

PROCESSING SYSTEMS

PREPARATION
LINES

CIP/SIP
SYSTEMS

ANCILLARY
SYSTEMS

BRAM-COR[®]
PHARMACEUTICAL TECHNOLOGIES

BRAM-COR PROCESSING SYSTEMS

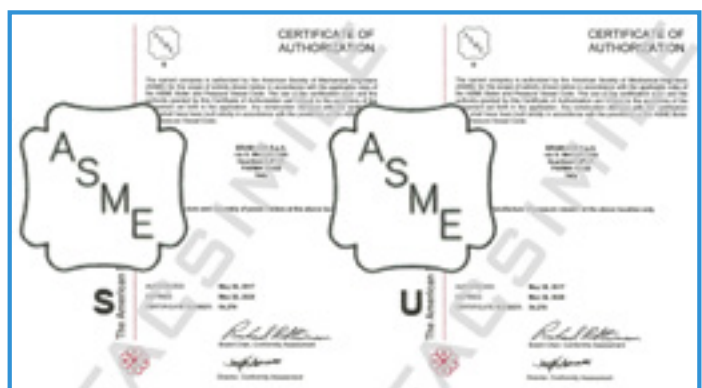
BRAM-COR designs, manufactures and installs complete Formulation & Preparation Plants starting from specific Product and User Requirements.

Sterile preparation or cleaning and sterilization of process vessels and contact equipment are common issues in the pharmaceutical industry and therefore a must in all our projects.

Specific manufacturing or sanitization & sterilization requirements can be satisfied by our processing systems. BRAM-COR solutions provide the optimum balance of performance with cost effective aseptic processing equipment including:

- MIXING TANKS & BIOREACTORS
- CIP/SIP SYSTEMS
- ANCILLARY SYSTEMS FOR FORMULATION LINES

Boilers and pressure vessels in BRAM-COR water treatment and processing systems are ASME certified ("S" and "U" stamp).



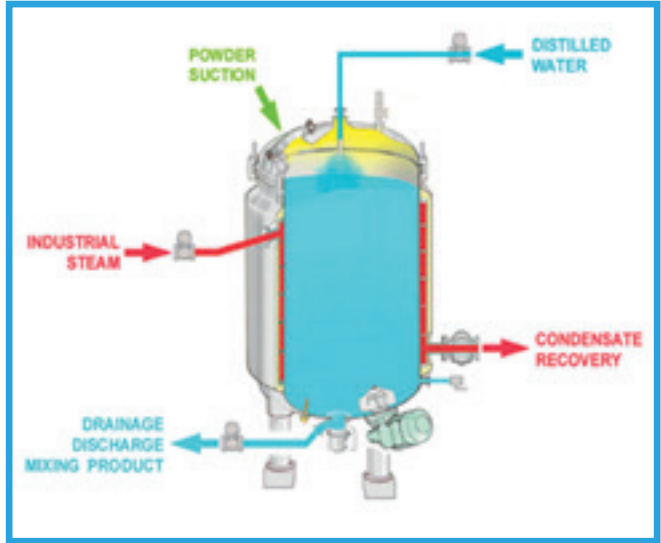
DISS	PREPARATION SYSTEMS	4
CIP/SIP	STATIONS	7
ANSY	ANCILLARY SYSTEMS FOR FORMULATION LINES	8
	TRANSFER PANELS	
	TRIBLENDERS	
	FILTRATION GROUPS	
	SOLUTION TRANSFER CIRCUITS THROUGH NITROGEN OR SANITARY PUMPS	
	LAMINAR AIR FLOW CABINETS	
	FILTRATION GROUPS	
	DEVOTED SCADA SYSTEMS	
	VESSELS LOADING PLATFORMS	
	AUTOMATIC BALANCES	



DISS PREPARATION SYSTEMS

BRAM-COR offers a complete range of preparation lines suitable for any pharmaceutical formulation including:

- **BIOREACTORS** (reactor vessels, pressure vessels)
- **MIXING TANKS** (pressure tanks, mobile mixing vessels)
- **CUSTOMIZED FORMULATION TANKS** (for high purity water mixing with powders)
- **ATMOSPHERIC TRANSFER TANKS**



The accurate finishing and the high quality of the materials used in the construction of all our equipment ensure aseptic drug manufacturing, in accordance with international cGMP and pharmacopoeias.

All vessels are in AISI 316L stainless steel, internally mirror polished, thermally insulated and clad in satin finish stainless steel. The design strictly follows PED standard. ASME and PED certification is also available for Pressure tanks.





COMPLETE FORMULATION LINES

BRAM-COR 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.

Safe platforms and staircases are provided to facilitate the management and inspection issues of larger plants.

CAPACITIES RANGE

From 50 to 25,000 l





PERMANENT QUALITY AND QUANTITY CONTROL OF CRITICAL PARAMETERS

Each tank 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 thermostating unit. Compact pre-wired mobile preparation units can be designed by Technical Department according to local space requirements.

BRAM-COR range of products can also be integrated by 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.





CIP/SIP STATIONS

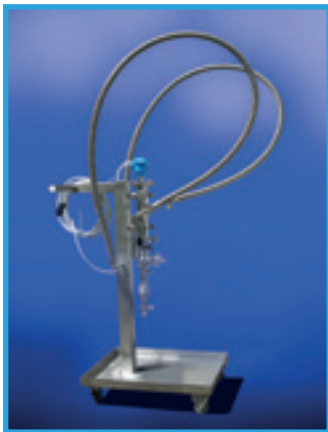
BRAM-COR Cleaning in Place / Sterilizing in Place systems are designed to fully meet cGMPs requirements in cleaning and sterilizing practices commonly applied in pharmaceutical process lines. BRAM-COR C.I.P./S.I.P. systems are supplied as fixed STATIONS or as MOBILE SKIDS, with manual, semiautomatic or automatic configuration.

C.I.P. systems can be equipped with different utilities for heating:

- **Electrical heater**
- **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**



CLEANING PARAMETERS

In CIP/SIP automatic stations, CIP critical parameters, such as:

- **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**
- **Tanks levels**

can be constantly monitored by the PLC and managed with cost-savings criteria. CIP/SIP System SW can be customized with different washing cycles.





ANSY ANCILLARY SYSTEMS FOR FORMULATION LINES

According to specific product requirements (viscosity, temperature, oxygen sensitivity, aseptic issues etc.), BRAM-COR integrates his formulation plants with state-of-the-art:

TRANSFER PANELS

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 SS 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.)

LOADING PLATFORMS

for safe and easy loading operation

AUTOMATIC BALANCES

for dispensing rooms



TRANSFER PANELS

Transfer panels allow an easy and proper connection of all sanitary pipes between tanks and return line. This system allows simultaneous connections between different piping from mixers outlet. The system, composed by removable stainless steel pipes, is designed to avoid "cross contamination" in the simultaneous phases of production and CIP/SIP operation. Each pipe is equipped with inductive sensors in order to allow the right identification by the PLC during the current phases.



TRIBLENDERS

Solid-liquid mixtures for IV solutions shall be prepared through a sanitary triblender for a proper dosage of solid intake and liquid flow. The triblender basically consists of a casing and a centrifugal-pump impeller with sanitary design, sanitary single mechanical seal, standard hopper of 40° and clamp connections. The suction side has a double-wall tube that keeps the inlet of solids separate from that of liquids, thus avoiding the formation of flocks before the material enters the casing.

The fluids enters the mixing chamber at a high velocity, thereby creating a vacuum on the center of the impeller, which causes the suction of the solids. The fall of the solids can be regulated by means of a valve situated on the bottom of the hopper. The system is suitable for quick and homogeneous mixing of a great variety of solids without air contact performing complete mixing with recirculation of the material.

Materials:

- **Parts in contact with the media:**
AISI-316L
- **Gaskets: EPDM according to FDA**
- **Mechanical seal (standard):**
C/ St.St / EPDM
- **Inside finishing: mirror polished,**
Ra<0.5 µm
- **Outside finishing: mirror polished**



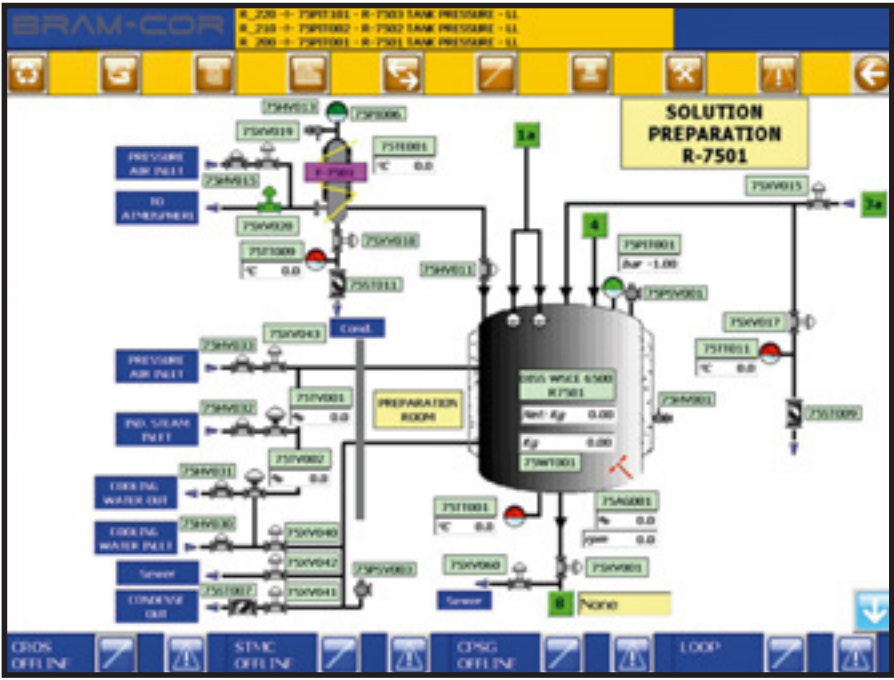
SOLUTIONS TRANSFER CIRCUITS

Each formulation plant can be integrated with a solution preparation circuit, composed of sanitary fittings and components, such as:

- Sanitary piping in AISI 316 L stainless steel, conforming to ASTM A 27A code, Ra< 0.5 µm finishing, Tri-clamp connections
- Sanitary flexibles in sanitary silicon, Tri-clamp connections
- Flow-sensors in AISI 316L, Tri-clamp In-Out connections
- Sanitary Centrifugal Pump, Finishing: internal - mirror polished Ra < 0,8 µm
- Inverter in AISI 316 L SS
- Pneumatic/Manual sanitary membrane valves
- Thermostatic steam trap on the pump drainage
- Security Sensors, in stainless steel IP68 protection grade.



SCADA SYSTEMS



Each preparation plant can be automated with a SCADA supervisory system to control process sequences and critical parameters such as:

- Recipe management
- Filling/emptying operation
- Cooling/heating phases
- Mixing speed
- Solution transfer
- CIP/SIP sanitization

Software development, based on validable platforms, follows GAMP 5 standard, while 21 CFR part 11 electronic signature & records practices are applied for safety management concerns, ensuring safe access policy, audit trails and back-up management.

LOADING PLATFORMS

Formulation plants are integrated with special heavy-duty 304 SS platforms, designed according to ISO safety standards, installed around the tanks to allow the operator to load the raw materials in the tanks, easing use and inspection issues of the plant. Suitable staircases with anti-slip steps and safe rails ensure easy reach of the loading level.



FILTRATION GROUPS

After the preparation line, BRAM-COR Filtration Group filter the solution before the filling process. All surfaces in contact with the product are polished to $Ra \leq 0.5 \mu\text{m}$. Our filtration groups are mainly composed of:

- Filter for Liquids, consisting in special 1,5 – 0.2 microns sterile cartridges, in Sanitary AISI 316 L stainless steel housings , tri-clamp connections
- Pressure Gauges
- Temperature Probe on air filter
- Thermostatic Steam trap on the Drainage
- Pneumatic/Manual sanitary membrane valves



DISPENSING SYSTEMS

Excipients to pharmaceutical solutions are prepared in the dispensing room and weighted on special balances. Coding and labelling of the batches is carried out through an operator panel. Each batch is identified by a label, printed with the bench-printer in the dispensing room.

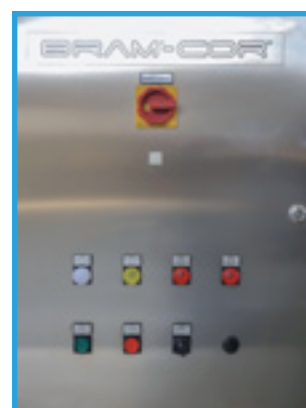
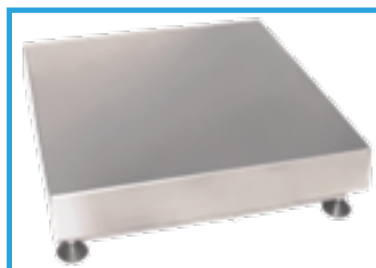
LAMINAR FLOW HOODS

BRAM-COR Laminar air flow cabinets are designed to prevent contamination during dosing operation in dispensing rooms. Air coming from the HVAC ducts is first filtered through pre-filters and then decontaminated through HEPA filters. Exhaust air is sucked and expelled through rear ducts, granting a correct air circulation.



SCALES

Special sets of electronic platform balances and desk balances can be provided to allow preparing the proper formulation in dispensing room. Scaling systems can be connected to a control unit (Operator panel or SCADA) for correct batch coding and equipped with thermal panel printers for batch identification and labeling.



BRAM-COR KEY DESIGN CONCEPTS

BRAM-COR engineering focuses on liquid/sterile drug and low/medium/high viscosity production processes, such as parenteral solutions, oral solutions, ophthalmic and oncology solutions, viscous emulsions, gel and pharmaceutical creams, cosmetic preparations.

BRAM-COR work flow structure consists of the following main activities: Design, Construction (mechanical, electro-pneumatic, software configuration), Testing, Documentation, Installation, Validation, Assistance.

Every step of the assembly follows rigorous quality approved processes and procedures. Specification, construction and verification steps within the lifecycle are carried out according to GAMP "V-model", considering risk assessment, architecture of system components, functional specification, sanitization and validation issues with special overview to include sustainability and maintenance of the system.



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WORLDWIDE SERVICES

We are currently delivering our machines and building complete water treatment systems and preparation lines all over the world. Top quality GMP equipment must necessarily be integrated through a proper high level of professional services including: **Technical Documentation, Factory Acceptance Test, Installation, Commissioning, Site Acceptance Test & Start-up, Training, Validation, After Sales Service.** Our worldwide network of skilled agents and our affiliated companies ensure assistance to our Clients in over 50 countries, from the very beginning of a pharmaceutical project throughout decades after start-up. Our **After Sales Dept.** grants punctual and quick deliveries of spares and ongoing technical support.



BRAM-COR
PHARMACEUTICAL TECHNOLOGIES

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