FilterTEF 0.2 micron

Validation Guide

SISTEMI DI FILTRAZIONE
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Summary

General information filter cartridges FilterTEF

This document give the necessary information for the use of *FilterTEF rated* 0,2 micron in pharmaceutical applications. .

FilterTEF filter cartridges 0,2 micron rated, are manufactures as per the procedures used for production of sterilizing grade filters.
Materials used for the assembly of the cartridges, both the teflon (PTFE) membrane and the Polypropylene used for the hardware, had been selected for the specific application meeting the current rules.

The assembly is made by thermo-bonding without any adhesive.
FilterTEF filter cartridges rated 0,2 micron are manufactured into a clean room with controlled contamination and tested prior to the shipment by the internal IPM labs in order to meet the high standards and the quality assurance as per internal procedures.
The identification of the FilterTEF filter cartridges is made per the following:

TEF	-	7	10	-	002	-	S	I	PH
		CARTRIDGE TYPE	LENGTH		FILTRATION RATING		GASKETS O-RINGS	INSERT	VERSION
Product identification: **TEF**		**D** = DOE (double open end) **2** = bayonet 2.226/flat **3** = 2.222/flat **5** = 3 bayonet 2.222/fin **7** = bayonet 2.226/fin **8** = 2.222/fin	10 = 10” 20 = 20” 30 = 30” 40 = 40”		001 = 0.1 µm 002 = 0.2 µm 004 = 0.45 µm		B = Buna N E = EPR S = Silicone V = Viton X = other VITON ® is a registered trade name of E.I. duPont de Nemours & Co. Inc	I = with SS insert (*) 0 = no SS insert (*) When filter has to be sterilized by steam	PH= Pharma version
		J = Junior Cartridge	02 = 2,5” 05 = 5”						

Should you need any more info please contact IPM technical support tel. +39 039 21 45 244 or visit the site www.ipmfilters.com

Technical characteristics FilterTEF rated 0.2 micron

Cartridges Materials:				
Membrane	Teflon (PTFE)			
Support Layers	Polypropylene (PP)			
Cartridges supprts	Polypropylene (PP)			
O-rings	Silicon			
Technical Characteristics of the cartridge:				
Filtration Area	0.78 m^2 per 10" modules			
Pore size	0.2 µm			
Length	Available cartridges as per the following dimensions: 5'' JUNIOR (125 mm), 10'' (250 mm), 20'' (500 mm), 30'' (750 mm)			
Retention characteristics of the cartridges:				
Bacteria Retention	Retention of 10^7 CFU/cm^2 Brevundimonas diminuta (ATCC 19146), as per ASTM F838-05.			
Mechanic Characteristics				
Resistance at Hydraulic Stress	*FilterTEF 0,2 µm* filter cartridges shown no diffusion and phisical changes when stressed by:			
	Water Pressure (bar)	N° strocks	Water temperature (°C)	Direction of the flow
	5,0	50	20±5	Forward
	2,0	50	20±5	Reverse
Resistance at Thermal Stress	*FilterTEF 0,2 µm* filter cartridges shown no diffusion and phisical changes when stressed by:			
	Temperature Test (°C)	Pressure Test (bar)	Cycle[1] time (hours)	N° of cicles (in autoclave)
	121	1.15	1	130
Estractables				
Extractables	*FilterTEF 0,2 µm* filter cartridges meet USP<661>.			
Conformity of materials to the rules for food contact	Materials of the *FilterTEF 0,2 µm* cartridge meet the requirements for food contact as per Reg. N° 1935/2004/EEC and "Code of Federal Regulations" FDA, 21 # 171-199.			
Biological Reactivity				
Material toxicity	All the materials of the *FilterTEF 0,2 µm* cartridges meet the rules as per USP<87> ("Biological Reactivity Test in vitro for Class VI Plastics") e USP<88> ("Biological Reactivity Test in vivo for Class VI Plastics – Safety Test").			
Release of particles and/or Endotoxins				
Bacteria endotoxins	< 0,125 EU/ml of aqueous extract as per USP<85>.			
No fibers releasing	*FilterTEF 0,2 µm* cartridges satisfy the rules as per USP<788>			

[1] **Total time considering a warming up rising of 15 min, 30 min at the test temperature and of 15 min. for room temperature cooling down**

Bacteria Removal efficiency

Several Authorities as FDA and EMA fix the standards for show that the sterilizing action of a filter has to be evidenced by tests before to be used in the pharmaceutical application. A filter is cannot be considered sterilizing grade only because the dimension of its pores.

In order to consider a filter as sterilizing grade it must challenged with an upstream concentration not less of 10^7 CFU/cm^2 of the bacterial *Brevundimonas diminuta.* It must get a sterile downstream.

Correlation between the microbiological retention and a non destructive integrity test is an other very important aspect of the validation of a filter cartridge pharmaceutical grade.
The Official Authorities had set up a procedure for control the filter both prior to the use and after the use.

On the followings you can find the Challenge tests results to confirm that the membrane used for the filter cartridges *FilterTEF 0,2 µm* can have full retention a bacteria charge of 10^7 CFU/cm^2 di *Brevundimonas diminuta* according to the ASTM F838-05 methodology.

You can also find the correlation between the retention and the diffusion test.
This is important to set the maximum diffusion flow acceptance limit to warranty the filter will get a sterile effluent.

On the followings tables are reported the correlation between the diffusion test (non destructive test) and the bacteria challenge (destructive test) for filter cartridges *FilterTEF 0,2 µm* Part Numbered: TEF J05 002 SI - PH ; TEF 710 002 SI - PH ; TEF 720 002 SI - PH.

Challenge Test - Filter cartridge TEF J05 002 SI - PH da 0.2 micron

20 (twenty) cartridges from the standard production had been tested. Any of them had been tested first to an integrity test by diffusion and then bacteria challenged by Brevundimonas diminuta >10^7 CFU/cm^2.
Table 1 shows the Tests results also shown by graphic on Fig 1.
As per the results the filter cartridge TEF J05 002 SI – PH - 0.2 micron is conform to the acceptance requirements.

Lot	Diffusion at 690 mbar (ml/min) **	Downstream Sterile	Titre Reduction
6818/22	4,0	Si	> 1,6 x 10^8
6818/25	4,8	Si	> 1,5 x 10^8
6117/06	5,1	Si	> 1,6 x 10^8
6118/05	5,3	Si	> 1,5 x 10^8
6117/18	5,4	Si	> 1,7 x 10^8
6118/23	6,0	Si	> 1,8 x 10^8
6777/11	6,5	Si	> 1,4 x 10^8
6771/16	7,0	Si	> 1,5 x 10^8
6512/01	7,3	Si	> 1,5 x 10^8
5943/09	7,3	Si	> 1,6 x 10^8
5836/14	7,4	Si	> 1,7 x 10^8
6132/12	7,5	Si	> 1,8 x 10^8
5981/17	7,6	Si	> 1,9 x 10^8
6091/19	7,6	Si	> 1,7 x 10^8
5643/02	7,9	Si	> 1,6 x 10^8
6843/13	8,0	Si	> 1,5 x 10^8
5643/05	8,0	Si	> 1,7 x 10^8
5643/11	8,0	Si	> 1,4 x 10^9
6777/15	8,5	No	1,3 x 10^6
6777/24	9,0	No	1,7 x 10^6
6818/03	10,5	Si	> 1,7 x 10^8

Tab. 1. Bacteria challenge results for FilterTEF J05 002 SI - PH - 0.2 µm

** Tested in 60% IPA / 40% DI Water

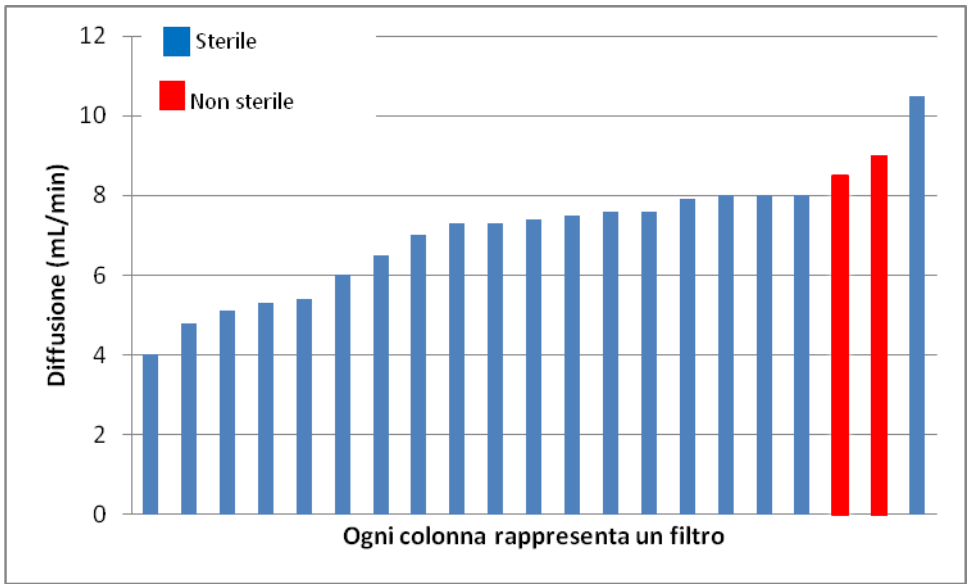

Fig. 1. Correlation between diffusion test and bacteria challenge ASTM F838-05 for filter cartridge FilterTEF J05 002 SI - PH - 0.2 micron

Conclusions:
Based upon the results the filter cartridge TEF J05 002 SI - PH - 0.2 micron meets the acceptance and has to be considered a sterilizing grade filter up to a maximum diffusion value of 8.0 mL/min.

➤ Correlation diffusion Vs cartridge retention TEF 710 002 SI – PH - 0.2 micron

20 (twenty) cartridges from the standard production had been tested. Any of them had been tested first to an integrity test by diffusion and then bacteria challenged by Brevundimonas diminuta >10^7 CFU/cm^2.
Table 2 shows the Tests results also shown by graphic on Fig 2.
As per the results the filter cartridge TEF 710 002 SI – PH - 0.2 micron is conform to the acceptance requirements.

Lot serial N#	Diffusion at 690 mbar ml/min **	Downstream Sterile	Titre Reduction
7095/10	12,0	Si	> 1,4 x 10^8
7095/15	12,3	Si	> 1,4 x 10^8
6827/34	13,0	Si	> 1,2 x 10^8
7095/43	13,3	Si	> 1,6 x 10^8
6869/05	13,4	Si	> 1,7 x 10^8
6726/18	13,7	Si	> 1,8 x 10^8
6726/06	14,0	Si	> 1,8 x 10^8
6366/30	14,1	Si	> 1,4 x 10^8
7095/03	14,3	Si	> 1,5 x 10^8
6566/42	14,3	Si	> 1,5 x 10^8
6827/05	14,4	Si	> 1,3 x 10^8
6726/15	14,5	Si	> 1,4 x 10^8
6366/14	14,6	Si	> 1,2 x 10^8
6566/19	14,6	Si	> 1,1 x 10^8
6366/19	14,9	Si	> 1,4 x 10^8
6827/21	15,0	Si	> 1,7 x 10^8
6566/02	15,0	Si	> 1,8 x 10^8
6366/27	15,0	Si	> 1,3 x 10^9
6827/16	15,5	No	1,6 x 10^6
6869/12	16,0	No	1,5 x 10^6
6366/21	17,5	Si	> 1,7 x 10^8

Tab. 2. Bacteria challenge results for FilterTEF 710 002 SI - PH - 0.2 µm

** Tested in 60% IPA / 40% DI Water

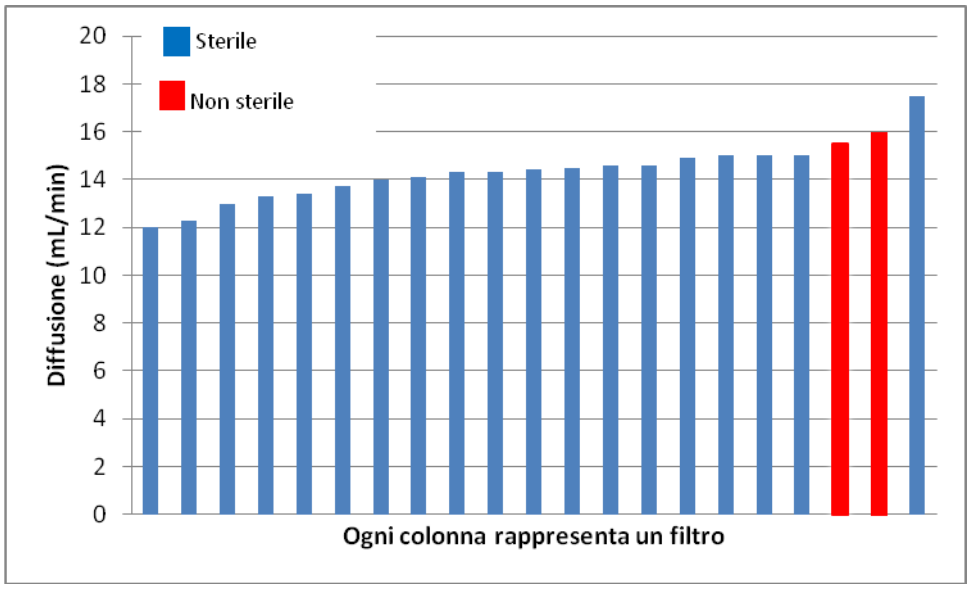

Fig. 2. Correlation between diffusion test and bacteria challenge ASTM F838-05 for filter cartridge FilterTEF 710 002 SI - PH - 0.2 micron

Conclusions:
Based upon the results the filter cartridge TEF 710 002 SI - PH - 0.2 micron meets the acceptance and has to be considered a sterilizing grade filter up to a maximum diffusion value of 15.0 mL/min.

➤ Correlation diffusion Vs cartridge retention TEF 720 002 SI – PH - 0.2 micron

20 (twenty) cartridges from the standard production had been tested. Any of them had been tested first to an integrity test by diffusion and then bacteria challenged by Brevundimonas diminuta >10^7 CFU/cm^2.
Table 3 shows the Tests results also shown by graphic on Fig 3.
As per the results the filter cartridge TEF 720 002 SI – PH - 0.2 micron is conform to the acceptance requirements.

Lot	Diffusion at 690 mbar ml/min **	Downstream Sterile	Titre Reduction
5823/14	26,0	Si	> 1,3 x 10^8
5823/23	26,2	Si	> 1,3 x 10^8
4713/23	27,0	Si	> 1,4 x 10^8
4713/12	27,1	Si	> 1,4 x 10^8
5901/05	27,4	Si	> 1,7 x 10^8
5901/16	27,7	Si	> 1,3 x 10^8
4961/12	28,2	Si	> 1,6 x 10^8
5823/24	28,3	Si	> 1,8 x 10^8
5901/22	28,5	Si	> 1,6 x 10^8
6004/11	28,7	Si	> 1,5 x 10^8
4239/19	28,7	Si	> 1,4 x 10^8
5097/03	29,1	Si	> 1,5 x 10^8
4713/18	29,4	Si	> 1,8 x 10^8
4239/15	29,5	Si	> 1,3 x 10^8
4713/19	29,8	Si	> 1,6 x 10^8
5097/32	29,9	Si	> 1,4 x 10^8
5097/17	30,0	Si	> 1,5 x 10^8
6004/15	30,0	Si	> 1,6 x 10^9
4713/32	30,4	No	1,7 x 10^6
5901/30	31,0	No	1,6 x 10^4
5823/04	32,7	Si	> 1,6 x 10^8

Tab. 3. Bacteria challenge results for FilterTEF 720 002 SI - PH - 0.2 µm

** Tested in 60% IPA / 40% DI Water

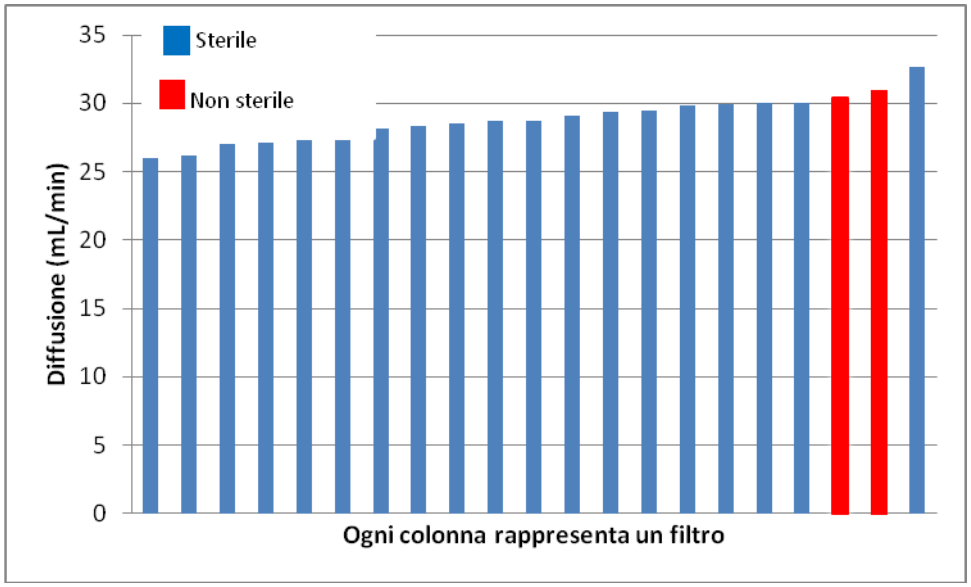

Fig. 3. Correlation between diffusion test and bacteria challenge ASTM F838-05 for filter cartridge FilterTEF 720 002 SI - PH - 0.2 micron

Conclusions:
Based upon the results the filter cartridge TEF 720 002 SI - PH - 0.2 micron meets the acceptance and has to be considered a sterilizing grade filter up to a maximum diffusion value of 30.0 mL/min.

Biological and extractables tests

➤ Bacteria endotoxyns

Test had been run according the Current USP<85> using the Chromogenic Method that gives the endotoxyn amount released by a filter cartridge type *FilterTEF 0,2 micron*.
The sample cartridge had been filled with a-pyrogenic water and ultrasound treated in order to better extract the endotoxins.

The lab test shows no Bacteria endotoxins release by the filter cartridge FilterTEF.

LOT	METHOD	RESULT
5795/03	cUSP<85>	<0.25 EU/mL
5901/17	cUSP<85>	<0.25 EU/mL
4713/29	cUSP<85>	<0.25 EU/mL

Tabella 4. LAL test Resilts

Chemical compatibility and extractables

On the following table the chemical compatibility of *FilterTEF 0.2 micron* challenged with several chemicals. However, in case of concerns, before using *FilterTEF 0.2 micron* with no experienced chemicals, please contact IPM.

CHEMICAL CLASSIFICATION	***COMPOUND*** *(Condizioni di prova: 7 giorni a 20°C)*	***FILTER TEF***
ACIDS	Acetic acid, 90%	R
	Acetic acid, 30%	R
	Acetic acid, 10%	R
	Hydrochloric acid, conc. (35%)	R
	Hydrochloric acid, 6N (20%)	R
	Hydrochloric acid, 1N (3.3%)	R
	Nitric Acid, conc. (67%)	R
	Nitric acid, 6N (27%)	R
	Sulfuric acid, conc. (96%)	R
	Sulfuric acid, 6N (16%)	R
ALCOHOLS	Amyl alcohol	R
	Benzyl alcohol	R
	Butanol	R
	Ethanol	R
	Isopropanol	R
	Methanol	R
AROMATIC HYDROCARBONS	Benzene	R
	Toluene	R
	Xylene	R
BASES	Ammonium hydroxyde, 3N (5.7%)	R
	Ammonium hydroxyde, 6N (11.4%)	R
	Potassium hydroxyde, 3N (15%)	R
	Sodium hydroxyde, 3N (11%)	R
	Sodium hydroxyde, 6N (22%)	R
ESTERS	Amyl acetate	R
	Butyl acetate	R
	Cellosolve acetate	R
	Ethyl acetate	R
	Isopropyl acetate	R
	Methyl acetate	R
ETHERS	Ethyl ether	R
	Tetrahydrofuran (THF)	R
	THF in water (50:50)	R
GLYCOLS	Ethylene glycol	R
	Glycerol	R
	Propylene glycol	R
HALOGENATED HYDROCARBONS	Carbon tetrachloride	R
	Chloroform	R
	Ethylene dichloride	R
	Methylene chloride	R
KETONES	Acetone	R
	Cyclohexanone	R
	Methyl ethyl ketone (MEK)	R
	Methyl isobutyl ketone	R
OILS	Cottonseed	R
	Peanut	R
MISCELLANEOUS	Acetonitrile	R
	Dimethylformamide (DMF)	R
	Formaldehyde (37%)	R
	Hexane	R
	Pyridine	R

Tabella 5. Chemical compatibility FilterTEF da 0.2 micron (R=Recomended, L=Limited Resistance, N=No Recomended)

Extractables as per USP<661>

Purpose of the following test is to verify the non volatile residuals amount that can be extract by WFI. Test had been run in static condition at 70°C for 24 h.
After the extraction procedure a sample had been dry evaporated to get the Non Volatile Residual (NVR)

LOT	NVR
5795/07	<5 mg
5901/16	<5 mg
4713/28	<5 mg

Tab. 6. FilterTEF 0.2 micron NVR by la cUSP<661>

Conclusions:
FilterTEF da 0.2 micron meet NVR by USP<661>.

Biological safety test

Test “in vitro” class V USP 87

The purpose of this test is to evaluate the biological toxicity of the filter cartridges FilterTEF da 0,2 micron.
The sample cartridges, including the o-rings, are treated by the solutions as per procedures described in the current USP<87> in the indicated rapport weigh /volume.
Test result is indicated as a grade of reactivity where 0 is no reactivity and 4 is high reactivity.
Results in the following table:

LOT	TEST	METHOD	RESULT
5795/08	citotossicità	cUSP<87>	Reacitivy grade 0
5901/10	citotossicità	cUSP<87>	Reactivity grade 0
4713/25	citotossicità	cUSP<87>	Reactivity grade 0

Tabella 7. tests by cUSP<87>

Conclusion:
No in vitro biological reactivity for the filter cartridges FilterTEF da 0,2 micron as per USP<87>.

➤ ”in vivo” Class VI plastic materials Safety Test (cUSP<88>)

Purpose of the test is to evaluate the ”in vivo” biological reactivity of the filter cartridges FilterTEF as per USP<88>.
Results had been evaluated as meeting the limit described in USP procedures.

LOT	TEST	RESULT
5795/10	Intracutaneous Test	Conform
	Systemic Injection Test	Conform
	Implantation Test	Conform
5901/11	Intracutaneous Test	Conform
	Systemic Injection Test	Conform
	Implantation Test	Conform
4713/22	Intracutaneous Test	Conform
	Systemic Injection Test	Conform
	Implantation Test	Conform

Tabella 8. Results by cUSP<88>

Conclusions:
No biological reactivity “in vivo” for the filter cartridges FilterTEF - 0,2 micron by USP<88>.

Phisical Proprieties

➤ Thermal stress test

Purpose of the test is to verify the resistance of the filter cartridge FilterTEF – at repetitive steam sterilizing cycles.
Test had been run at 121°C, 35 min., per cycle.
Sample is tested by diffusion integrity test and tested each 10 cycles by diffusion.

Tab. 9. shows the schedule.

FASE	TEMPERATURE (°C)	PRESSURE (bar)
STERILIZATION	121±1	1.14±0.04
WARMIG UP	121→96	1.12→0.00

Tab. 2. Sterilizing cycle program

Diffusion integrity test run at 690 mbar with acceptance limit of di 15,0 mL/min.
Tab.10. Shows the results.

LOT	DIFFUSION BEFORE (mL/min)	DIFFUSION AFTER (mL/min)
6827/02	13,0	14,0
6566/10	14,0	14,5
7095/26	13,5	13,0
6366/05	13,0	14,0
7095/19	12,5	13,5
6726/16	14,5	13,5
6566/12	13,0	14,5
6869/18	14,5	15,0
6566/35	13,0	13,5

Tab. 3. Thermic stress FilterTEF

Conclusion:
The filter has high resistance when challenged at several sterilizing cycles.

Pressure drop Vs water flow rate

The following table shows the pressure drop Vs. air flow rate at 20±5°C for the filter TEF per 10” module.

In the typical range of use of the filterTEF cartridges the initial Delta P are less than 0,2 bar (flow rate <1200 L/h per 10”).

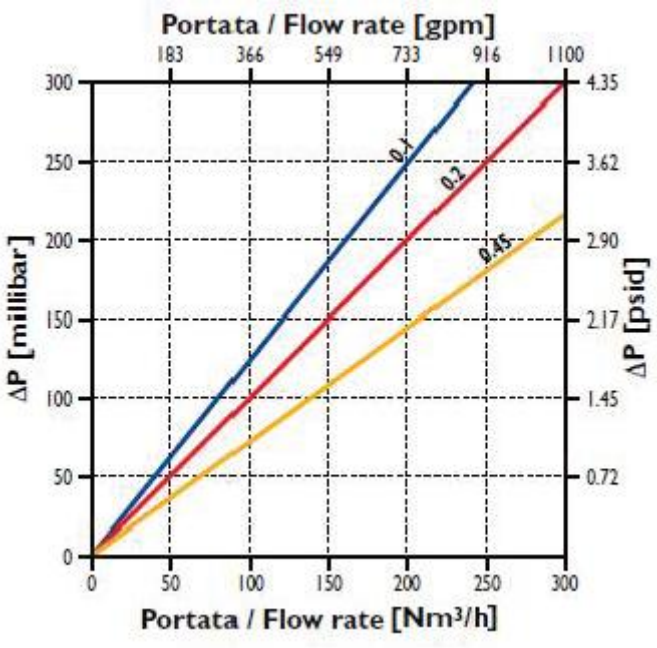

Fig. 2 – Flow rate – Delta P FilterTEF per 10” module

TEF	-	7	10	-	002	-	S	I	PH
Product identification: **TEF**		**CARTRIDGE TYPE**	**LENGTH**		**FILTRATION RATING**		**GASKETS O-RINGS**	**INSERT**	**VERSION**
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		J = Junior Cartridge	02 = 2,5” 05 = 5”						

attached

➤ Certificate of Conformity

Every cartridge for pharma use comes with a CofC like the following fac-simile:

IPM
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E-mail: ipm@ipmfilters.com
www.ipmfilters.com

CERTIFICATO DI CONFORMITÀ
CERTIFICATE OF CONFORMITY
CERTIFICAT DE CONFORMITE
CERTIFICADO DE CONFORMIDAD

XXXXXXXXX

Data di produzione
Date of production
Date de production
Fecha de producción
01/01/2013

Cliente - Customer
Client - Cliente
XXXXXXXXXXXXXXXXX

Rif. Cliente - Rif. Customer
Ref. Client - Ref. Cliente
Ord. N.XXXXXX
del 31/12/2012

TIPO DI FILTRO
FILTER TYPE
TYPE DE FILTRE
TIPO FILTRO
Filter TEF

MOD.
TEF710.002-S1

LOT.
L/N: XXXX

Controllo visivo e dimensionale:
Visual and dimensional check:
Contrôle visuel et dimensionnel:
Inspección visual y control dimensional:
✓

Risultato - Result - Résultat - Resultado:
ACCEPTED

Test di integrità (diffusione):
Integrity test (diffusion):
Test d'intégrité (diffusion):
Prueba de integridad (difusión):
✓

Limite di accettabilità:
Accepted values:
Limite de tolérance:
Valor límite aceptable:
As per IPM QC procedures

IL CONTROLLO DI QUALITÀ - QUALITY CONTROL
CONTRÔLE DE QUALITÉ - CONTROL DE CALIDAD

Fig. 3. Certificate of conformity released by IPM S.r.l.