# Characterization and Extrusion Qualification Process of Introducers/Dilators at Edwards Lifesciences Puerto Rico

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## Abstract

Edwards Lifesciences is experiencing a high demand for Introducers/Dilators. The company decided to produce the Introducers/Dilators single lumen catheters shafts tubing in Añasco, Puerto Rico site. To implement this new production, a qualification process needed to be conducted, involving characterization study to demonstrate equivalency of the material used for component, as well as the qualification of an extrusion process for the catheter's shafts tubing at Puerto Rico. After several iterations, the study of the material demonstrated the equivalence for its use. Also, as results the new extrusion process was achieved to sustain demand.

## Introduction

Edwards Lifesciences is a global company focused on medical innovations centered on structural heart disease, as well as critical care and surgical monitoring. The component is single lumen shaft tubing designed to be used to access blood vessels for the insertion of vascular catheters. The sheath Introducer set comes with a Hydrophilic coating designed for ease used of insertion, and for low profile access in cardiac surgery interventions. The main purpose of is design is to allow space to replace a diseased aortic valve with an artificial valve in the heart. This component acts to stretch the opening in the skin and blood vessel allowing the insertion of the sheath, then is removed, leaving only the sheath inserted, providing a port through to insert the catheter. They are made from a specific resin material that is composed of LDPE DOW 722 (59%), HDPE DOW 8907 (20%), BaSO 4 (20%) and TiO 2 (1%). This shaft tubing come in different French sizes, and they are identified in the hub located at the proximal area for easy identification.

The company is currently experiencing a high demand of the Introducers/Dilators. The company decided to expand the component's production of the Introducers/Dilators. The shafts tubing, which was previously bought from a third party supplier, will now be produced at Edward's site in Añasco, Puerto Rico. This new solution will help not only to produce more units to meet demand, but also to avoid buying the component from the external suppliers. The objective of this project is to present the strategy of design, development and delivery of one of the main components of the sheath Introducer set, at the same time qualified the extrusion manufacturing process to produce the single lumen catheters shafts tubing in a clean room.

## Methodology

The process was to perform a characterization study to demonstrate the equivalency of a material already qualified by an external supplier. A feasibility study was conducted with objective evidence and summarized all results of consistency in the material tested and documented the achieve results in a feasibility report. After the completion, the material was challenged in the extrusion process at the window operation limit settings for critical parameters to meet pre-determined requirements per drawings critical dimension and following ISO standards regulations [1]. The results were satisfactory, and the extrusion parameters were also documented OQ/PQ report [2].

## Methodology

### Material Qualification

To demonstrate the equivalency of the resin material used to produce the Introducers/Dilators single lumen catheters shafts tubing, conduct a feasibility study to summaries the objective evidence. The material Characterization study tests to be conducted are mentioned in following Figure 1.

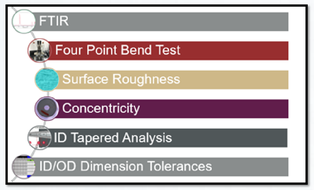


**Figure 1 Characterization Study Tests**

The FTIR test, is an infrared scan test technique used to identify by light the chemical properties of the material [3]. The Four Point Bend test, is used to measure the force required to bend a material. The Surface Roughness test used to indicate the level of surface finish of the component [4]. The concentricity test, is conducted performing a cross-section of the shaft tube, compare between wall tubing thickness minor wall and maximum wall, to calculate the actual level of concentricity [5]. The ID Tapered analysis, is performed by cutting the shaft tubing to different lengths in the formed tip area and inspect the inside diameter [5]. The ID/OD Dimension Tolerances, is performed by measuring dimension to and verified that are within the limit's specification as per drawing requirements [6].

### Qualification of the Extrusion Process

Perform an Operational Qualification (OQ) extrusion process challenge, at the extrusion machine using operating window limit settings range, under worst case conditions and provide objective evidence that the process produces acceptable product. After the completion of the OQ qualification, the last phase of the validation process required to conduct a Performance Qualification (PQ) extrusion process, running an operational production process at normal operating paraments and provide objective evidence that the process produces acceptable product under normal operating conditions. After having obtained satisfactory results of the Performance Qualification (PQ), the approval of OQ/PQ report was completed along with disposition of the material.

## Results and Discussion

The tests results obtained in the Material Characterization Study demonstrate the equivalency.

**FTIR:** The resin material and the data points comparison between sample and reference spectra matches by 99.72%, this is considered similar actual resin versus the actual shaft tube.

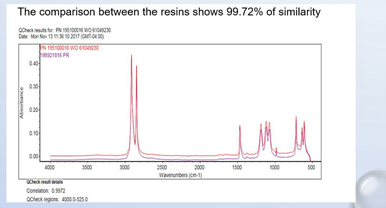


**Figure 2 FTIR**

## Results and Discussion

**Four Point Bend Test:** The results show than current shaft tube product is between the results obtained when challenging de validated parameters at low and high, therefore, the new extruded shaft tube will not represent a risk to the patient.

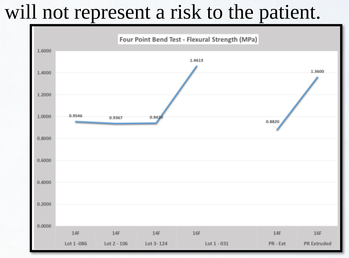


**Figure 3 Characterization Study Tests**

**Concentricity:** After inspected the dimension the concentricity was calculated for the shaft tubing per diameters. As the inside became narrower, the inside diameter became less centered. The bore began to become off-center at approximately 2.00" from the tip. Base on the circular symmetry it was established to set a tolerance for OD and ID.

**Surface Roughness:** Based on the results of Table 1, the extruded shafts are considered more rough than current shaft. Since the parts past through a coating process with a hydrophilic solution, this should help the part to mitigate the lack of solution and help in the bonding in the tube surface, therefore new extruded shaft compares satisfactory to current.

**Table 1 Surface Roughness result**

| 22F current | 22F Low | 22F High |
|---|---|---|
| 0.5177 | 0.3644 | 0.3693 |

**ID/OD Dimension Tolerance:** As results in Table 2, the samples from the extruded tubing show to met the product specification limits (LSL and USL) per drawing.

**Table 2 Dimension Results**

| | Introducer 14F | | Introducer 16F | | Introducer 18F | | Introducer 20F | |
|---|---|---|---|---|---|---|---|---|
| No. | OD | ID | OD | ID | OD | ID | OD | ID |
| 1 | 0.064 | 0.037 | 0.065 | 0.037 | 0.066 | 0.039 | 0.064 | 0.040 |
| 2 | 0.063 | 0.037 | 0.065 | 0.038 | 0.066 | 0.039 | 0.062 | 0.040 |
| 3 | 0.065 | 0.037 | 0.065 | 0.039 | 0.065 | 0.037 | 0.065 | 0.039 |
| 4 | 0.065 | 0.038 | 0.065 | 0.039 | 0.066 | 0.038 | 0.065 | 0.040 |
| 5 | 0.065 | 0.037 | 0.063 | 0.037 | 0.065 | 0.037 | 0.065 | 0.039 |
| | Dilator 22F | | Dilator 16F | | Dilator 18F | | Dilator 20F | |
| No. | OD | ID | OD | ID | OD | ID | OD | ID |
| 1 | 0.062 | 0.040 | 0.064 | 0.039 | 0.067 | 0.037 | 0.064 | 0.038 |
| 2 | 0.066 | 0.039 | 0.065 | 0.039 | 0.065 | 0.038 | 0.066 | 0.039 |
| 3 | 0.065 | 0.039 | 0.065 | 0.039 | 0.065 | 0.039 | 0.065 | 0.039 |
| 4 | 0.067 | 0.040 | 0.064 | 0.039 | 0.066 | 0.039 | 0.064 | 0.039 |
| 5 | 0.065 | 0.039 | 0.065 | 0.037 | 0.065 | 0.037 | 0.065 | 0.039 |
| OD Spec. | 0.065±.005) | | | | | | | |
| ID Spec. | 0.039±.002) | | | | | | | |

In Table 3 are the process at the window limit pre-stablished process parameters.

**Table 3 Operational extrusion process parameters**

| PROCESS PARAMETER | Process Range: | Run (Low) | Run (High) |
|---|---|---|---|
| Barrel Zone #1 (°F) | 365-370 | 360 | 375 |
| Barrel Zone #2 (°F) | 365-370 | 360 | 375 |
| Barrel Zone #3 (°F) | 375-380 | 370 | 385 |
| Hd/Clmp Zone #4 (°F) | 375-380 | 370 | 385 |
| Die Zone #1 (°F) | 375-380 | 370 | 385 |
| Die Zone #2 (°F) | 365-370 | 360 | 375 |
| Line Speed (ft/m in) | 31.5 – 47.5 | 30 | 50 |

As results in Table 4, the OD was measured, and it was successfully produced within the parameter window limits for extrusion process. As continued build plant for PQ, the Extrusion process also conducted at the nominal settings to demonstrates that the manufacturing process can produce a consistent for extrusion process. As show in Table 5 the results were successfully satisfactory.

## Results and Discussion

**Table 4 OQ Dimension Results**

| Test | 63812295 (18F) Low | | | | Result |
|---|---|---|---|---|---|
| | Mean | STDEV | LTL | UTL | |
| OD | 0.063 | 0.001 | 0.062 | 0.064 | Pass |
| ID | 0.039 | 0.001 | 0.038 | 0.040 | Pass |
| | 63812297 (18F) High | | | | |
| | Mean | STDEV | LTL | UTL | |
| OD | 0.062 | 0.000 | 0.062 | 0.063 | Pass |
| ID | 0.038 | 0.000 | 0.038 | 0.039 | Pass |
| | 63812299 (20F) Low | | | | |
| | Mean | STDEV | LTL | UTL | |
| OD | 0.063 | 0.001 | 0.062 | 0.064 | Pass |
| ID | 0.039 | 0.001 | 0.038 | 0.040 | Pass |
| | 63812298 (20F) High | | | | |
| | Mean | STDEV | LTL | UTL | |
| OD | 0.063 | 0.001 | 0.062 | 0.064 | Pass |
| ID | 0.040 | 0.002 | 0.038 | 0.041 | Pass |

**Table 5 PQ Dimension Results**

| Test | 63813717 (18F) Nominal | | | | Result |
|---|---|---|---|---|---|
| | Mean | STDEV | LTL | UTL | |
| OD | 0.063 | 0.001 | 0.062 | 0.064 | Pass |
| ID | 0.039 | 0.000 | 0.038 | 0.039 | Pass |
| | 63813718 (20F) Nominal | | | | |
| | Mean | STDEV | LTL | UTL | |
| OD | 0.064 | 0.000 | 0.063 | 0.065 | Pass |
| ID | 0.039 | 0.000 | 0.039 | 0.040 | Pass |

## Conclusion

The objective of this paper was achieved by presenting that the extrusion runs do not show any material degradation and Qualification of the manufacturing process for the Introducers/Dilators was achieved with no limitation and following the regulatory GMP, GxP's guidelines and regulations, and standard operating procedures for qualification process and sustain demand for next year. After the completion of this qualification is necessary to continued monitoring the process to avoid any implication or influences that might arise in the future.

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