

WATER TREATMENT SYSTEMS

PURIFIED
WATER

WATER FOR
INJECTION

PURE STEAM



BRAM-COR

PHARMACEUTICAL TECHNOLOGIES

BRAM-COR WATER TREATMENT LINES

BRAM-COR **Pharmaceutical Water Treatment Systems** are designed to produce compendial:

- **PW** PURIFIED WATER
- **HPW** HIGHLY PURIFIED WATER
- **WFI** WATER FOR INJECTION
- **PS** PURE STEAM

Pre-treatment options, monitoring of critical parameters, regulatory requirement for product quality, consumptions, microbiological control, operation and maintenance requirements, lifecycle costs are taken into considerations in the design of all processing steps, from feed water to the point of use.

Special care is given to the choice of sanitary materials. Product-contact surfaces are in certified AISI 316L stainless steel, with standard roughness $\leq 0.4 \mu\text{m}$.

PTFE gaskets ensure perfect sealing. Advanced Process Analytical Technologies are applied for monitoring issues and professional **GAMP** compliant automation is provided for system control.

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MMF 4600



ADUF 4600



PRT 8000



PRTW WATER PRE-TREATMENT SYSTEMS

BRAM-COR **Water Pre-Treatment Systems** are customized upon a thoroughful evaluation of feed-water 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) through different steps, including:

- 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. Upon request, for an effective microbial control strategy to prevent biofilm formation, most pre-treatment systems can be supplied in hot water sanitizable version.

CAPACITIES RANGE

From 100 to 20,000 lph



ADD HWS 2000



ADD HWS



CROS REVERSE OSMOSIS SYSTEMS

CROS Reverse Osmosis Systems are designed to produce compendial purified and highly purified water through several water treatment steps, according to 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, may include:

- Sodium hypochloride dosing station for water disinfection and oxidation of organic substances, reducing the bacterial charge
- Sodium metabisulphite dosing station for neutralization of calcium carbonate and chlorine
- 25 μ m + 5 μ m filtration system to eliminate solid substances in inlet water
- Single or double osmotic stages
- Electrodeionizer
- UV lamp



CROS EDI 500



CROS SINP 20000

CAPACITIES RANGE

From 100 to 20,000 lph

PURIFIED WATER GENERATION

Purified water is usually obtained through **single stage RO + Electrodeionization**, **double stage RO** and **double stage RO + EDI**. In each RO stage, water is processed through thin film composite RO membranes, offering the highest rejection of contaminants. Two different flows are generated by the RO system: permeate water, corresponding to PW specification, and RO concentrate, which is recycled in the system in order to obtain a higher recovery with a lower consumption of inlet water. **CROS** equipments, with a range of capacity spanning from 100 up to 20,000 lph, are manufactured according to all cGMP and FDA rules, including:

- Centrifugal booster pump in AISI 316L stainless steel, completely mirror polished both internally and externally
- AISI 316L stainless steel membrane vessels
- Sanitary in-line instrumentation to monitor product critical parameters, such as conductivity and temperature
- Full automation managed through GAMP-compliant hardware and software
- Framework and control board in AISI 304 stainless steel satin finished
- CIP sanitization or HOT WATER sanitization.

VESSELS DETAIL





STMC VAPOR COMPRESSION DISTILLERS

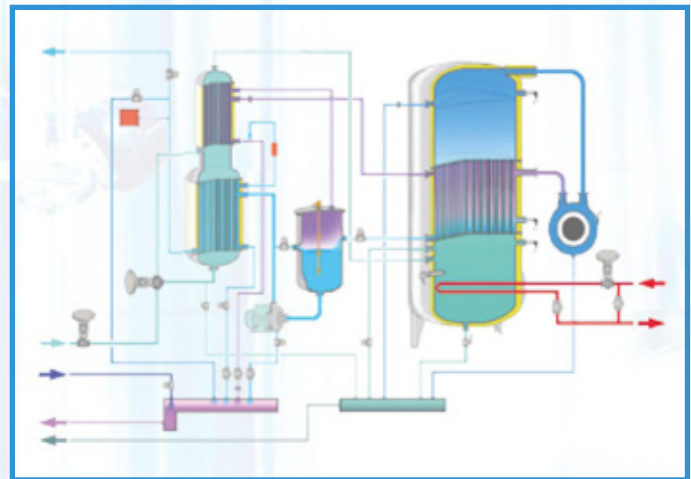
BRAM-COR **STMC Vapor Compression Distillers** produce compendial distilled water for pharmaceutical applications, such as I.V. solutions, injectables, washing systems and special solutions where both quality factors, such as the sterility, elimination of the pyrogens and of the chlorine solvents with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

STMC vapor compression distillers can operate:

- With electrical heating
- With steam heating
- Both with electrical and steam heating systems

CAPACITIES RANGE

From 20 to 12,000 lph, with single or double compressor



WFI AT EXTRA LOW MANAGEMENT COST

The **STMC** distiller can produce both cold distillate at a temperature and hot distillate with huge savings of energy costs and with no 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 the infeed water, the Pure Steam and the 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)



STMC ST 3000



STMC EL 60

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

Access policy and records can be managed according to 21 CFR PART 11.



SMPT ST6 1300

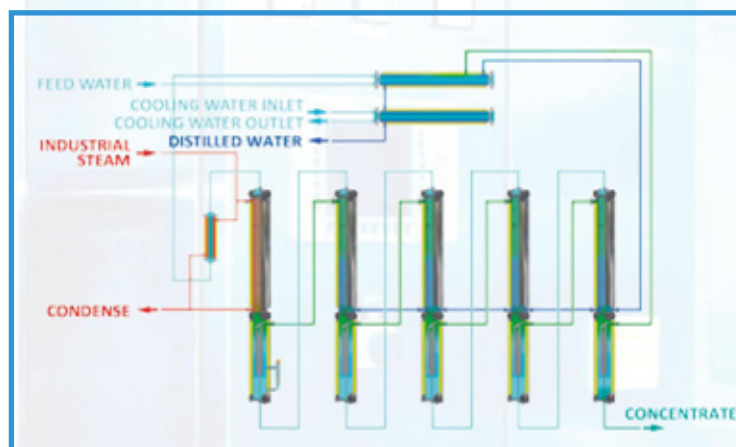


SMTP MULTIPLE EFFECT DISTILLERS

BRAM-COR **Multiple Effect Distillers** are designed and manufactured according to cGMP to produce compendial Water for Injection. 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 PS.

CAPACITIES RANGE

From 50 to 15,000 lph, with three-eight columns configurations



WFI FROM MULTIPLE DISTILLATION

Heating for evaporation and cooling for condensation processes are performed by double tube sheet heat 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 installed at the top of each column separates the steam generated by the evaporation process from entrained substance in the steam itself. The result is a pure, "dry", pyrogen-free steam, condensed in compendial Water for Injection. Pressure vessels are designed according to PED regulation, and the equipment features:

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



SMPT ST8 3000

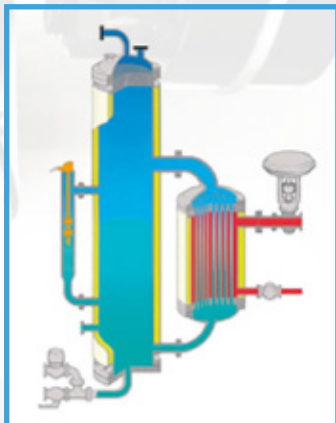
CPSG ST 150



CPSG ST 2500



CPSG PURE STEAM GENERATORS



Our **CPSG Pure Steam Generators** produce dry, saturated steam, suitable for sterilization of pharmaceutical production plants, for direct contact with 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 centrifugal and gravity separation methods.

CAPACITIES RANGE

From 20 to 5,000 Kg/h

PHARMACEUTICAL PURE STEAM

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

- 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 Heat 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 Heat Exchanger is typically industrial steam at 100 to 120 psig (7.9 to 2.0 bars).

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

KPSG ST 4500



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

DPSG EL 50



DPSG SINGLE EFFECT DISTILLERS

PS & WFI from a single effect distiller: each **DPSG** equipment is both a **Single Effect Distiller** and a **Pure Steam Generator**. This equipment produces dry, saturated steam to be used as sterilizing agent.

The Pure Steam, when condensed through a double tube sheet condenser, meets the requirements of international pharmacopoeias for Water for Injection. The system can therefore provide a simultaneous production of Pure Steam and Water for Injection. The production process consists in PW water evaporation followed by Pure Steam 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. All pipes are orbital welded when possible, with inert gas protection. Moreover:

- Active surfaces are passivated.
- The parts in contact with the pure steam are polished ($Ra \leq 0.4 \mu m$)
- The Skid is in stainless steel AISI 304 satin finished
- The Control Cabinet is in stainless steel AISI 304 satin finished

DPSG equipments are available in electrically or steam heated versions.





LOOP DISTRIBUTION SYSTEMS

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

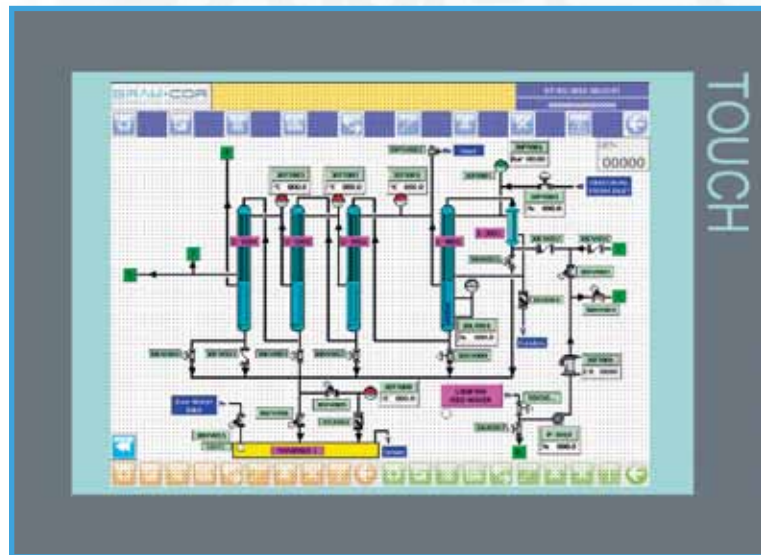
- **Maximum instantaneous flow rate**
- **Pressure & temperature requirements**
- **Sanitization issues**
- **Periodic consumption requirements and duration**
- **Method of delivery (automatic or manual)**



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 acceptance criteria, to check **quality of welds, effective passivation, hydrostatic tightness, full drainability, absence of dead-legs, fluid dynamics.**



A thoroughful loop documentation, including isometric drawings, welding reports, boroscopy records, passivation certificate and test reports is provided to complete the supply.



SCADA CONTROL SYSTEMS

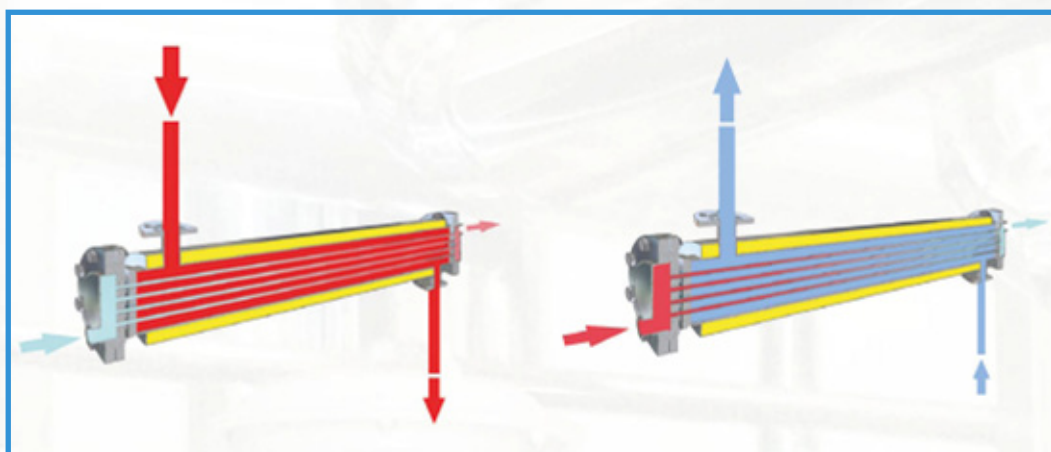
BRAM-COR **GAMP-Compliant Automation**: from equipment control to production line supervision, **SCADA Systems** provide full management control throughout the plant lifecycle. Data management includes: **trends and electronic records, electronic signatures and alarms management, audit trails, lifecycle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

GAMP-COMPLIANT AUTOMATION

The software is usually configured on WinCC Flexible platform. Other platforms may be used upon request, as A/B Rockwell. Secure access policy, according to 21 CFR PART 11, includes three different access levels. Each authorized user shall log-in by digiting user ID + password, the combination of which is unique and may be changed by the Customer in runtime. BRAM-COR control systems are configured to store and show live-data for one year. Different needs shall be highlighted by the Customer and involve HD of bigger size for a different configuration of WinCC Flexible program.



All historical data can be exported and saved by the Customer for long lasting backup. All parameters modified by the customer are stored and limited, all parameters and I/O (analogic and digital) of the system 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 by the Customer on a USB key or Ethernet.



SCAM HEAT/COOL EXCHANGERS

A heat/cool exchanger is due to heat up, cool down or keep process water temperature to the desired values, by heat transfer between two fluid media. For efficiency, BRAM-COR **Double Tube Sheet Heat/Cool Exchangers** are designed to maximize the surface area of the wall between the two fluids, while minimizing resistance to fluid flow through the exchanger.

Tube diameters, thickness, length and number are calculated to withstand internal tube pressure and shell overpressure in accordance to space and performance requirements.



SCAM DTS 172-2

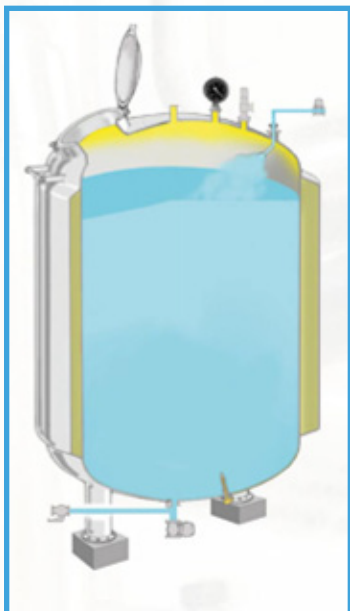
In pharmaceutical processes, BRAM-COR **SCAM DTS** exchangers are typically used for high pressure application, for hot water sterilization of loops and tanks, for water cooling/heating user points. All product contact surfaces are built in AISI 316 L stainless steel, internally mirror polished, $Ra \leq 0,4 \mu m$.

The exchangers are insulated and clad with 304 SS satin finished. Tube ends are manually expanded to fit in the tube sheet. All materials are fully traceable. Non-destructive tests are carried out by skilled personnel to ensure compliance to cGMP and Pressure Equipment Directive.

SCAM DTS may be embedded in the equipment (ex. in **SMPT** distiller) or on self-standing skid, and fitted with sanitary valves and pumps, steam trap, temperature probe.



SCAM DTS 06420



STOC STORAGE TANKS

BRAM-COR **STOC Storage** line includes a complete range of **pharmaceutical holding tanks** for storing **compendial or non-compendial water**.

HIGH QUALITY PHARMACEUTICAL VESSELS

Material and components traceability and certification are assured in all BRAM-COR vessels. Rigorous sanitary piping welding and inspection procedures, ND testing procedures in compliance to international standards for pharmaceutical equipment are enforced in our workshop. Basic features of our **fully cleanable** storage tanks:

- **Certified AISI 316L stainless steel mirror-polished ($Ra \leq 0,4 \mu m$) product contact surfaces and components**
- **"Tank in tank" insulation bottom and wall**
- **Vertical or Horizontal design**
- **Customized heat and cool jackets, clad in satin finish AISI 304 stainless steel**
- **Manhole**

The capacities range from 100 up to 25.000 litres, while sizes and shapes are scaled up according to specific URS, in order to fit different space requirements including for instance:

- **Any instrumentation / control / management system**
- **Heating and cooling systems**
- **Platforms and stairs**
- **PED certification upon request**



STOC WSIE 2000 HORIZONTAL

All tanks can be integrated with BRAM-COR **SCADA** computerized 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.



STOC PSIA 1500



KOMB COMBINED WFI + PS GENERATORS

BRAM-COR **KOMBO** 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, shrinking space needs.

A central **SCADA** controls the two units, providing separate or concurrent outlet of Water for Injection or/and Pure Steam.



GENO OZONE GENERATORS

Thanks to its high oxidation potential, ozone is proven to be one of the most effective and safe methods to remove antibacterial, anti-viral, and anti-fungal activity.

STERILIZING PW LOOPS PW STORAGE TANKS

BRAM-COR full-stainless steel **GENO Ozone Generators** are conceived for pharmaceutical application, i.e. for water disinfection and loop sanitization.

Ozone quantity during and after sanitization is constantly monitored by ozone analyzers, while residual ozone in water is automatically destroyed by a sanitary UV lamp before the use in the process.

Sanitary piping, valves, pumps and instruments complete each **GENO** unit.



STDA STANDARD ACCESSORIES AND COMPONENTS



UV LAMP DETAIL

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

- 316L SS housings for water filters
- 316L SS housings for air filters
- UV Lamps & Controls



WATER FILTER



AIR FILTER

BRAM-COR KEY DESIGN CONCEPTS

A full understanding of the drug production process is the key concept for correct design. BRAM-COR engineering focuses on fluid drugs sterile production processes, such as parenteral solutions, oral solutions, ophtalmic solutions. The definition, assessment and monitoring of critical parameters directly affecting product quality are the baseline for the application of suitable Process Analytical Technologies for in-line and at-line quality control. BRAM-COR work breakdown structure consists in following main activities:

- Design
- Construction (mechanical, electro-pneumatic, SW configuration)
- Testing
- Documentation
- Installation
- Validation
- Assistance

Every process follows rigorous cGMP-compliant Standard Operative 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 a sustainable maintenance of the system.



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.

