BRAM-COR Water Treatment Systems

STMC VAPOR COMPRESSION DISTILLER

A clear vision about vapor compression distillation in pharmaceutical environment

BRAM-COR
PHARMACEUTICAL TECHNOLOGIES

STMC *Performance*

SAFE PRODUCTION OF WATER FOR INJECTION ACCORDING TO GMP AND FDA RULES.

STMC models produce sterile WFI virtually with any type of water supply, thanks to many water pretreatment technologies, integrated on the same skid of the machine.

BRAM-COR project drivers are aimed at satisfying all pharmaceutical regulatory and QA requirements, aligning the Vapor Compression Distiller manufacturing to the international cGMP (Good Manufacturing Practices) and Pharmacopoeias.

BRAM-COR target in design, manufacturing, documentation, testing and validation activities focuses on the overall compliance of equipment to the needs of the pharmaceutical and biotechnology industry.

Capacities range:
from 70 to 25,000 Kg/h

Destination of use	**Production of Water for Injection for pharmaceutical use and laboratories (different WFI outlet temperatures available). STMC distillers produce sterile and free from pyrogen water, in accordance with cGMP and FDA regulations.**
Technology	**Feed water evaporation through vapor compression, followed by Pure Steam separation and condensation. The produced WFI is fully compliant to USP, JP, CP, IP and EP Pharmacopoeias.**
Technical features	**• cGMP design and construction**
	• All product contact surfaces in AISI 316 L stainless steel
	• Jackets, frame and control board in AISI 304 stainless steel
	• All welds are executed by qualified welders
	• Gaskets in EPDM or PTFE or Silicone
	• Column type: AISI 316L Stainless steel with sight glass
	• 0.2 µm vent filter with stainless steel housing
	• Recirculating tank
	• Sanitary pump
	• Pneumatic membrane valves
	• ASTM C-795 – compliant insulation
	• Instruments: conductivity meter, pressure transducers, temperature probes, level transmitter
	• Double manifold system for feedwater discharge and sanitary discharge
	• Self-sanitizable
	• Available pure steam production from the distillation column
	• WFI efficiency on feed water up to 95%
	• Possibility to be feed with softened water, water from industrial single-stage osmosis, Purified Water
	• Available in steam operated, electrically operated model or hybrid steam + electrical models
	• Stainless steel compressor available upon request
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** **• Recipes formulation / Batch • 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 (customer operator receives a message / a text message / a warning mail)** **• Server-side data centralization (customer can centralize data on his service, or Bram-Cor provides it)**
Sanitization	**Sanitization of the Vapor Compression Distiller can be performed as one-shot selection before production start or as a single phase, to be periodically performed on the WFI system.**

STMC *WFI Generation*

TO MEET ANY WFI REQUIREMENT

BRAM-COR STMC, pharmaceutical Vapor Compression Distiller, can produce both cold Distillate or hot Distillate with huge savings of energy costs and with **no need of cooling water**. It can work with electric heating (**STMC EL**), with steam heating (3 bar) exclusively (**STMC ST**), or both with electrical and steam heating (**STMC STEL**).

The last type of heating is useful when the distiller usually works 24 hours/day, and when there is a lack of industrial steam overnight. There are also STMC models that work with integrated water pretreament systems (available on the same skid or in separate skid, too, according to the requirements of the factory lay-out):

- **STMC AEL** (electric heating) and **STMC AST** (steam heating) operate the pretreatment with water softeners;
- **STMC REL** (electric heating) and **STMC RST** (steam heating) operate the pretreatment with water softeners and reverse osmosis system.

BRAM-COR
PHARMACEUTICAL TECHNOLOGIES

STMC *Documentation*

COMMISSIONING & QUALIFICATION PACKAGE

BRAM-COR **STMC** documentation is composed by:

• GMP collection of plant-specific drawings, technical specifications, materials certificates, calibration certificates, hardware and software specifications, welding documentation, plant manuals (TECHNICAL DOCUMENTATION);

• DATASHEETS & MANUALS BOOK, containing all the datasheet and manuals of the commercial components (valves, instruments, pumps, etc) installed on the equipment.

DOCUMENT	MAIN CONTENTS IN BRIEF
TECHNICAL DOCUMENTATION (for each equipment / line)	GENERAL DOCUMENTATION AND CONSTRUCTIVE SPECIFICATIONS (WITH DQ, RISK ASSESSMENT, DRAWINGS AND CONFORMITY DECLARATIONS)
	COMPONENTS, VALVES AND INSTRUMENTS DOCUMENTATION (WITH 3.1 MATERIAL CERTIFICATES FOR PRODUCT-CONTACT SURFACES AND CALIBRATION CERTIFICATES FOR CRITICAL INSTRUMENTS)
	PIPING, FITTINGS AND WELDING DOCUMENTATION
	MANUALS AND SPARE PARTS LIST (INCLUDING USE & MAINTENANCE MANUAL AND OPERATING MANUAL)
DATASHEETS & MANUALS BOOK	MANUFACTURERS' DATASHEETS AND INSTRUCTION MANUALS FOR COMMERCIAL COMPONENTS
F.A.T. PROTOCOL FACTORY ACCEPTANCE TEST	TEST PRE-REQUISITES
	MECHANICAL COMPONENTS ACCEPTANCE TEST
	ELECTRICAL HARDWARE ACCEPTANCE TEST
	SOFTWARE ACCEPTANCE TEST
	FUNCTIONAL TEST
	FAT REPORT APPROVAL
S.A.T. PROTOCOL SITE ACCEPTANCE TEST	TEST PREREQUISITES
	MECHANICAL COMPONENTS ACCEPTANCE TEST
	ELECTRICAL HARDWARE ACCEPTANCE TEST
	SOFTWARE ACCEPTANCE TEST
	FUNCTIONAL TEST & TRAINING
	DOCUMENTATION VERIFICATION
	SAT REPORT APPROVAL

DOC. TYPE		MAIN CONTENTS IN BRIEF
VALIDATION PACKAGE	DQ	QUALITY PLAN
		FUNCTIONAL DESIGN SPECIFICATION
		HARDWARE DESIGN SPECIFICATION
		SOFTWARE DESIGN SPECIFICATION
		RISK ASSESSMENT
	IQ	DOCUMENTATION VERIFICATION
		AS-BUILT VERIFICATION
		COMPONENTS VERIFICATION
		INSTRUMENTS VERIFICATION
		HARDWARE VERIFICATION
		SOFTWARE INSTALLATION VERIFICATION
		PRODUCT CONTACT MATERIALS VERIFICATION
		SAFETY VERIFICATION
		UTILITIES & BOUNDARIES CONNECTION VERIFICATION
	OQ	HMI AND COMMUNICATION VERIFICATION
		ACCESS VERIFICATION
		INPUTS/OUTPUTS VERIFICATION
		ALARMS VERIFICATION
		FUNCTIONAL VERIFICATION AND TRENDS REPORTS VERIFICATION
		POWER FAILURE VERIFICATION
		AUDIT TRAILS AND CSV VIOLATION VERIFICATION (FOR SCADA SYSTEMS ONLY)
		TRAINING VERIFICATION AND FINAL REPORT

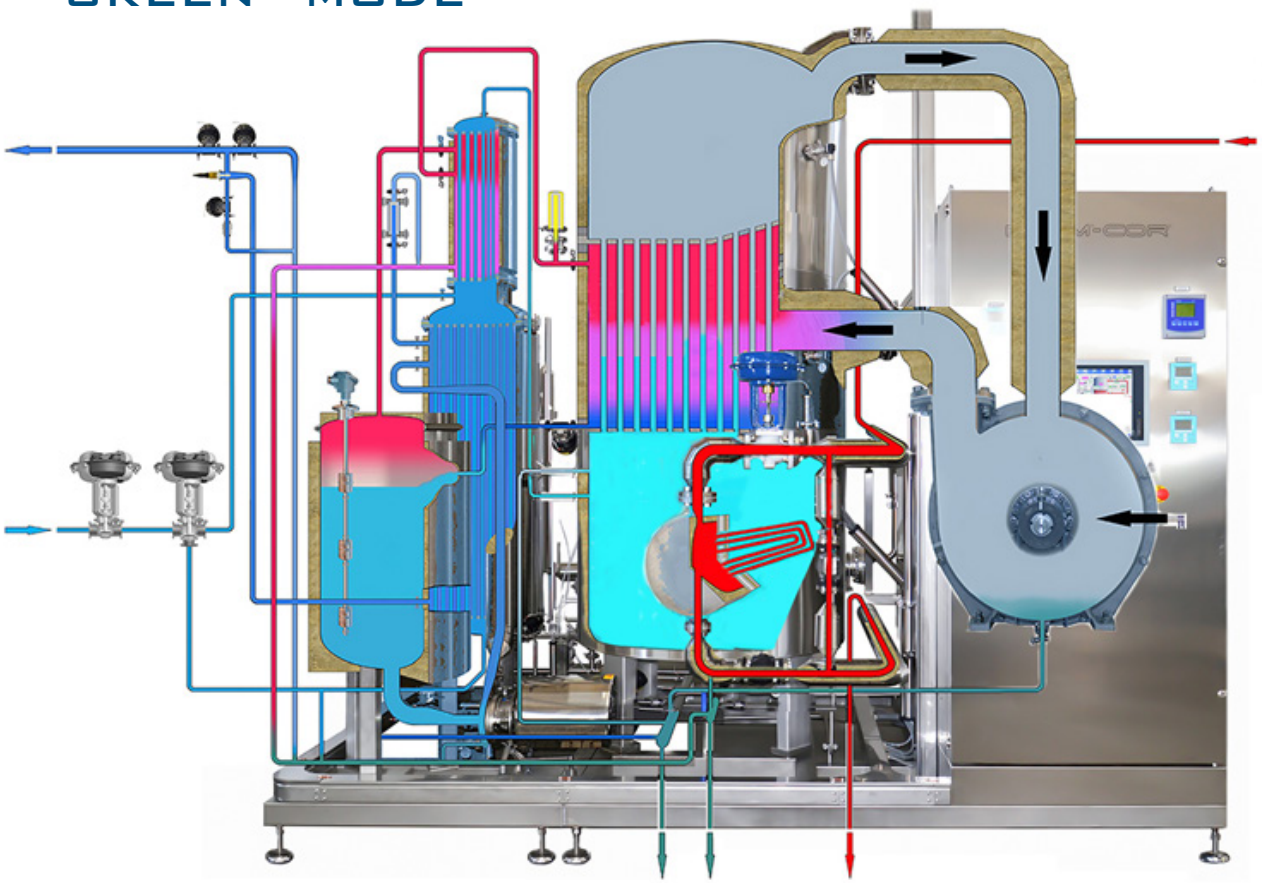
WATER FOR INJECTION IN BULK*		
PHISICAL / CHEMICAL	EU.PH.	USP
Appearance	Colorless, clear	Not defined
Conductivity	≤ 1.1 µS/cm@20°C	≤ 1.3 µS/cm @25°C
TOC	≤ 0.5 mg/L	≤ 0.50 mg/L
Nitrates NO_3	≤ 0.2 ppm	Not defined
Aluminium	≤ 10 ppb	Not defined
MICROBIOLOGICAL	EU.PH.	USP
Bacterial count	≤ 10 CFU/100 ml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

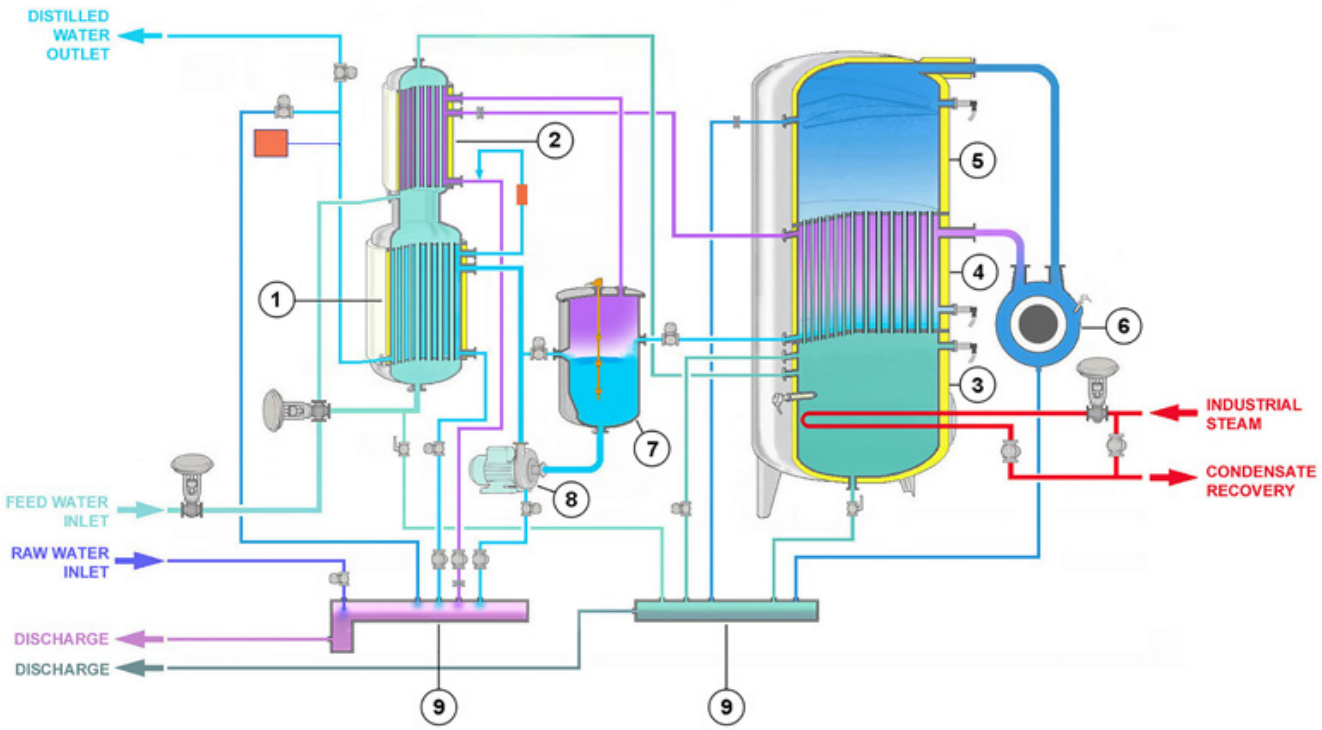
*update: January 31, 2021

BRAM-COR PHARMACEUTICAL TECHNOLOGIES

STMC *Process*

CONTINUOUS HEAT RECOVERY TO PRODUCE WFI IN A "GREEN" MODE





STMC ST (Steam heating) diagram:
(1) Heat exchanger (for Feed Water preheating and WFI cooling)
(2) Heat exchanger (incondensable gas condenser)
(3) Distiller tank
(4) Condenser
(5) Dome
(6) Blower
(7) Recirculating tank
(8) WFI pump
(9) Drain manifolds

BRAM-COR STMC Vapor Compression Distillation process runs as follows:

STEP 1 Feed-water enters into the first (optional) heat exchanger (1) (tube side) and is pre-heated, cooling at the same time the WFI to the temperature set in the HMI.

STEP 2 An automatic system (optional) regulates feed-water flow passing through phase 1, thus regulating WFI temperature.

STEP 3 Feed water goes into in the second heat exchanger (2) (tube side), and is furthermore pre-heated, condensing the gas generated by WFI production process.

STEP 4 Heated water flows in tank (3). Water level is controlled by an automatic system. The pipes in condenser (4) are partially filled by feed-water.

STEP 5 The heater (either electric and/or steam-heated) increases feed-water temperature to evaporation temperature. The generated pure steam occupies the dome (5). An automatic system regulates the thermal intake of the heating system, in order to keep the pressure in the dome at the set value.

STEP 6 A blower (6) sucks in the pure steam present in the dome (5) compressing it into the shell side of the condenser.

STEP 7 PS condenses in the shell side of the condenser (generating WFI) yielding energy to the feed-water contained in the condenser pipes, which now evaporates, generating other PS.

STEP 8 The produced WFI comes out of the condenser and flows into the recirculating tank (7). The gases released during WFI production process go into the shell side of the heat exchanger (2).

STEP 9 WFI is then collected in the recirculating tank (7) and pressurized by the pump (8), through the heat exchanger (1) (optional), where it reaches the temperature, set in the HMI.

STEP 10 A measuring system continuously monitors WFI quality (conductivity and temperature), and diverts WFI to the storage tank (conform WFI) or to the distiller drain manifolds (9) (substandard WFI).

STMC *Benefits*

MANY ADVANTAGES IN PRODUCING WFI

STARTING FROM SAVING, THE FIRST APPEAL

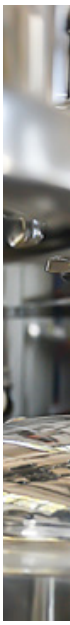
There is a lot of secure benefits in the use of BRAM-COR Vapor Compression distillation system:

- **Low energy consumption, no need of cooling water to condensate the pure steam**
- **No need for high quality inlet water (in some cases even softened water can feed the VC still)**
- **Very high quality of the WFI thanks to the strong degassying process**
- **No need to pressurize the inlet water**
- **WFI outflow at high pressure (1 – 1.5 bar) without any additional pump**
- **Extreme safe process, with no risk of any cross contamination through plant steam or inlet water**
- **Highest flexibility in terms of capacities and WFI temperatures**
- **Reduced maintenance**

The circuit of the WFI is separated from the circuit of the feed water. Moreover, the circuit of the distillate is under positive pressure. In case there should be any leakage it will be the WFI flowing out to the circuit of the feed water and never the opposite. The usual contamination problems that can arise by any multiple effect distiller after some 4-6 years of operation could therefore never happen in case of BRAM-COR Vapor Compression technology.

The special feature of the Vapor Compression Distiller, allowing to produce WFI at any temperature between 25°C and 99°C, together with the possibility to produce any quantity of WFI desired (from 0 to the maximum capacity of the plant), allows to adapt to any customer need. The same distiller can produce WFI for LVP as for antibiotics (heat sensitive injectables).
BRAM-COR Vapor Compression systems offer, thanks also to a wide range of available optional devices, not only the lowest degree of energy and water consumption of the market but also offer the highest possible output flexibility in terms of:

- Possibility to change the hourly capacity from 0 to the highest plant capacity (this interesting option allows to drastically reduce distiller starts/stops)
- Possibility to produce distillate at any temperature from 25°C up to 99°C
- Possibility to heat the equipment by steam and/or by electricity (for instance by steam, during the day and by electricity during the night, when the cost/kW is lower)
- Possibility to use feed water not only from pre-treatment plants such as the Reverse Osmosis and Demineralizers, but also from simple and low cost softeners.



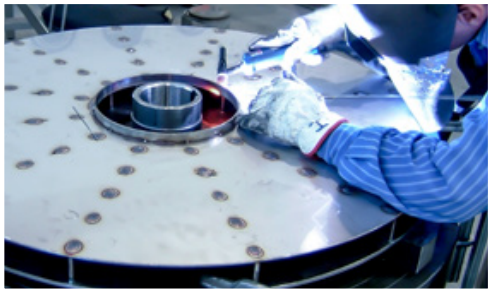
PHARMACEUTICAL WATER DISTILLATION SYSTEMS
MULTIPLE EFFECT VS VAPOUR COMPRESSION TECHNOLOGY

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 quantity 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 challenge)	Yes	Yes
HEAVY METALS	Free	Free + elimination of chlorine solvents
MOVING PARTS	Feed pump	Compressor, Recirculation pump
PURE STEAM 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 15 min for steam heating	SCADA 15÷40 min for steam heating

STMC *Blower*

PERFORMANCE OF THE BELT DRIVEN COMPRESSOR

AFFORDABLE INVESTMENT, EXTREME RELIABILITY



We focuse on the choice of the drive type for the “turbo blower”, which mechanically compresses vapor inside the boiler. The blower is the main mechanical part in motion in a VC distiller; it can be either direct driven or belt driven. In the first case the drive shaft and the rotor coincide; in the second case the impeller shaft is belt driven by the underlying motor shaft.

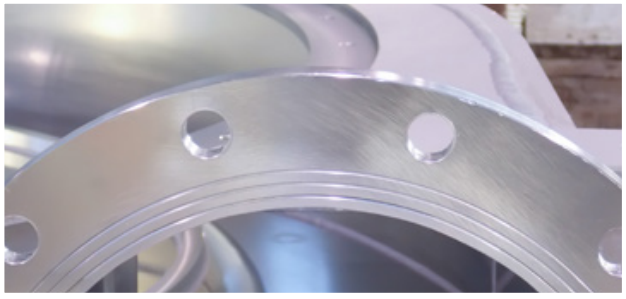
Both systems have positive and negative aspects on operation and maintenance which should be carefully taken into account when choosing a distiller, but we have chosen the belt driven compressors for our STMC distillers, for many reasons, below shown:

– The reduction of the capital cost for the equipment: a proven cost-effective technology for an affordable initial investment.

- The reliability, based on the extreme structural simplicity, ensuring an easy replacement of spare parts which can be commonly found on site.

In BRAM-COR distillers, all spares can be easily replaced by non-expert mechanical staff, with reduced plant shutdowns and production stops. Even the ball bearings of the shaft can be easily replaced in short time. On one hand, STMC equipment design is conceptually advanced (minimal tolerances for impeller and heads, high performance, optimized consumption). On the other hand, each STMC is conceived for a clean, sanitary separation of the product-contact blower from the electrical motor, which is safely placed below the blower, to prevent contamination. Every piece is in sight, everything is perfectly reachable.

A few minutes are needed to open the protection carters and periodically verify the condition of the belts; common mechanical skills are required to substitute the ball bearings of the blower shaft, the risk of shutdown becomes really negligible.



Two critical factors affect direct driven compressors, due to the high number of revolution: an accelerated bearing wear and a reduced lifecycle. The replacement of rotor ball bearings, as soon as they start deteriorating, is more complex, requiring prolonged shutdowns and specialized technicians and tools.

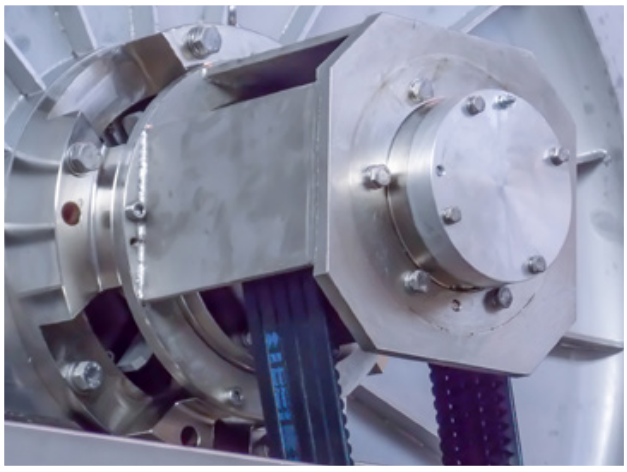
NO CONTAMINATION, HIGHEST SAFETY

- Safety from contamination: in direct drive, the rotor is firmly anchored to a ball bearing systems lubricated by pressurized oil, which is cooled by a radiator with a pump. This compact solution has the undoubted advantage of a restrained size, but does not ensure total safety against undesired contamination from oily sediments coming from the rotor.

In BRAM-COR belt driven compressor there is no lubrication circuit. Therefore there is no oil contamination risk, if not hypothetical: the ball bearings of the impeller shaft, in fact, are lubricated with the original grease; there is no physical-mechanical stress causing grease leaks. Moreover, the process side (internal side of the compressor) is always at higher pressure than the outern side, because no pressurized oil is used for lubrication. In other words, the highest safety against oil contamination can be reached when the shaft, moving the impeller, is different from the rotor.

LONG LIFE FOR A CONSTANT WFI QUALITY

– Long lifecycle: belt driven blowers ensure a long life to the distiller and a constant WFI quality, in compliance with the international pharmacopeias, ensuring an easy validation of the equipment.
Lip seals and ball bearings are due to be replaced often up to 10000 working hours. Indirect drive allows belt compressors to be “oil contamination free”, therefore suitable for pharmaceutical application.



Key design concept

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, low / medium / high viscosity emulsions, 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, considering risk assessment, architecture of system components, functional specification, sanitization and validation issues with special overview to include sustainability and maintenance of the system.

Worldwide services

We deliver BRAM-COR machines all over the world and our high quality cGMP equipment is supported through our high level professional services including: Technical documentation, Factory Acceptance Test, Installation, Commissioning, Site Acceptance Test & Start-up, Training, Validation, and After sales service. Our worldwide network ensures assistance to our clients in over 50 countries, from the very beginning of a pharmaceutical project and for decades after start-up. Our ***After sales dept***. provides punctual and quick deliveries of spares and ongoing technical support.

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