DE NOVO CLASSIFICATION REQUEST FOR TORNIER PYROCARBON HUMERAL HEAD

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Shoulder joint humeral (hemi-shoulder) ceramic head / metallic stem cemented or uncemented prosthesis. A shoulder joint humeral (hemi-shoulder) ceramic head / metallic stem cemented or uncemented prosthesis is a device using a replacement humeral head made of ceramic materials, such as pyrolytic carbon, and a stem made of alloys, such as cobalt-chromium-molybdenum. It is intended to be implanted to replace the articular surface of the proximal end of the humerus and to be fixed with or without bone cement (§ 888.3027). This device is not intended for use in total shoulder arthroplasty.

NEW REGULATION NUMBER: 888.3695

CLASSIFICATION: Class II

PRODUCT CODE: QKW

BACKGROUND

DEVICE NAME: Tornier Pyrocarbon Humeral Head

SUBMISSION NUMBER: DEN220012

DATE DE NOVO RECEIVED: February 8, 2022

SPONSOR INFORMATION:

Tornier SAS
% Tornier, Inc.
10801 Nesbitt Avenue South
Bloomington, Minnesota 55437

INDICATIONS FOR USE

The Tornier Pyrocarbon Humeral Head is indicated as follows:

The Tornier Pyrocarbon Humeral Head associated with the Tornier Flex Stem is indicated for use as a replacement of deficient humeral heads disabled by:

- Non-inflammatory degenerative joint diseases (osteoarthritis, avascular necrosis)
- Traumatic arthritis.

The Tornier Pyrocarbon Humeral Head Shoulder Prosthesis, combined with the Tornier Flex Humeral Stem, are to be used only in patients with an intact or reconstructable rotator cuff and if the native glenoid surface is intact or sufficient, where they are intended to increase mobility, stability, and relieve pain.

Note: The coated humeral stem is intended for cemented or cementless use. The non-coated humeral stem is for cemented use only

LIMITATIONS

The sale, distribution, and use of the Tornier Pyrocarbon Humeral Head are restricted to prescription use in accordance with 21 CFR 801.109.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

Implant Description

The Tornier Pyrocarbon Humeral Head (**Figure 1**) is a prescription use device that is comprised of the pyrolytic carbon (pyrocarbon) articulating surface and a cobalt chromium alloy double taper neck. The humeral head is provided pre-assembled to the double taper to the end user and is compacted onto 510(k) cleared compatible humeral stems (K151293) for replacement of deficient humeral heads disabled by non-inflammatory arthritis, or traumatic arthritis. The pyrocarbon articulating surface is made of a graphite substrate core, coated with a layer of pyrolytic carbon deposited onto the substrate via chemical vapor deposition. The pyrocarbon articulating surface is pressed into the cobalt chromium alloy double taper neck during the manufacturing process, is provided as a singular construct to the end user, and is not intended to be disassembled by the end user. Compatible monoblock humeral stems are available in titanium plasma spray coated or uncoated versions. The humeral stems are designed with a female taper connection to accept the mating male taper connection of the pyrocarbon humeral heads.

Figure 1: Tornier Pyrocarbon Humeral Head, with the pyrocarbon articulating surface pre-assembled onto the cobalt chromium alloy double taper neck alone (left), and with the Tornier Flex Shoulder humeral stem in a hemi-shoulder arthroplasty configuration (right)

Instrument Description

The Tornier Pyrocarbon Humeral Head and compatible humeral stems are implanted using Class I surgical instruments regulated under 21 CFR 888.4540, product code LXH; trials regulated under 21 CFR 888.4800, product code HWT; class II instruments previously cleared with the compatible humeral stems (K151293); and the following device specific instrumentation specific to facilitate implantation of the Tornier Pyrocarbon Humeral Head:

- Spring impactor, impactor tip supports, and pyrocarbon head impactor tip: Reusable instruments designed to deliver an appropriate amount of energy to impact the Tornier Pyrocarbon Humeral Head onto the humeral stem without damaging the pyrolytic carbon articulating surface.
- Manual planar reamers and reamer tip: Reusable instruments provided for reaming the humeral cut surface following stem implantation to ensure the bone cut is perfectly aligned so as to not interfere with seating of the Tornier Pyrocarbon Humeral Head.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The Tornier Pyrocarbon Humeral Head is manufactured from the following patient contacting materials:

Table 2: Manufactured Materials of Patient-Contacting Device Components

Description	Material	Direct Patient Contact	Contact Duration
Articulating Surface	Pyrocarbon	Yes	Permanent (>30 d)
Double Taper	Cobalt Chromium Alloy per ISO 5832-7 (Implants for surgery — Metallic materials — Part 7: Forgeable and cold-formed cobalt-chromium-nickel-molybdenum-iron alloy)	Yes	Permanent (>30 d)
Patient-contacting Instruments	Medical Grade Stainless Steel, Polypropylene, and Silicone	Yes	Limited (≤24 h)

Biocompatibility evaluation has been completed according to 2020 FDA Guidance, Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process."

For the permanent implant, the **Table 3** shows the biocompatibility testing performed and the results, which were acceptable for a permanent implant in contact with bone/tissue:

Table 3: Implant Biocompatibility Testing Performed

Test Description	Result
Cytotoxicity (per ISO 10993-5 (Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity))	Non-cytotoxic
Irritation (per ISO 10993-10 (Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization))	Non-Irritant
Sensitization (per ISO 10993-10 (Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization))	Non-Sensitizing
Implantation Effects (per ISO 10993-6 (Biological evaluation of medical devices — Part 6: Tests for local effects after implantation))	Null to Minimal Reactivity
Material Mediated Pyrogenicity (per ISO 10993-11 (Biological evaluation of medical devices — Part 11: Tests for systemic toxicity))	Non-Pyrogenic

Acute/Subacute/Subchronic/Chronic Systemic Toxicity, Genotoxicity and Carcinogenicity (addressed through chemical characterization and toxicological risk assessment per ISO 10993-18 (Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process)/ISO 10993-17 (Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances)	Non-systemically toxic/genotoxic/carcinogenic

For the reusable silicone instruments, the **Table 4** shows the biocompatibility testing performed and the results, which were acceptable for instruments in limited contact with bone/tissue:

Table 4: Silicone Instrument Biocompatibility Testing Performed

Test Description	Result
Cytotoxicity (per ISO 10993-5 (Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity))	Non-cytotoxic
Irritation (per ISO 10993-10 (Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization))	Non-Irritant
Sensitization (ISO 10993-10 (Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization))	Non-Sensitizing
Acute Systemic Toxicity (per ISO 10993-11 (Biological evaluation of medical devices — Part 11: Tests for systemic toxicity))	Non-Toxic

In addition to the biocompatibility testing of silicone instruments, reference to a master file was provided to support the Material Mediated Pyrogenicity Endpoint to demonstrate the instrument is non-pyrogenic.

For the reusable stainless steel and polypropylene instruments, a manufacturing rationale was provided to demonstrate acceptable biocompatibility for instruments in limited contact with bone/tissue.

STERILITY / PACKAGING AND SHELF-LIFE / PYROGENICITY

Sterility:

The Tornier Pyrocarbon Humeral Head is a single-use device provided clean and sterile to the end user. Gamma Sterilization of the device has been validated to provide a Sterility Assurance Level (SAL) of 10^{-6} based on the VDmax[25] method as recommended by FDA Recognized Consensus Standard series ANSI/AAMI/ISO 11137-1 (Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices)/-2 (Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose).

Packaging and Shelf-Life:

The sterile barrier system consists of a double blister package sealed with Tyvek lids which is placed into a protective cardboard box. Sterilized samples accelerated aged to 5 years were used to determine the sterile shelf-life of the device. The mechanical performance of the device is not expected to degrade over time. Distribution testing (ASTM D4169 (Standard practice for performance testing of shipping containers and systems)), package integrity testing (bubble leak test, ASTM F2096 (Standard test method for detecting gross leaks in packaging by internal pressurization (bubble test))), and seal strength testing (ASTM F88/F88M (Standard test method for seal strength of flexible barrier materials)) were used to validate the sterile shelf-life of the device. Non-clinical performance testing of the implant was used to assess the shelf-life of the device. The testing confirmed a 5 year shelf-life.

Pyrogenicity:

Bacterial endotoxins testing (BET) was performed to determine whether the Tornier Pyrocarbon Humeral Head met pyrogen limit specifications. All tested devices passed with a reported value of ≤1 EU/device, meeting the recommended endotoxin limits per ANSI/AAMI ST72:2011 ("Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing").

Reprocessing:

Certain instruments for use with the Tornier Pyrocarbon Humeral Head are provided non-sterile and are to be cleaned and sterilized by the end user. Validated reprocessing instructions are included in their own separate labeling document.

Steam sterilization method was validated per ISO 17665 Half Cycle Method (Sterilization of health care products – Moist heat – Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices) and AAMI ST79 (Comprehensive guide to steam sterilization and sterility assurance in health care facilities) to ensure that a minimum SAL of 10^{-6} is achieved. Instruments are to be sterilized using a pre-vacuum steam autoclave. For the pre-vacuum steam autoclave cycle, the validated parameters call for an exposure time of 4 minutes at 270°F (132°C) and a dry time of 20 minutes at 270°F (132°C). Users are advised to use an FDA- cleared sterilization wrap.

MAGNETIC RESONANCE (MR) COMPATIBILITY

The Tornier Pyrocarbon Humeral Head was not evaluated for safety and compatibility in a Magnetic Resonance Environment.

PERFORMANCE TESTING – BENCH

A summary of non-clinical mechanical performance evaluations is provided in **Table 5:**

Table 5: Summary of Non-clinical Mechanical Performance Evaluations

Test	Purpose	Method	Performance Criteria	Results
Construct fatigue endurance	The aim of this test is to assess the risk of component loosening and potential damage following fatigue for the worst-case devices and test parameters.	5 million cycles of compressive load was applied in a worst-case orientation.	The implants were required to survive 5 million cycles to the pre-specified test parameters without any cracks, breakage, damage, or dissociation.	All tested implants survived 5 million cycles without any cracks, breakage, damage, or dissociation from the stem.
Taper disassembly resistance – axial pull-off	The aim of this test is to assess the disassembly resistance of the humeral head sub-components and of the humeral head from the humeral stem to axial pull-off in the worst-case configuration.	The test method follows recommendations described in ASTM F2009 (Standard test method for determining the axial disassembly force of taper connections of modular prostheses).	No pre-determined acceptance criteria were defined. Disassembly results were compared to another humeral head with the same intended use.	The minimum pull-off load for the Tornier Pyrocarbon Humeral Head exceeded the pull off load of another humeral head.
Taper disassembly resistance – torque off	The aim of this test is to assess the disassembly resistance of the humeral head sub-components and of the humeral head from the humeral stem to torque-off in the worst-case configuration.	Test methods were adapted for shoulder prostheses from methods described in ISO 7206-13 (Implants for surgery - Partial and total hip joint prostheses - Part 13: Determination of resistance to torque of head fixation of stemmed femoral components).	The torsional resistance force between the Pyrocarbon articulating surface and the CoCr double taper neck must exceed anticipated clinically relevant loading conditions including an appropriate factor of safety.	All samples met the pre-determined acceptance criteria for torsional resistance.
Taper disassembly resistance – lever-off	The aim of this test is to assess the disassembly resistance of the humeral head sub-components and of the	A static lever-off load was applied at a constant rate until dissociation or	No pre-determined acceptance criteria were defined. Disassembly results were compared to	The minimum lever-off load for the Tornier Pyrocarbon Humeral Head exceeded the lever-

Test	Purpose	Method	Performance Criteria	Results
	humeral head from the humeral stem to lever-off in the worst-case configuration.	breakage of the components.	another humeral head with the same intended use.	off load of another humeral head.
Fretting and corrosion resistance	The aim of this test is to evaluate the fretting and corrosion resistance of the humeral prostheses for worst-case compatible components.	5 million cycles of compressive load were applied in a worst-case orientation in a physiologic environment.	No pre-determined acceptance criteria were defined. Visual scoring, ion release analysis, and particulate analysis results were compared to another humeral head with the same intended use.	Qualitative damage determined by visual scoring, ion release analysis, and particulate analysis demonstrated comparable performance to another humeral head with the same intended use.
Humeral head burst testing (static compression)	The aim of this test is to evaluate the maximum compressive load that the humeral head may experience prior to breakage when considering worst-case components.	Static compressive load to failure testing was adapted to evaluate shoulder components from methods described in ISO 7206-10 (Implants for surgery - Partial and total hip-joint prostheses - Part 10: Determination of resistance to static load of modular femoral heads).	A safety factor was derived from FDA guidance document: "Guidance Document for the Preparation of Premarket Notification for Ceramic Ball Hip System," and the fatigue load requirements for femoral stems from ISO 7206-4 (Implants for surgery — Partial and total hip joint prostheses — Part 4: Determination of endurance properties and performance of stemmed femoral components). This safety factor was applied to the mean fatigue load to determine a minimum acceptance criteria for burst.	All samples met the pre-determined acceptance criteria.
Humeral head subcritical crack propagation	The aim of this test is to evaluate the risk of delayed component fracture of the humeral head for worst-case components and	Incremental load release testing was adapted to evaluate shoulder implants from methods described in ISO	A safety factor was derived from FDA guidance document: "Guidance Document for the Preparation of	All samples met the pre-determined acceptance criteria.

Test	Purpose	Method	Performance Criteria	Results
	orientation due to subcritical crack growth.	11491 (Implants for surgery — Determination of impact resistance of ceramic femoral heads for hip joint prostheses).	Premarket Notification for Ceramic Ball Hip System," and the fatigue load requirements for femoral stems from ISO 7206-4 (Implants for surgery — Partial and total hip joint prostheses — Part 4: Determination of endurance properties and performance of stemmed femoral components). This safety factor was applied to the mean fatigue load to determine a minimum acceptance criteria for burst.	
Third body wear	The aim of this test is to evaluate the articular wear of the humeral head in an abrasive condition to debris circulating within the joint.	Abrasive wear conditions were simulated on the bench referencing literature, ASTM F2028 (Standard test methods for Dynamic Evaluation of Glenoid Loosening or Disassociation, and ISO 14242 (Implants for surgery — Wear of total hip-joint prostheses).	No pre-determined acceptance criteria were defined. Abrasive wear results were compared to another humeral head with the same intended use.	Tornier Pyrocarbon Humeral Head demonstrated lesser surface roughening when exposed to an abrasive condition compared to another humeral head with the same intended use. Wear particulate analysis demonstrated wear particulates were consistent with wear particulates from other arthroplasty devices.
Range of motion (ROM)	The aim of this test is to characterize the ROM of the humeral prosthesis for worst-case components.	Smallest and largest components were evaluated when paired with virtual scapula models to determine the ROM of the system prior to implantation in accordance with ASTM F1378 (Standard	Performance criteria were defined from ASTM F1378 (Standard specification for shoulder prostheses): Flexion shall be equal to or greater than 90°. Extension shall be equal to or	All simulated constructs met the pre-determined acceptance criteria.

Test	Purpose	Method	Performance Criteria	Results
		specification for shoulder prostheses).	greater than 45°. Abduction shall be equal to or greater than 90°. Internal Rotation shall be equal to or greater than 90°. External rotation shall be equal to or greater than 45°.	
Spring impactor testing	The aim of this test is to assess the function of the impactor instrument in response to both fatigue testing and extended cycles of cleaning and sterilization.	The spring impactor was cycled through extended simulated use, cleaning, and sterilization cycles.	The performance of the instrument (e.g., spring stiffness and ability to impact the humeral head onto the stem) should not be impacted from repeated use, cleaning, or sterilization.	The spring impactor's performance was not impacted from extended cycles of simulated use, cleaning, or sterilization of the device.

SUMMARY OF CLINICAL INFORMATION

Study Design

The sponsor conducted a prospective, multi-center, single-arm investigational study under IDE G140202 – Pyrocarbon IDE Study. A total of 157 subjects were enrolled across 18 sites within the US. While the study was originally designed as a performance goal study, the study design changed to a non-inferiority historically controlled study with Propensity Score (PS) analysis at FDA's request. Control data originated from the Aequalis Post-Market Outcomes Study dataset for a 510(k) cleared cobalt chromium humeral head hemiarthroplasty device (i.e., Tornier Flex Cobalt Chromium Humeral Head). A blinded independent statistician implemented a two-stage, outcome-free PS design, and after PS matching, 169 control subjects were selected. The purpose of the study was to evaluate the safety and effectiveness of the pyrocarbon humeral head as a hemiarthroplasty for patients with non-inflammatory arthritis or post-traumatic arthritis when compared to cobalt chromium humeral heads. Subjects were followed to Month 24 post-treatment for study endpoint analysis.

Subject Demographics

A total of 157 subject were enrolled for the investigational trial. After PS matching, 169 control subjects were selected from the Aequalis Post-Market Outcomes Study dataset. The two treatment groups were similar in terms of demographics and baseline characteristics, with an overall mean age and standard deviation of 52.1 ± 10.8 years for the Pyrocarbon group, and 54.9 ± 11.4 years for the control group. The study population was 79% male for the Pyrocarbon group and 72.8% for the control group with average body mass index (BMI) of 30.4 ± 7.0, and 29.2 ± 5.9, respectively. The primary diagnosis in both treatment groups was primary glenohumeral arthritis, comprising 86.6% of patients for the Pyrocarbon group and 82.8% of the control group.

Breakdown of age (beyond mean), race, and ethnicity specific data were not reported in the clinical study. **Table 6** presents a summary of the baseline characteristics for the Pyrocarbon group and control groups (with and without outcome data):

Table 6: Patient Baseline Characteristics

Measure	Pyrocarbon	Control (Overall)	Control (with outcome data)	Control (without outcome data)
N	157	169	73	96
Age, years	52.1 ± 10.8	54.9 ± 11.4	55.9 ± 10.2	54.1 ± 12.2
BMI, kg/m^2	30.4 ± 7.0	29.2 ± 5.9	29.2 ± 5.9	29.2 ± 5.9
Constant Activity Score	7.8 ± 3.7	6.9 ± 3.2	6.8 ± 3.4	7.1 ± 3.3
Constant Pain Score	4.9 ± 3.2	3.4 ± 2.2	3.4 ± 2.3	3.3 ± 2.3
Adjusted Constant Score	49.1 ± 17.4	46.0 ± 17.5	47.4 ± 17.8	44.9 ± 17.6
Sex = Male, %	79.0%	72.8%	78.1%	68.8%
Diagnosis, %				
Avascular Necrosis	7.6%	10.7%	6.9%	13.5%
Post-traumatic Arthritis	5.7%	6.5%	8.2%	5.2%
Primary Glenohumeral Arthritis	86.6%	82.8%	84.9%	81.3%
Dexterity = Right, %	86.0%	91.1%	90.4%	91.7%
Operated Shoulder = Right, %	58.0%	59.2%	65.8%	54.2%
Hospital with Large Number of Beds, %	65.6%	72.8%	75.3%	70.8%
Private Institution, %	62.4%	79.9%	82.2%	78.1%

Primary Endpoint

The primary composite endpoint for the study was defined as the rate of patient success at 24 months. A patient was considered a success at 24 months if:

- Their change in Constant score is ≥ 17;
- They did not have revision surgery;
- There is no radiographic evidence of system disassembly or fracture; AND
- They did not have a system-related serious adverse event.

For the intent to treat set, using multiple imputation to account for missing data, the success rate was 82.7% for the Pyrocarbon group, and 66.8% for the control group. The success rate of Pyrocarbon group led the control by 15.9%. For the per protocol set, after imputation, the success rate was 87.9% for the Pyrocarbon group, and 63.1% for the control group, success rate for Pyrocarbon group was 24.8% higher than for the control group. The sponsor applied a two-way generalized linear model to adjust for propensity score subclass, and used model results to support the non-inferiority claim. Results are presented in **Table 7** for all study subjects.

Table 7: Primary Endpoint Success at Month 24 Post-treatment

	Pyrocarbon			Control		
Outcome	**N**	**n**	**%**	**N**	**n**	**%**
Free of Revision	157	154	98.1%	169	160	94.7%
Constant Score improved 17+ points	143	121	84.6%	67	49	73.1%

	Pyrocarbon			Control		
Outcome	**N**	**n**	**%**	**N**	**n**	**%**
Free of disassembly or fracture	157	157	100.0%	169	169	100.0%
Free of device related SAE	157	152	96.8%	169	160	94.7%
Composite Clinical Success (CCS)	157	--	82.7%	169	--	66.8%
CCS – Completers	146	120	82.2%	73	49	67.1%
CCS – Best Case	157	131	83.4%	169	49	29.0%
CCS – Worst-case	157	120	76.4%	169	145	85.8%

While the historical control group was missing a significant portion of outcome data, all control subjects with missing data are conservatively assumed to be a success in the primary endpoint analysis. To assess for potential selection bias, the sponsor provided an analysis of baseline characteristics for control completers comparing with control subjects with missing data. The analysis indicated that there are no significant differences in baseline demographics or comorbidity characteristics between control completers and control subjects with missing data. The performance of the control group was also compared to literature, noting that the revision rate and the mean improvement in Constant Score are consistent with published data in literature and real-world data, as presented in **Table 8**.

Table 8: Control Group Performance Comparison to Literature and Real World Data

Name	Endpoint	Average Follow Up (months)	Sample Size	Estimate
Historical Control	Revision Rate	24	169	5.3%
Meta Analyses of Hemiarthroplasty Literature	Revision Rate	55	835	11.1%
Australian Joint Registry 2021	Revision Rate	24	5332	5.45%
Historical Control	Constant Score Change from baseline	24	57	28.6±19.9
Meta Analyses of Hemiarthroplasty Literature	Constant Score Change from baseline	56	626	31.8±10.3
Fonte et. al. Meta Analysis[1]	Constant Score Change from baseline	14-240	341	29.6

In addition to the comparison of baseline characteristics between control subjects with or without complete outcome data, and the comparison of outcome data of the control subjects to literature, a tipping point analysis was conducted to analyze the sensitivity of missing data. Compared to the multiple imputation model, the tipping point analysis does not require the same statistical assumptions as it analyzes every possible combination of the missing data. Based on modeling where all possible combinations of missing data were used to assess success or failure in the

[1] Fonte H, Amorim-Barbosa T, Diniz S, Barros L, Ramos J, Claro R. Shoulder Arthroplasty Options for Glenohumeral Osteoarthritis in Young and Active Patients (<60 Years Old): A Systematic Review. J Shoulder Elb Arthroplast. 2022;6:24715492221087014. Published 2022 Mar 23. doi:10.1177/24715492221087014

overall success measurement, only 68 of the 1,164 (5.8%) scenarios would change the study conclusions. The overall success criterion was met in the other 1,096 (>94%) potential missing data combinations. This indicates that the tipping point analysis, along with the multiple imputation analysis and supporting information, demonstrate that the non-inferiority result is insensitive to the presence of missing data.

Secondary Endpoints

Secondary endpoints assessed during the study included the Constant Score, Adjusted Constant Score, American Shoulder and Elbow Surgeons (ASES) Score, Single Assessment Numeric Evaluation (SANE), EQ-5D, Pain measured by a visual analog scale (VAS), ROM, and strength. The Adjusted Constant Score change of 40.5 points in 24 months, observed in the Pyrocarbon IDE study is greater than the minimally clinical important differences (MCID) determined by Holmgren et al who defined a MCID in the Adjusted Constant score for subjects treated conservatively for subacromial pain to be between 17-24 points.[2] The Constant Score change of 34.3 observed in the Pyrocarbon IDE study is greater than the MCID determined by additional literature that reports the MCID in Constant Score for shoulder arthroplasty to be 5.7-9.4.[3] The ASES change of 43.4 in 24 months, observed in the Pyrocarbon IDE study is greater than the MCID determined by Tashjian et al (12-17 points) for rotator cuff disease (tendonitis or tears).[4] The SANE change of 49.5 points observed in the Pyrocarbon IDE study is greater than the MCID determined by Zhou et al (27.25 points) for rotator cuff repairs.[5] EQ-5D change of 0.21 points observed in the Pyrocarbon IDE study is greater than the MCID determined by Hao et al (0.02-0.11) for subacromial pain.[6]

Pain was assessed in the study using a 10-pt (0=no pain at all, 10=pain as bad as it can be) pain VAS (taken from the pain portion of the ASES standardized score). The mean subject reported pain went from 5.5 to 1.1 on the VAS scale with a mean change of -4.2 ± 2.8. The change observed in the Pyrocarbon IDE study is greater than the MCID determined by Hao et al (-1.5) for subacromial pain. The ROM change observed in the Pyrocarbon IDE study at two years are consistent with the results observed by Sowa et al who assessed change in ROM at an average of four years after shoulder hemiarthroplasty.[7] The mean change in strength observed was 5.0±7.6 lbs. at 24 months. These results in the Pyrocarbon IDE study at 24 months are consistent with the

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[2] Holmgren T, Oberg B, Adolfsson L, Björnsson Hallgren H, Johansson K. Minimal important changes in the Constant-Murley score in patients with subacromial pain. J Shoulder Elbow Surg. 2014;23(8):1083-1090. doi:10.1016/j.jse.2014.01.014

[3] Dabija DI, Jain NB. Minimal Clinically Important Difference of Shoulder Outcome Measures and Diagnoses: A Systematic Review. Am J Phys Med Rehabil. 2019;98(8):671-676. doi:10.1097/PHM.0000000000001169

[4] Tashjian RZ, Deloach J, Green A, Porucznik CA, Powell AP. Minimal clinically important differences in ASES and simple shoulder test scores after nonoperative treatment of rotator cuff disease. J Bone Joint Surg Am. 2010;92(2):296-303. doi:10.2106/JBJS.H.01296

[5] Zhou L, Natarajan M, Miller BS, Gagnier JJ. Establishing Minimal Important Differences for the VR-12 and SANE Scores in Patients Following Treatment of Rotator Cuff Tears. Orthop J Sports Med. 2018;6(7):2325967118782159. Published 2018 Jul 26. doi:10.1177/2325967118782159

[6] Hao Q, Devji T, Zeraatkar D, et al. Minimal important differences for improvement in shoulder condition patient-reported outcomes: a systematic review to inform a BMJ Rapid Recommendation. BMJ Open. 2019;9(2):e028777. Published 2019 Feb 20. doi:10.1136/bmjopen-2018-028777

[7] Sowa B, Thierjung H, Bülhoff M, et al. Functional results of hemi- and total shoulder arthroplasty according to diagnosis and patient age at surgery. Acta Orthop. 2017;88(3):310-314. doi:10.1080/17453674.2017.1280656

12-month results observed by Sperling et al who assessed change in strength after total shoulder arthroplasty on subjects with an intact rotator cuff.[8]

Safety Analysis

There were no Unanticipated Adverse Device Effects as determined by the independent medical monitor. All device- and procedure-related serious adverse events (SAEs) were considered expected complications for total shoulder arthroplasty. In the IDE data, there were 3 revisions (3/157, 1.91%) and zero instances of humeral head fracture and/or disassembly at 24 months for the Pyrocarbon group. In Historical Control, SAEs reported include 9 revisions (9/169, 5.33%), which is consistent with the hemiarthroplasty revision rate (5.45%) reported in the 2021 Australian joint registry.

SAEs possibly related to the device include rotator cuff tear (2/157, 1.27%). SAEs possibly related to the procedure include: arthrofibrosis, atelectasis, biceps rupture, brachial plexus palsy, deep vein thrombosis, pain, pulmonary emboli, rotator cuff tear, stroke, and infection.

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

LABELING

The labeling consists of the following: device description, indications for use, instructions for use including surgical steps (e.g., device selection and placement), principles of device operation, identification of device materials, contraindications, warnings, precautions, a list of potential adverse effects, and importance of patient compliance with postoperative activity restrictions. Furthermore, the sterile packaging includes a shelf-life for the device. The labeling meets the requirements of 21 CFR 801.109 for prescription devices.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of the shoulder joint humeral (hemi-shoulder) ceramic head / metallic stem cemented or uncemented prosthesis and the measures necessary to mitigate these risks.

Identified Risks to Health	Mitigation Measures
Adverse events of the index shoulder including pain, unanticipated adverse device effects, subsequent surgical interventions, wear of the native bone, osteolysis, loosening and migration, and revision, including revision due	Clinical data Non-clinical performance testing Biocompatibility evaluation

[8] Sperling JW, Kaufman KR, Schleck CD, Cofield RH. A biomechanical analysis of strength and motion following total shoulder arthroplasty. *Int J Shoulder Surg*. 2008;2(1):1-3. doi:10.4103/0973-6042.39579

Identified Risks to Health	Mitigation Measures
to device wear, component dissociation, or device brittle fracture	
Adverse tissue reaction due to • Device materials • Fretting and corrosion • Wear particulates	Biocompatibility evaluation Non-clinical performance testing
Infection	Sterilization validation Reprocessing validation Shelf-life testing Pyrogenicity testing Labeling
Insufficient range of motion	Non-clinical performance testing

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the shoulder joint humeral (hemi-shoulder) ceramic head / metallic stem cemented or uncemented prosthesis is subject to the following special controls:

1. Clinical data must demonstrate that the device performs as intended under anticipated conditions of use and include the following:
    a. Evaluation of improvement of shoulder function and reduction of symptoms, including pain and function, for the indications for use; and
    b. Evaluation of adverse events, including pain, unanticipated adverse device effects, subsequent surgical interventions, wear of the native bone, osteolysis, loosening and migration, and revision, including revision due to device wear, component dissociation, or device brittle fracture.
2. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use and include the following:
    a. Evaluation of the mechanical function (mechanical fatigue strength including evaluation of fretting and corrosion, static mechanical strength, modular component disassembly strength, and wear analysis) and durability of the implant; and
    b. Evaluation of worst-case device range of motion.
3. All patient-contacting components of the device must be demonstrated to be biocompatible.
4. Performance data must support the sterility and pyrogenicity of the device components intended to be sterile.
5. Performance data must validate the reprocessing instructions for the reusable components of the device.
6. Performance data must support the shelf-life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf-life.
7. Labeling must include the following:
    a. Validated methods and instructions for reprocessing of any reusable components; and

b. A shelf-life.

BENEFIT-RISK DETERMINATION

BENEFITS:

1) The clinical study demonstrates Tornier Pyrocarbon Humeral Head leads to clinically meaningful improvements in shoulder function and symptoms (e.g., reduction in pain) that are maintained over time to at least 24 months;
2) Performance has demonstrated to be non-inferior to Cobalt Chrome Hemiarthroplasty;
3) Literature on clinical use and in vitro testing demonstrate decreases in native glenoid wear when compared to Cobalt Chrome devices;
4) The Tornier Pyrocarbon Humeral Head secondary endpoint results (Constant Score, ASES, SANE, VAS, Strength, and Revision Rate) support clinically meaningful, patient-valued benefits at a magnitude similar to, or numerically greater than, those observed with the Control device; AND
5) Improvement in long-term implant survival rates and delay of TSA conversion.

RISKS:

1) Adverse events of the index shoulder including pain, unanticipated adverse device effects, subsequent surgical interventions, wear of the native bone, osteolysis, loosening and migration, and revision, including revision due to device wear, component dissociation, or device brittle fracture;
2) Adverse tissue reactions due to device materials; fretting and corrosion; and wear particulates;
3) Infection; AND
4) Insufficient range of motion.

Based on the totality of the evidence, the Tornier Pyrocarbon Humeral Head demonstrated a reasonable assurance of safety and effectiveness for the device for its intended use/indications for use and while there is a medium degree of uncertainty in this finding due to missing data from the control group in the clinical study, the risks are not greater than the current standard of care. In addition, the pyrocarbon humeral head demonstrated lower revision rates over the course of the clinical study, and literature and *in vitro* testing demonstrate a probable benefit of decreased glenoid wear when compared to a cobalt chrome hemiarthroplasty. In conclusion, the benefits of using the Tornier Pyrocarbon Humeral Head for its intended use/indications for use outweigh the risks to health.

PATIENT PERSPECTIVES

Patient perspectives considered for the Tornier Pyrocarbon Humeral Head during the review include:

The primary composite study endpoints included assessment of improvement in pain and function using patient reported metrics (e.g., Constant score) at month 24.

Additionally, pre-specified secondary effectiveness study endpoints included the following scales: Constant score, ASES, SANE, EQ5D, VAS Pain Scale, ROM, and change in strength to evaluate the treatment effect at 24 months. These patient reported outcomes (PROs) are used to demonstrate a clinically meaningful improvement in pain and function.

BENEFIT/RISK CONCLUSION

In conclusion, given the available information above, for the following indication statement:

> "The Tornier Pyrocarbon Humeral Head associated with the Tornier Flex Stem is indicated for use as a replacement of deficient humeral heads disabled by:
> - Non-inflammatory degenerative joint diseases (osteoarthritis, avascular necrosis),
> - Traumatic arthritis.
>
> The Tornier Pyrocarbon Humeral Head Shoulder Prosthesis, combined with the Tornier Flex Humeral Stem, are to be used only in patients with an intact or reconstructable rotator cuff and if the native glenoid surface is intact or sufficient, where they are intended to increase mobility, stability, and relieve pain.
>
> Note: The coated humeral stem is intended for cemented or cementless use. The non-coated humeral stem is for cemented use only"

The probable benefits outweigh the probable risks for the Tornier Pyrocarbon Humeral Head. The device provides benefits, and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo for the Tornier Pyrocarbon Humeral Head is granted and the device is classified as follows:

> Product Code: QKW
> Device Type: Shoulder joint humeral (hemi-shoulder) ceramic head / metallic stem cemented or uncemented prosthesis
> Regulation Number: 21 CFR 888.3695
> Class: Class II