

COLLIN® Medical and Pharmaceutical Technology



FDA-compliant lines provide the highest production standard
Full support for qualification and validation according to FDA

Single-Screw Extruders

Types: ME 16, ME 20, ME 25, ME 30, ME 45

Length of processing unit is 25:1 L/D or 30:1 L/D. Barrier screws are available for 30 mm and 45 mm screw diameters. The barrels are water-cooled as are the asynchronous servo drives. These extruder series cover a wide range of throughputs from 0.05 kg/h to 45 kg/h.

The control system is microprocessor-based with an LCD display as user interface. For fast and safe data access, a data wheel is included. Touch screen is available as an option.

A melt pump can be integrated into the control system.

The ability to adjust the height and angle of the extruder's axis permits easy adjustment and good access for cleaning.



Twin-Screw Compounders

Types: MZK 12, MZK 16, MZK 25, MZK 35

All machines can be changed easily from co-rotating to counter-rotating. For fast and easy cleaning, all barrel elements are designed with a C-clamp and are water-cooled.

The machines cover a wide range of throughputs from 0.05 kg/h to 70 kg/h.

The control system is similar to that of the single-screw extruders.

A melt pump can be integrated in the control system.

High-precision gravimetric dosing systems are available in each configuration.



Catheter Tubes

*Mono- and multilayer tubes
Mono- and multi lumen tubes*



Various types of extruders between ME16 and ME30 provide a throughput range from 0.05 kg/h up to 15 kg/h. The modular design of the line components assures high flexibility in production. The product range consists of coating wires, mono-layer, multilayer, mono-lumen, multi-lumen catheters.



The materials used are polyolefins and polyurethanes, flexible PVC and polyamides. The line covers the diameter range between 0.5 mm

and 5 mm at a maximum line speed of 100 m/min. Diameter-controlled haul-off speed provides tight diameter tolerances.

Infusion Bags

For the production of 3, 5 or 7 layer water cooled blown film for infusions bags and secondary packaging



Vertical extrusion into a water cooling ring provides optimum film transparency. The new spiral distribution die



provides accurate thickness distribution. The maximum lay-flat width is 530 mm. Throughput is up to 100 kg/h.

All modular components such as extruders, coextrusion dies, haul-off, winders and data acquisition are fine tuned for perfect operation.

Pills Forming

Calenders for continuous production of drug loaded polymers



Calender Types: PK 110 and PK 200

These machines are based on the COLLIN® measuring roll mills, which are well-established in the R&D departments of polymer material producers around the world for more than thirty years. Rigid machine construction and true-running rolls provide the basis for maximum machine accuracy.

The calenders are designed for nip forces up to 10 t. Automatic nip width adjustment and nip width control ensure precisely formed pills. Nip forces and torques are measured and reported for quality assurance. When combined with a compounder from the MZK series, melt pump, flat film die and cooling belt, a complete

pill production line can be established. A touch screen system controls the process and gives a wide range of parameters for filing, evaluation and reporting.

Pelletizing Lines

For the production of Pellets of drug loaded polymers for further extrusion and injection moulding.

The **MZK 16**, **MZK 25** and **MZK 35** compounders can be converted into production pelletizing lines when combined with a melt pump, strand die, cooling belt and pelletizer.

Mono-, dual- and triple-strand dies are available.

High-precision gravimetric dosing stations ensure a dosing accuracy of $\pm 1\%$. The throughput range is from 0.15 kg/h to 70 kg/h.

Different types of cooling belts provide the best cooling capacity for each throughput and strand type.

Available belt cooling:

- Natural convection and roll systems for compact extension of the cooling length.
- Additional air cooling directly on the strand combined with recooling of the belt by cold water.



High-Precision Strands

For the production of drug loaded strands for subcutaneous implants.

The extruders are equipped with melt pumps and pressure / speed control for accurate throughput of the line.

Through use of a multi-layer die, the strand is extruded directly into a water bath vertically. This process eliminates any influence of a calibration system and gravity guarantees the high precision in diameter and ovalness.

Controlled water flow ensures an absolutely calm water surface at product entry into the cooling vessel. The diameter range is between 1 mm to 10 mm at a maximum line speed of 25 m/min.

The touch screen control system is ergonomically designed and files all process and quality parameters.

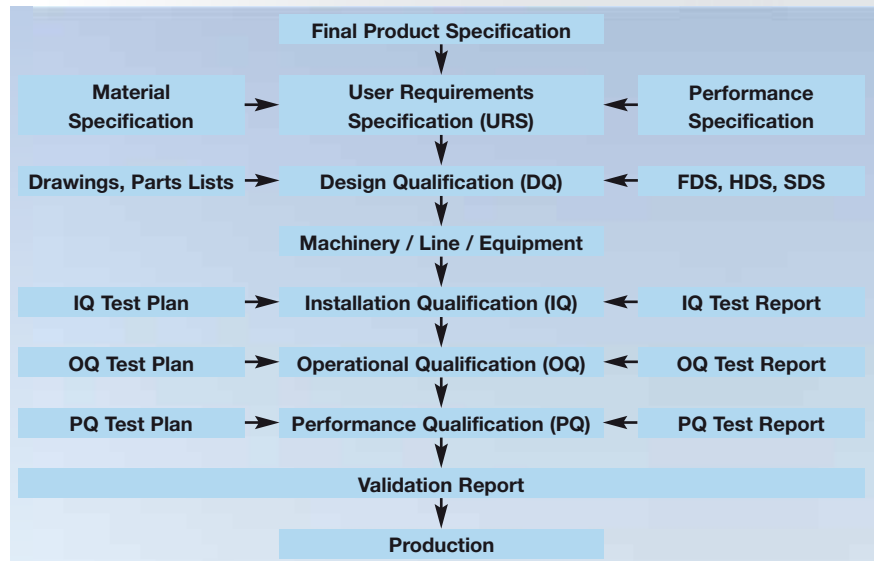


Validation Master Plan

COLLIN® has a well-trained and experienced team to give full support to fulfill all FDA requirements during

- Design
- Production and installation of the equipment
- Qualification and validation
- Documentation

The team follows the Validation Master Plan, which is tailored individually to the current project, strictly.



ISO 9001 and Design Rules

The quality management system of COLLIN® guarantees that all processes in all phases of machine design/construction are documented and controlled properly.

The basic rules outlined in 21 CFR, Part 11 are observed when designing proper FDA software.

Instructions for the mechanical and electrical design ensure that all FDA requirements concerning

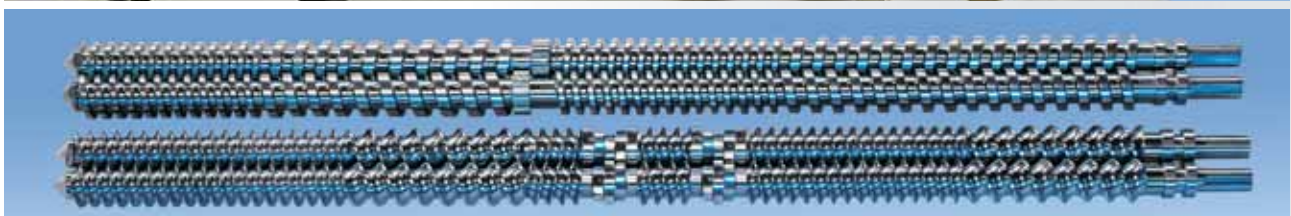
- Materials
 - Surface shapes
 - Surface treatments
 - Electrical components
 - Wiring
 - Heating and cooling systems
- are satisfied completely.

Every detail of a COLLIN® line is designed to provide easy and fast access for cleaning and maintenance.



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Pharmaceutical and Food Compounding Technology



Drug loading of polymers, waxes and cellulose
Pellets for pills production
FDA-compliant lines provide the highest production standard
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Food Plant Twin-Screw Compounder ZK 35

Compounder

This production machine is designed for a throughput range between 10 and 70 kg/h. The diameter of the screw is 35 mm and the length can be varied for up to 56:1 L/D.

For fast and easy cleaning of the screw and the barrel, the machine base is divided into a drive section and a processing section. Both can be separated by a motor drive, making the screw accessible for work.



Feeding systems

A wide variety on feeding systems is possible. For low accuracy, volumetric systems are sufficient. Higher accuracy requires use of gravimetric systems in any combination of gravimetric feeders for liquids and solids at any position on the machine.

The image at the lower left shows an example with 4 solid feeders and 3 liquid feeders.



Pharma Twin-Screw Extruders MZK 25 and MZK 35

Extrusion in pharmaceutical processes

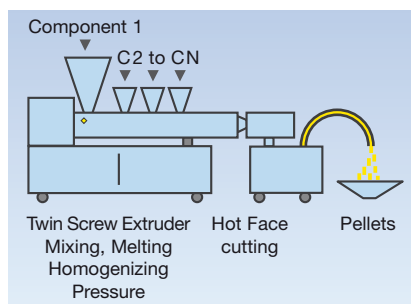
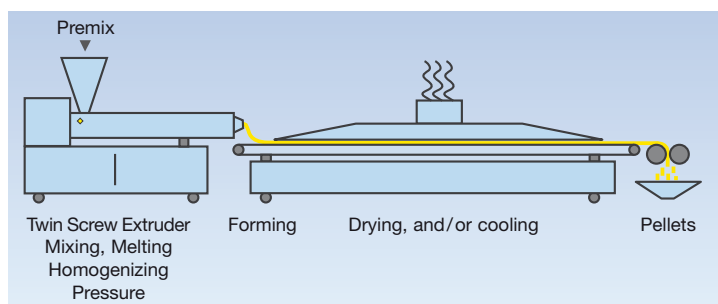
The extrusion process is appropriate to

- Drug incorporation into vehicle materials like Waxes, cellulose, starch, polymers
- Degassing of volatile parts in the recipe
- Pelletizing of premixes for pills
- Continuous forming of pills
- Pelletizing of materials for further extrusion and injection molding processes



Two main types of processes

- Wet extrusion
 - Solid powders are mixed into liquids
 - After forming the product has to be dried
- Melt extrusion
 - The components of the recipe are incorporated into the melted vehicle material
 - After forming the material is cooled down



Benefits of the extrusion

- Optimal Homogenization
- Wide range of process temperatures (RT to 300°C)
- Accurate temperature control in each heating zone
- Short residence times in each processing unit
- Short times for production changes
- Self cleaning twin screws
- Steady-state, continuous process
- Reliable process with maximum reproducibility of the quality



Basic Design Elements

Barrel

The barrel is formed from individual segments with different designs. The positioning of each barrel segment on a single slide and the C-clamp connection permit fast and easy dismantling and cleaning. They can be removed easily to put them into a washer. All parts in contact with the product are made of FDA-approved stainless steels. Each element is water-cooled, which makes them suitable for clean room production. As an option, motordriven axial movement of the barrel is available. This makes product changes and cleaning procedures even faster and simpler.



Screws

The heart of every extruder is the screw, because its geometry defines the process behavior and the quality of the final product. Co-rotating twin screws are segmented, as is the barrel. The screw segments are arranged on a shaft. A wide variety of geometries permits the screw geometry to be adapted to individual process requirements by rearranging the segments. The screw kits include tightly intermeshing or open profiles, single- and double-flighted mixing and shearing elements.



Basic Design Elements

GMP design

All surfaces are made of precision-ground stainless steel or painted with a clean room - accredited color. They are resistant to all commonly used sanitizing agents.

The shape of each surface and design details are made with consideration of cleaning validation. All outer machine covers can be removed quickly and easily by hand.

Drive unit

The MZK 25 is driven by an AC synchronous motor with closed-loop speed control. Power is transferred via a bevel gear to the distributor gear. This is designed for high torque and back pressure.

The power components and the main switch are combined in a separate control cabinet, which forms the machine base.

Downstream

The standard downstream equipment consists of a cooling belt and pelletizer.

Different types of cooling belts provide the best cooling capacity for each throughput and strand type.

Available belt cooling:

- Natural convection and roll systems for compact extension of the cooling length.
- Additional air cooling directly on the strand in conjunction with recooling of the belt by cold water

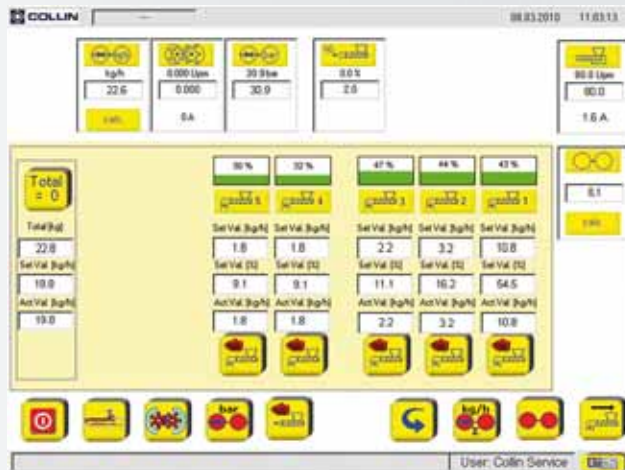
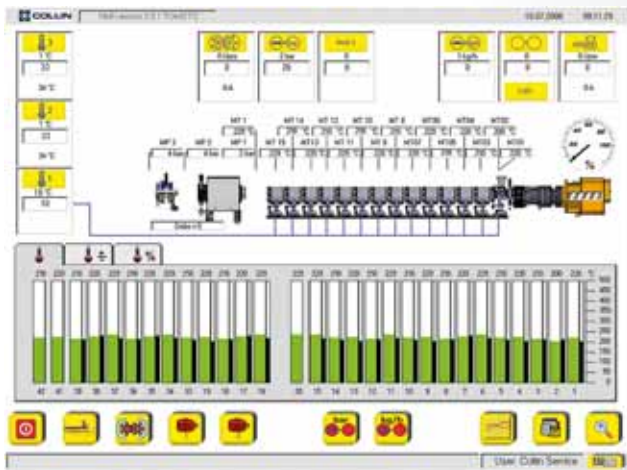


Control system

It consists of a human-engineered touch screen for the gravimetric system and the extruder integrated into one control panel. Self-explanatory graphs provide all parameters (actual and set values) of the machine.

Recipe management of each individual component ensures the high reproducibility of production.

The basic rules outlined in 21 CFR, Part 11 are observed when designing proper FDA software.

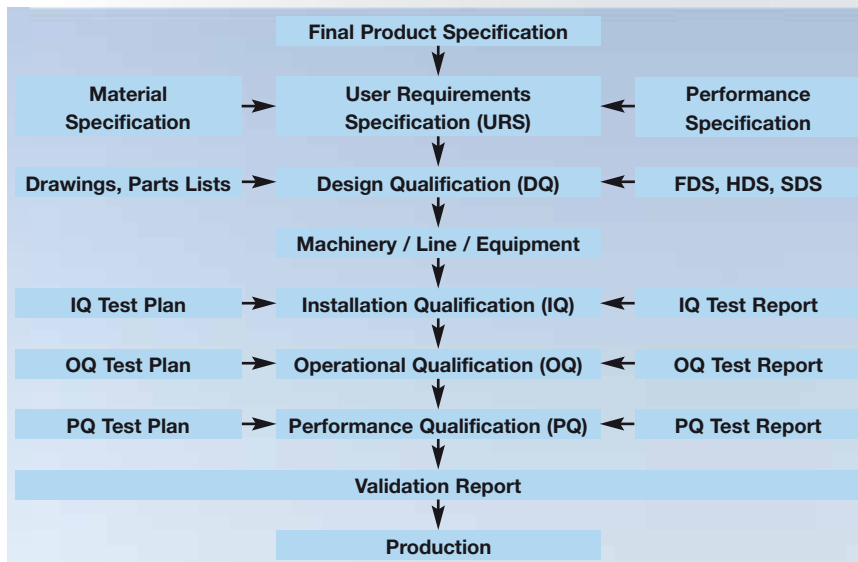


Good Manufacturing Practice (GMP)

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Extrusion lines for catheter tubing

High-precision lines for the production of medical tubing



Mono-layer and multi-layer tubes
Mono-lumen and multi-lumen tubes
Extrusion with supporting wire

Extrusion lines for medical catheters

Areas of application

Catheter tubing is used for a variety of medical applications. The tubes vary in diameter, wall thickness, polymer material or layer thickness. Most of these varieties require highly flexible production lines.

The lines have the following properties:

- very small diameters of 0.5 to 5 mm
- low wall thickness (0.07 to 0.5 mm)
- extremely narrow tolerances
- mono-layer, double-layer or three-layer structure

- take-off speed of up to 100 m/min.
- fast product change-over
- all line components comply with clean-room standards
- central control with acquisition, documentation and validation of all process data

Main components of a catheter extrusion line

Extruder

A finely-tuned range of extruders of 16, 20, 25, 30, 45 mm diameter covers the required wide throughput range from 0.05 up to 10 kg/h. High-precision screw speed control and a highly constant temperature control ensure reproducible quality and a continuous throughput. The processing of a wide range of polymers is optimized with the use of exchangeable feed bushings.

Melt pumps

The use of melt pumps ensures extreme low throughput variations and therefore exact diameters and smallest wall thickness variations.

Gravimetric feeding

Gravimetric feeding is a proven tool for ensuring control, precise setting and documentation of the layer thickness ratios.

Dies

The die design is of crucial importance for the quality of both mono-layer and multi-layer tubings. Characteristics such as

- bypass lines for fast purging,
- short flow length,
- prevention of dead spots,
- possibility to adjust the consistency of individual layers, even at a 2 or 3-layer coextrusion die,
- improved control for homogeneous temperature level

are the main features of a die designed for very narrow diameters and layer thickness tolerances.

Vacuum calibration and cooling

High-quality vacuum calibration promotes high-precision tube diameters.



Melt pumps with multi-layer die



View of an open calibration tank

EXTRUSION LINES FOR CATHETER TUBING

Constant and reproducible production conditions are possible through:

- Control of the water flow in the calibration and the cooling tank,
- Control of the temperature of the water in the calibration, even with heating,
- Air knife to blow off the water, prior to measuring the diameter.
- Closed loop control of the vacuum, by measuring the diameter,
- Closed loop control of take-off speed,
- Closed loop control of pressure and circulating volume of the supporting air.

In addition, the tanks have generous dimensions to allow for easy and safe feeding of the tube. The tanks are fitted with transparent lids to permit visual checks throughout the process.

Diameter control

A laser gauge measures the diameter of the tube in two places each offset at 90°.



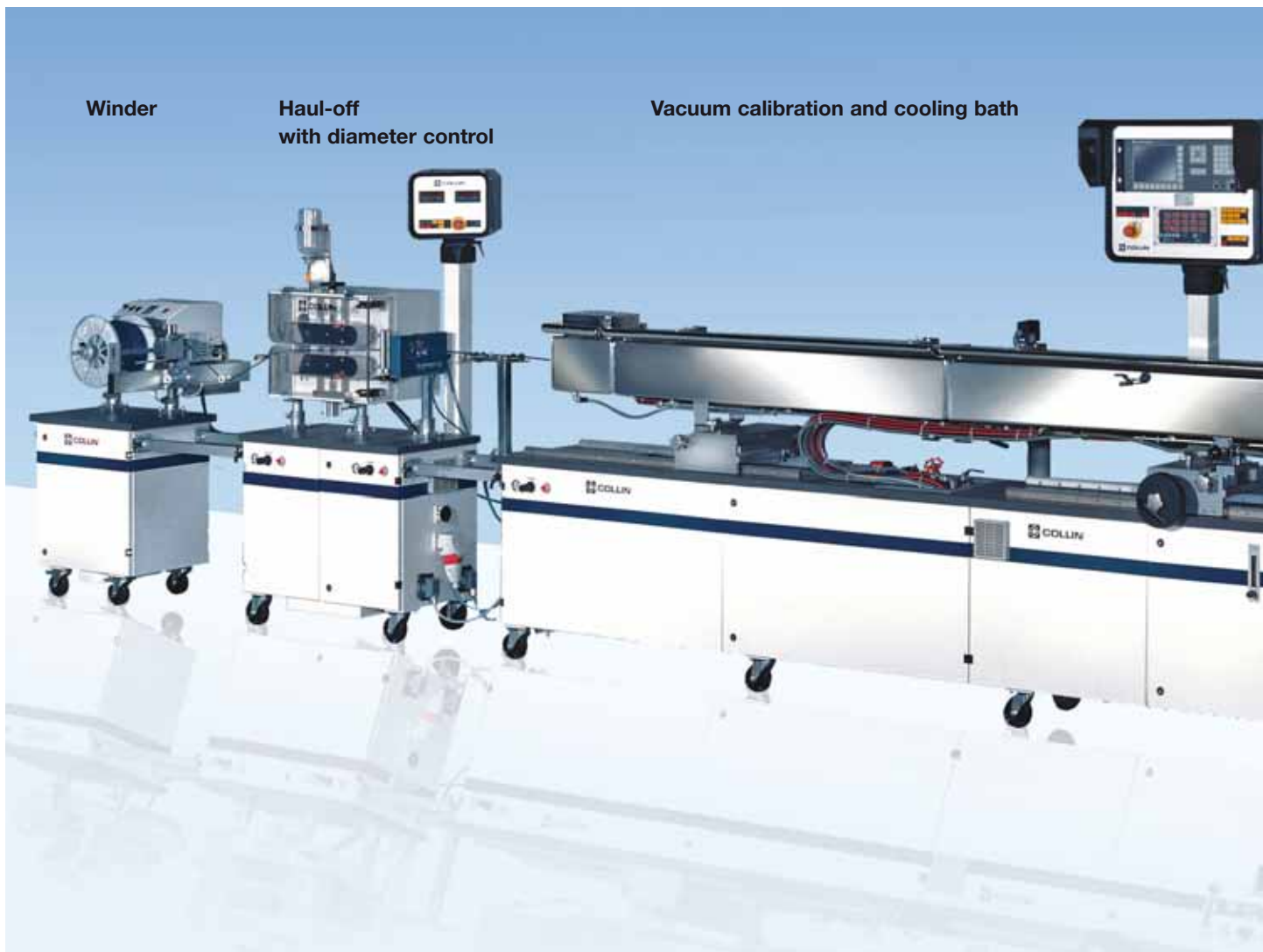
The acquired diameter and ovality values are registered and logged. In addition to this, an ultrasonic wall thickness gauge can be used for efficient die gap adjustment and wall thickness optimization.

Haul-offs

Both belts of the double-belt haul-off are operated by synchronized AC-drives to ensure a highly consistent take-off speed and therefore consistency of tube diameter and wall thickness.

Winders

After haul-off, the tubes are either wound or cut off. Winding is best carried out by central winders with a balance roller system for fine adjustment of the tension. By a fine-adjustable traversing system, an exact positioned cross-winding of the tubes is guaranteed.



From polymers to healthcare

Winder



Cutting units

Alternatively, cutting systems provide the following:

- a.) high cutting frequency to allow high-speed cutting of short tube length.
- b.) selection between good parts and rejects (controlled by the thickness gauge) and assortment of quality classes.

Unwinder for supporting wire

For certain tubing, extrusion onto a wire is a well tried and tested method for ensuring a high-precision inner diameter. Suitable tension-controlled unwinding systems with straighteners are available.

Preheating systems

Extrusion coating to manufacture so-called braided tubing, i.e. cover wire supporting fabrics, require a preheating achievable with a hot air oven.

Process control with protocolling

Besides sophisticated mechanical equipment and controls, this type of line requires a state of the art data

acquisition and evaluation system for controlling the whole process, generate the relevant protocols, facilitate and improve the reproducibility and offer the tools for a validation.

Clean-room conditions

All components of the catheter extrusion line are suitable for clean-room environment. Naturally, this requires the use of suitable materials, complete covering of all drives and heaters, smooth, homogeneous surfaces and easy cleaning of all surfaces.

Die and die carriage

Preheating system

Unwinder for supporting wire



Two-Layer High-Precision Strand Line

The extruders are equipped with melt pumps and pressure / speed control for accurate throughput of the line. Through use of a multi-layer die, the strand is extruded directly into a water bath vertically. This process eliminates any influence of a calibration system and gravity guarantees the high precision in diameter and ovalness. Controlled water flow ensures an absolutely calm water surface at the product entry into the cooling vessel. The diameter range is between 1 mm to 10 mm at a maximum line speed of 25 m/min.



Control system

The touch screen control system is ergonomically designed and stores all process and quality parameters. Each extruder has its own touch screen from which all extruder and gear pump parameters can be managed. Closed-loop pressure/ screw speed control ensures that

maximum throughput accuracy is achieved. The line is equipped with a two-axis diameter measuring system. The laser measuring of the diameter controls the haul-off speed and reports the ovalness as a quality criterion. The COLLIN® VISUAL FECON soft-

ware integrates all components of the line so that the process can be managed from one central user panel. It stores all parameters of the line, shows trend analysis for each parameter and documents them for quality control purposes.

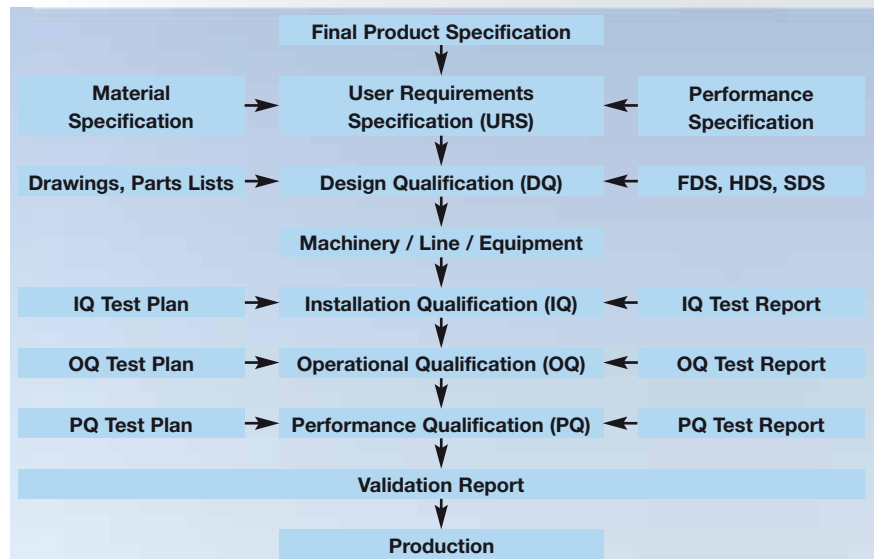


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