



Pharmaceutical Production Sites Europe

OEM Division, October 2009

Pharmaceutical Production Sites Europe

- **Germany**
 - [Berlin](#)
 - [Melsungen](#)
- **Spain**
 - [Jaén](#)
 - [Rubí](#)
- **Switzerland**
 - [Crissier](#)

Where do we fill...

| | Infusion solutions | | | Injectables | | | Parenteral Nutrition | | | | Others | | | |
|-----------|-----------------------|--------------------|--------------------|----------------------|--------------|--------------|----------------------|----------------------|-----------------|-------------------|----------------|----------------------|---------------|----------------|
| | Elektrolyte solutions | Standard solutions | Volume Replacement | Standard Injectables | Concentrates | Various APIs | Anesthetics | Amino Acid Solutions | Lipid Emulsions | Glucose Solutions | Trace Elements | Irrigation Solutions | Topical drugs | Dry substances |
| Berlin | | | | ✓ | | ✓ | ✓ | | ✓ | ✓ | | | | |
| Crissier | ✓ | ✓ | ✓ | | | | | ✓ | | ✓ | | ✓ | | ✓ |
| Jaén | ✓ | ✓ | | ✓ | | ✓ | ✓ | | | ✓ | | | ✓ | ✓ |
| Melsungen | ✓ | ✓ | ✓ | ✓ | | | ✓ | ✓ | ✓ | ✓ | | ✓ | | |
| Rubí | ✓ | ✓ | ✓ | | | ✓ | ✓ | | | ✓ | | ✓ | | |

... and in which container type?

| | Glass ampoules | Glass vials | Glass bottles | Mini-Plasco® | Ecoflac® plus | Ecotainer® | Ecobag® | Multi-Chamber-Bags | Ecolav® | Tubes/containers for topical drugs |
|-----------|----------------|-------------|---------------|--------------|---------------|------------|---------|--------------------|---------|------------------------------------|
| Berlin | ✓ | | | ✓ | | | | | | |
| Crissier | | | | | ✓ | | ✓ | ✓ | | |
| Jaén | ✓ | ✓ | | | | | | | | ✓ |
| Melsungen | | ✓ | ✓ | | ✓ | ✓ | | ✓ | | |
| Rubí | | | ✓ | ✓ | ✓ | | | | ✓ | ✓ |



Germany: [Berlin](#)

B. Braun Melsungen AG
Mistelweg 2
12357 Berlin
Germany

Production area: 3500 m²
Employees: 330

Berlin: Filling possibilities

Filling possibilities

- Standard injectables
- Various APIs
- Anesthetics
- Lipid emulsions

Additional services

- Upon agreement

Berlin: Containers

Containers

- Glass ampoules
1, 2, 3, 5, 10, 20 ml
- Plastic ampoules (Mini-Plasco®[®], Mini-Plasco® connect)
5, 10, 20 ml

Container material

- Glass ampoules: class I
- Plastic ampoules: low density polyethylene



Berlin: Technology

Technology

- Glass ampoule filling
- Bottelpack®

Filling method

- Blow-fill-seal technology
- Down level filling of ampoules
- Pre- and past gassing (N²)

Sterilization method

- Glass ampoules: rinsing method in autoclave 121°, 15 min, no steam
- Plastic ampoules: „below-water-method“

Berlin: Quality Control

All chemical test methods:

- HPLC (high performance liquid chromatography)
- GC (gas chromatography)
- Ph. Eur. (European Pharmacopoeia)
- Microbiological test methods
- Trace element analysis
- Pyrogen tests

Berlin: Certification

- EU GMP + production permit acc. to German Drug Law
- DIN ISO 14001 (Environmental protection management system)
- DIN ISO 13485:2003



Germany: [Melsungen](#)

B. Braun Melsungen AG
Carl-Braun-Straße 1
34212 Melsungen
Germany

Production area: 11000 m²
Employees: 400

Melungen: Filling possibilities

Filling possibilities

- Electrolyte solutions
- Standard solutions
- Plasma volume replacement solutions
- Standard injectables
- Various APIs
- IV Anesthetics
- Amino acid solutions
- Lipid emulsions
- Glucose solutions
- Irrigation solutions

Additional services

- Upon agreement

Messungen: Containers

- Glass Vials
50, 100 ml
- Glass bottles
50, 100, 250, 500, 1000 ml
- Plastic bottles (Ecoflac® plus in LIFE)
100, 500, 1000 ml
- Plastic container (Ecotainer®)
250, 500, 1000 ml
- Bags (Ecobag®, NuTRIflex®)
500 ml mono-chamber
(other volumes on request)
625, 1250, 1875, 2500 ml 3-chambers



Messungen: Containers

Container material

- Infusion glass bottle: class I + II
- Injection glass bottle: class I + II
- Plastic bottle (Ecoflac® plus): low density polyethylene, polypropylene
- Plastic container (Ecotainer®): low density polyethylene, polypropylene
- Bags: multi-layer co-extruded films

Melungen: Technology

Technology

- Bottelpack®
- Standard filling of glass bottles and plastic containers
- Bag filling

Filling method

- Blow-fill-seal technology
- Standard filling with sterilization with or without evacuation and/or nitrogen gasing

Sterilization method

- Hot water sprinkling sterilization with or without rotation

Messungen: Quality Control

Quality Control

- Full range of analytical methods available

Water purification method

- Deionisation: tap water → deionised water
- Distillation: deionised water → water for injection

Meldungen: Certifications

- EU GMP
- OHSAS 18001 *date of issue 2005-12-09*
- DIN ISO 13485:2003 *date of issue 2005-11-30*
- DIN ISO 9001-2000
- DIN EN ISO 14001:2005 *date of issue 2005-12-09*
- Approved for delivery of medicinal products to the Japanese market



Spain: [Jaén](#)

B. Braun Medical S.A.
Ronda de los Olivares, 5
Polígono Industrial Los Olivares
23009 Jaén
Spain

Production area: 3.880 m²
Employees: 100

Jaén: Filling possibilities

Aseptic filling of parenterals

- Water for Injection
- Electrolyte solutions
- Analgesics
- Anti-inflammatories
- Psychotropic drugs
- Anesthetics
- Corticosteroids
- Adrenaline, Atropinesulfat
- Heparine (Sodium)
- Other injectable drugs

Topical drugs

(creams, gels, ointments, liquids)

- Antibiotics
- Analgesics
- Anti-inflammatories
- Anesthetics
- Corticosteroids
- Fungicides
- Antivirals
- Hydratants
- Other topical drugs

Jaén: Containers

- Glass ampoules
1, 2, 5, 10, 20 ml
- Glass Vials
with liquids
2, 3, 5, 10, 20, 50 ml
with powder
100 mg - 4 g according to customer's request
- Bottles for topical use with cap and atomizer
10 - 1,000 ml according to customer's request
- Tubes/containers for topical drugs
diameter from 13,5 mm - 35 mm
weight from 2 g - 140 g
according to customer's request



Jaén: Containers

Container material

- Glass ampoules: class I
- Glass vials: class I+II
- Bottles for topical use: plastic and glass
- Tubes/containers for topical drugs: plastic and aluminum

Jaén: Technology

Injectables

- Washing machine
- Sterilization-despirogenation tunnel
- Filling machine for vials and ampoules

Topical drugs

- 2 tanks 1.000 kg for large preparations
1 tank 50 kg for small preparations
2 fusion tanks for pre-preparation 350 kg + 500 kg
- Room classes
laminar flow (class A), filling-environment (class C), room preparation (class C)
- Creams, gels and ointments
UNI pac machine → aluminium and plastic tubes
- Liquids (lotions, etc)
ELF machine → glass and plastic bottles (with atomizer or with cap)

Jaén: Technology

Filling method

- Aseptic filling (triple filtration 0.22 μm)
- Room classes: A filling (environment class B)
- Pre, during and past gassing (N_2)

Sterilization method (heat treatment)

- Steam or pressurized hot water autoclave
Standard cycle: 121°C / 15 – 30 min
others according to customers' specification
- By time f_0

Jaén: Quality control

Quality control

- Analytical methods executed by internal laboratories
 - All chemical test methods:
HPLC (high performance liquid chromatography), others
- Required biological test methods: sterility, endotoxines, bioburden quantification of antibiotics

Water purification method

- Drinking water → highly water → WFI by distillation-> bulk preparation

Jaén: Certifications

- EU GMP since 1994
- ISO 9001:2000 since 07/2006
- ISO 14001:2004 since 07/2006



Spain: Rubí

B. Braun Medical SA
Carretera de Terrassa, 121
08191 Rubí
Spain

Production area: 12.000 m²
Employees: 1200

Rubí: Filling possibilities

Filling possibilities

- Electrolyte solutions
- Standard solutions
- Plasma volume replacement solutions
- Various APIs
- Anesthetics
- Glucose solutions
- Irrigation solutions

Additional services

- Stability testing
- Galenic development and formulation studies
- Development and validation of analytical methods
- Support in regulatory affairs
- Warehousing

Rubí: Containers

- Plastic ampoules (Mini-Plasco®)
5, 10, 20, 30 ml
- Glass bottles
100, 250 ml
- Plastic bottles (Ecoflac® plus)
100, 250, 500, 1000 ml
- Plastic container for irrigation solutions (Ecolav®)
30, 100, 250, 500, 1000 ml
500 and 1000 ml with external bags sterile
- Bags (Ecobag®)
5000 ml



Rubí: Containers

Container material

- Plastic ampoules: low density, polyethylene (PE)
- Glass bottles: class I+II
- Plastic bottles: low density polyethylene, polypropylene
- Plastic container: low density polyethylene, polypropylene
- Bags: multi-layer co extruded film

Rubí: Technology

Technology

- Bottelpack ®

Filling Method

- Blow-fill-seal technology

Sterilization method *

- Autoclave
 - 121°C for glass bottles
 - < 112°C for plastic bottles (111,5°C for Ecoflac® and Miniplasco®)

* Attention: no sterilization tunnel for empty glass bottles available ! (std for LVP glass bottles)

Rubí: Quality Control

Quality control

- Complete chemical and biological tests executed by internal laboratories
- Polymerase chain reaction (PCR) analysis: analysis of RNA for bioburden test

Water purification method

- Drinking water → highly purified water → WFI by distillation → bulk preparation

Rubí: Certifications

- EU GMP since 1992
- ISO 9001 since 7/1998. Version 9001:2000 since 1/2004
- EN 46001:1996 since 7/1998 → ISO 13485:2003 since 2/2005
- ISO 14001 since 2003. Version 14001:2004 since 4/2005
- OHSAS 18001:1999 since 7/2006



Switzerland: Crissier

**Route de Sorge 9
1023 Crissier
Switzerland**

**Production area: 2000 m²
(+ 5000 m² under construction)**

Employees: 320

Crissier: Filling possibilities

Filling possibilities

- Electrolyte solutions
- Standard solutions
- Plasma volume replacement solutions
- Amino acid solutions
- Glucose solutions
- Irrigation solutions
- Dry substances

Additional services

- Stability testing
- Validation of analytical methods
- Registration support
- Bag development

Crissier: Containers

- Plastic bottles (Ecoflac® plus)
500 ml
- Mono-chamber bags (Ecobag®)
50, 100, 250, 500, 1000,
2000, 3000, 5000 ml
- Multi-chamber bags (Nutiflex®, NuTRIflex®)
1000, 1500, 2000 ml (2-chambers)
1250, 1875, 2500 ml (3-chambers)
only empty 3-chamber-bags
- PVC bags
50, 100, 200, 300 ml



Crissier: Containers

Container material

- Plastic bottle: low density polyethylene, polypropylene
- Mono-chamber bag: PVC or multi-layer co-extruded film - non PVC
- Multi-chamber bag: multi-layer co-extruded film - non PVC, overwrapped

Crissier: Technology

Technology

- Bottelpack®
- High frequency welding (PVC)
- Thermic welding (non-pvc)
- Spray drying (API)

Filling method

- Blow-fill-seal technology
- Fully GMP conform
- No aseptic filling

Sterilization method

- Bags: air-steam mixture
- Plastic bottles: water cascading

Crissier: Quality Control

Quality Control

- Executed by internal laboratories

Water purification method

- Softening & reverse osmosis → distillation

Crissier: Certifications

- GMP
- DIN ISO 9001:2000 *date of issue 2007-07-24*
- DIN ISO 13485:2003 *date of issue 2007-08-01*
- DIN ISO 14 001
- OHSAS 18001 *date of issue 2008-05-14*



Thank you for your attention

OEM Division, October 2009

B | BRAUN
SHARING EXPERTISE