Validation of biomedical coatings

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Established in 1989, Medical Group presently has five subsidiary companies specialising in the biomedical field: Medical Coating, Medical Packaging, Medical Biomat, Medical Manufacturing and Medical Lab. All of these organisations are EN ISO 13485 certified.

Medical Lab offers a comprehensive Performance Qualification service for medical devices: coating, cleaning, packaging and sterilisation validations. The purpose of these qualifications is to assure clients that their medical devices comply with European (EC) and US (FDA) regulations.

**THE COATINGS**

There are various process methods for applying coatings to implants:
- Porous coating by bead sintering
- Creation of a surface 3D structure composed of wire
- Plasma spraying
- Surface macro-roughness by spark-erosion or machining

The various types of coatings resulting from these processes are:
- metallic (titanium – chrome cobalt)
- ceramic (hydroxyapatite – aluminium).

The choice of couple process / coating to apply to an implant depends on the final characteristics of the desired coating.
STANDARDS AND REGULATIONS

MEDICAL LAB, within the framework of its coating validation services, follows the guidelines below:


Guideline HAP: 510(k) Information needed for Hydroxyapatite coated orthopedic implants (February 20, 1997)

Guideline FDA HA Solubility products Ksp: 510(k) Information needed for Hydroxyapatite coated orthopaedic implants

ASTM A 967: Standard Specification for Chemical Passivation Treatments for Stainless Steel Parts


ASTM F1160: Standard Test Method for Shear and Bending Fatigue Testing of Calcium Phosphate and Metallic Medical and Composite Calcium Phosphate.

ASTM F 1609: Standard Specification for Calcium Phosphate Coatings for Implantable Materials


ISO 7206-4: Implants for surgery - Partial and total hip joint prostheses – Part 4: Determination of endurance properties of stemmed femoral components

ISO 7206-6: Implants for surgery - Partial and total hip joint prostheses – Part 6: Determination of endurance properties of head and neck region of stemmed femoral components

ISO 13779-2: surgical implants - Hydroxyapatite part 2 : hydroxyapatite-based coatings

ISO 13779-3: Implants for surgery - Hydroxyapatite - Part 3: Chemical analysis and characterization of crystallinity and phase purity

ISO 13779-4: Implants for surgery - Hydroxyapatite - Part 4: Determination of coating adhesion strength
THE VARIOUS TYPES OF TESTS

1. Mechanical tests: Static tensile strength testing

   The aim of this test is to assess the tensile adhesive strength of coating layer to the substrate. Coated tests specimens 25 mm in diameter are linked to uncoated coupons with a FM1000 or 3M-2214 structural adhesive. A tensile stress is applied to separate the coating and the substrate. The maximum tensile adhesive stress is recorded. Usually, this test is performed on at least five coated coupons.

2. Mechanical tests: Static shear strength testing

   The aim of this test is to assess the shear adhesive strength of coating layer to the substrate. Coated tests specimens 19 mm in diameter are linked to uncoated coupons with a FM1000 or 3M-2214 structural adhesive. A shear stress is applied to separate the coating and the substrate. The maximum shear adhesive stress is recorded. Usually, this test is performed on at least five coated coupons.

3. Mechanical tests: Shear Fatigue Testing

   The aim of this test is to assess the fatigue shear adhesive strength of coating layer to the substrate. Coated tests specimens 19 mm in diameter are linked to uncoated coupons with a FM1000 or 3M-2214 structural adhesive. A fatigue shear stress is applied to separate the coating and the substrate. Test is stopped at 10 million cycles or after the testing specimen failure. Usually, this test is performed on at least five coated coupons.

4. Mechanical tests: Bending Fatigue Testing

   Realization of a coating on a substrate can impair the strength of the substrate. The aim of this test is to assess the bending fatigue strength of the substrate covered with the coating in comparison to the uncoated substrate. Test on specimen is stopped at 10 million cycles or after the testing specimen failure with a bending testing machine. Usually, this test is performed on at least five coated coupons.

5. Mechanical tests: abrasion

   The aim of this test is to assess the abrasion resistance of the coating layer. A coating disc, 100 mm in diameter is abraded in a 5151 TABER abraser tester with an H-22 wheel during 100 cycles. The weight loss of the specimen is recorded after 2, 5, 10 and 100 cycles. This test is performed on at least 6 coated coupons plus 1 coated reference coupon.
6. **Physicals tests: thickness / porosity / roughness / pores sizes**  

The aim of this test is to assess the thickness, porosity, roughness and pore size of the coatings. A metallographic cut is done on a coated sample. After cutting and polishing, the cut is analysed by a numerical camera coupled with an optical microscope. This test is to be done on real implants for coating process performance qualification (PQ) on product.

7. **Chemicals tests: chemical composition (ICP)**  

The aim of this test is to assess the chemical elements content in the HA powder and coating. The analysis is performed by ICP/SEA emission spectrometry machine. If required, other methods can be used according to the nature of the material analysed and chemical elements to be assessed.

8. **Chemicals tests: XRD**  
*Reference standard: ISO 13779-3: Surgical implants - Hydroxyapatite – chemical analysis and characterisation of the crystallinity and purity phase*

The aim of this test is to assess the XRD composition of the HA powder and coating. This method gives access to crystalline phases content, crystallinity, Ca/P ratio and estimation of crystallite size by Scherrer method.

9. **Chemicals tests: IR**  
*Reference standard: FDA Guidelines and ISO 13779-3: Surgical implants - Hydroxyapatite – chemical analysis and characterisation of the crystallinity and purity phase*

The aim of this test is to assess the FTIR composition of the HA powder and coating. According to the wavelength, the functional groups of Hydroxyapatite and possible impurities can be detected and interpreted.

10. **Chemicals tests: Helium density**  
*Reference standard: Guidelines FDA*

The aim of this test is to assess the density of the fully dense HA powder and coating. The results are done with a Helium pycnometer.

11. **Chemicals tests: dissolution**  

The aim of this test is to assess the dissolution rate of the HA powder and coating. At the different sampling intervals, the pH and the quantity of Ca element are measured. Initial and final dissolution rates are analysed. The standard describes the possibility to do the test on coated coupons. For FDA, the test shall be done on particles scraped from the coating.

12. **Chemicals tests: corrosion**  
*Reference standard: ASTM A 967: Standard Specification for Chemical Passivation Treatments for Stainless Steel Parts*

Even if medical grade metals resist to corrosion, different parameters can impair their inertness: local heating during the manufacturing of the implant or coating, association of dissimilar materials for the substrate and the coating, lack of homogeneity of the raw material batch, etc... The aim of this test is to assess the corrosion of the implant. Different methods are described by the standard: immersion test, ferritic test... he most appropriate method has to be chosen according to the nature of the metal to assess.
IQ, OQ and PQ VALIDATION

In order to guarantee reproducibility of the coatings on implants, the coating production processes shall be IQ, OQ and PQ validated. Two sets of standards can be taken in reference:


The WHO guide relating to standards of good manufacturing practices (GMP) (WHO/VSQ/97.02, Part 2: Validation, 1997)

Installation Qualification (IQ)
Tests and checks are performed on the processes installed to verify that they comply with previously established specifications. When the process is subcontracted, this part of the process is the responsibility of the coating service provider.

Operational Qualification (OQ)
After setting the standard adjustment parameters for obtaining a sample result meeting the specifications, the OQ enables validation of these standard parameters, even when the process is carried out under degraded conditions (validation of adjustment parameters and critical cases). When the process is subcontracted, this part of the process is the responsibility of the coating service provider.

Performance Qualification (PQ)
This serves to demonstrate that the system yields a reproducible, correct result on the product. The PQ is therefore conducted in two phases:

Process PQ: when the process is subcontracted, this test is carried out by the coating service provider. This establishes the long-term reproducibility of the process. It is conducted on coupons.

Product PQ: even if the process is subcontracted, this part of the validation is carried out under the supervision of the product manufacturer. This establishes compliance of the process result on the product (usually by performing sections of the coating on the product).

PQ VALIDATION OF COATINGS ON PRODUCTS

In order to compile one's coating validation dossier, it is first necessary to consider the guidelines used in countries where implants are sold, as the tests asked for in the validation dossiers are not necessarily the same.

Once the guidelines or the target market has been identified, the tests to be conducted in order to compile one's coating validation dossier are identified.

Next, it is necessary to find out from one's coating service provider which tests he has conducted or routinely conducts, and under what conditions (of thickness and of substrate). By using the information collected above, one can begin compiling the coating validation dossier. All that remain to complete this coating validation dossier are the missing tests which must be conducted in a laboratory on the implant.
Here are examples of several possible cases to illustrate the above comments:

1. The coating service provider has a coating validation dossier, a process performance qualification and the characteristics of thickness and of substrate tested are consistent with those of the coated implants;
   In this case, only the test for thickness on the coated implants is to be conducted. This verification of thickness on the implant is necessary since, depending on the geometry of the implants (stems, cups, condyles, etc.), shadowing or discrepancies in the coating might occur during the coating application procedure.

2. The coating service provider has a coating validation dossier, a process performance qualification and the characteristics of thickness and of substrate tested are not consistent with those of the coated implants;
   In this case, all of the tests involving thicknesses / substrate (for e.g. mechanical strength of the coating: tensile, shear, fatigue...) are to be conducted or a rational shall be constructed to explain why the substrate and coating thickness will not have influence on the results (according to the regulatory institutions and countries, this rational is not always accepted).

3. The coating service provider does not have a coating validation dossier but conducts a process performance qualification and the characteristics of thickness and of substrate tested are consistent with those of the coated implants;
   In this case, the routine tests conducted by the coating service provider must be retrieved and completed along with the other tests required by the validation dossier.
DESIGN: QUESTIONS TO ASK

- Is a coating validation dossier required in the country where my products are sold?
- What are the guidelines for the countries where my products are sold?
- What is the list of required tests for my coating validation dossier?
- Can I forego the tests to be conducted and rely on the experience of my coating service provider?
- Does my coating service provider have a coating validation dossier which I can draw on to compile my coating validation dossier?
- Does my coating service provider have a process performance qualification on which I can draw?
- After I have got back the tests from my coating service provider, what list of tests should I conduct?
- What are my implant categories (groupings based on substrates, thickness, type of coating, geometry of the pieces)?
- What sample size should I choose for my coating validation (all sizes / minimum or maximum size / critical sizes)?
REASONS FOR CHOOSING MEDICAL GROUP

- We offer customised solutions to meet your requirements. We work with majors as well as star-up companies.
- Coating used on over 1.5 million implants worldwide.
- Over 20 years’ experience.
- Operations in 30 countries spread over 5 continents.
- Unrivalled responsiveness.
- Quality of the highest standard.
- A full service partner.
- A multilingual sales team (English, German, Italian, Spanish, Arabic, Chinese...).
- Our experts can assist you with your regulatory processes.
- ISO 13485:2003 certified.
- Our collaborative interaction helps you limit your suppliers, save time in having your batches released and reduce your transport costs.
- A highly qualified technical team that is very knowledgeable about French, European and US regulatory requirements.
- We work with medical device manufacturers in various fields such as orthopaedic, dental, spinal, biomaterials, single and multi-use instrumentation.
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