Pharmaceutical Equipment

at a glance

BRAM-COR

PHARMACEUTICAL TECHNOLOGIES

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BRAM-COR S.p.A.

Made in Italy, made in Parma: our headquarters is located in a highly specialised industrial district, heart of the Italian food valley and of the European Food Safety Authority (EFSA). Parma is the capital of advanced technologies in industrial food machineries and production lines. Dating back to 1964, our diversified know-how and field experience in developing and manufacturing water treatment systems from COR S.r.l., and filling lines and packaging equipment from BRAM S.p.A. are today joined together in BRAM-COR S.p.A., a leading company in customised pharmaceutical technologies and in biopharmaceutical turnkey plants.

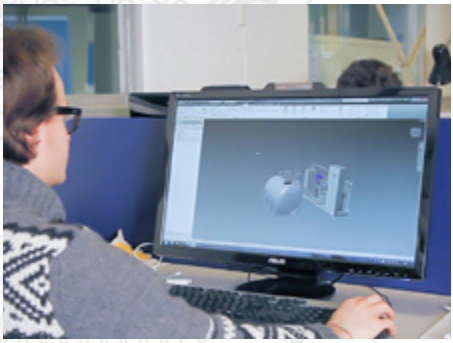
OUR QUALITY SYSTEM

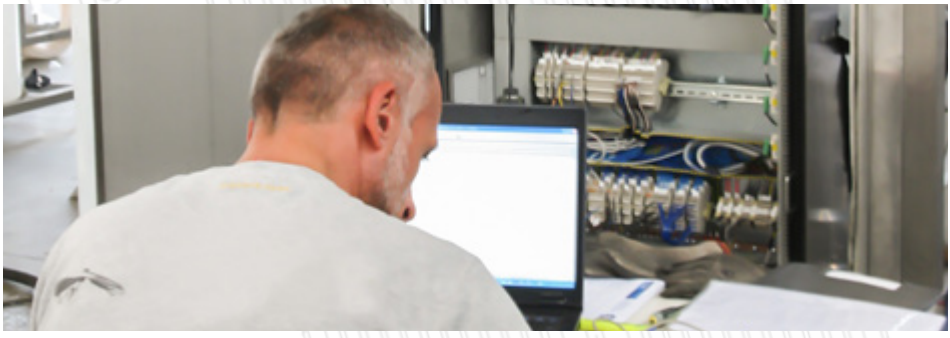
We focus all our activities on ensuring that our equipment meets the needs of the pharmaceutical industry. To meet this objective, our work is guided by cGMP - International Good Manufacturing Practices and Pharmacopoeias, and all our operations meet ISO 9001:2008 standards.

By continually assessing and revising our working procedures in response to any non-conformity, we strive for continuous quality improvement. The BRAM-COR team is committed to providing professional support throughout the system lifecycle.

DESIGN KEY
CONCEPT

Correct system design requires an understanding of the whole drug production process. BRAM-COR engineering focuses on liquid and sterile drugs and low, medium, and high viscosity production processes, such as parenteral solutions, oral solutions, ophthalmic and oncology solutions, ointments, creams and cosmetic preparations. To implement suitable Process Analytical Technologies for in-line and at-line quality control, critical parameters directly affecting product quality must be identified, assessed, monitored. There are five main activities in our project cycle: design, construction (mechanical, electro-pneumatic, SW configuration), testing, documentation, installation, validation, and assistance. Every process follows rigorous cGMP compliant Standard Operating Procedures.





STAINLESS-STEEL CONSTRUCTION EXPERTISE

AISI 316L S/S piping and vessels are welded by qualified welders following BRAM-COR Sanitary Piping procedures. Certified sanitary fittings and components are assembled on the line, ensuring good access to all items for easy maintenance operation. Non-destructive tests are performed during construction. Each component is identified by a unique TAG for total traceability to the relevant technical documentation. Experts in automation ensure functional testing, paying close attention to critical parameters. Our project management services include documentation, inspection, and field testing.

CUSTOMER CARE & WORLDWIDE SERVICES

Documentation, inspection and field testing are our project management services. This includes: Technical Documentation, Factory Acceptance Test, Installation, Commissioning, Site Acceptance Test & Start-up, Training, Validation, After Sales Service. Our worldwide network of skilled agents and affiliated companies ensures assistance in more than 50 countries, while our After Sales Department ensures timely and efficient delivery of spare parts and ongoing technical support.

WATER TREATMENT

Bram-Cor Pharmaceutical Water Treatment Systems are designed to produce compendial:

- PW PURIFIED WATER
- WFI WATER FOR INJECTION
- PS PURE STEAM

In designing all processing steps, from feed water to point of use, we consider pretreatment options, monitoring of critical parameters, regulatory requirements for product quality, consumptions, microbiological control, operation and maintenance requirements, and analytical costs. Special care is given to the choice of sanitary materials. Product-contact surfaces are in certified AISI 316L stainless steel, with standard roughness ≤ 0.4µm. PTFE gaskets ensure perfect sealing. Advanced Process Analytical Technologies are used to handle monitoring issues and professional GAMP compliant automation is provided for system control.

A full range of Bram-Cor distillers and generators are available with electric heating.

WATER PRE-TREATMENT SYSTEMS

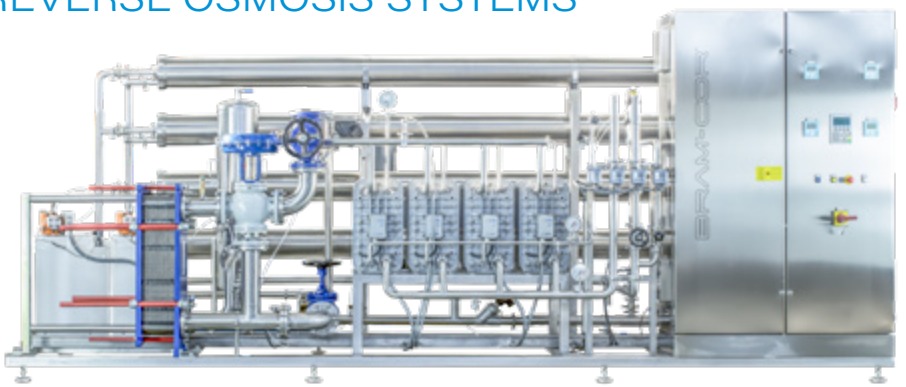
Bram-Cor Water Pre-Treatment Systems are customized following a thoroughful evaluation of feedwater quality using the customer's water analysis. Raw water can be pre-treated to remove contaminants (such as particulates, calcium and magnesium salts, heavy metals, organics and bacteria) via different steps, including:

- ***Uvitron UV lamps***
- ***Ozone units***
- ***Cartridge microfiltration***
- ***Ultrafiltration units***
- ***Multimedia filters***
- ***Automatic duplex softeners***
- ***Industrial RO***

Chemical dosing stations are added for water disinfection and / or chlorine neutralization. Pretreated water quality is constantly monitored to ensure suitability to feed downstream water treatment equipments, such as RO units or distillers. Standard versions are designed for CIP sanitization.

To prevent biofilm formation, most pre-treatmentsystems can be supplied in a hot water sanitization version upon request. Capacities range: from 100to 50,000 lph.

CROS
REVERSE OSMOSIS SYSTEMS



CROS Reverse Osmosis Systems are designed to produce compendial Purified Water (PW), Ultrapure water and/or "cold" Water for Injection (WFI) through several water treatment steps, depending on feed water quality and production needs. Water treatment steps, which are necessary to separate the water from organic substances, high and medium molecular weight ions and from some bacteria and pyrogenes, can include:

- Chemicals dosing station for water disinfection and oxidation of organic substances, reducing the bacterial charge;

- Chemicals dosing station for neutralization of calcium carbonate and chlorine;

- Microfiltration system to eliminate solid substances in inlet water;

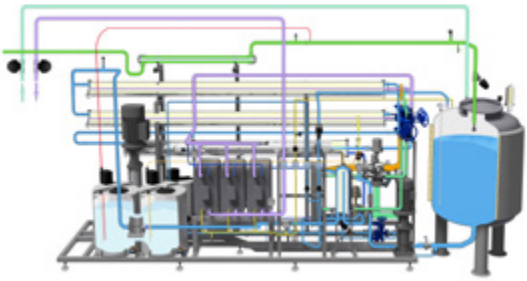
- Single or double osmotic stages;

- Electrodeionizator; UV reactor;

- Ultrafiltration

(**UF,** producing "cold" WFI for pharmaceuticals or Ultrapure water for other uses**).**

Capacities range: from 100 to 50,000 lph



Purified Water is usually obtained through ***single RO stage + Electrodeionization***, ***double RO stage*** and ***double RO + EDI stage***.

WFI production requires PW polishing through a final ultrafiltration unit (UF stage, see the CROS model below). In each RO stage, water is processed through thin film composite RO membranes, offering the highest level of contaminants rejection.

Two different flows are generated by the RO system: permeate water (corresponding to PW specifications), and RO concentrate, which is recycled in the system in order to obtain a higher recovery with a lower consumption of inlet water. **CROS** equipment are manufactured according to all cGMP and FDA rules, including:

- Centrifugal pump in AISI 316L;

- AISI 316L stainless steel membrane vessels;

PURIFIED WATER IN BULK*		
PHISICAL / CHEMICAL	Ph. Eur.	USP
Appearance	Colorless, clear	Not defined
Conductivity	≤ 4.3 µS/ cm@20°C	≤ 1.3 µS/ cm@25°C
TOC	≤ 0.5 mg/l	≤ 0.50 mg/L
Nitrates NO_3	≤ 0.2 ppm	Not defined
MICROBIOLOGICAL	Ph. Eur.	USP
Bacterial count	≤ 100 CFU/ml	≤ 100 CFU/ml
Bacterial endotoxins	< 0.25 IU/ml	-

WATER FOR INJECTION IN BULK*		
PHISICAL / CHEMICAL	Ph. Eur.	USP
Appearance	Colorless, clear	Not defined
Conductivity	≤ 1.1 µS/ cm@20°C	≤ 1.3 µS/cm @25°C
TOC	≤ 0.5 mg/L	≤ 0.50 mg/L
Nitrates NO_3	≤ 0.2 ppm	Not defined
Aluminium	≤ 10 ppb	Not defined
MICROBIOLOGICAL	Ph. Eur.	USP
Bacterial count	≤ 10 CFU/100 ml	≤ 10 CFU/100 ml
Bacterial endotoxins	< 0.25 IU/ml	< 0.25 EU/ml

*update: January 31, 2023

- In-line instrumentation to monitor product critical parameters;

- Full automation (GAMP-compliant hardware and software);

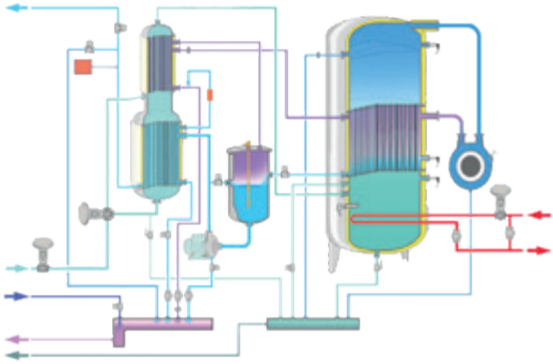
- Framework & control board in AISI 304 satin finished;

- CIP sanitization or HOT WATER sanitization.

STMC
VAPOR COMPRESSION DISTILLERS

BRAM-COR **STMC Vapor Compression Distillers** produce compendial Water for Injection for pharmaceutical applications, such as I.V. solutions, injectables, washing systems and special solutions where both quality factors (sterility, elimination of pyrogens and of chlorine solvents with low molecular weight), and economical factors, as well as the low production costs, are critical for the success of the pharmaceutical process.

Note that any **water pre-treatment system** (softeners, reverse osmosis, ...) can be combined on the same skid of the distiller; so STMC can work with virtually any type of water. Capacities range: from 20 to 20,000 lph, with single or double compressor.



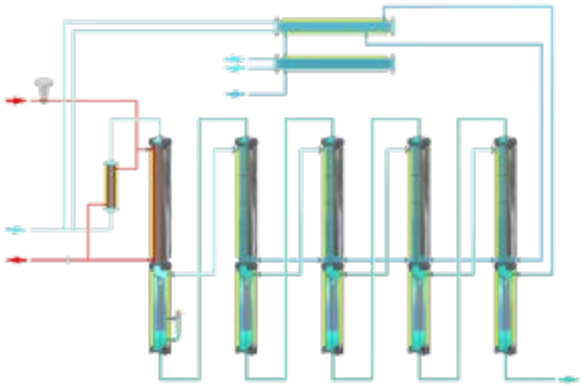
STMC vapor compression distillers can operate with **electrical heating** or with **steam heating** or a combination of the two (**electrical and steam heating systems**). STMC distillers can produce both cold distillate at a defined temperature and hot distillate with huge savings of energy costs and without the need of cooling water. The design, construction and documentation of STMC distiller strictly complies with cGMP and FDA regulations, ensuring an easy certification by the relevant authorities.

In detail:

- ***The distiller is made in certified AISI 316L stainless steel;***
- ***All internal parts in contact with infeed water, Pure Steam and Distillate are mirror-polished;***
- ***AISI 304 frame, jackets and control board;***
- ***All hydraulic connections are sanitary tri-clamp or flange connection;***
- ***All gaskets are made in PTFE;***
- ***All weldings are T.I.G.*** (Tungsten Inert Gas).

Vapor is compressed by a special blower. A full automation ensures easy operation and total monitoring of critical parameters, by means of certified in-line instruments and of a related alarm policy.

SMPT
MULTIPLE EFFECT DISTILLERS



BRAM-COR **SMPT Multiple Effect Distillers** are manufactured according to cGMP to produce compendial Water for Injection (WFI). Each unit contains a number of boiling columns (or effects), with the first column producing Pure Steam, which is either condensed in the following columns decreasing the operational costs, or used as Pure Steam (PS).

Capacities range: from 50 to 15,000 lph, with three-ten columns configurations.

Heating through evaporation and cooling through condensation are performed by double tube sheet heath and cool exchangers. Condensation is achieved by means of the thin-falling film system. The process is repeated in each column; the higher the number, the lower the consumption of the equipment.

A special labyrinth-separator inst-alled at the top of each columnseparates the steam generated by evaporation from substances trapped in the steam itself. The result is a pure, ”dry”, pyrogen-free steam, condensed in compendial WFI. Pressure vessels are designed according to ASME (S+U stamp) and PED regulations.

WATER DISTILLATION SYSTEMS MULTIPLE EFFECT VS VAPOUR COMPRESSION TECHNOLOGY		
parameters	MULTIPLE EFFECT DISTILLER	VAPOR COMPRESSION DISTILLER
OUPUT FLEXIBILITY	Reduced output modulation	Capacity ranging from 0 to max. cap. of the still
TEMPERATURE FLEXIBILITY	WFI output 85÷99°C	WFI output from infeed water T + 10°C till 99°C
HEATING MEDIA FLEXIBILITY	Industrial steam or electricity	Industrial Steam and/or electricity
COOLING WATER	High consumption depending on Nos. of columns	No cooling water required
FEED WATER	SI02 < 1 ppm, Amines free resins (in case of DI), double stage RO preferred	SI02 <30 ppm, Single stage RO or even softened water acceptable
FEED WATER INPUT	Must be higher than primary steam pressure	< 1 bar
WFI OUTPUT	Atmospheric pressure	1 / 1.5 bars
WFI QUALITY	0.2÷0.5 microS/cm with FW <5mS	0.15÷0.4 microS/cm with FW <5mS
PREVALIDATION (endotoxin chall.)	Yes	Yes
HEAVY METALS	Free	Free + elimination of chlorine solvents
MOVING PARTS	Feed pump	Compressor, Recirculation pump
PS FROM 1ST COL.	Possible	Possible
STRESS CORROSION	Very high “Rouging” percentage higher	Very low
CLEANABILITY	More tough than VCD	More easy than MED
START UP	SCADA 15m for steam heating	SCADA 15÷40m for steam heating

Bram-Cor SMPT water distillers line features:

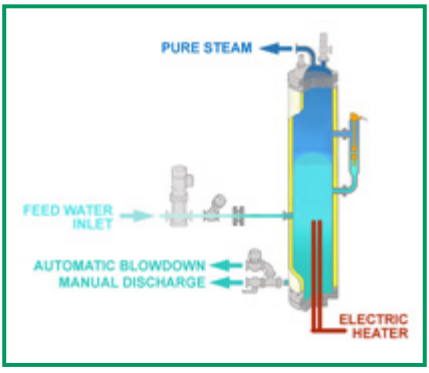
- ***Double tube sheet heat exchangers;***
- ***Certified AISI 316L SS mirror-polished and passivated product contact surfaces;***
- ***AISI 304 frame, jackets and control board;***
- ***PTFE gaskets;***
- ***Pneumatic valves with PTFE membranes and AISI 316L SS eletro-polished body***
- ***AST C-795 compliant insulation***

CPSG
PURE STEAM GENERATORS

BRAM-COR **CPSG Pure Steam Generators** produce dry, saturated steam, suitable for sterilization of pharmaceutical production plants, for direct contact with API (Active Pharmaceutical Ingredients), for parenteral and non-parenteral dosage form applications. The steam, when condensed, meets USP requirements for Water for Injection. The steam is purified using a demister and gravity separation methods.
Capacities range: from 20 to 5,000 Kg/h.

cGMP and **PED** standards are baseline criteria in our **CPSG** design and construction: material and instruments are certificated and all welds are made by qualified welders.

The evaporation column is designed to minimize steam speed to avoid the entrainment of water droplets, which are separated from the steam by means of a special separator. A Double Tube Sheet Heath Exchanger provides heating of pre-treated feed water above the boiling temperature, generating Pure Steam which expands into the evaporation column. Heating medium in the DTS Heath Exchanger is typically industrial steam at 100 to 120 psig (7.9 to 2.0 bars). Small **CPSG** can be electrically operated.



Pure Steam pressure is maintained by an electronic control system, modulating the supply steam control valve and monitoring the evaporator feed water.
The system should be fed with Purified Water (PW).

KPSG Kettle Pure Steam Generators provided with a horizontal evaporation chamber with kettle end, are also available for special space needs.

DPSG
SINGLE EFFECT DISTILLERS

Each **DPSG** equipment is both a **Single Effect Distiller** and a **Pure Steam Generator**. This equipment, available in electrically or steam heated versions, produces dry, saturated steam to be used as sterilizing agent. The PS, when condensed through a double tube sheet condenser, meets the requirements of international pharmacopoeias for WFI. The production process consists in PW evaporation followed by PS separation and condensation. The steam is purified using centrifugal and gravity separation methods. The equipment is made in AISI 316L stainless steel for all parts in contact with the process fluid and steam, and it is designed according to European PED pressure regulation. Additionally:

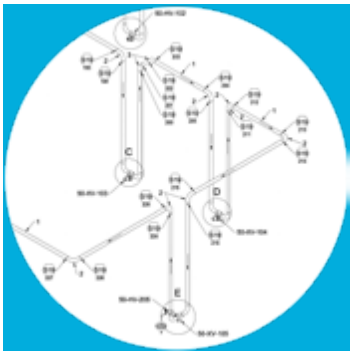
- Active surfaces are passivated.
- The parts in contact with the pure steam are polished (Ra ≤ 0.4 µm);
- Skid and control cabinet are in AISI 304 Stainless Steel satin finished.

KOMB
COMBINED WFI + PS GENERATORS

BRAM-COR **KOMB** is a unique equipment for the simultaneous production of WFI and PS, combining the double functions of a Multiple Effect Distiller and of a Pure Steam generator on a single skid, minimizing any space needs.

A central **SCADA** controls the two units, providing separate or concurrent outlet of WFI or / and PS.

LOOP
DISTRIBUTION SYSTEMS

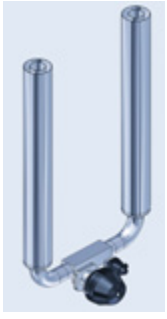


BRAM-COR integrates **PW-WFI-PS Generation Equipment** with advanced distribution loops. Loop design is the result of a careful evaluation of Points of Use delivery criteria such as:

- Maximum instantaneous flow rate;
- Pressure & temperature requirements;
- Sanitization issues;
- Periodic consumption requirements and duration;
- Method of delivery (automatic or manual).

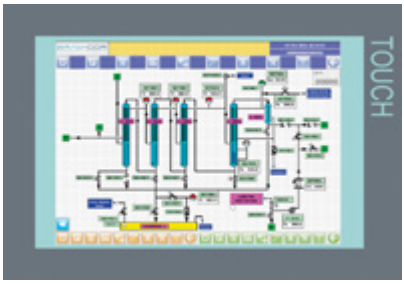
Loop construction is carried out by qualified welders following BRAM-COR sanitary piping procedures, according to ASME standards.
All pipelines are passivated and inspected, according to ASME/BPE criteria, to check **quality of welds, effective passivation, hydrostatic tightness, full drainability, absence of dead-legs and fluid dynamics.**

A full loop documentation, including isometric drawings, welding reports, borescopy records, passivation certificate and test reports is provided to complete the supply. Our water distribution systems are completely validable and suitable for use in FDA and EMA regulated facilities.

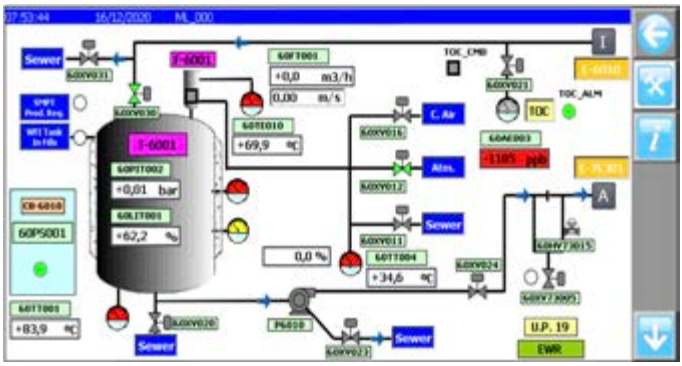


BRAM-COR **Points of Use** features:
- *Tube-in-tube insulation in cleanrooms;*
- *Automatic or manual ZDL valves;*
- *Sampling valves;*
- *Local control panels*.

SCADA
CONTROL SYSTEMS



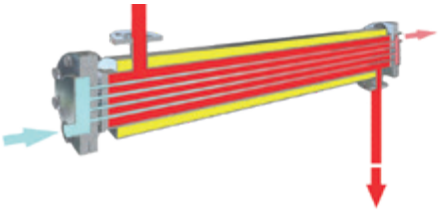
Our **GAMP-Compliant Automation Systems** offer full management control across the plant lifecycle, from equipment control to production line supervision. Data management includes: **trends and electronic records, electronic signatures and alarms management, audit trails, lifecycle check counts, display of manuals and documentation.**

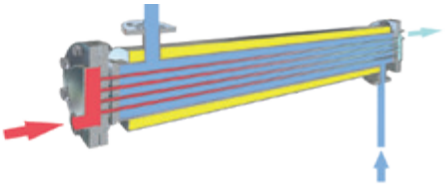


Secure access policy, according to 21 CFR PART 11, includes three different access levels. All historical data can be exported and saved for long lasting backup. All parameters are stored and limited, all parameters and I/O (analogic and digital) can be printed on the report, allowing a quicker assistance, in accordance to 21 CFR PART 11. Start/stop of operating modes are recorded on the audit trail. Audit trail file can be exported on a USB flash drive or Ethernet.

Control system	**Functions operated by the PLC (Programmable Logic Controller):** **• Input of measured values and setting of limit values** **• Automatic Sequences (production, sanitization, ...)** **• Control Functions (PID control for valves and speed of pump)** **• Alarm management and Verification of parameters** **• Input of measured values and setting of limit values** **• Output commands for digital and analogic values**
Visualization system	**HMI (Human Machine Interface):** **• Display of machine state • Controls management • Verification of alarms** **• Set points inserting and limit values setting • Graphic interface** **SCADA (Supervisory Control And Data Acquisition) / SCADA SERVER:** **• All HMI values and controls • Data historicization • Historical alarms** **• Trend • Report • Data backup / Restore** **All automation systems can be in compliance to 21 CFR PART 11 or Siemens Operator Panel, through audit management and electronic signature. Access management included (user/password).**
Communication system	**Bram-Cor automation systems can virtually communicate with all network partners through maximum security protocol (Ethernet, Profinet, OPC Unified Architecture, ...). Options:** **• Teleservice (malfunctions managed remotely by Bram-Cor)** **• Remote Control (operator receives a message/text message/warning mail)** **• Server-side data centralization (customer can centralize data on his service, or Bram-Cor provides it)**

DTS
HEAT / COOL EXCHANGERS





Usually mounted on self-standing skid, BRAM-COR **Double Tube Sheet Heat/Cool Exchangers** are designed to maximize the surface area of the wall between two fluids, while minimizing resistance to fluid flow through the exchanger, in order to increase efficiency. Our **DTS** exchangers are typically used for high pressure application, for hot water sterilization of loops and tanks and also -wall mounted- for water cooling/ heating user points.

All product contact surfaces are manufactured in AISI 316 L S/S, internally mirror polished. The exchangers are insulated and clad with 304 S/S satin finished. Non-destructive tests are carried out to ensure compliance to cGMP and Pressure Equipment Directive. **DTS** exchangers can be incorporated in the equipment (i.e., in **SMPT** distiller) and fitted with sanitary valves and pumps, steam trap and temperature probe.

STOC
STORAGE TANKS

BRAM-COR **STOC Storage Tanks** are supplied with complete material and components traceability. In our workshop, strict procedures for sanitary piping welding and inspection, and ND testing are enforced in accordance with international standards for pharmaceutical equipment. Basic features of our fully cleanable storage tanks, usually combined with PW or WFI loop, include:

- Certified AISI 316L S/S mirror-polished (Ra ≤ 0,4 µm) product contact surfaces and components;
- "Tank in tank" thermal insulation (wall or wall and bottom insulation, aisi 304 cladded);
- Vertical or horizontal design;
- Customized heath and cool jackets:
- Manhole access.

Capacities range: from 100 up to 30.000 litres (networking volume). Sizes and shapes are scaled up according to specific URS, to fit different space requirements, including:

- Any control/management system;
- Heating and cooling systems;
- Platforms and stairs;
- PED/ASME certification (upon request).

Tanks can be integrated with our SCADA control system, managing PW or WFI generators, loop and user points, which also records and produces the files and documents necessary for the international pharmaceutical validation.

GENO

OZONE GENERATORS

Thanks to the high oxidation potential, ozone is proven to be one of the most effective and safe methods to promote bacterial, viral, and fungal removal. BRAM-COR full-stainless steel **GENO Ozone Generators** are conceived for pharmaceutical application, i.e. for water disinfection and loop sanitization. Ozone concentration, during production and sanitization, is constantly monitored by ozone analyzers, while residual ozone in water is automatically removed by a sanitary UV lamp before PW use in the process. Sanitary piping, valves, pumps and instruments complete each **GENO** unit.

UVITRON

UV REACTORS

We manufacture and customize a full range of UV Reactors for pharmaceutical purposes, from one to multiple lamp units, following strict cGMP-compliant SOPs.

STDA

STANDARD ACCESSORIES AND COMPONENTS

Special sanitary components in AISI 316L are manufactured by BRAM-COR to fit our water treatment systems, such as:

- 316L S/S housings for solution filters
- 316L S/S housings for air filters

PROCESSING

We design, manufacture, and installs complete formulation and preparation plants, starting from User Requirements. This includes sterile drugs and low/medium/high viscosity emulsions, and a full range of production processes (parenteral, oral, ophthalmic, and oncology solutions, ointments, creams, cosmetic preparations).

Our processing systems can meet specific manufacturing and sanitization & sterilization requirements. BRAM-COR solutions combine performance with cost effective aseptic processing equipment including:

- ***MIXING VESSELS***
- ***HOMOGENIZERS AND DISSOLUTORS***
- ***BIOREACTORS AND PREPARATION SYSTEMS***
- ***CIP/SIP SYSTEMS***
- ***ANCILLARY SYSTEMS FOR FORMULATION LINES***

DISS
PREPARATION SYSTEMS

BRAM-COR offers a complete range of preparation lines suitable for any pharmaceutical formulation, including **BIOREACTORS** and **MIXING TANKS.**
In accordance with international cGMP and pharmacopoeias, all our equipment is accurately finished and constructed with high quality materials. All vessels are in AISI 316L S/S, internally mirror polished, thermally insulated and clad in satin finish stainless steel. The design strictly follows PED standard. PED certification is also available for Pressure tanks. Our formulation tanks are sized according to any batch production need, upon careful calculation of production shifts, optimizing product flows according to the specific lay-out. Capacities Range: from 50 to 25,000 liters.
Each **DISS** is equipped with a complete set of fittings for quality and quantity control such as:

- ***Temperature probes;***
- ***Sampling valve;***
- ***Level control;***
- ***Outlet valve;***
- ***Safety valve;***
- ***Vent filter;***
- ***Manhole with sight glass;***
- ***Cleaning spray balls;***
- ***Solution interception valve;***
- ***Load cells.***

Temperature control of the vessel can be performed through a thermostatting unit. Compact pre-wired mobile preparation units can be designed by our Technical Dept. following local space requirements. We offer a wide range of ancillary systems for solution preparation, and all necessary devices to clean and sterilize the manufacturing line, such as stationary or mobile C.I.P. units.

DISS SYSTEMS FOR SOLUTIONS

Pharmaceutical solutions are liquid preparations containing one or more substances dissolved in the molecular state, in a solvent or mixture of solvents. When the final drug is an injectable, WFI is commonly used as the solvent. BRAM-COR process systems are suitable for the production of:

- ***Injectable solutions***
- ***Solutions for infusions***
- ***Dermal solutions***
- ***Oral solutions***
- ***Solutions for inhalations***

BRAM-COR's experience in pharmaceutical processing has enabled the development of a wide range of tanks and filtration systems dedicated to:

- ***Formulation / mixing / homogenization***
- ***Sterile filtration***
- ***Transfer and storage.***

BRAM-COR range of tanks offers a variety of customizable options based on the required process, regulatory requirements and production technology.

DISS SYSTEMS FOR DISPERSIONS

Dispersions are biphasic systems with two substances, one called dispersed/discontinuous phase that is distributed in the form of particles or droplets throughout another substance called continuous, dispersant, or external phase. Our processing technology is used to produce pharmaceutical dispersions in their most-used form called suspension (where solid particles are insoluble in the dispersing medium). The technology can be used for:

- ***Suspensions for oral use***
- ***Suspensions for topical use***
- ***Suspensions for injectable use***
- ***Emulsions*** (made up of 2/3 components and immiscible liquid phases, one of which is dispersed in the other).

DISS SYSTEMS FOR SEMI-SOLID CREAMS, MEDIUM/HIGH-VISCOSITY GELS

Semi-solid pharmaceutical forms are suitable for the treatment of skin disorders and are mainly designed for topical use. The following are the main groups of semisolid preparations

- ***Ointments***: consist of a monophasic base, in which solid and/or liquid substances can be dispersed. This type of drug formulated to allow skin penetration of the active ingredients dispersed in the drug, or to provide an emollient, lubricating or protective action;
- ***Creams***: multiphase preparations consisting of a lipophilic phase and an aqueous phase; they are generally formulated as either water-in-oil or oil-in-water emulsions;
- ***Gels***: semi-solid preparations that contain small inorganic particles or large organic molecules that form a lattice to retain the dispersing liquid phase;
- ***Pastes***: semi-solid preparations for dermal/topical application that contain solids in large percentages/quantity, finely dispersed in a base (in general, the percentage of dispersed solid is between 30% and 70%). They are characterized by high viscosity.

CIP / SIP
STATIONS

BRAM-COR Cleaning in Place systems are designed to fully meet cGMPs requirements in cleaning and sterilizing practices commonly followed in pharmaceutical process lines. Our **CIP** systems are supplied as fixed STATIONS or as MOBILE SKIDS, with manual, semiautomatic or automatic configuration. CIP systems can be equipped with different utilities for heating: ***Electrical heater or Heat exchanger by industrial steam.***

Each equipment is designed (in single or multitank configuration) to achieve the most effective and easily validable cleaning systems, starting from:

- Type and size of equipment to wash;
- Required type of water and chemical agent;
- Pharmaceutical product to remove;
- Cleaning nozzles type;
- Washing sequence, automation level.

In all of our automatic stations, CIP critical parameters can be constantly monitored through the PLC and managed with cost-savings criteria. The parameters include:

- Contact time of solution;
- CIP supply temperature;
- CIP return temperature;
- Chemical conductivity (pH) for wash solutions;
- Final rinse resistivity;
- CIP solution flow rate;
- Supply pressure and Tanks levels.

CIP System units can be customized with different washing cycles. Steam sterilization of the pharmaceutical plants takes place after CIP, as a further sterilization step, with the use of PS (Pure Steam, produced by generators such as BRAM-COR CPSG). SIP (Sterilization-in-place) process ensures that any microorganism still active in the plant is eliminated.

ANSY - ANCYLLARY SYSTEMS
FOR FORMULATION LINES

Following specific product requirements (viscosity, temperature, oxygensensitivity, aseptic issues, etc.), we are able to integrate all of our formulation equipment and plants with state-of-the-art ancillary systems, such as:

FLOW TRANSFER UNITS
to transfer process fluids through multiple process lines.

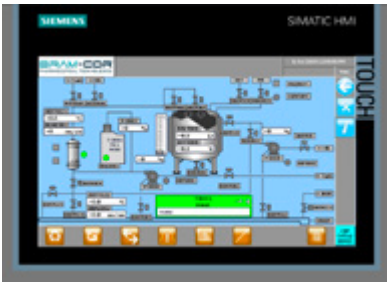
TRIBLENDERS
for air-free homogeneous mixing of liquids and solids.

SOLUTION TRANSFER CIRCUITS
through sanitary pipelines, pumps, fittings.

LAMINAR FLOW CABINETS
ensuring aseptic operation in the working area.

FILTRATION GROUPS
including sanitary cartridge filters in stainless steel housings, pressure gauges, temperature probes, steam traps and membrane valves.

DEVOTED SCADA SYSTEMS
for control of automatic sequences (i.e. startup, filling, mixing, heating-cooling, transfer, etc.).



AUTOMATIC BALANCES
for dispensing rooms.

VESSELS LOADING PLATFORMS
for safe and easy loading operation.

FILLING

BRAM-COR pharmaceutical bags or bottles filling machines are intended for automatic, semiautomatic or manual use, for different bags or plastic/glass bottle sizes, depending on production requirements (from min. 50 ml). In addition to ensuring trouble-free operation, our equipment reduces maintenance costs and ensures long-term reliability. Complete bottle lines are integrated with washing machines, capping and crimping machines, labelling lines and belt conveyors. Our Filling & Packaging lines:

- ***FILLING MACHINES FOR BAGS***
- ***VISUAL INSPECTION LINES FOR BAGS***
- ***FILLING MACHINES FOR BOTTLES***
- ***WASHING, STOPPERING, CAPPING MACHINES FOR BOTTLES***
- ***INTEGRATED LINES INCLUDING CIP/SIP SKIDS***
- ***TURNKEY PLANT FOR BAGS AND BOTTLES***

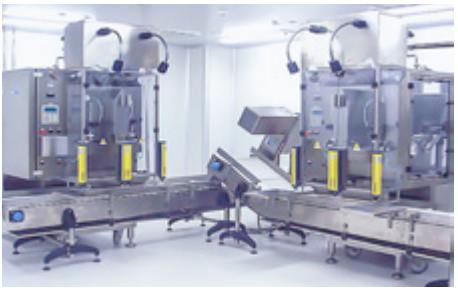
BFIL
FILLING MACHINES FOR BAGS

BRAM-COR manufactures bags linear filling equipment Mod. **BFIL** according to CGMP regulations. The equipment is completely validable with all parts in contact with the fluids in AISI 316L mirror polished S/S and with PLC controlled electronics. Upon request it is possible to modify the software and thus the operation of the machine including vacuum extraction, gas or sterile air injection, etc.

Three different ranges of equipment are available: **BFIL T** (Manual Bags Filler), **BFIL S (Semiautomatic Bags Filler), BFIL A** (Automatic Bags Filling & Capping machine).

One of the most important innovations of the **BFIL** is the hydraulic circuit: since it is completely linear and steady, the cleaning and sterilization processes are simplified, ensuring a perfect sterilization of the equipment. A special drop grill to collect any droplet or leakage of solution is installed on each model. Each BFIL can be integrated with a devoted **CIP/SIP** station. The dosage precision varies according to the adopted flowmeter and can reach ±0.1%. The volume of the bag can range from 50 up to 5000 ml.

The capping process of the **BFIL S** and **BFIL A** models is automatic and eliminates the need to manually insert plugs into the filling pipe. The feeding of the plugs can be both manual or automatic, through vibrators, the capacity of which depends on the kind of plug used.



A wide range of optional extras, such as dedicated sterile laminar air flow hoods, integrated conveyor belts, ink jet printers are available for all **BFIL** models. Each station only requires one operator.
Up to 4 different **BFIL A** stations can be integrated in one line.

FFIL
FILLING MACHINES FOR BOTTLES

Our **FFIL** pharmaceutical linear filling machine for bottles represents an evolution in the systems of filling for pharmaceutical rigid vessels, combining:

- Maximum reliability
- High precision in metering
- Low maintenance costs

The process has been designed in order to offer the maximum functional easiness:

- The bottles are fed through a special sanitary belt and a mechanical system ensures the correct positioning of each bottle under the filling system;
- Special slides drive the filling nozzles onto the bottles reducing. The nozzles have a special design avoiding the production of foam even at high filling speed;
- The mass flow-meters provide for the metering of the solution with high precision and reliability, allowing a perfect sterilization in place through pure steam;
- The nozzles raise and the separators move in order to let the bottles feed.

The FFIL filling machine in standard version is designed for bottles from 50 upto 1000 ml with capacities upto 12.000 bph.

NTOS-NTE-TARO

CONVEYORS AND TURNTABLES

Our customised conveyor belts are designed to meet any requirement in the handling of pharmaceutical containers throughout the drug packaging process. Feed-lines and output lines to and from production equipment can be tailored forcontainer type (i.e., glass bottles, PP bottles) and volume (small and large bags). Suitable materials, sanitary and safety concerns are the baseline for the design of our belt conveyors: ***first-class, easy-to-clean product handling components, sanitary belts, stainless steel frame, adjustable frame support components, sheltered moving parts, smooth product flow, emergency push button.***

Conveyor lines can be fitted with our stainless steel rotating (or turn) tables Mod. **TARO**, to suit different machines and even out the flow of containers.

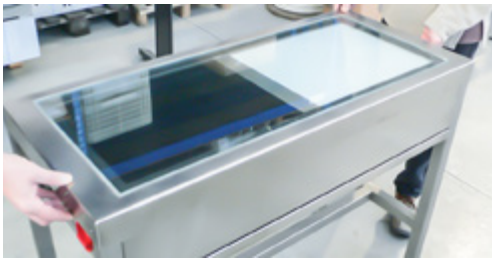
GHA-SCP

CAPPING AND STOPPERING SYSTEMS

In support of our installations, the **CAPPING MACHINES** ensure a fully automatic sealing operation. Special optical sensors provide fault detection and smooth product flow. Product critical parameters are constantly checked and alarmed. Transparent panels provide clear visibility of the operation. Moving parts are protected by stainless steel panels and all mechanical details are carefully designed to increase productivity.

With Alu Caps: Pressurized capping for rubber closures & rotating head crimping machine for aluminum ferrules. ***With Euro Cap*** or other plastic plugs: by heat-sealing.
With Screw Caps for canisters: closing by rotating system with or without plastic or aluminum sheet sealing on the container mouth.

VIS
BAGS INSPECTION LINES



Parenterals should be manufactured and inspected to ensure the highest quality, meeting the requirements set forth in Pharmacopoeias. As they are typically injected, parenterals have the potential to go directly into the bloodstream which can result in adverse reactions to contamination and particulates.

Particulate matter in finished pharmaceuticals can come from multiple sources, such as the ingredients, processing equipment, or the container closure system. Visual inspection is necessary to reduce or eliminate the risk of non conformities in the products.

Filled bag are difficult to inspect automatically due to their special characteristics (soft, warm, potential risk of air intrusion, etc) and therefore most of the I.V. fluid companies perform the activity manually or semi-automatically. Particulate matter in parenteral solutions can be detected through BRAM-COR systems with black/white background for human inspection, using our **Manual Visual Inspection desks** and **Semi automatic Visual Inspection Lines**.

We care for our equipment

BRAM-COR
PHARMACEUTICAL TECHNOLOGIES

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