

FilterNYL 0.2 micron

VALIDATION GUIDE

Summary

➤GENERAL INFORMATION ABOUT FILTER CARTRIDGES FILTERNYL	3
➤FILTER CARTRIDGES FILTERNYL 0.2 µM-TECHNICAL CHARACTERISTICS	4
➤BACTERIA REMOVAL EFFICIENCY	5
➤FILTER CARTRIDGE TYPE NYL 7 10 002 S I – PH: CORRELATION DIFFUSION VS RETENTION	6
BIOLOGICAL AND EXTRACTABLES TESTS	7
➤BACTERIAL ENDOTOXINS – CURRENT USP <85>	7
➤ESTRACTABLES – CURRENT USP<66 I>	7
➤CHEMICAL COMPATIBILITY	8
BIOLOGICAL SAFETY TEST	9
➤”IN VITRO” BIOLOGICAL REACTIVITY TEST - CLASS VI PLASTIC MATERIALS (CURRENT USP<87>).....	9
➤”IN VIVO” BIOLOGICAL REACTIVITY TEST -CLASS VI PLASTIC MATERIALS – SAFETY TEST (CURRENT USP<88>)	10
PHYSICAL CHARACTERISTICS	11
➤HYDRAULIC STRESS TEST	11
➤THERMAL STRESS TEST	12
➤ DIFFERENTIAL PRESSURE VS WATER FLOW RATE.....	13
ATTACHMENT	14

➤General information about filter cartridges FilterNYL

In a pharmaceutical production process, filtration is a very important step. It guarantees the depletion of any particles or microbial contaminants from the drug being processed. The filtration process must meet high and well defined quality standards.

Filter cartridges validation is mandatory to ensure purity, security and effectiveness to a pharmaceutical product.

The purpose of this document is to supply with useful information every End User of FilterNYL filter cartridges. 0.2 µm rated, operating in pharmaceutical applications. The document provides all references about test methods used and results obtained confirming cartridges conformity to the applicable requirements.

FilterNYL filter cartridges 0.2 micron rated are designed and manufactured for use in production of sterile liquids in pharmaceutical industry. Materials used for the assembly of the cartridges, both the Nylon membrane and the Polypropylene polymer used for the hardware supports, had been selected for the specific application meeting the current regulations.

All the assembling steps are carried out by means of thermal bonding processes, without adding adhesive material. *FilterNYL* are made in controlled contamination clean room and tested prior shipment by QA & QC IPM labs, following internal procedures, in order to meet the reference values set.

A wide range of product configurations are available. IPM Filters assigns a unique ID number to each product specific to its source of supply to enable traceability in combination with its lot number. The identification of the *FilterNYL* filter cartridges are made using the following part number guide:

NYL	D	10	002	S	I	PH
	Cartridge type	Lenght	Filtration rating	Gaskets/ O-rings	Insert	Version
Product identification NYL	2= bayonet 2.226/flat 3= 2.222/flat 5= bayonet 2.222/fin 7= bayonet 2.226/fin 8= 2.222/fin	10=10" 20=20" 30=30" 40=40"	002= 0.2 µm 004= 0.45 µm 006 = 0.65 µm 008 = 0.8 µm 012 = 1.2 µm	B= buna N E= EPR S= silicone V= Viton® X= other** ** pl.se contact IPM	I= SS insert* 0= no SS insert * use SS insert when you steam sterilize the filter	PH= Pharma version
	J= Junior cartridge	02=2.5" 05=5.0"				

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

► Filter cartridges FilterNYL 0.2 µm-technical characteristics

Materials of construction				
Membrane	Nylon 6,6 (NYL)			
Support layers	Polypropylene (PP)			
Cartridge supports	Polypropylene (PP)			
O-rings	Silicone			
Technical characteristics				
Filtration area	0.78 m ² (10'' module)			
Pores size	0.2 µm			
Length	Cartridges are available with the following dimensions: 5'' JUNIOR (125 mm), 10'' (250 mm), 20'' (500 mm), 30'' (750 mm)			
Retention characteristics				
Bacteria retention	Retention of 10 ⁷ CFU/cm ² Brevundimonas diminuta (ATCC 19146), as per ASTM F838-05.			
Mechanical characteristics				
Hydraulic Stress Resistance	FilterNYL filter cartridges 0.2 µm rated showed to retain their diffusion and integrity characteristics after the following hydraulic stress tests			
	Water Pressure (bar)	N° of strokes	Water temperature (°C)	Flow direction
	5.0	50	20±5	Forward
	2.0	50	20±5	Reverse
Thermal Stress Resistance	FilterNYL filter cartridges 0.2 µm rated showed to retain their diffusion and integrity characteristics after the following thermal stress tests			
	Temperature Test (°C)	Pressure Test (bar)	Cycle Time ¹ (hours)	N° of cycles (in autoclave)
	121	1.15	1	50
Estractables				
Estractables	FilterNYL 0.2 filter cartridges meet USP<661>.			
Conformity of materials to the rules for food contact	The materials used to produce the FilterNYL 0.2 µm cartridge filters were confirmed to be compliant with the requirements for food contact prescribed in Reg. N° 1935/2004/EEC and meet the FDA Indirect Food Additive requirements cited in 21 CFR 177 – 182.			
Biological reactivity				
Toxicity of materials	All the materials of the FilterNYL 0.2 µm filter cartridges meet the requirements of USP<87> ("Biological Reactivity Test in vitro for Class VI Plastics") and USP<88> ("Biological Reactivity Test in vivo for Class VI Plastics – Safety Test").			
Release of particles and/or Endotoxins				
Bacterial endotoxins	< 0.25 EU/mL of aqueous extract as per USP<85>.			
Non-fibre releasing	FilterNYL 0.2 µm filter cartridges satisfy the requirements as per USP<788>			

¹ Total time considering warming up time of 15 minutes; 30 minutes at test temperature and 15 minutes for cooling down to ambient temperature.

►Bacteria removal efficiency

Regulator Authorities FDA and EMA, set the rule to demonstrate the sterilizing action of a filter before to start to use it in pharmaceutical applications. Therefore, the sterilizing grade of a filter cannot be set only by the rating of pores dimension.

In order to consider a filter of sterilizing grade it must be submitted to a process simulation challenging it by a bacterial suspension of *Brevundimonas diminuta* ATCC 19146 at the concentration of not less than 10^7 CFU/cm². The downstream fluid must be sterile.

This must be done both for the qualification of the membrane, using 47 mm discs, and for the qualification of the production process of cartridges and / or filter capsules.

The correlation between the microbial retention and the non-destructive integrity test is another very important aspect of the validation of a pharmaceutical grade filter cartridge.

The Regulator Authorities require a procedure to control the filter both prior and after the use.

According to the ASTM F838-05 method, the tests demonstrate the ability of membranes, used to produce FilterNYL, to fully retain a *Brevundimonas diminuta* bacterial charge of 10^7 CFU/cm².

Hereinafter are reported the Challenge tests results made on a 10" FilterNYL filter cartridges 0.2 µm rated, to validate its process of production.

You can also find the correlation between the retention and the diffusion test.

This correlation is important to set the maximum diffusion flow acceptance limit to guarantee that the filter will produce a sterile effluent.

►Filter cartridge type NYL 7 10 002 S I – PH: correlation diffusion vs retention

To perform the test, 20 filter cartridges were withdrawn from normal production. Each cartridge has been tested by diffusion test at 2750 mbarg and then challenged by a suspension of *Brevundimonas diminuta* at the concentration $>10^7$ CFU/cm². Numerical results are reported in Table 1. The filter cartridges NYL 7 10 002 S I – PH meet acceptability criteria on performance basis.

LOT N°	DIFFUSION AT 2200 mbar (ml/min)	DOWNSTREAM STERILITY	TITRE REDUCTION
6634/31	5.5	Yes	$> 1.4 \times 10^8$
6634/22	6.0	Yes	$> 1.4 \times 10^8$
6213/12	6.5	Yes	$> 1.2 \times 10^8$
6114/07	7.0	Yes	$> 1.6 \times 10^8$
5974/12	7.5	Yes	$> 1.7 \times 10^8$
5764/30	8.0	Yes	$> 1.8 \times 10^8$
5764/12	8.1	Yes	$> 1.8 \times 10^8$
5949/33	8.4	Yes	$> 1.4 \times 10^8$
5764/18	8.4	Yes	$> 1.5 \times 10^8$
5935/35	8.7	Yes	$> 1.5 \times 10^8$
5882/05	8.9	Yes	$> 1.3 \times 10^8$
6435/26	9.0	Yes	$> 1.4 \times 10^8$
6465/19	9.3	Yes	$> 1.2 \times 10^8$
6354/14	9.3	Yes	$> 1.1 \times 10^8$
6215/37	9.5	Yes	$> 1.4 \times 10^8$
6215/34	9.8	Yes	$> 1.7 \times 10^8$
6215/02	10.0	Yes	$> 1.8 \times 10^8$
6632/46	12.0	Yes	$> 1.3 \times 10^9$
6176/17	13.5	No	1.6×10^6
6989/12	13.5.0	No	1.5×10^6
6045/22	13.0	Yes	$> 1.7 \times 10^8$

Table 1- Filter NYL: NYL 7 10 002 S I - PH filter cartridges 0.2 μ m
Results of bacterial retention test

On performance basis, FilterNYL filter cartridges NYL 7 10 002 S I - PH 0.2 micron rated meet acceptability criteria and are considered to be a sterilizing filters within a maximum diffusion value of 12.0 mL/min.

► Biological and extractables tests

► Bacterial endotoxins – current USP <85>

The test was used to measure bacterial endotoxins released from FilterNYL filter cartridge 0.2 micron rated. The test was carried out according to the Current USP<85> using the Chromogenic Method to measure the amount of endotoxins released by a filter cartridge type FilterNYL 0.2 micron.

The sample cartridge was filled with a pyrogen-free water and then treated by an ultrasonic device in order to enhance endotoxins extraction.

Water samples obtained was then submitted to the analysis.

The lab test shows bacterial endotoxins level released by the filter cartridge FilterNYL.

The test results demonstrate the absence of endotoxins release from FilterNYL cartridges.

LOT N°	METHOD	RESULTS
5967/03	cUSP<85>	<0.25 EU/mL
5876/21	cUSP<85>	<0.25 EU/mL
6111/15	cUSP<85>	<0.25 EU/mL

Table 2-LAL test results

► Extractables – current USP<661>

Test scope is to measure the amount of non-volatile residual released by the cartridge treated with WFI water. The extraction tests were run in static conditions for 24 hours at 70 °C. A portion of liquid extracted was evaporated to dryness and then submitted to non-volatile residual (NVR) measure.

NVR test results are reported in table 3.

LOT N°	NVR
5967/05	<5 mg
5876/22	<5 mg
6111/16	<5 mg

Table 3-Results of tests carried out according to cUSP<661>

FilterNYL 0.2 micron meet USP<661> requirements.

►Chemical compatibility

The following table lists chemical compatibility of FilterNYL filter cartridge 0.2 micron rated, when challenged with chemical products. Chemical compatibility is influenced by several parameters (temperature, concentration, contact time). IPM suggests that the Customers check chemical compatibility running a test at the same process conditions, before to use a FilterNYL cartridge 0.2 micron. IPM remains available, if requested, to supply the Customer with technical support.

CHEMICAL CLASSIFICATION	COMPOUND (Test Conditions 7days at 20°C)	RESULTS
ACIDS	Acetic acid, 90%	N
	Acetic acid, 30%	N
	Acetic acid, 10%	N
	Hydrochloric acid, conc. (35%)	N
	Hydrochloric acid, 6N (20%)	N
	Hydrochloric acid, 1N (3.3%)	N
	Nitric Acid, conc. (67%)	N
	Nitric acid, 6N (27%)	N
	Sulphuric acid, conc. (96%)	N
ALCOHOLS	Sulphuric acid, 6N (16%)	N
	Amyl alcohol	R
	Benzyl alcohol	L
	Butyl alcohol	R
	Ethanol (Ethyl alcohol)	R
	Isopropanol	N
AROMATIC HYDROCARBONS	Methanol	R
	Benzene	R
	Toluene	R
	Xylene	R
BASES	Ammonium hydroxide, 3N (5.7%)	R
	Ammonium hydroxide, 6N (11.4%)	R
	Potassium hydroxide, 3N (15%)	R
	Sodium hydroxide, 3N (11%)	R
	Sodium hydroxide, 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	L
	Methylene chloride	L
KETONES	Acetone	L
	Cyclohexanone	R
	Methyl ethyl ketone (MEK)	R
	Methyl isobutyl ketone	R
OILS	Cottonseed	R
	Peanut	R
MISCELLANEOUS	Acetonitrile	L
	Dimethyl-Formamide (DMF)	L
	Formaldehyde (37%)	R
	Hexane	R
	Pyridine	N

Table 4 - FilterNYL 0.2 micron cartridges Chemical Compatibility
(R=recommended; L=Limited resistance; N=Not Recommended; « - » Insufficient Data)

► Biological Safety Test

► "In vitro" Biological Reactivity Test - Class VI Plastic Materials (current USP<87>)

Test scope is to evaluate biological toxicity of FilterNYL cartridges 0.2 micron . The cartridge (O-rings included) is submitted to extraction with extractive solutions following related recipes provided for by current USP <87>. Test results are recorded as reactivity degree ranging from 0 (none reactivity) to 4 (high reactivity)

LOT N°	TEST	METHOD	RESULTS
5876/25	cytotoxicity	cUSP <87>	Reactivity grade = 0
6111/01	cytotoxicity	cUSP <87>	Reactivity grade = 0
5831/53	cytotoxicity	cUSP <87>	Reactivity grade = 0

Table 5-Results of tests carried out according to current USP<87>

Test results carried out according to USP<87>,.demonstrate lack of "in vitro" biological reactivity by FilterNYL filter cartridges 0.2 micron rated.

► "In Vivo" Biological Reactivity Test -Class VI Plastic Materials – Safety Test
(current USP<88>)

Test scope is to evaluate the "in vivo" reactivity of FilterNYL cartridge according to the method provided for by USP <88>.

Test results are compared with USP acceptability limits.

LOT N°	TEST	RESULTS
5876/01	Intracutaneous Test	Conform
	Systemic Injection Test	Conform
	Implantation Test	Conform
6111/19	Intracutaneous Test	Conform
	Systemic Injection Test	Conform
	Implantation Test	Conform
5831/11	Intracutaneous Test	Conform
	Systemic Injection Test	Conform
	Implantation Test	Conform

Table 6-Results of the tests carried out according current USP<88>

Test results carried out according to USP<88>, demonstrate lack of "in vivo" biological reactivity by FilterNYL filter cartridges 0.2 micron rated.

►Physical characteristics

►Hydraulic stress test

Test purpose is to demonstrate the capability of FilterNYL 0.2 micron cartridges to tolerate hydraulic stress at ambient temperature (20 ± 5 °C). 10" FilterNYL cartridges were installed inside an holder, wetted with water and fluxed at 2 bar during 20 minutes at least. After the wetting cycle was run a diffusion test.

If the cartridge passes the diffusion test, is then washed with a direct flux during 10 minutes, with 50 sudden pressure strokes from 0 to 5.0 bar. The same cartridge is then back-flushed at 2.0 bar per 10 minutes, with 50 sudden pressure strokes from 0 to 5.0 bar.

This test is repeated 50 times in both flux directions- Every 10 stress cycle every single cartridge is controlled by integrity diffusion test.

Diffusion test is performed at 2750 mbar. Acceptability limit of diffusion test was set at 12.0 mL/min. The following table reports diffusion test results run before and after 50 cycles of stress test.

LOT N°	DIFFUSION BEFORE STRESS TEST (mL/min)	DIFFUSION AFTER 50 CYCLES OF STRESS TEST (mL/min)
6633/41	8.2	7.7
6213/37	8.5	8.7
6114/19	8.5	9.0
5974/35	8.7	9.2
5764/09	9.0	8.8
5935/07	8,7	8.4
5831/45	8.6	8.5
5994/31	8.0	8.4
6213/50	9.0	9.0

Table 7-Results of hydraulic stress test run on FilterNYL filter cartridges

Test results confirm the high resistances of FilterNYL filter cartridges to hydraulic stress, even changing pressure and flux direction.

► Thermal stress test

The purpose of this test is to determine FilterNYL filter cartridges (10") resistance to multiple steam sterilization. The test has been carried out at 121 °C as provided for an appropriate steam sterilization. After a diffusion test the cartridge is submitted to 50 sterilization cycles. Every 10 cycles diffusion test is repeated.

Sterilization cycles follow the schedule below

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

Table 8 -Sterilising cycle program

Diffusion tests were run at 2750 mbar. Acceptability limit of diffusion test was set at 12.0 mL/min.

The following table reports diffusion test results run before and after the stress test of 50 steam sterilizations:

LOT N°	DIFFUSION BEFORE STRESS TEST (mL/min)	DIFFUSION AFTER 50 STEAM STERILIZATIONS STRESS TEST (mL/min)
6633/44	7.5	8.0
6213/26	9.0	9.5
6114/13	8.5	9.5
5974/11	8.4	9.0
5764/01	8.0	8.5
5935/54	9.0	8.5
5831/32	8.7	8.4
5994/12	9.5	9.5
6213/02	7.7	8.8

Table 9-FilterNYL cartridges Thermal Stress Test results

Test results confirm the high resistances to thermal stress of FilterNYL filter cartridges submitted to repeated thermal stress in autoclave.

► Differential pressure vs water flow rate

The test measures the pressure drop when different flow rates are fluxed across the filter cartridge membrane.

All data are referred to temp of 20 ± 5 °C.

10" FilterNYL cartridges typical pressure drop vs flow rate curve, is shown in the following graph.

Within the typical flow rate range of usage, FilterNYL cartridges guarantee initial pressure drops less than 0.2 bar (flow rate <1200 L/h per 10" cartridge)

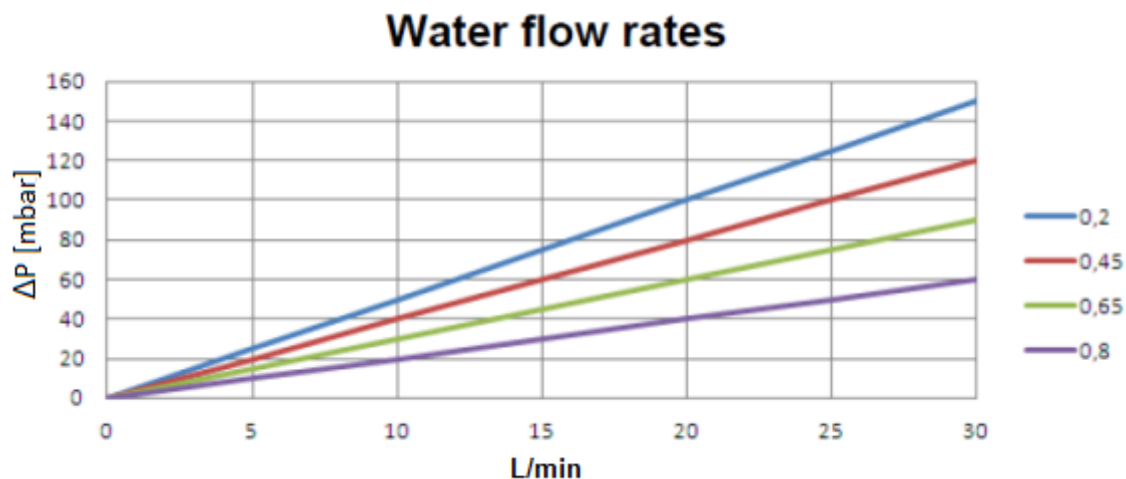


Figure 1-Water Flow Rate vs pressure drop graph.

► Attachment

- Sample of Certificate of Conformity (CoC) enclose in every packaging of cartridge type –PH

Every cartridge type –PH (which can be used in pharmaceutical productions) is shipped together with a Conformity Certificate (CoC) / Lot traceability. Here following a facsimile:

 Via Machi Teresa, 22 20035 Cinisello - Italy Tel +39 039 2145244 Fax +39 039 2145245 E-mail: ipm@ipmfilters.com www.ipmfilters.com		Data di produzione Date of production Date de production Fecha de producción 01/01/2013	
CERTIFICATO DI CONFORMITÀ CERTIFICATE OF CONFORMITY CERTIFICAT DE CONFORMITÉ CERTIFICADO DE CONFORMIDAD		XXXXXXX	
Cliente - Customer Client - Cliente		XXXXXXXXXXXXXXXXXXXX	
TIPO DI FILTRO FILTER TYPE TYPE DE FILTRE TIPO FILTRO		Filter NYL	
MOD.		NYL710.002-S1	
L.O.T.		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 test di integrità come sopra specificato, è stato eseguito su ogni singolo cartoccia di questo lotto e risponde alle procedure interne del controllo qualità IPM certificate le cartucce filtranti IPM sopra descritte sono state controllate in ambiente controllato. Materie di costruzione: I componenti del filtro rispondono alle specifiche per i test di biocompatibilità previste dalla USP classe VI per materie plastiche a 121 °C e a quanto previsto per fluidi in contatto con alimenti secondo CFR Title 21 parte 170-199. Questo prodotto risponde a tutti gli standard qualitativi IPM. L'ipotesi non è frutto casuale. IPM dichiara che questo certificato di conformità risponde al vero e sostituisce quanto da lui richiesto. Tutti i test sopra descritti sono stati condotti secondo procedure. La merce ed i materiali sono privi di difetti. Integrity test has been run on every cartridge of this batch and meets the internal QC procedures. IPM hereby certifies that the above IPM filter cartridge has been manufactured in a controlled environment. The filter components have met the specifications for biological tests listed in the current revision of the United States Pharmacopoeia (USP) for Class VI plastics at 121 °C. These filter also are used from materials listed for food contact usage per Title 21 of the U.S. Code of Federal Regulation (CFR) parts 170-199. Contact IPM for more information regarding materials of construction. This product has met all IPM standards for manufacturing inspection and traceability. The above are true supplier claims. IPM hereby certifies that this certificate of conformity is true and correct and meet y our order requirements. All the above (and) has performed as per our procedures. The end is certify goods and materials have no defect. Le test d'intégrité spécifique ci-dessus a été effectué sur chaque cartouche du lot et remplit toutes les exigences internes du contrôle de qualité IPM certifie que les cartouches filtrantes IPM indiquées ci-dessus ont été fabriquées en milieu contrôlé. Matières de construction: Les composants du filtre répondent aux critères pour procéder de biocompatibilité prévue par USP, classe VI pour matières plastiques à 121°C définies pour les liquides en contact alimentaire selon le Title 21 de CFR parties 170-199. Ce produit correspond aux standards de qualité IPM. Le produit n'est pas fruit casuel. IPM déclare que ce certificat de conformité correspond à la réalité et substitue toutes vos exigences. Tous les tests décrits ci-dessus ont été effectués selon la procédure. La marchandise et les matériaux n'ont aucun défaut. Todos y cada uno de los cartuchos de este lote han sido sometidos al test de integridad según las especificaciones antes descritas, y cumplen con los procedimientos internos del control de calidad IPM certifica que los cartuchos filtrantes IPM antes descritos han sido fabricados en ambiente controlado. Materiales de construcción: Los componentes del filtro cumplen los criterios para pruebas de biocompatibilidad de la USP clase VI para plásticos a 121 °C y con todos los requisitos para No los en contacto con alimentos según el Title 21 de CFR partes 170-199. Este producto cumple todos los parámetros de calidad IPM. El producto no es un resultado casual. IPM declara que los datos de conformidad de conformidad son verídicos y se corresponden con los requisitos de su pedido. Todos los pruebas antes citadas se han llevado a cabo con arreglo a sus procedimientos. Los productos y los materiales están libres de defectos.			
IL CONTROLLO DI QUALITÀ - QUALITY CONTROL CONTRÔLE DE QUALITÉ - CONTROL DE CALIDAD			

Figure 3- Sample of Conformity Certificate released by IPM Sistemi di Filtrazione

IPM Sistemi di Filtrazione s.r.l – Via Madre Teresa, 22 -20851 Lissone (MB) - ITALY

IPM Filters, FilterNYL are trademark
of IPM Filters.

Doc n° VGNYL02EN rev 210119
printed in Italy 02/2021

IPM reserves the right to
change any and all
characteristic of the items
to offer the best product
to the customer. Please
check with IPM if any
doubt about.

Ordering & Info request

E-mail: ipm@ipmfilters.com

Tel. +39 0392145244

Fax. +39 0392145245

To learn more about us:

www.ipmfilters.com

