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Technical Overview of Permallon® Avant Alumina Matrix Composite Ceramic Material

White Paper

Permallon® Avant

Technical Overview of Permallon® Avant Alumina Matrix Composite Ceramic Material Manufactured by CoorsTek Bioceramics

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History of Alumina Matrix Composites

The use of ceramic oxide materials for hip arthroplasty was pioneered in France during the 1970's by Prof Pierre Boutin who used Aluminum Oxide (Alumina) femoral heads to provide a solution to high wear rates of metal on polyethylene bearing couples. The combination of low wear rates combined with Alumina's excellent biocompatibility provided a successful approach to reducing clinical issues associated with polyethylene wear[1].

The latest generation of ceramic materials used for bearing surfaces in Total Hip Arthroplasty are Alumina Matrix Composites that aim to provide the proven properties of Alumina with the added mechanical benefits of Zirconium Oxide (Zirconia) but with greater in vivo stability. Willmann[2] presents a thorough technical overview of Alumina and Zirconia in orthopaedics and the evolution of Alumina Matrix Composites like Permallon® Avant.

Permallon® Technical Review

CoorsTek Permallon® Avant is an implant grade Alumina Matrix Composite ceramic material governed by the ISO 6474-2 Type X (Extra High Strength) material standard. The material is a fully dense 75% Alumina and 25% Zirconia composite ceramic. The microstructure of Permallon® Avant is engineered to incorporate advanced toughening mechanisms to improve the mechanical integrity of the material. The chemical composition and physical makeup of the material is also designed to be biocompatible, stable, and to provide excellent wear performance.

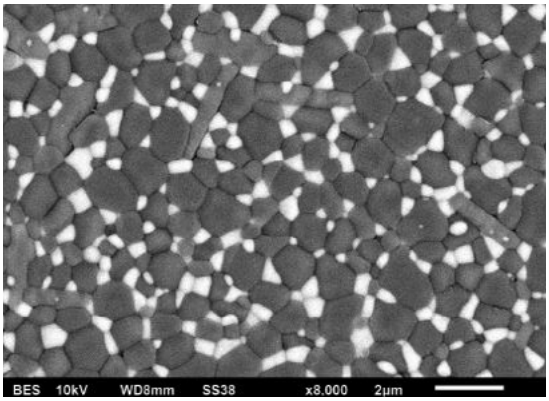
Typical properties including chemical composition, mechanical properties, and physical properties are shown in Table 1.

Table 1: Typical Material Properties of Permallon® Avant

TEST	TEST STANDARD	ISO 6474-2 TYPE X REQUIREMENT	PERMALLON® AVANT
Composition (wt. %)	ISO 12677 / ISO 6474-2	60-90% Al_2O_3 10-30% ZrO_2+ HfO_2 ≤ 10% Additives ≤ 0.2% Impurities	75% Al_2O_3 25% ZrO_2 ≤ 10% Additives ≤ 0.2% Impurities
Density (% Ultimate)	ISO 18754	≥ 99%	4.36g/cm^3 (100%)
Elastic Modulus (GPa)	ASTM C1198	≥ 320	350
4pt. Flexural Strength (MPa)	ISO14704	≥ 1000	1198
Fracture Toughness (MPa m$^{1/2}$)	ISO 23146	≥ 4.0	6.0
Vickers Hardness (GPa)	ISO 14705 / ASTM C1327	≥ 16.0	16.6

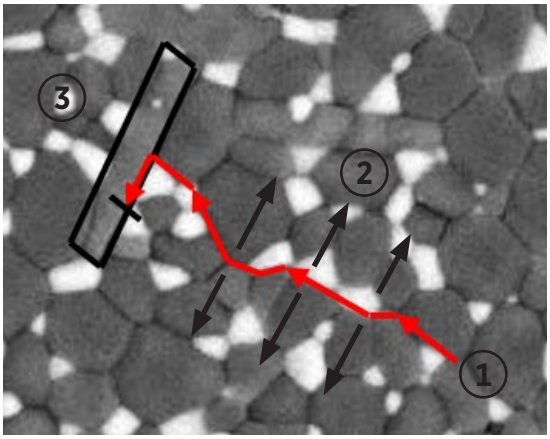
The chart is intended to illustrate typical properties. Specific property values may vary. Data contained herein is not to be construed as absolute and does not constitute a representation or warranty for which CoorsTek Bioceramics assumes legal responsibility.

Figure 1 Permallon® Avant microstructure



A scanning electron microscope image of Permallon® Avant is shown in Figure 1. In addition to the Alumina Matrix (dark grains) the material also contains β-Alumina platelets (dark-elongated grains) and a Zirconia phase (white grains)—both of which increase fracture toughness.

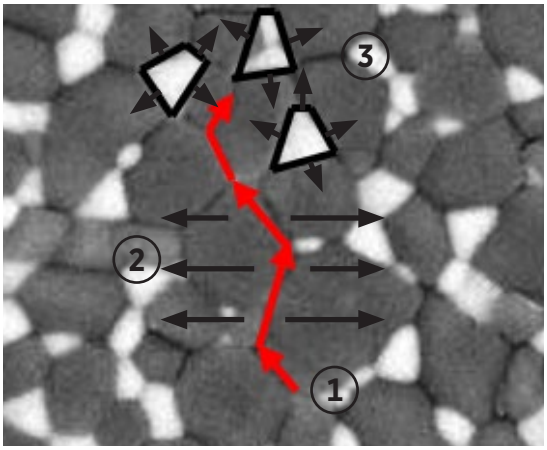
Figure 2: Crack Deflection at the β-Alumina Platelets



The microstructure of Permallon® Avant enhances toughness by two mechanisms: The first toughening mechanism is crack deflection that occurs at the β-Alumina platelets. The second toughening phenomenon is crack compression, which is promoted by the homogeneous distribution of Zirconia particles within the Alumina Matrix. These toughening mechanisms are depicted in Figures 2 and 3.

1: Crack Forms → 2: Crack advances in tensile field → 3: β-Alumina grain deflects the crack away from the tensile field and arrests propagation.

Figure 3: Crack Compression by Zirconia Particles



1: Crack Forms → 2: Crack advances in tensile field → 3: Zirconia particles expand as the crack advances which compresses the fracture and arrests propagation.

Permallon® Avant Material Testing Protocol

Chemical, Physical, and Mechanical Properties

Permallon® Avant material is tested on a batch basis and is certified to meet the requirements for Surgical Implant Grade Alumina Matrix (Ceramic) Composite material per ISO 6474-2 (Type X, Extra High Strength). A list of the baseline testing conducted, and performance criteria follows in Table 2.

Table 2: Testing Protocol per ISO 6474-2 Type X

TEST	TEST METHOD / STANDARD	ACCEPTANCE REQUIREMENTS PER ISO 6474-2 TYPE X
Average Relative Bulk Density	ISO 18754	≥ 99% Ultimate Density
Chemical Analysis	ICP/XRF ISO 12677 / ISO 6474-2 (Type X)	60 – 90 wt.% Al_2O_3 10 – 30 wt.% ZrO_2 + HfO_2 ≤ 5 wt.% HfO_2 in ZrO_2 ≤ 10 wt.% additives ≤ 0.2 wt.% impurities
Microstructure		
• Grain Size	ISO 13383-1 / EN 623-3	Alumina: ≤ 1.5 µm Zirconia: ≤ 0.6 µm
• Standard Deviation		Alumina: ≤ 25% Zirconia: ≤ 40%
Material Strength		
• 4pt. Flexural Strength	ISO 14704	≥ 1000 MPa
• Weibull Modulus	ASTM C1239	≥ 8
Radioactivity	ISO 13356	≤ 200 Bq/kg
Fracture Toughness	ISO 23146	
• SEVNB (single edge V-notch bending) Test		≥ 4.0 MPa $\sqrt{m}$
Vickers Hardness	ASTMC1327 / ISO 14705	≥ 16.0 GPa
Young's Modulus	ASTM C1198	≥ 320 GPa
Cyclic Fatigue	ISO 22214	No failure during cyclic loading in 4-point bending, 10^7 cycles at 400 MPa
Accelerated Hydrothermal Aging		
• Mean Biaxial Flexural Strength	ISO 6474-2 (Type X) / ASTM C1499	Degradation ≤ 20% vs. pre-autoclave. Meet other values noted previously for un-aged
• Cyclic Fatigue	ISO 22214	No failure during cyclic loading in 4-point bending, 10^7 cycles at 320 MPa
• Wear	ISO 6474-2 (Type X)	Wear volume increase ≤ 20% of aged as compared to un-aged

Effects of Hydrothermal Aging

Alumina Matrix Composites that incorporate Zirconia materials (such as Permallon® Avant) can be susceptible to hydrothermal degradation. This degradation process has been shown to take place in vivo over long periods of time, based on retrieval studies of Zirconia femoral heads[3]. To address these concerns, the Zirconia-containing ceramics used for implantable applications must be designed in such a manner to reduce the sensitivity of the material to this aging process. In the case of Permallon® Avant, this stabilization is achieved via constraint of the Zirconia phase by the surrounding Alumina matrix.

The international standard for implant grade Alumina Matrix Composites (ISO 6474-2 (Type X)) requires the performance characteristics are successfully maintained after subjecting the material to hydrothermal (accelerated) aging. The protocol detailed in ISO 6474-2 (Type X) requires ten hours of hydrothermal aging at 134°C of steam pressure. This simulation has the theoretical effect of 3-4 years of in vivo exposure for every hour of aging[3]. Using this theoretical model, the ISO 6474-2 (Type X) protocol for hydrothermal aging simulates 30-40 years of in vivo aging. The Permallon® Avant material has been tested and certified to meet the requirements of this hydrothermal accelerated aging test protocol as detailed above.

Biological Properties

A review of available literature investigating the biocompatibility of Alumina Matrix Composite ceramics shows that such ceramics exhibit biocompatibility for implantable applications such as Total Hip Arthroplasty.

Piconi, et al.[4] published a comprehensive literature review of biocompatibility studies on Alumina and Zirconia bioceramics, which are the main constituents of Permallon® Avant. This demonstrates that both materials are suitable candidates for human implantation. This is reinforced further by the long clinical history behind the use of such ceramics in dental and orthopaedic applications.

CoorsTek Bioceramics has conducted a full range of biocompatibility testing on Permallon® Tru materials according to ISO 10993. Out of the family of Permallon® materials, Permallon® Tru was chosen for biological testing as it contains all the constituents contained in Permallon® Avant at similar percentages. Additionally, Permallon® Tru alumina matrix composite has a chromium oxide additive for improved performance which results in increased hardness and strength. This testing strategy was chosen as it is a common practice to conduct Biological testing on the most complex material formulation in a given material family. Biocompatibility testing is not available for Permallon® Avant at this time. Tests were chosen based upon guidance given in ISO 10993-1. The testing demonstrates that CoorsTek Bioceramics Permallon® materials are biocompatible for long term implantation. A list of tests conducted follows in Table 3.

Table 3: Biocompatibility Testing on Permallon® Tru*

ISO 10993-1 REQUIREMENT	TEST METHOD / STANDARD	TESTING CONDUCTED	PERMALLON® RESULT
Cytotoxicity	ISO 10993-5	MEM Elution	**Pass:** No Reactivity
Sensitization	ISO 10993-10	Maximization Sensitization	**Pass:** No Sensitization Response
Irritation / Intracutaneous Reactivity	ISO 10993-10	Intracutaneous Reactivity	**Pass:** Non-irritant
Systemic Toxicity (acute)	ISO 10993-11, ISO 10993-17/18	Acute Systemic Toxicity, Toxicological Risk Assessment	**Pass:** Non-toxic
Subacute and Subchronic Toxicity	ISO 10993-11	Rabbit Pyrogen, Subacute Intraperitoneal Toxicity	**Pass:** Non-pyrogenic, Negative for signs of systemic toxicity
Genotoxicity	ISO 10993-3	Mutation Assay (AMES), In Vitro Mouse Lymphoma Assay, In Vivo Mouse Micronucleus	**Pass:** Non-mutagenic
Implantation	ISO 10993-6	Intra-muscular Implant	**Pass:** Non-irritant

*Formerly known as CeraSurf® -p

Product Description

Ceramic femoral heads are manufactured by CoorsTek Bioceramics from Permallon® Avant Alumina Matrix Composite according to implant grade specifications per ISO 6474-2 Type X. The heads are precision ground and polished ceramic single-use components designed for replacing the body's natural femoral head. Permallon® Avant femoral heads are provided to customers of CoorsTek Bioceramics non-sterile and ready for subsequent processing, including final cleaning, packaging, labeling, sterilization, and kit assembly. Our customers combine Permallon® Avant femoral heads with other components such as acetabular liners/shells and femoral stems to create a total hip replacement system. Such hip replacement systems are indicated for use in primary Total Hip Arthroplasty in skeletally mature patients with non-inflammatory degenerative joint disease, trauma, or other indications for use as validated and detailed by customers of CoorsTek Bioceramics.

CoorsTek produces femoral heads for total hip replacement in a wide range of custom sizes using Permallon® Avant material.

Manufacturing Detail for Permallon® Avant Femoral Heads

Ceramic Material Preparation: Ceramic powder is produced including addition of a binder to aid in pressing and forming.

Ceramic Pressing/Forming: The ceramic powder is pressed into a blank shape and formed to a shape representing the final geometry of the product.

Sintering/Hot Isostatic Pressing: The ceramic component is sintered using heat to achieve full density. The sintering schedule includes a hot isostatic pressing process.

Grinding/Polishing: As precision surfaces are required, the ceramic component is ground and polished. After this process, the ceramic has achieved the final dimensional and finish specification.

Dimensional Inspection: Inspection is conducted in accordance with the approved manufacturing control plan to verify the dimensional and finish specifications. The component is measured for conformance to product specifications using calibrated equipment.

Laser Etching: The component is marked with identifying information such as the Articulating Diameter, Offset, and Taper Type (as applicable for femoral heads), Taper Size, Manufacturing Lot, Serial Number, Manufacturer's Logo, and Conforming Material Standard.

Testing/Visual Inspection: The component is tested and visually inspected, including the use of a dye penetrant to analyze for defects.

Cleaning: A cleaning process is utilized to remove processing compounds.

Packaging: After cleaning, the component is packaged to protect from damage during transit.

Quality Assurance Review/Shipment: The component and the manufacturing documentation are reviewed against the applicable standards to ensure conformance to product/process specifications. After the Quality Assurance Review the component is prepared for shipment, then shipped along with the appropriate certificates, documents, and reports.

Manufacturing Quality Systems and Relevant Regulations

CoorsTek Bioceramics operates a quality system, including inspection processes, which are certified as complying with the requirements of ISO 13485 (Medical devices - Quality management systems - Requirements for regulatory purposes). CoorsTek Bioceramics quality system complies with the applicable requirements of 21 CFR 820 (U.S. FDA Quality System Regulation (QSR)).

Product Testing

Permallon® Avant femoral heads have been tested with the objective of assessing the structural integrity and mechanical fixation required of ceramic components used as bearing surfaces in Total Hip Arthroplasty and have been found to meet the applicable requirements of the orthopaedic industry. A list of the test protocols and acceptance criteria are included in Table 4.

Table 4: Permallon® Avant Femoral Head Testing Protocol

TEST	TEST STANDARD	ACCEPTANCE REQUIREMENTS
Axial Burst Test	ISO 7206-10	Avg > 46kN, Min 20kN (FDA Guidance for femoral heads[8])
Axial Fatigue	ASTM F2345	10 Million cycles at 14kN without failure (FDA Guidance for femoral heads[8])
Post Fatigue Axial Burst	ISO 7206-10	Min 20kN (FDA Guidance for femoral heads[8])
Pull Off	ISO 7206-10	>250 N criteria for predicate Ceramic Hip Systems[7]

Product Testing Protocols

Structural Integrity

As the ceramics used in hip arthroplasty are subject to in vivo loading, it is important to characterize the strength of the components. This characterization should be conducted such that the components can be reasonably expected to survive the lifetime of the hip system. The testing protocols subject the components to loads that, although sometimes different in orientation, well exceed the expected physiological loading conditions[7]. For example, given a body mass of 75kg (165lbs)[7], the axial fatigue loading of 14kN is 19 times body weight and static axial compression requirement (based on FDA guidance[8]) of >46kN average is greater than 63 times body weight.

Mechanical Fixation

It is important that the modular interface between the femoral stem and head are adequately fixed to eliminate the possibility of dissociation of the ceramic during use. In service, the predominant forces generated are compressive, and therefore will work to keep the modular components attached. However, there are some frictional forces and adverse conditions that apply opposing loads to the ceramic hip system. To assess the integrity of the fixation mechanism, tests were conducted applying axial load to dissociate the modular interface between the femoral stem and head. For Permallon® Avant femoral heads these tests included a Pull Off test (static tension) in which a load is applied along the axis of the taper connection (detailed in ISO 7206-10).

Discussion of Product Testing

Structural Integrity

Permallon® Avant femoral heads met the acceptance criteria for mechanical strength testing. The worst-case configuration 28-12/14 L (+3.5mm) against the titanium test taper has a 123kN mean and 118kN minimum axial burst strength. This exceeds the FDA Guidance[8] of >46kN mean and >20kN minimum by a safety factor of 2.7X and 5.9X respectively. The axial burst strength of the Permallon® Avant femoral head at 123kN compares favorably to Biolox®Delta 28-12/14 L (+3.5mm) ceramic heads with a 90kN mean[9] (both tested against Titanium tapers) as shown in Figure 4. All Permallon® Avant femoral head samples passed fatigue testing and are well in excess of the FDA Guidance[8] for post fatigue burst.

The Permallon® Avant femoral heads were subjected to loading that exceeds physiological conditions[7]. In addition, these components are well in excess of the industry standards for strength. Given these results Permallon® Avant femoral heads are expected to provide adequate structural integrity for the lifetime of the hip implant system[7].

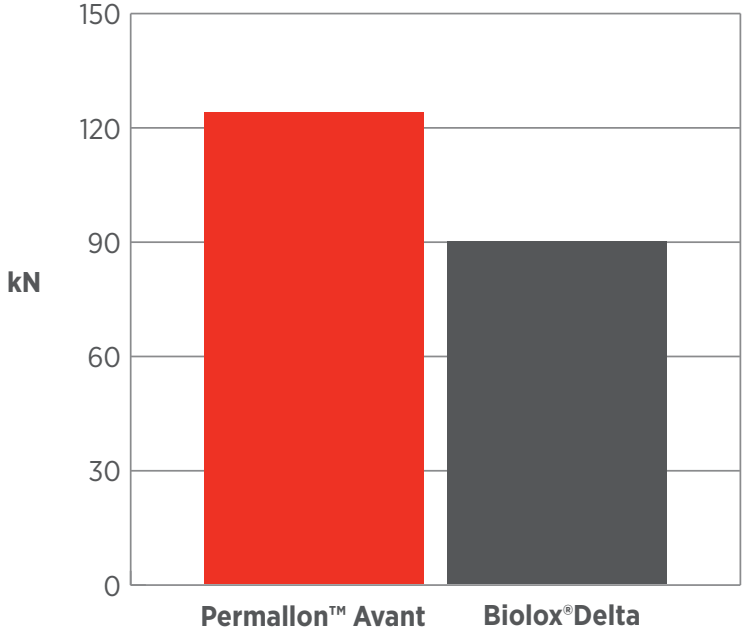
Mechanical Fixation

All samples met the acceptance criteria for mechanical fixation. The performance of the Permallon® Avant femoral heads has been shown to exceed expected physiological conditions[7], and is comparable to available historical test data from predicate ceramic hip systems[7]. These results along with performance from fatigue testing support proper mechanical fixation of the Permallon® Avant femoral head in Total Hip Replacement systems.

Summary

Permallon® Avant material has been tested and found to meet the requirements for chemical, physical, and mechanical performance related to the intended use as a permanent load bearing implant. The material has been evaluated from a technical standpoint and the results exceed the requirements for implant grade Alumina Matrix Composite material. Femoral heads produced from Permallon® Avant material have been tested using applicable protocols, worst-case configurations, comparisons to predicates, and industry standardized acceptance criteria. These tests verify the performance of Permallon® Avant products with respect to the demands of ceramic femoral heads used in Total Hip Arthroplasty. These results support the use of Permallon® Avant as a high-performance ceramic bearing material for use in Total Hip Arthroplasty.

Figure 4: Axial Burst Strength (ISO 7206-10) 28-12/14 L (+3.5mm) / Titanium Taper



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Standards

21 CFR 820 "Quality System Regulation" U.S. Food and Drug Administration

ASTM C1198 "Standard Test Method for Dynamic Young's Modulus, Shear Modulus, and Poisson's Ratio for Advanced Ceramics by Sonic Resonance"

ASTM C1239 "Standard Practice for Reporting Uniaxial Strength Data and Estimating Weibull Distribution Parameters for Advanced Ceramics"

ASTM C1499 "Standard Test Method for Monotonic Equibiaxial Flexural Strength of Advanced Ceramics at Ambient Temperature"

ASTM F2345 "Standard Test Methods for Determination of Static and Cyclic Fatigue Strength of Ceramic Modular Femoral Heads"

EN 623-3 "Advanced technical ceramics - Monolithic ceramics - General and textural properties - Part 3: Determination of grain size and size distribution (characterized by the linear intercept method)"

ISO 10993 "Biological Evaluation of Medical Devices"

ISO 10993-1 "Biological Evaluation of Medical Devices — Part 1: Evaluation and testing within a risk management process"

ISO 12677 "Chemical analysis of refractory products by X-ray fluorescence (XRF) - Fused cast-bead method"

ISO 13356 "Implants for surgery - Ceramic materials based on yttria-stabilized tetragonal zirconia (Y-TZP)"

ISO 13383-1 "Fine ceramics (advanced ceramics, advanced technical ceramics) – Microstructural characterization – Part 1: Determination of grain size and size distribution"

ISO 13485 "Medical devices – Quality management systems – System requirements for regulatory purposes"

ISO 14705 "Fine ceramics (advanced ceramics, advanced technical ceramics) - Test method for hardness of monolithic ceramics at room temperature"

ISO 18754 "Fine ceramics (advanced ceramics, advanced technical ceramics) - Determination of density and apparent porosity"

ISO 22214 "Fine ceramics (advanced ceramics, advanced technical ceramics) - Test method for cyclic bending fatigue of monolithic ceramics at room temperature"

ISO 23146 "Fine ceramics (advanced ceramics, advanced technical ceramics) - Test methods for fracture toughness of monolithic ceramics - Single-edge V-notch beam (SEVNB) method"

ISO 6474-2 "Implants for surgery – Ceramic materials Part 2: Composite materials based on a high-purity alumina matrix with zirconia"

ISO 7206-10 "Implants for surgery – Partial and total hip prostheses – Part 10: Determination of resistance to static load of modular femoral heads"

About CoorsTek

CoorsTek is a leading global manufacturer of technical ceramics and advanced materials. With over 400 proprietary material formulations, vast process capabilities, and vertically integrated systems, CoorsTek is the international partner of choice for companies requiring the unique, high-performance properties of technical ceramics.

For over 100 years, industry leaders have turned to CoorsTek for solutions to the world's most perplexing engineering and manufacturing challenges. CoorsTek meets these challenges with unsurpassed expertise in materials engineering, broad research and development capabilities, operational excellence, and a commitment to building reliable, collaborative relationships. We partner with industry leaders to engineer next-generation technology applications.

With locations across three continents, CoorsTek expertise is available to help design better, more efficient, and longer-lasting products.

Learn more at www.coorstek.com

CoorsTek Bioceramics

Located in Grand Junction, Colorado, USA, CoorsTek Bioceramics is dedicated to state-of-the-art manufacturing of technical ceramics for the medical device industry. Since its inception in 2005, CoorsTek Bioceramics has manufactured over six million critical implantable ceramic components under an ISO 13485 certified and FDA compliant quality system. Our focus is orthopaedic reconstruction with a primary concentration on ceramic bearing components for Total Hip Arthroplasty. Additionally, CoorsTek Bioceramics components can be found in other implantable devices such as Spinal Disc Replacements, Cochlear Implants, Pacemakers, and Neurostimulators.

The manufacture of Permallon® femoral heads and acetabular liners begins with the production of the raw material and continues all the way to the testing and inspection of the finished components. This vertical integration allows for the finest control of the manufacturing process, guaranteeing consistent, high-quality performance.

Devices incorporating CoorsTek Bioceramics' products are registered by our customers. Check for regulatory approval in your area: www.coorstek.com/bioceramics-regulatory

Learn more at www.permallon.com.

About the Author

Jon Haftel has been in the technical ceramics industry since 1996 and has a wide range of experience in ceramics processing and ceramic material engineering/development. He has spent his career in Engineering and Manufacturing Operations, and has managed projects for a variety of industries including health care, semiconductor, and electronics. Jon has been responsible for the engineering of materials and processes since the launch of CoorsTek Bioceramics (formerly C5 Medical Werks) in 2005, and currently manages the technical and operational aspects of the business. Jon received a Bachelor of Science in Mechanical Engineering with honors from Colorado State University, where he worked on research of biomedical materials. He also holds a Master's in Metallurgical and Materials Engineering from the Colorado School of Mines, with a focus on Advanced Ceramic Materials and graduate research on ceramic-metal seals. Jon is involved with his local community in Grand Junction, Colorado, supporting the Engineering Program at Colorado Mesa University where he provides industry guidance, assistance with material laboratories, and sponsors student engineering projects.

To learn more about CoorsTek Bioceramics and Permallon® Orthopaedic Ceramics, contact us:

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