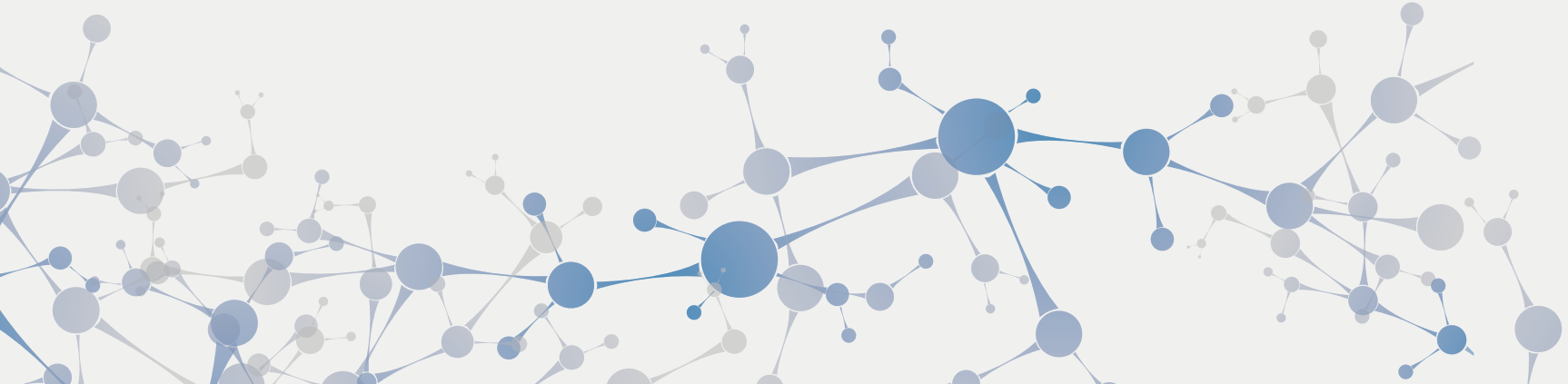
BSP PHARMACEUTICALS

# Sterile Injectable



# ONE STOP SHOP IN THE SUPPLY CHAIN OF ANTICANCER PRODUCTS


BSP Pharmaceuticals is a Contract Development and Manufacturing Organization focused on production of anticancer and cytotoxic drugs as small molecules and ADC compounds.

BSP Pharmaceuticals provides a full range of integrated services aimed to support the entire life cycle of a product.

From the formulation and process development/optimization, through scale up/scale down studies, we can drive the product to cGMP manufacturing for clinical and commercial needs.

QC laboratories are equipped to run all analytical testing (chemical and microbiological) on raw materials, components, in process controls, release and stability testing.

Internal Regulatory Affairs team to manage data collection and document preparation for DMF and CMC to support filing activities.

**DEVELOPMENT**
Formulation, Process, Analytical methods

**SCALE UP/DOWN**
Process Robustness and Characterization

**QUALITY CONTROL**
Release, Stability, Process comparability testing

**MANUFACTURING**
Clinical and Commercial Supply

**REGISTRATION**
Regulatory Support for DMF and CMC Preparation


The Manufacturing plant is located in Italy, 40 miles southbound of Rome. A single campus extended to more than 58 acres hosts all the main buildings supporting the capacities to manage a wide range of batch sizes.

**1 DEVELOPMENT LABORATORY**
**6 STERILE SUITES with more than 1800 sqft fully dedicated to production anticancer and cytotoxic drugs**

This work mode and the proper combination of expertise allows:
- To switch quickly from **development to commercial** production
- To make the **scale-up** of the product internally without the need to transfer the product elsewhere
- To **reduce** technical issues and constraints when changing manufacturing suites.

The **FULLY INTEGRATED** services we offer are suitable to manage **BREAK-THROUGH DESIGNATED COMPOUNDS** and **FAST TRACK APPROVED PRODUCT** for which an increased demand of manufacturing capacity can be necessary in a short timeframe and a robust technical package needs to be developed in order to minimize post approval changes.

# INJECTABLE
## CAPABILITIES

With the highest level of technology and the **most innovative** solutions applied to all manufacturing areas, BSP can fulfill the most stringent requirements for handling **conventional** cytotoxic High Potent Drugs as well **the next generation** of anticancer products characterized by complex formulations

### CONVENTIONAL CAPABILITIES

- LYOPHILIZED VIALS
- LIQUID VIALS BY ASEPTIC FILLING AND TERMINAL STERILIZATION

### SPECIAL CAPABILITIES

- LIPID BASED FORMULATIONS
- ORGANIC SOLVENT BASED FORMULATIONS
- ADCs FROM CONJUGATION TO FILL-FINISH

### SPECIAL CAPABILITIES
(non conventional formulation)

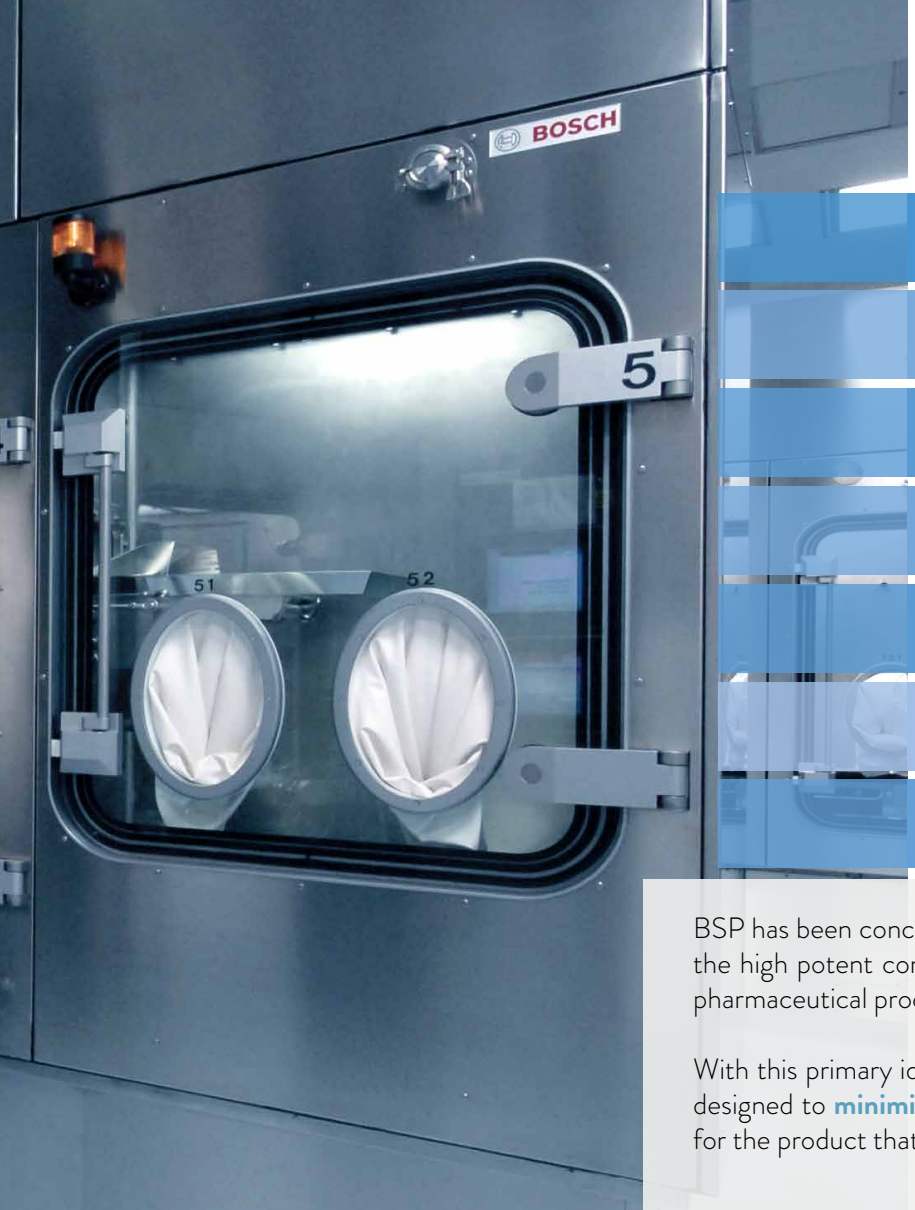
All Sterile filling lines are equipped to handle **Organic Solvent based formulations** as well a **oxygen-sensitive products**.

**Lipid-based formulations**, such as emulsion and suspension, can be manufactured by using special technologies and equipments, including:

- MICROFLUIDIZER
- HIGH PRESSURE HOMOGENIZER
- EXTRUSION


# AN HIGH CONTAINMENT FACILITY

DESIGNED TO HANDLE HIGH POTENT AND CYTOTOXIC COMPOUNDS




The plant has been designed to achieve an Occupational Exposure Limit (OEL) :

**<10 nanograms/m$^3$**

## CONTAINMENT GRANTED BY

- **INSULATING SYSTEM**
  ISOLATOR, cRABS, CONTAINMENT VALVES
- **PRESSURE CASCADE FROM OPERATIONAL**
  TO SURROUNDING AREAS
- **CONTINUOUS MONITORING**
  OF DIFFERENTIAL PRESSURES AND RELATED ALARM SYSTEM
- **DEDICATED AIR HANDLING SYSTEM**
- **100% EXHAUST AIR (NO RECIRCULATION)**
- **ABSOLUTE FILTER** OF EXHAUST AIR
- **CONTAMINATED WASTED MATERIAL**
  SEGREGATION, INACTIVATION AND DISPOSAL

BSP has been conceived starting from a basic but essential operating requirement: **segregate** the high potent components from the surrounding and create a system suitable to manage pharmaceutical processes.

With this primary idea in mind, layouts, flows of materials and personnel, air flows have been designed to **minimize** the risk of contamination for the environment, for the employees and for the product that is intended for patients with low level of immune defenses.

# STERILE SUITES CAPABILITIES

## CLINICAL AND COMMERCIAL MANUFACTURING

A UNIQUE MANUFACTURING SYSTEM **SPECIALLY DESIGNED** FOR ANTICANCER DRUGS, WITH THE FLEXIBILITY TO MANAGE **SMALL MOLECULES** AND **THE COMPLEXITY OF ADCs**

| | STERILE 2 | STERILE 6 | STERILE 1 | STERILE 4 | STERILE 5 | STERILE 3 |
|---|---|---|---|---|---|---|
| **LYO SURFACE** | 1x16 sqft | 2x65 sqft | 2x107 sqft | 2x215 sqft | 2x215 sqft | 2x323 sqft |
| **VIAL SIZES** range | from 2 ml to 100 ml | from 2 ml to 100 ml | from 2 ml to 100 ml | from 2 ml to 100 ml | from 2 ml to 100 ml | from 2 ml to 100 ml |
| **ISOLATOR AND CLOSED RABS** to have the highest level of sterility assurance and containment | Isolator | cRABS | cRABS | cRABS | cRABS | cRABS |

ALL THE EQUIPMENT USE **FIRST-IN-CLASS TECHNOLOGY** WITH AN HIGH LEVEL OF AUTOMATION TO REDUCE THE NEED OF MANUAL INTERVENTIONS.

**SIX STERILE MANUFACTURING SUITES**
equipped to handle liquid and lyophilized vials

**PRODUCT LINES ARE FULLY CUSTOMIZED**
and designed according to specific characteristics and criticality of each product and process

**FILLING LINES**
designed to minimize shear stress: possibility to use rotary piston pumps and peristaltic dosing systems

**HIGH SPEED FILLING LINE**
designed to manufacture products with short holding times

**CRYOGENIC LYOPHILIZERS**
enable a very accurate and efficient temperature's management during each step

**AUTOMATIC LOADING & UNLOADING SYSTEMS (ALUS)**
designed for a rapid introduction of the vials into the lyo chamber to minimize product's exposure to room temperature

**DEDICATED COLD STORAGE AREAS**
for BDS, mAb, toxin and finish product (+2/+8°C; from -20°C up to -80°C)

**DEDICATED AREAS**
for manual/automatic Thawing activities

**TEMPERATURE CONTROL**
during manufacturing

**CIP AND SIP SYSTEM**
to prevent microbiological and chemical carry over

**LOW LEVEL OF RESIDUAL PEROXIDE**
to prevent protein degradation

**DEDICATED PRODUCT CONTACT PARTS**
(stainless steel, disposable systems) and **SPECIFIC CLEANING PROCEDURES** to avoid contamination/degradation


ST4-061


ST4-021
Modulo c-RABS
CARICO/SCARICO LYO 1

# DEVELOPMENT

## CAPABILITIES

**BSP Sterile Department** has dedicated laboratories and skilled scientists to support formulation, process development and process optimization services.

**BSP Development Team** works on both conventional and innovative formulations including ADCs and Lipid Based Formulations such as nano/microemulsion and liposomes.

BSP can also perform all their ancillary studies that can support process characterization and robustness aimed to facilitate the product scale-up delivering the product from R&D to cGMP stage.

**THERMAL PROFILE**
characterization, by DSC and cryomicroscope

**LYO CYCLE**
development, optimization, robustness

**2 FREEZE-DRYERS**
of 2.1 sqf and 4.5 sqft installed under isolator

**STRONG INTEGRATION**
between development and cGMP manufacturing

**ANALYTICAL METHODS DEVELOPMENT AND OPTIMIZATION**
to support manufacturing during early stages

All the pharmaceutical forms produced, can be manufactured in the development laboratories with pilot scale machines that reproduce the operating conditions of industrial lines
An extended working team that integrates scientific backgrounds and manufacturing expertise supports the characterization of the products transferred within the plant, contributing to an accurate comprehension of the criticality of either process and product.

# ANALYTICAL SERVICES

All conventional analytical testing and instruments are available to support IPC and final release testing

- METHODS DEVELOPMENT & OPTIMIZATION
- METHODS VALIDATION & TRANSFER
- CLEANBILITY & COMPATIBILITY STUDIES
- CLEANING METHODS DEVELOPMENT AND VALIDATION
- STABILITY & PHOTOSTABILITY STUDIES
- IN PROCESS CONTROLS
- RAW MATERIALS TESTING
- FINAL RELEASE

**SUPPORT**
FORMULATION/PROCESS DEVELOPMENT

**DEVELOP**
OPTIMIZE VALIDATE AND TRANSFER ANALYTICAL METHODS

**CHARACTERIZE**
PRODUCT STABILITY PROFILE

**PROCESS**
COMPARABILITY TESTING

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## HEADQUARTER AND MANUFACTURING PLANT

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6th WORLD adc AWARDS 2019
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WORLD adc AWARDS 2015

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LEADERSHIP AWARDS 2019
CAPABILITIES, EXPERTISE, RELIBILITY, SERVICE

LEADERSHIP AWARDS 2018
CAPABILITIES, COMPATIBILITIES, EXPERTISE
RELIBILITY, QUALITY, DEVELOPMENT