UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF INDIANA
SOUTH BEND DIVISION

IN RE: BIOMET M2a MAGNUM HIP IMPLANT PRODUCTS LIABILITY LITIGATION (MDL 2391)	)	CAUSE NO. 3:12-md-2391
This Document Relates to All Cases	)	

ORDER

Biomet's Retrieval Analysis Protocol, Exhibit A in Section II of the Explant Preservation Order entered on March 7, 2013, is attached hereto and incorporated by reference in that order [Doc. No. 279].

SO ORDERED.

ENTERED: March 8, 2013

/s/ Robert L. Miller, Jr.
Judge, United States District Court
Northern District of Indiana

Biomet's Retrieval Analysis Protocol

EXHIBIT A

1. SCOPE

This document describes the protocol for the retrieval and analyses of Explanted Biomet Devices. The objective of this protocol is to enable preservation and analysis of Explanted Biomet Devices and surrounding tissues in a manner that may constitute evidence related to this litigation, as well as to permit Biomet to comply with its postmarket surveillance obligations pursuant to Section 522 of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 3601. The investigation of the Explanted M^2a Devices is non-destructive and will be performed on all reasonably available Explanted M^2a Devices.

2. REFERENCES

ASTM F561 – 05a (Reapproved 2010): Standard Practice for Retrieval and Analysis of Medical Devices, and Associated Tissues and Fluids

ISO 12891-1: 2011 Implants for surgery – Retrieval and analysis of surgical implants, Part 1: Retrieval and handling

ISO 12891-2: 2000 Implants for surgery – Retrieval and analysis of surgical implants, Part 2: Analysis of retrieved metallic surgical implants

ASTM E860 – 07: Standard Practice for Examining and Preparing Items That Are Or May Become Involved in Criminal or Civil Litigation

ASTM E1188 – 05: Standard Practice for Collection and Preservation of Information and Physical Items by a Technical Investigator

ASTM E620: Standard Practice for Reporting Opinions of Scientific or Technical Experts

ASTM E678: Standard Practice for Evaluation of Scientific or Technical Data

3. TERMS AND DEFINITIONS

Metal on metal component: a component of a total hip replacement whereby the articulating surfaces of both the ball and socket are intended to be Co-28Cr-6Mo per ASTM F75 or F1537.

Reasonably available retrieval: any Explanted M^2a Device obtained by a Party pertaining to a Plaintiff in this litigation.

4. PROCEDURES FOR RETRIEVAL, HANDLING AND PACKAGING

Institutional guidelines for the retrieval, handling and packaging of potentially infectious materials shall be utilized. In situations where institutional guidelines do not exist, the specifications outlined in ISO 12891-1 can be utilized.

Specific requirements for this retrieval study:

- When handling, packaging and shipping the retrieved components, the hospital or clinic should avoid putting all the components in the same container without separating packaging.

Ideally, each retrieved component should be individually wrapped and stored in its own container, then placed in a larger container with all the other retrieved components. This will prevent further damage to the explants, which can be difficult to distinguish from *in situ* damage.

- Shortly after removal, a detailed record of any damage caused to the components during extraction should be performed , especially in the presence of the operating surgeon. Adequate 'macro' photography can also be helpful. This information should be labeled adequately and should accompany the explanted components. This will make it easy to differentiate between damaged regions caused in vivo and those caused during extraction.

- It is imperative to label the retrieved parts adequately for future identification.

- The retrieved components should be marked in a non-destructive way to indicate their orientation *in situ* before removal. If the implants are not marked before extraction or immediately after, then the true location of the wear scars can only be guessed. This can be avoided easily by marking the superior rim of the cup and the base of the femoral head.

- Sterilization of metal on metal components should be performed utilizing cold techniques. Do NOT sterilize metal on metal components by steam autoclave as this may alter features or surfaces which may be essential in determining failure modes.

    - In situations where the device has already been sterilized by steam autoclave prior to coming into Biomet's control, the investigator may still perform the retrieval analysis taking into consideration the potential confounding factors introduced by the steam autoclave procedure.

    - Where residual tissues are retained on or within the components, fixation by 10% buffered formalin and/or ethanol and/or other fixative will be included in the sterilization procedure.

5. COLLECTION OF CLINICAL HISTORY OF THE IMPLANT AND PATIENT

Whenever possible, the clinical history of the Plaintiff and the Explanted M2a Device shall be obtained and recorded.

This clinical history shall include at least the following, if available:

- the name or identification number of the patient as permitted by HIPAA or other applicable national regulations;

- the original diagnosis which resulted in the use of the surgical implant;

- the identification of the components inserted, including part number and lot number;

- an X-ray of the surgical implant in situ taken after the insertion operation;

- an X-ray of the surgical implant in situ taken prior to the retrieval operation;

- the patient's activity level including the ability to perform work, sports and recreational activities;
- metal ion analysis of blood or serum for levels of cobalt and chromium;
- the patient's medical history relevant to the surgical implant, including the hospital or clinic at which the surgical implant was implanted;
- information on the patient's experience with the surgical implant just before surgical implant retrieval including any audible noises emanating from the joint;
- sex, height and weight of the patient;
- the date of the insertion operation;
- the date of the retrieval operation;
- observations during the retrieval operation including stability of the cup or dark staining of the surrounding tissues;
- the reason for explantation of the components;
- the hospital or clinic at which the surgical implant was inserted;
- the hospital or clinic at which the surgical implant was retrieved.

The information obtained will be treated as confidential by the Parties.

6. COLLECTION OF TISSUE AND FLUID SAMPLES NEAR THE IMPLANT

In order to assist in the determination of the failure mode for the retrieval, it is recommended that local tissue and fluid samples are obtained during the retrieval operation. The general procedure for this collection is contained within section 3.4 of ISO 12891-1 which is excerpted below:

> *Taking into account the need for patient safety, if tissue and/or fluid samples are to be collected for analysis, then these shall be retrieved in a manner which causes as little damage as possible to both the surgical implant and the tissues.*
>
> *For microbiological investigation, swabs, tissue and/or fluid samples shall be taken from a location adjacent to the implant as soon as possible after the surgical implant has been exposed. Where and how the specimens are taken shall be recorded.*
>
> *For histological examination, tissue samples shall be taken from a location adjacent to the implant and/or from other relevant sites (e.g. lymph nodes or any tissue with abnormal appearance). When possible, tissue samples for histological examination shall include portions extending into the normal tissue.*

The site of the tissue excision and the orientation of the tissue relative to the surgical implant shall be indicated and recorded. Where possible, the proximal end of the tissue shall be marked (e.g. with a suture). Where necessary, the original length of the tissue shall be maintained (e.g. with plastic muscle biopsy clamps or by pinning the tissue to a corkboard or by other means, which avoid contact with metal which could corrode).

The tissue samples for histological examination shall be transferred as early as possible to an appropriate fixative or other media. The type of fixative used and the time between excision and placement in the fixative or media shall be documented. The tissue sample shall be treated in a routine manner as required for histological examination, unless a special method is needed for special investigations. If appropriate, the media used to preserve tissue attached to a retrieved surgical implant shall be selected so as not to affect the surgical implant. When it is not possible to preserve the tissues without affecting the retrieved surgical implant, the portions of the retrieved surgical implant to be analysed should be determined and the tissue preserved accordingly.

Fluids obtained by aspiration shall be appropriately preserved for examination unless a special method is needed for special investigations. The preservation method should be chosen taking into account the intended analysis.

7. PHOTOGRAPHIC RECORD OF THE EXPLANTED DEVICE AND TISSUES

Where appropriate, photographic records shall be made of the surgical implant *in situ*, of the surgical site and of the explanted surgical implant and any associated tissue specimens.

Where appropriate, the orientation of all removed surgical implant components in relation to each other and their placement in relation to the body and associated excised material shall be recorded. If not self-explanatory, the proximal end and the orientation in the transverse plane of the implant shall be marked and documented. Any observed abnormalities in the appearance or condition of the device shall be recorded.

8. CONTAINING, LABELING, CLEANING, DECONTAMINATING, PACKAGING AND SHIPPING OF RETRIEVED IMPLANT, TISSUE, OR FLUID SAMPLES

General instructions for labeling, cleaning, decontaminating, packaging and shipping of retrieved implants, tissue, or fluid sample are found in sections 3.6, 3.7, 3.8, 3.9, & 3.10 of ISO 12891-1.

In addition to these general instructions

- When handling, packaging and shipping the retrieved components, the hospital or clinic should avoid putting all the components in the same container without separating packaging. Ideally, each retrieved component should be individually wrapped and stored in its own container, then placed in a larger container with all the other retrieved components. This will prevent further damage to the explants, which can be difficult to distinguish from *in situ* damage.

- Shortly after removal, a detailed record of any damage caused to the components during extraction should be performed, especially in the presence of the operating surgeon. Adequate 'macro' photography can also be helpful. This information should be labeled adequately and should accompany the explanted components. This will make it easy to differentiate between damaged regions caused in vivo and those caused during extraction.

- It is imperative to label the retrieved parts adequately for future identification.

- The retrieved components should be marked in a non-destructive way to indicate their orientation *in situ* before removal. If the implants are not marked before extraction or immediately after, then the true location of the wear scars can only be guessed. This can be avoided easily by marking the superior rim of the cup and the base of the femoral head.

- Sterilization of metal on metal components should be performed utilizing cold techniques. Do NOT sterilize metal on metal components by steam autoclave as this may alter features or surfaces which may be essential in determining failure modes.

- As soon as possible, ship the following:

    - Clinical information per section 5

    - Photographic records per section 7

    - Retrieved implants

    - Tissue or fluids, if applicable

    To the following address:

    Clinical Studies – MOM Litigation Retrieval
    Biomet Orthopedics
    56 E. Bell Drive
    Warsaw, IN 46582

9. ANALYSIS OF TISSUE AND FLUIDS

Analysis of tissue and fluids will be performed per ISO 12891 and/or ASTM F561. In addition to these protocols, an ALVAL histological score for the tissue shall be made pursuant to the following reference:

> Campbell P, Ebramzadeh E, Nelson S, Takamura K, De Smet K, & Amstutz HC, Clinical Orthopaedics and Related Research, 2010; 468(9):2321-7.

*A number of new consensus standards are currently under development within ASTM committee F04. Where appropriate and reasonable, new standards will be considered for studies.

10. ANALYSIS OF RETRIEVED COMPONENTS – VISUAL ANALYSIS

Visual analysis will be performed on all reasonably available retrievals. Visual analysis shall include the observation of the components with the unaided eye or with the aid of a stereomicroscope. If the retrieval contains more than one component, each component should be analyzed. The following information shall be recorded:

- Unique retrieval code to identify the components

- Catalogue and lot number of each component along with device description
- Markings found on the implant, such as logos, part numbers, or lot numbers
- Date of analysis
- Date retrieved
- Implant duration, if available
- Reason for explantation, if available

Examination of the component will include all surfaces of the components looking for evidence of in service or iatrogenic damage. The following features shall be documented for presence, size/area, location, and severity/degree:

- Bearing surface(s)
    - Wear
    - Scratches
    - 3rd body damage
    - Corrosion
    - Embedded particles
    - Discoloration or staining
    - Impingement
    - Edge damage/subluxation
    - Equatorial contact
    - Stripe wear formations, both superior and inferior stripes on cup and head
    - Evidence of, or exclusion of, a polished main wear zone
    - Surface pitting
    - Wear scars exceeding to the cup rim and beyond
- Taper junction(s)
    - Fretting
    - Corrosion

- Discoloration or staining
- Evidence of head or adapter stuck on neck taper

- Non-bearing surfaces
  - Cup front face damage
  - Cup edge/rim damage, both superior and inferior edges
  - Backside damage, i.e. any damage to the backing of the cup (e.g. removal of porous coating) or bottom face of the femoral head
  - Fretting damage caused by fixation screws, if present

The location of these features will be indicated by performing concise wear mapping of the worn features on both articulating and non-articulating surfaces.

11. ANALYSIS OF RETRIEVED COMPONENTS AND RECORDS – PHYSICAL ANALYSIS

If the following minimal clinical history/information is available:

- Date of implantation
- Date of explantation
- X-rays
  - Post-operative
  - Prior to explantation
- Cup inclination
- Cup anteversion
- Sex, Height and weight of patient
- Activity level of patient

and after patient consent has been obtained, the following physical analyses will be performed:

- If an explanted device is determined to have been well-positioned *in situ* and is associated with adverse tissue reactions, or has obvious high wear/damage, then every effort should be made to estimate the total volumetric wear from the explanted components. A suggested technique includes a three-dimensional coordinate measuring machine (CMM) to measure

changes in component radius of curvature of both worn and unworn surfaces. Estimations of volumetric wear can then be determined using 3D modeling software.

- Surface roughness measurements of damaged and undamaged Co-Cr-Mo surfaces, including at least: average roughness (Ra or Sa), surface texture (Rz or Sz), maximum scratch height (Rp or Sp) and skewness (Rsk or Ssk), plus be accompanied by close-up photographs for each measurement site to provide a visual indication of the amount of wear that took place and what wear processes were involved

- Scanning electron microscopy to examine microstructural features such as topography, carbide morphology, grain structure (if visible), along with EDS to determine surface chemistry , for both the bearing surfaces and the taper junction. The analysis should include investigation of any material transfer, embedded debris or corrosion product on the surfaces.