SLOVENSKI STANDARD
SIST EN 12006-1:2000

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Neaktivni kirurġki vsadki (implantati) ï Posebne zahteve za srļ noģilne vsadke (kardiovaskularne implantate) ï 1. del: Nadomestki srļ ne zaklopke

Non active surgical implants - Particular requirements for cardiac and vascular implants - Part 1: Heart valve substitutes

Nichtaktive chirurgische Implantate - Besondere Anforderungen für Herz- und Gefäßimplantate - Teil 1: Herzklappenprothesen

Implants chirurgicaux non actifs - Exigences particulieres pour les implants cardio-vasculaires - Partie 1: Protheses valvulaires cardiaques

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11.040.40	Implantanti za kirurgijo, protetiko in ortetiko	Implants for surgery, prosthetics and orthotics

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Non active surgical implants - Particular requirements for cardiac and vascular implants - Part 1: Heart valve substitutes

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This European Standard was approved by CEN on 19 June 1999.

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Foreword

This European Standard has been prepared by Technical Committee CEN/TC 285 "Non-active surgical implants", the secretariat of which is held by NNI.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by January 2000, and conflicting national standards shall be withdrawn at the latest by January 2000.

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive(s).

For relationship with EU Directive(s), see informative Annex ZA, which is an integral part of this standard.

There are three levels of European Standards dealing with non-active surgical implants. These are as follows, with level I being the highest:

- level 1: General requirements for non-active surgical implants;
- level 2: Particular requirements for families of non-active surgical implants;
- level 3: Specific requirements for types of non-active surgical implants.

This standard is a level 2 standard and contains requirements that apply to all non-active surgical implants in the family of heart valve substitutes.

The level 1 standard, EN ISO 14630:1997, contains requirements that apply to all non-active surgical implants.

Level 3 standards apply to specific types of implants within a family such as bone plates and hip joints.

To address all requirements it is recommended to start with a standard of the lowest available level.

Working group 3 "Cardiac Vascular Implants" of CEN/TC 285 collaborated closely with the International Organization for Standardization (ISO/TC 150) in order to come to a standard for Heart Valve Substitutes, which is as harmonized as possible. The table at the informative Annex G indicates for each EN 12006-1 clause, whether the requirements are covered by compliance with the corresponding ISO 5840 clause.

According to the CEN/CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom.

Introduction

This European Standard provides, in addition to the requirements in EN ISO 14630:1997, a method to demonstrate compliance with the relevant essential requirements as outlined in general terms in Annex 1 of the Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, as they apply to cardiac and vascular implants - heart valve substitutes.

1 Scope

This standard specifies particular requirements for heart valve substitutes.

This European Standard is not applicable to heart valve substitutes composed in whole, or in part, of human tissue.

With regard to safety, it gives requirements for intended performance, design attributes, materials, design evaluation, manufacturing, sterilization, packaging and information supplied by the manufacturer.

This European Standard specifies a number of test methods and requirements regarding the performance characteristics of equipment to be used to determine the physical, biological and chemical properties of heart valve substitutes and of the materials and components of which they are made.

Recommendations are also made for *in vivo* testing and clinical evaluation, and for the reporting of results of all types of testing and evaluation covered in this European Standard. These recommendations do not purport to comprise a complete test programme (see annex F for rationale).

2 Normative references

This European Standard incorporates by dated or undated reference, provisions from other publications. These normative references are cited at the appropriate places in the text and the publications are listed hereafter. For dated references, subsequent amendments to or revisions of any of these publications apply to this European Standard only when incorporated in it by amendment or revision. For undated references the latest edition of the publication referred to applies.

EN ISO 14630:1997	Non-active surgical implants - General requirements (ISO 14630:1997)
EN ISO 10993-1:1997	Biological evaluation of medical devices - Part 1: Evaluation and testing (ISO 10993-1:1997)
ISO 5840	Cardiovascular implants - Cardiac valve prostheses

3 Definitions

For the purposes of this standard the definitions given in EN ISO 14630:1997 apply together with the following:

3.1 anticoagulant-related haemorrhage: Internal or external bleeding that causes death or stroke, or that requires transfusion, operation or hospitalization [ISO 5840].

NOTE: This definition is restricted to patients who are receiving anticoagulants and/or antiplatelet drugs.

3.2 arterial diastolic pressure: Minimum value of the arterial pressure during diastole [ISO 5840].

3.3 arterial peak systolic pressure: Maximum value of the arterial pressure during systole [ISO 5840].

3.4 biological heart valve substitute: Heart valve substitute composed wholly or partly of animal tissue (ISO 5840).

3.5 cavitation: Erosive mechanism caused by the generation and collapse of gas bubbles in a fluid system.

3.6 closing volume: Component of the regurgitant volume that is associated with the dynamics of valve closure during a single cycle (see figure 1) [ISO 5840].

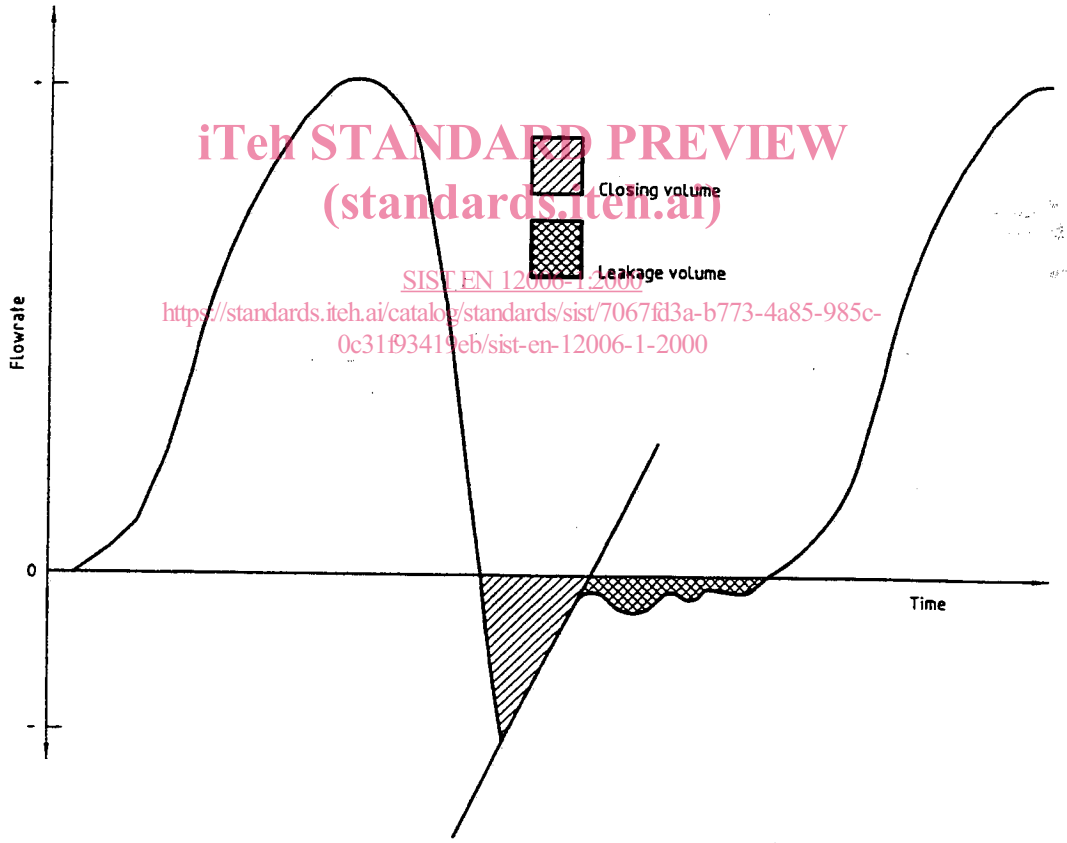

Figure 1 : Simulated flow wave-form showing regurgitant volume (closing volume plus leakage volume) for one cycle.

3.7 cycle: One complete sequence in the action of a test heart valve substitute under pulsatile flow conditions [ISO 5840].

3.8 cycle rate: Number of complete cycles per unit of time, usually expressed as cycles per minute (cycles/min) [ISO 5840].

3.9 external sewing ring diameter: Maximum external diameter of a heart valve substitute, including the sewing ring (see figure 2) [ISO 5840].

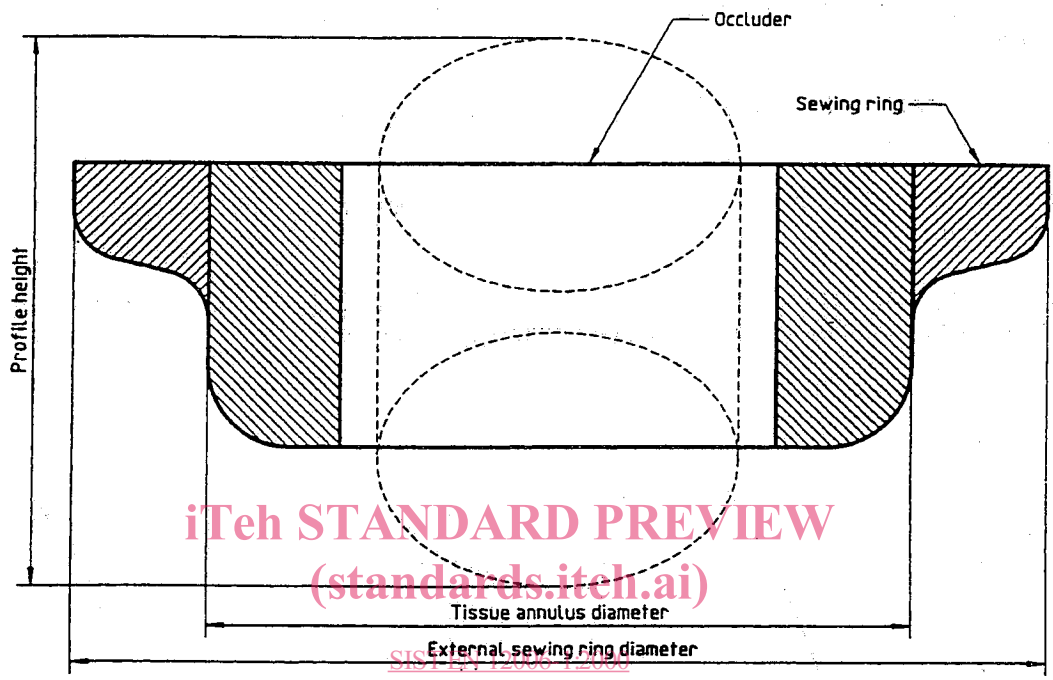

Figure 2 : Designation of dimensions of heart valve substitutes

3.10 forward-flow phase: Portion of the cycle time during which forward flow occurs through a test heart valve substitute [ISO 5840].

3.11 heart valve substitute: Device used to replace or supplement a natural valve of the heart, categorized according to the position in which they are intended to be used (valve type) [ISO 5840].

3.12 internal orifice area: Minimum projected area normal to the plane of the heart valve substitute, excluding the occluder(s) [ISO 5840].

3.13 leakage volume: Component of the regurgitant volume that is associated with leakage through the closed valve during a single cycle (see figure 1) [ISO 5840].

NOTE: The point of separation between the closing and leakage volumes is obtained according to a defined and stated criterion (the linear extrapolation shown in figure 1 is just an example).

3.14 mean arterial pressure: Time-averaged arithmetic mean value of the arterial pressure during one cycle [ISO 5840].

3.15 mean pressure difference; (deprecated: **mean pressure gradient**): Time-averaged arithmetic mean value of the pressure difference across a heart valve substitute during the forward-flow phase of the cycle [ISO 5840].

3.16 mean volume flow: Time-averaged arithmetic mean value of the flow across a heart valve substitute during the forward-flow phase of the cycle [ISO 5840].

3.17 mechanical heart valve substitute: Heart valve substitute composed wholly of synthetic materials [ISO 5840].

3.18 non structural dysfunction: Abnormality resulting in stenosis or regurgitation of the heart valve substitute that is not intrinsic to the valve itself [ISO 5840].

NOTE: This dystfunction is exclusive of valve thrombosis, systemic embolus or infection diagnosed by reoperation, autopsy or *in vivo* investigation. Examples include entrapment by pannus or suture, paravalvular leak, inappropriate sizing, and significant haemolytic anaemia.

3.19 occluder: Component(s) of a heart valve substitute that move(s) to inhibit reflux [ISO 5840].

3.20 operative mortality: Death from any cause during operation or within 30 days after operation [ISO 5840].

3.21 polymeric leaflet heart valve substitute: Heart valve substitute with flexible leaflets composed in part or wholly of synthetic polymer(s).

3.22 profile height: Maximum axial dimension of a heart valve substitute in the open or closed position, whichever is greater (see figure 2) [ISO 5840].

3.23 prosthetic valve endocarditis: Infection involving a heart valve substitute [ISO 5840].

NOTE: Diagnosis is based on customary clinical criteria including an appropriate combination of positive blood cultures, clinical signs (fever, new or altered cardiac murmurs, splenomegaly, systemic embolus, or immunopathologic lesions), and/or histologic confirmation of endocarditis at reoperation or autopsy. Morbidity associated with active infection such as valve thrombosis, embolus, or paravalvular leak is included under this category and is *not* included in other categories of morbidity.

3.24 reference valve: Heart valve substitute used to assess the conditions established in the test device employed to evaluate the test heart valve substitute [ISO 5840].

NOTE: The reference valve should approximate the test valve in type, configuration and tissue annulus diameter; it may be an earlier model of the same valve, if it fulfils the necessary conditions. The characteristics of the reference valve should be well documented with both *in vitro* and clinical data available in the literature.

3.25 regurgitant fraction: Regurgitant volume expressed as a percentage of the stroke volume [ISO 5840].

3.26 regurgitant volume: Volume of fluid that flows through a test heart valve substitute in the reverse direction during one cycle; it is the sum of the closing volume and the leakage volume (see figure 1) [ISO 5840].

3.27 root mean square (r.m.s.) volume flow: Square root of the time-averaged arithmetic mean square value of the volume flow through a test heart valve substitute during the forward-flow phase of the cycle [ISO 5840].

3.28 simulated cardiac output: Net fluid volume flowing forward through a test heart valve substitute per minute [ISO 5840].

3.29 stroke volume: Volume of fluid moved through a test heart valve substitute in the forward direction during one cycle [ISO 5840].

3.30 structural deterioration: Change in the function of a heart valve substitute resulting from an *intrinsic* abnormality that causes stenosis or regurgitation [ISO 5840].

NOTE: This definition excludes infection or thrombosis of the heart valve substitute as determined by reoperation, autopsy or *in vivo* investigation. It includes intrinsic changes such as wear, stress fracture, occluder escape, calcification, leaflet tear and stent creep.

3.31 systemic embolism: Clot or other particular matter, not associated with infection, originating on or near the heart valve substitute and transported to another part of the body [ISO 5840].

NOTE: Diagnosis may be indicated by a new, permanent or transient, focal or global neurological deficit (exclusive of haemorrhage) or by any peripheral arterial embolus unless proved to have resulted from another cause (e.g. atrial myxoma). Patients who do not awaken post-operatively or who awaken with a stroke or myocardial infarction are excluded. Acute myocardial infarction that occurs *after* operation is arbitrarily defined as an embolic event in patients with known normal coronary arteries or who are less than 40 years of age.

3.32 tissue annulus diameter: External diameter of a heart valve substitute, including any covering, where it is intended to mate with the smallest diameter of host tissue (see figure 2) [ISO 5840].

NOTE: The use of "mounting diameter" for this term is deprecated.

3.33 valve size: Manufacturer's designation of the dimensions of the heart valve substitute [ISO 5840].

3.34 valve thrombosis: Blood clot, not associated with infection, causing dysfunction of the heart valve substitute [ISO 5840].

NOTE: Diagnosis may be proved by operation, autopsy, or clinical investigation (e.g. echocardiography, angiocardiography, or magnetic resonance imaging).

4 Intended performance

In addition to the requirements of EN ISO 14630:1997 and to the description of the intended performance of the heart valve substitute, details of the heart valve substitute and its components shall be described using the system for the description of heart valve substitutes as given in annex A.

5 Design attributes

The requirements of clause 5 of EN ISO 14630:1997 apply. Additionally the manufacturer shall supply heart valve substitutes sterile.

6 Materials

The requirements of clause 6 of EN ISO 14630:1997 on materials apply.

7 Design evaluation

7.1 General

The requirements of clause 7 of EN ISO 14630:1997 apply, together with the following:

7.1.1 Introduction

All heart valve substitutes to be tested shall be of quality suitable for human implantation.

Before testing, each valve substitute shall have been sterilized by the process used or intended to be used by the manufacturer for production purposes. In the case of a heart valve substitute that may be re-sterilized by the user, it shall also have been subjected to the maximum number of re-sterilization cycles recommended, using the method stated by the manufacturer to be the worst case procedure.

7.1.2 Description

Details of each test heart valve substitute and reference valve, including their identity, type (e.g. aortic or mitral), tissue annulus diameter, external sewing ring diameter and profile height shall be provided.

Details of each test heart valve substitute, including the materials of which it is made, and if appropriate, the specific gravity, mass and travel of the occluder shall be provided.

7.2 Pre-clinical evaluation

References to and descriptions of possible materials and component testing of heart valve substitutes are given in annex B.

In addition to EN ISO 14630:1997 the following applies:

7.2.1 Testing of materials

7.2.1.1 Requirements and procedures

All materials used shall have been identified and their characteristics specified: the methods of identification and of specifying characteristics shall be relevant to the materials under test (see annex C).
Evaluation for biological safety and compatibility shall be performed in accordance to EN ISO 10993-1. The test results shall be documented.

7.2.1.2 Test report
The test report shall include the following information:

a) the rationale for the test;
b) the identity of the material tested (e.g. chemical generic name or biological source);
c) sample identification (e.g. batch number);
d) the number of specimens tested;
e) the test method used and, where a test method other than a test specified in a published standard is used, full details of the procedure;
f) test results.

7.2.2 Testing of components

7.2.2.1 Requirements, procedures and results
Representative samples of the heart valve substitute components shall be tested for biological compatibility, durability and mechanical characteristics, and the results documented.

NOTE 1: Testing of the complete heart valve substitute may satisfy the requirement for testing of components.

NOTE 2: Standards that may be applicable for testing materials and components of heart valve substitutes are listed in annex C.

7.2.2.2 Test reports
The test report shall include the following information:

a) the rationale for the test;
b) a description of the item(s) tested;
c) the number of specimens tested;
d) details of the test method used;
e) test results.

7.2.3 Mechanical testing of a heart valve substitute

7.2.3.1 General
The aim of these procedures is to generate information on the mechanical performance of the heart valve substitute.

For the following procedures, at least three heart valve substitutes of each of the largest, medium and smallest size tissue annulus diameter plus at least one valve of each intermediate size shall be tested.

7.2.3.2 Sewing ring tear-off and tear-out forces
a) principle:
The aim of this test procedure is to generate information on the sewing ring such that it satisfactorily withstands the force specified by the manufacturer without separating it from other parts of the valve or tearing;

b) procedure:
One single pass suture shall be applied in one particular area and tested to a force specified by the manufacturer. Four positions (at 90°) to each other shall be tested. The manufacturer shall report the results of the tests and comparative data from the reference valve.

NOTE: An example of a test apparatus is given in D.1.

7.2.3.3 Torque of rotatable valves

a) principle:
The aim of this test is to provide information on the torque required to rotate the valve within its sewing ring if appropriate;

b) procedure and results:
The specific rotator shall be used to measure the torque required to rotate the valve. The range of torques and effects of applying such forces on the valves shall be documented. The test shall be carried out for the worst case (dry or wet) as specified by the manufacturer.

NOTE: An example of a test apparatus is given in D.2.

7.2.3.4 Static pressure testing

a) principle:
The aim of this test procedure is to provide information on the static pressure the manufacturer indicates the heart valve substitute can withstand without impairment of function;

b) procedure and results:
The manufacturer shall document the test procedure the results.

7.2.3.5 Distortion

If applicable, tests shall be documented to examine ring stiffness, occluder sticking and/or dislodging. The values shall be indicated in newtons.

a) principle:
The aim of this test procedure is to provide information on the performance of the heart valve substitute under application of a force equivalent to that which can be applied by the myocardium during a cardiac cycle;

b) procedure and results:
The manufacturer shall document the testing procedure and describe the different design related problems that could occur when the heart valve substitute is submitted to a given range of forces.

NOTE: An example of a suitable test apparatus is given in D.3.

7.2.4 Hydrodynamic testing

7.2.4.1 Principle

The aim of the test procedure is to generate in vitro information on the fluid mechanical performance of the heart valve substitute under conditions of steady and pulsatile flow.

7.2.4.2 Steady forward flow testing

a) measurement equipment accuracy and test fluids:
The measurement equipment shall fulfil the following conditions:

1) the test apparatus shall have had its properties and performance established by means of a standard nozzle (in accordance with E.1), and these characteristics shall be monitored by means of regular re-testing using a standard nozzle (see E.1);

2) the pressure difference measurement system accuracy shall be at least 0,15 kPa (± 1mmHg);

3) all other measurement equipment used shall have a measurement accuracy of at least ± 5% of the full scale reading.

The physical and chemical properties (e.g. specific gravity, viscosity at working temperature) of the test fluid shall be defined.

NOTE: Test fluids which have been found acceptable include isotonic saline solution, blood and blood-equivalent fluid.

b) test apparatus:
The following test apparatus shall be used:

1) steady flow testing for aortic and mitral heart valve substitutes shall be conducted in a 35 mm internal diameter straight tube;

2) the test system shall be capable of generating flow rates of at least 30 l/min;

3) flow entering the test chamber shall be relatively non-disturbed, which can be achieved with a flow straightener upstream of the heart valve substitute;

4) pressure taps shall be located one tube diameter upstream and three tube diameters downstream from the midplane of the heart valve substitute sewing ring. If sufficient data can be provided to demonstrate comparable results, other pressure tap configurations may be used;

5) the pressure taps shall be flush with the inner wall of the tube;

6) a standard nozzle, as given in E.1, shall be used to characterize the forward flow pressure and flow measuring equipment.

c) Test procedure
At least three heart valve substitutes of each tissue annulus diameter shall be tested.
All measurements and visual assessments shall be carried out over a flow rate range from 5 l/min to 30 l/min (83 ml/s to 500 ml/s).
At least five measurements of each variable shall be made, and the mean and standard deviation shall be determined. The following parameters shall be determined:

1) include pressure drop measurement of a flow rate range from 5 l/min to 30 l/min in 5 l/min increments and conduct identical measurement using the standard nozzle (see E.1);

2) the stated flow rates during pressure measurement;

3) pressure drop across the heart valve substitute or standard nozzle (see E.1).

d) test report:
The test report shall include the following information:

1) a description of the test fluid, including its biological origin and/or chemical components as well as its temperature, viscosity and specific gravity and other characteristics as appropriate under the test conditions;

2) a description of the test apparatus for steady flow testing as specified in b), and major components of the test loop and associated apparatus, including a schematic diagram of the system giving the relevant chamber dimensions, details of the location of the pressure-measuring sites relative to the mid-plane of the valve sewing ring and a representative pressure-flow curve of mean volume flow;

3) an assessment, including appropriate documentation, of the test valve behaviour during pressure-flow measurement and of a standard nozzle (see E.1);

4) details of the mean, range, and standard deviation of the performance test variables at each simulated condition for each test heart valve substitute and standard nozzle (see E.1), shall be presented in tabular or graphical form:

a) steady flow rate in l/min;

b) pressure differences (mmHg and kPa);

c) effective orifice area (cm^2).

The effective orifice area shall be calculated taking into account the pressure recovery downstream from the test valve.

NOTE: Example for the calculation of the effective orifice area (EOA), based on the Carnot-Equation:

$$EOA = \frac{A}{1 + \sqrt{\frac{2\Delta P}{\rho v^2}}}$$

Where:
A is the cross-sectional area of the tube
ΔP is the mean pressure difference across heart valve substitute
υ is the cross-sectional average velocity in the tube
ρ is the density of test fluid