BEAPURE

presentation of "Animal Free" filters

Purification Control Technology

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«BEAPURE»

OUR FILTRATION PRODUCTS SPECIFICALLY DESIGNED AND PRODUCED FOR *PHARMACEUTICAL INDUSTRY*

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More than 50 years of experience in filtration

BEA Technologies
Answers ready, effective and dedicated service to the specific needs of the customer.

Who choose **Bea Technologies** has found the right partner: quality, reliability, cooperation over the time, oriented to customer satisfaction.

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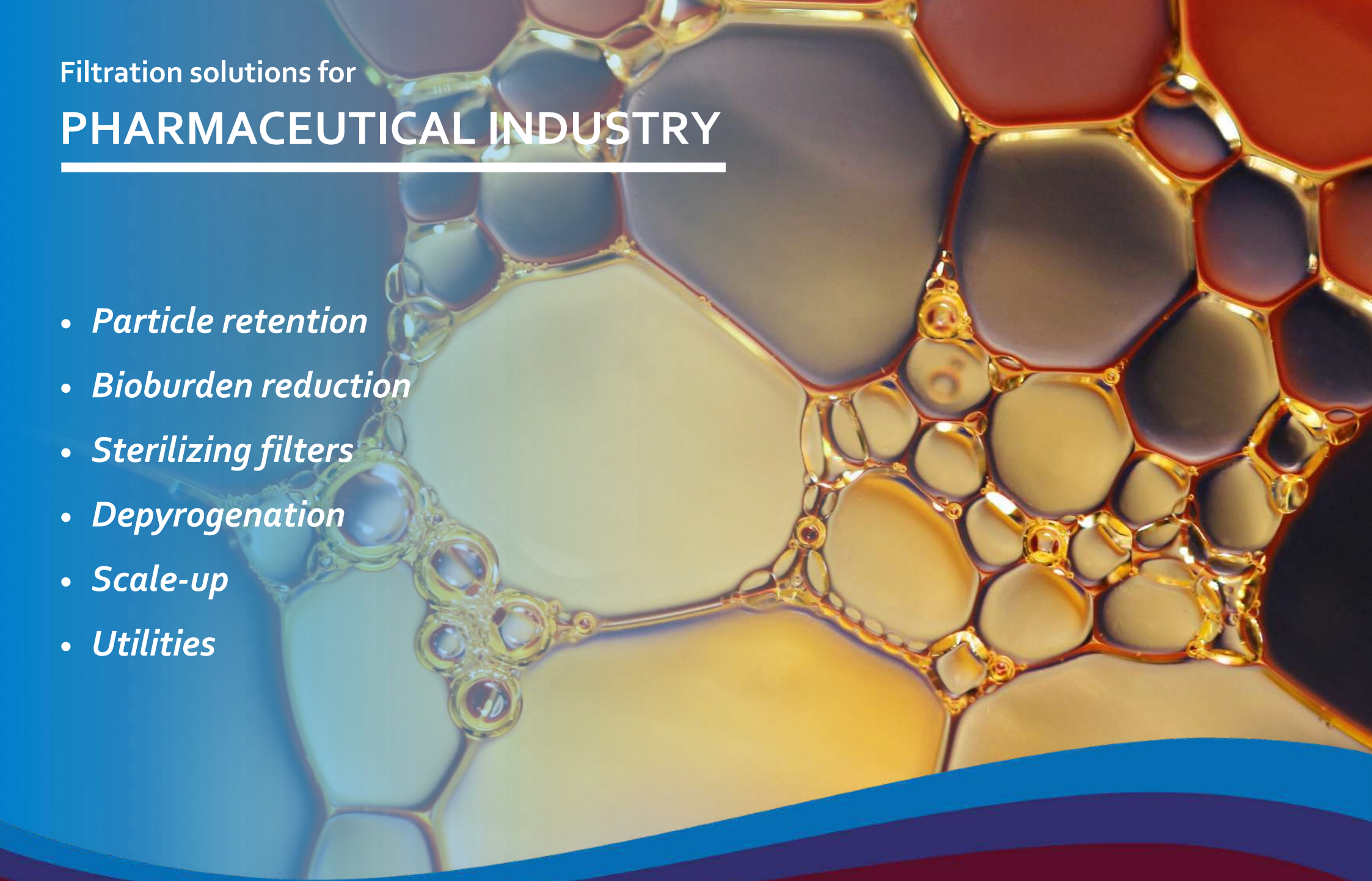
Filtration solutions for

PHARMACEUTICAL INDUSTRY



- *Particle retention*
- *Bioburden reduction*
- *Sterilizing filters*
- *Depyrogenation*
- *Scale-up*
- *Utilities*

Company History

1976 — In 1976 the Company focuses on the construction of filter elements with an absolute degree of filtration, used for applications that require precision filtration.

1984 — In 1984 has created the BEA Laboratory Service for R&D activities on Pre Post assistance. The filter is produced with an absolute filtration rating of 0.2 micron.

1987 — In 1987 the laboratory has been equipped with a laser particle counter to check the efficiency of the filters and the MICROBIOLOGY department is set up, to executive tests of bacteria retention and bacteria challenge on sterilizing membrane filter elements.

1990 — In 1990 the CAD system was introduced for design of pressure vessels.

1994 — In 1994 obtained the UNI-EN 29001 CERTIFICATION (ISO 9001) for the Quality System.

1996 — In 1996 a new CLEAN ROOM has been built for the production of filter element in compliance with pharmaceutical standards.

1998 — In 1998 the "PYROGEN FREE" water plant has been installed with the consequent expansion of production activity of the Clean Room for the bio-medical sector.

2002 — In 2002 the production capacity of micro-filtration increased with expansion of the CLEAN ROOM and the CAD system enhanced with the latest generation of software in the modernization of the entire IT system.

2004 — In 2004 changed the company name into BEA Technologies SpA in order to identify the mission of providing innovative products to customers.

2011 — In 2011, it has triple-increased the production capacity thanks to the expansion of the WHITE CAMERA and the introduction of new updated machinery and at the most modern production processes.

2017 — In 2017, as a part of the National Industry 4.0 Plan, BEA invests in technologies and machinery to support digital transformation, and therefore increase efficiency and improve competitiveness.

2019 — In 2019, the launch of the new series of filter elements "BEAPURE" characterized by the new philosophy to be "Animal Free" without additives of animal origin.

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SCOPE OF PROJECT:

Redefine the materials of construction and filter media to avoid substances of ANIMAL ORIGIN.

The manufacturers of many polymers are adding additives to improve the characteristics for moulding and extrusion

- **1st PHASE:** check the composition of actual materials and polymers
- **2nd PHASE:** request certification of materials to manufacturers
- **3rd PHASE:** check composition of filters with new materials

HISTORICAL DEVELOPMENT: RECEIVING THE REQUEST TO SUPPLY <<ANIMAL-FREE>> FILTERS.

The customer's request was forwarded to us at the end of 2017 and it all started with an important big Pharma customer. In particular, compliance with the EMA/410/01 Rev. 3 guideline (relating to the inactivation of substances of animal origin) was not deemed sufficient.

The customer's specific request was to have products **"Free of substances of animal origin"**. From the finished product (API) backwards, the customer's request has been extended to all contact materials. BEA filters, being the last purification step in production process, were involved first…

Typical «BSE/TSE statement» by resin manufacturers

The typical statement is based on following factors to demonstrate the use of "TALLOW" in production of polypropylene resin in our product poses a very low risk in the transference of transmissible spongiform encephalopathy (TSE) or bovine spongiform encephalopathy(BSE):

1) The polypropylene resins used to mold plastic parts may contain bovine tallow used as an additive to their process. This tallow supply comes from North America, Europe and Asia. The suppliers state that prior to use, the tallow goes through the hydrolysis conditions of 260 degrees C at 48 bar for 1.5-2 hours, complying with EMEA/410/01 Rev3. These hydrolysis conditions exceed those rigorous conditions outlined in section 6.4 of hydrolysis of 200 degrees C, under appropriate corresponding pressure for 20 minutes.

2) It is claimed that BSE has never been found in beef tallow and the World Health Organization (WHO) said that tallow does not represent a risk for human and animal health (OMS/CDS/VPH/95.145).

Typical «BSE/TSE statement» by resin manufacturers

3) The polypropylene resins are then subjected to high temperatures again during the extrusion and molding process. Polypropylene resins are typically molded at temperatures above 230 degrees F.

4) The use of animal derived stearates in polyolefin resin is very common. Based on this knowledge, the resin manufacturers conclude that the use of polypropylene resin poses essentially low risk in the transference of transmissible spongiform encephalopathy(TSE) or bovine spongiform encephalopathy (BSE).

«BSE/TSE Statement»

Please note:

- All information filled into the "BSE/TSE statement" have to be written and confirmed by the respective manufacturer.
- All documentation attached to "BSE/TSE statement" , have to be signed with date:

1) The statement and relative questionnaire is primarily based on the "Note for Guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products" (EMA/410/01 Rev. 3), available on

http://www.ema.europa.eu/docs/en GB/document librarv/Scientific guideline/2009/09/WC500003700.pdf

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Our Research & Development started to study the request to search for *«Animal-free»* polymers and materials:

- check of chemical compatibility
- test on extractables
- review of certifications
- studies on contact with specific fluids

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From results of research
BEA Technologies
has selected the
«Animal-free»
materials & polymers

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SPECIFIC FEATURES OF «BEAPURE»FILTER ELEMENTS

Declared «Animal-Free»

BEAPURE filters comply with the latest European and FDA regulations

Traceabilty of materials used in production

Production in clean room facility

Periodical controls in BEA laboratory

Final controls on assembled filters

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BEAPURE
Animal Free filters

Filter elements « Animal free»

BEAPURE filter elements are manufactured using materials and polymers (polypropylene,polyester,Nylon, PES, PTFE) which are completely free from substances of animal origin (stearates), generally added during production process of polymers to facilitate extrusion and moulding.

Otherwise, the filters that are only in compliance with the «BSE/TSE» requirements contain substances of animal origin that have only been «deactivated» to prevent the potential transmission of BSE and TSE.

BEAPURE filter elements are full in compliance with latest European and FDA

Here below are listed the names of BEAPURE range of filter elements:

STERYKLEAR ADM FREE BEA CODE – KSEA filter elements with PES membrane
STERINYL ADM FREE BEA CODE – KLEA filter elements with NYLON 66 membrane
STERYFLON ADM FREE BEA CODE – PTFA filter elements with PTFE membrane
POLYVER ADM FREE BEA CODE – PLVA filter element with borosilicate filter media
POLYSAN ADM FREE BEA CODE – PKPA filter elements with PP filter media
POLIXSTER ADM FREE BEA CODE – PKEA filter element with PE filter media

These filter elements, «Animal-free» are in compliance with the requirements for pharmaceutical use and to latest Europen and FDA regulations.

STERYKLEAR - KSEA ADM line of PES single/double membrane filter elements, with high filtration surface, designed to filter high volume of liquid solutions.

BEA Technologies provides

- Micron rating Single/double membrane 0.1 , 0.2, single membrane 0.45.
- Full validation guide and documentation for validation on site
- Documentation for Regulatory support files

STERINYL - KLEA ADM line of NYLON 66 single and double membrane filter elements, highly hydrophilic and resistant to solvents, designed to filter specific types of liquid solutions.

BEA Technologies provides

- Micron rating Single/double membrane 0.1 , 0.2, single membrane 0.45 and 0.65 micron.
- Full validation guide and documentation for validation on site
- Documentation for Regulatory support files

STERYFLON – PTFA ADM line of PTFE membrane filter elements, specific for air & gas filtration, reinforced for repeated steam sterilization.

BEA Technologies provides

- Range of micron rating 0.1 , 0.2
- Full validation guide and documentation for validation on site
- Documentation for Regulatory support files

POLYVER - PLVA ADM line of filter elements with borosilicate microfibers, specific for retention of collioidal and fine particles.

BEA Technologies provides

- Range of micron rating 0.5 , 0.65, 1.0, 2.5
- Full validation guide and documentation for validation on site
- Resistant to repeated steam sterilization.

POLYSAN - PKPA ADM line of filter elements with PP filter media, neutral, reinforced for repeated steam sterilization.

BEA Technologies provides

- Range of micron rating 0.6 , 1.2, 2.5, 4.5, 6.5, 10,0
- Full validation guide and documentation for validation on site
- Resistant to repeated mechanical stress.

POLIXSTER – PKEA ADM line of filter elements integrally made in Polyster to allow better compatibiity to solvents.

SCOPE OF FILTRATION:

Retention of Fine particles in solvents

- 1st FILTRATION: POLIXSTER grade rating 5.0 micron
- 2nd FILTRATION: POLIXSTER grade rating 1.0 micron
- FINAL FILTRATION: POLIXSTER rating 0.5 micron

Our filtration knowledge at the service of the PHARMA INDUSTRY

APPLICATIONS:

The customer requesting “Animal-free”, ADM free products has decided to standardize all the filtration of finished products with filter elements belonging to this category. For this reason the “Animal-free” filter elements have become of compulsory use in production also for all filter elements in contact with utilities.

Production processes where have been installed «Animal-free» filters:

We are here reporting 2 processes where are installed BEA «Animal-free» filters.

Process 1: Decoloration process

Flow sheet: reactor with mixer + plate&frame filter + final cartrige filter; destination of filtered product: stockage in tank waiting for crystallization.

Process Data:

Solution: metanol – DMF – purified water – API + addition of activated carbon
Operative temperature: 77° C
Batch volume: 2000 l
Flow rate: 2000 l/h
Operative pressure: 0,8 – 1,5 barg (pressurized with N_2 gas)
Filtration time: 60 min. (excluding decoloration time)

SCOPE OF FILTRATION:

Retention of FINE activated carbon particles

Clarification of solutions to retain the exhausted activated carbon particles

- **PREFILTRATION: POLYSAN 2.5 - 1.2 micron**
- **FILTRATION: POLYVER (Pleated borosilicate fibers) 0.5 micron**

or

- **FINAL FILTRATION: STERYKLEAR (PES) 0.2 micron**

Production processes where have been installed «Animal-free» filters:

Case history 2: Decoloration process

Flow sheet: reactor with mixer + Filter sheets + final cartridge filter; product destination: storage in tank waiting for crystallization .

Process data:

Solution: API diluted in acetone + addition of activated carbon particles
Temperature: 56° C (product stating crystallization at 40-43°C)
Batch volume: 3500 l
Flow rate: 1000 l/h
Operative pressure: 0,5 – 1,0 barg (pressurized by N_2 gas)
Filtration time: 210 min. (excluding decoloration time)

SCOPE OF FILTRATION:

Retention of FINE particles and haze

Purification of active ingredients

- **1st FILTRATION: POLYSAN - PKPA**
- **(PP pleated) 2.5 -1.2 micron**

- **2nd FILTRATION: POLYVER - PLVA**
  (Borosilicate pleated fibers) 0.65 micron

- **FINAL FILTRATION: STERYKLEAR – KSEA**
  (PES membrane) 0.2 micron

Production processes where have been installed «Animal-free» filters:

3- Retention of fine particles:

-Retention of activated carbon fine particles downstream decoloration process.
-Retention of fines by resins.
-Separation of metallic catalyzers to be wasted.
-Separation of precipitated salts

These operations are based on liquid solvents or mix of different solvents.

Used Filter types: Polyver – Polysan – Polixster ADM free versions.

Filter material: selected with reference to compatibility to solvents and temperature.
Filtration rating and sizing of filter system: selected on batch size and contamination level

SCOPE OF FINE-FILTRATION:

Retention of activated carbon particles, fine particles and various aggregates.

- **POLYSAN**
  ADM Free (PP pleated filter elements) rating 0.65, 1,2, 2,5, 5.0, 10.0 micron

- **POLYVER**
  ADM Free (Pleated borosilicate fibers) 1.0 micron

- **POLIXSTER**
  ADM Free (Pleated Polyester filter media) 0.5 micron

Production processes where have been installed «Animal-free» filters:

1)Filtration of air/nitrogen in following operations:

- Fluid beds Dust handling
- Fluid handling in time / pressure mode
- Blow molding systems
- Stabilization and inertization of plants with nitrogen

Installed filter element: Steyflon Plus – PTFA ADM free

Separation of fine particles from vents and exhausts released by mixers and granulators

SCOPE OF FILTRATION:

Retention of powder that can be exhausted to internal environment of production site.

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1) FILTRATION: POLYSAN (PP pleated) rating 10.0 micron

or

2) FILTRATION: POLYSAN (PP pleated) rating 2.5 micron

or

3) FILTRATION: STERYFLON (PTFE membrane) 0.2 micron

Production processes where have been installed «Animal-free» filters:

1) Filtration on production of Purified Water.

Products: Steryklear ADM free rated 0.2 micron

Know-how
and expertise
to ensure

filtration
solutions

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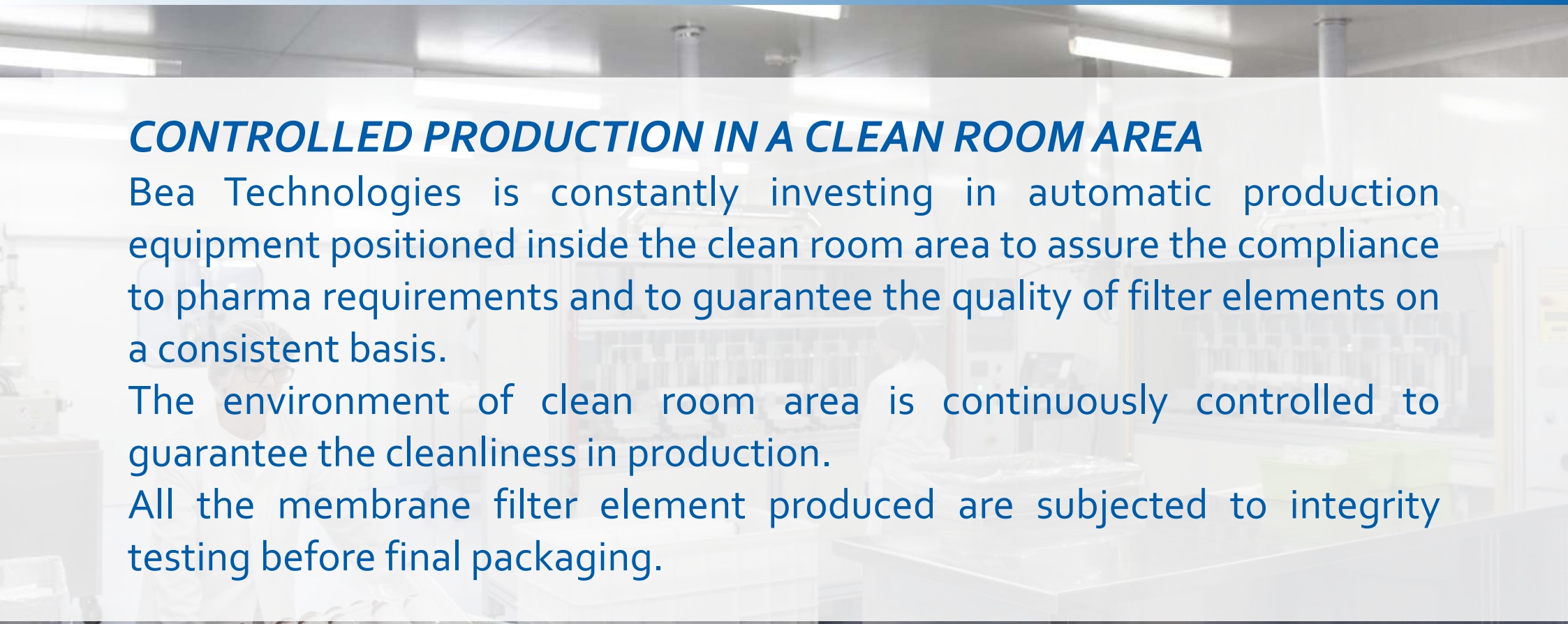
Our production process is conducted in a certified clean room with highly trained personnel



CONTROLLED PRODUCTION IN A CLEAN ROOM AREA

Bea Technologies is constantly investing in automatic production equipment positioned inside the clean room area to assure the compliance to pharma requirements and to guarantee the quality of filter elements on a consistent basis.

The environment of clean room area is continuously controlled to guarantee the cleanliness in production.

All the membrane filter element produced are subjected to integrity testing before final packaging.

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We execute the final integrity testing on each single membrane filter to guarantee product quality

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QUALITY MANAGEMENT & CERTIFICATIONS

The activities of BEA Technologies are regulated by the Quality Management procedures for the design, production, distribution and after-sale assistance of filtration products.

The Quality management System of the company is certified by an international body and recognized in compliance with ISO 9001 e ISO 3834 requirements and standards.

Life Science

Microfiltration filter elements for pharmaceutical companies are manufactured in a cleam room environment to meet the pharma requirements and maintain safety and traceability parameters.

PRODUCT TRACEABILITY

Production is carried out internally to ensure the product quality and reliability of a controlled supply chain. The highly trained production team benefit from direct support from the management and Research & Development department to maintain the efficiency in production and effectivenes in problem solving.

BEA Technologies can guarantee the traceability of materials used ant the process controls at each single stage of assembling. The company is able to support customers in the validation operations for the use of its filters in pharmaceutical production lines.

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PERIODICAL CONTROLS IN BEA LABORATORY

To assure the compliance of materials and filter elements to certifications, BEA Laboratory Service carries out periodical controls on charateristics and performances of materials and produced filter elements .

- **Analisis of extractables**
- **Bacterial challenge tests.**
- **Resistance to mechanical stress and Steam sterilizations.**

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Animal Free filters

RESEARCH & DEVELOPMENT

The BEA Technologies Research & Development Team provide the technical knowledge to identify the most advanced filtration solutions capable to meet the customer's needs in various applications.

- **Feasibility studies.**
- **Support to Installation, operational, performance *qualifications.***
- ***Training courses on filtration,***
- **Assistance to Start up and survey of filtration lines.**
- **Particle analysis.**
- **Microbiological analysis.**
- **Material chemical compatibility.**

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Next « Animal Free» CAPSULES

for filtration of small batches

Capsule will have following features:

- Type of membrane : PTFE
- Validation guide and documentation for validation on site
- Easy opening of vent and drain valves with gloves
- Indicated for filtration of solvents, venting, gas pressurization of tanks and bioreactors

MAKING THE DIFFERENCE

BEA Technologies provides

- Effective and dedicated service to the customer's needs
- Flexible production
- Prompt reply to your requests
- Wide range of different filter elements, housings and filtration systems to satisfy most of the current applications.

HEADQUATER and CONTACTS:

CONTACT US AT
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BEA Technologies Spa

Wish to thank you for
partecipation and your kind attention

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DEVELOPING
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QUESTIONS and ANSWERS