

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forced area by providing maximum fixation/reinforcement strength to minimize tack dislodgement and provide enhanced handling during alignment. Currently, Atrium is completing its experimental and pre-clinical testing with its proprietary Omega 3 coating chemistry with several Pharma agents to investigate ways to help minimize pain, further improve visceral organ healing following surgical intervention, and to help minimize local infection when required. We will keep you informed of our experimental findings and results.

## QUESTION 2

**What benefits are there for using C-QUR™ mesh products in primary and secondary hernia repair?**

It's common knowledge that the human body has a limited repertoire for healing bluntly dissected soft tissue, or electro-cauterized tissue, and/or tissue which has been neatly dissected or "sealed" by use of ultrasonic cutting and coagulating devices. Uncontrolled connective tissue formation, particularly in abdominal wall reconstruction and hernia repair, are well published complications, frequently observed with all synthetic polymer mesh and composite PTFE barrier mesh products. Such abdominal wall repairs and/or surgical interventions often require use of synthetic reinforcement material for connective tissue formation and stabilization, particularly in the surgical reduction of a hernia, and for tissue reinforcement following take down of a highly vascularized or densely overgrown connective tissue attachment. In particular, for those dense scar-like connective tissue attachment conditions which involve the bowel, the common denominator for such visceral organ involvement is "connective tissue" stimulation and overgrowth, due to the body's natural healing response to injury and trauma. Such clinical conditions, if left uncontrolled and/or not mechanically separated by use of a coated mesh or tissue separating material, can result in a "tightly compacted" connective tissue attachment. Such conditions are known to begin at the time of injury, and evolve throughout the entire healing phase of the surgically manifested soft tissue injury, whether created by ultrasonic cutting and/or high

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