



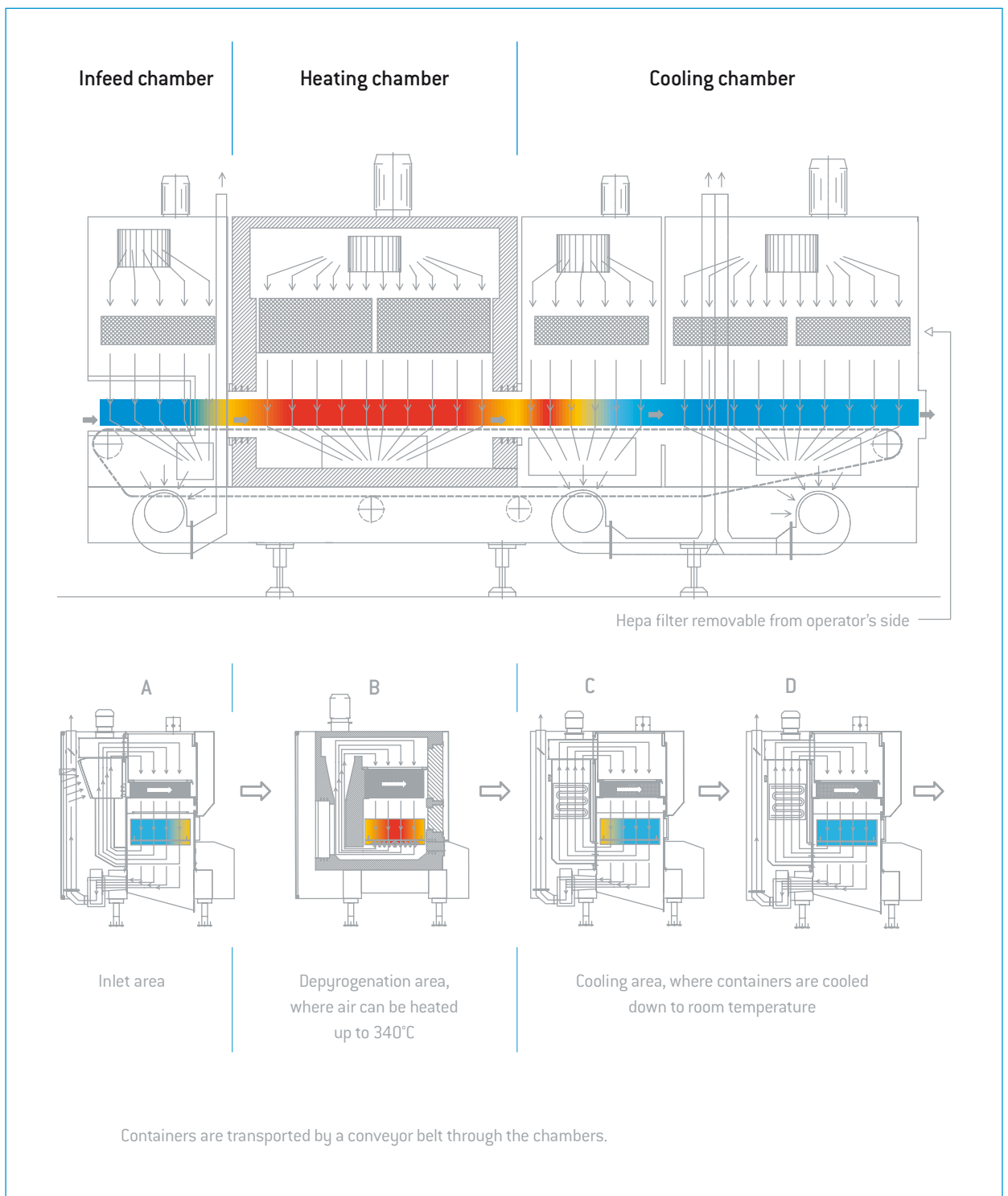
Macofar T 600 / T 800

Depyrogenation Tunnels

Depyrogenation Process Description

A pyrogen is defined as any substance that can cause a fever. A pyrogen can either be an endotoxin or an exotoxin, although most pyrogens are endogenous. Endotoxins are lipopolysaccharide molecules found as part of the cell wall of gram-negative bacteria and are primarily released upon cell lysis. In the manufacturing of parenteral pharmaceutical products, depyrogenation is the process of removal of pyrogens from the product and its containers and closures.

T 600 and T 800 Macofar tunnels have been designed to sterilize and depyrogenate glass containers by means of a continuous process based on heated dry unidirectional air flow. An ISO 5 environment according to ISO 14644-1 requirements is kept inside the whole length of the tunnel.



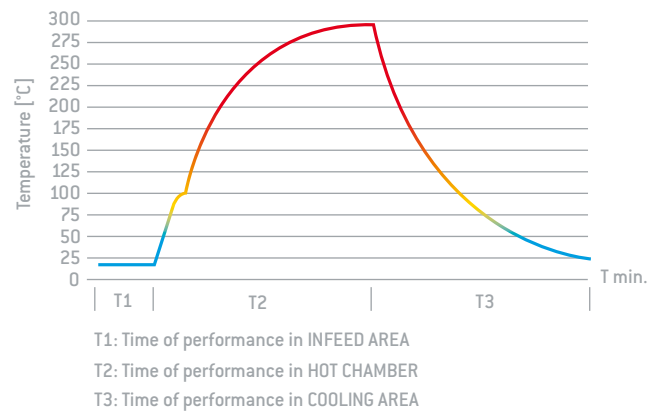
T 600 / T 800

Pyrogens resistance to depyrogenation can be identified by their D-value which is the time required to reduce the initial load of pyrogens by one logarithm at a defined constant temperature T_{ref} VTH. D-value can be experimentally measured and it depends on pyrogen type. Macofar tunnels have been developed in accordance to the most demanding requirements, using E.coli endotoxin as the reference pyrogen ($D = 5$ minutes at 250°C constant T_{ref}).

Another important parameter is Z-value which is the temperature increment to reduce D-value by a factor of 10 ($Z = 46.4^{\circ}\text{C}$ for E.coli endotoxin).

As containers treated in any tunnel are subject to a certain temperature variation, it is therefore necessary to calculate the equivalent treatment time to constant temperature of 250°C in order to establish the endotoxins reduction value.

Typical profile of vials temperature inside tunnels



The equivalent time FH is the time theoretically required to keep the container at a fixed T_{ref} temperature (250°C) necessary to obtain the same depyrogenation process carried out inside a tunnel at variable temperature.

$$FH = \int_0^t 10^{\frac{T-250}{46.4}} dt$$

Where T is the actual instantaneous temperature of the containers in the tunnel and t is the overall actual treatment time.

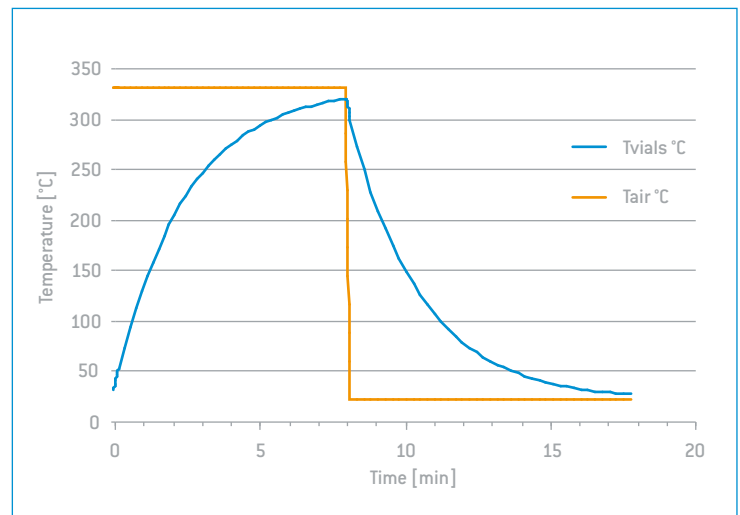
Macofar tunnels can either be used for 3 Log or 6 Log pyrogens reduction. A 3 Log reduction means that containers are subjected to a thermal cycle equivalent to a 15 minutes treatment at a constant temperature of 250°C . A 6 Log reduction means a 30 minutes treatment





Depyrogenation Validation

The depyrogenation qualification is carried out by measuring the temperatures of the containers while running through the tunnel and by measuring the temperature of the air in the hot and cool chamber. Temperature profiles are determined by directly placing temperature probes inside the containers. The collected values can then be compared with microbiological tests results (LAL test).



Limulus Amebocyte Lysate (LAL) test is the most sensitive and specific way to detect and measure endotoxins. It is the most commonly used method to qualify the depyrogenation process.

Inspection window



Tunnel main features

Containers conveyed on a stainless steel wire mesh belt and by two side guides running at the same speed to avoid friction.

The conveyor is conveyed inside the infeed and discharge area and it is always protected by the vertical unidirectional air flow. During its return, outside the heated area, the conveyor is in a closed and sealed-off environment.

The seal of the absolute filters is assured by ceramic fibre gaskets. The area surrounding the filter frames is connected to their relative fan inlet to create a depression between the up-stream area and the down-stream sterile area. This prevents accidental infiltration of non-sterile air through the gaskets.

Proper air speed uniformity across the whole tunnel width is ensured by adjustable flaps located in the hot chamber, this optimizes heat and temperature.

Automation

- Parameters are set by recalling production recipes through HMI panel
- Recording of main process parameters available on paper or electronic files
- 21CFR part 11 compliance upon request
- Automatic start-up and shut-down sequences
- System validation documentation and testing according to GAMP guidelines

Process control

According to PAT (Process Analytical Technology) requirements, in-line monitoring of the main parameters is essential to fully understand and keep a production process under control.

Macofar tunnels are therefore equipped with:

- Air pressure monitoring and balance management between chambers and between tunnel and external environment
- Air temperature monitoring
- Pressure differential monitoring across filters
- Particles counting with isokinetic probes
- Anemometers to check unidirectional air flow speed

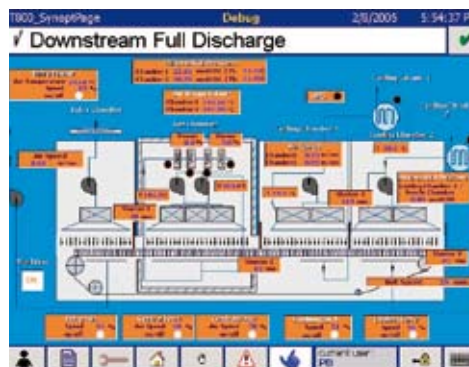
Tunnels main options

- Cooling chamber dry heat sterilization
- Automatic containers unloading at the batch end
- Automatic height adjustment of gates between chambers
- Chiller for cooling water

Parameter printer



HMI panel





Full aseptic line competence

Built on Macofar's early reputation as an expert in aseptic powder handling by developing a range of equipment to complement its superb microdosing machines, Macofar is now a recognized global supplier of technologically advanced and highly innovative aseptic lines for both solids and liquids. Macofar does not only offer a machine, but full lines for aseptic filling. We can offer lines including washers for vials and ampoules, sterilizing tunnels, filling and dosing equipment for both liquids and powders as well as capping machines. And to complete the line, we can also offer cartoners and case packers.

Romaco is your single source supplier for fully customized, state of the art aseptic lines. Starting from the first project meeting, integration into existing equipment, set up, training qualification, validation and service Romaco is your partner.



1 Washer

Macofar automatic washing machines, which have a mechanical speed of between 9.000 and 24.000 vials/ampoules per hour, handle vials and/or ampoules through a unique system of universal grippers to ensure stable, reliable and efficient transport of cylindrical containers. The key features of the balcony design machine includes separated working and mechanical areas, modular washing cycles and self draining washing circuits.

2 Depyrogenation Tunnel

Macofar depyrogenation tunnels are designed to sterilize and depyrogenate ampoules, vials, bottles and other glass containers based on the laminar flow principle using hot sterile air (max. 340 °C).

3a Powder Dosing Micro 9/18

Macofar offers a range of intermittent motion machines, with mechanical speeds of 9.000 and 18.000 vials per hour, featuring volumetric vacuum/pressure dosage for filling sterile antibiotic powders into round glass vials closed by rubber stopper.



3b



4

5

3b Liquid Filling VF 18

(alternative to powder dosing machine)

Macofar offers an aseptic liquid filling machine with speeds up to 18.000 vials per hour. This slim design machine features outstanding performance and reliability and is the benchmark in aseptic liquid filling.

4 Capping Machine

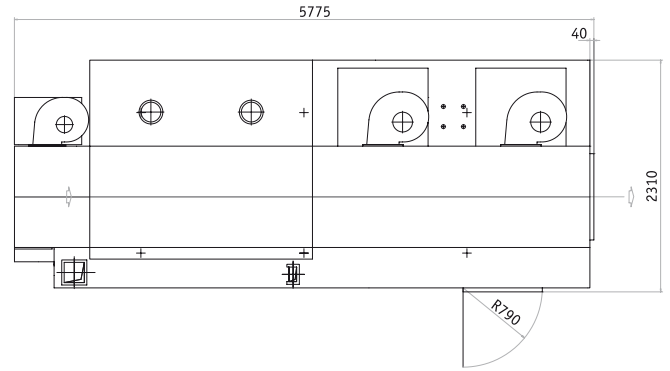
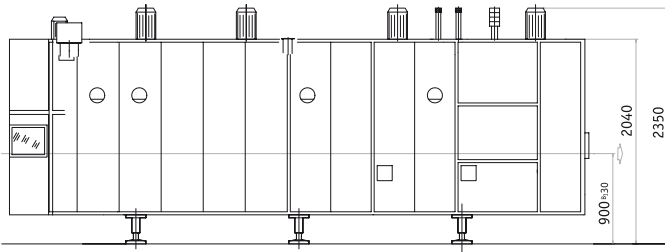
The automatic continuous motion capping machine offers a mechanical speeds up to 10.000 and 24.000 vials per hour. The range of capping machines is suitable to close cylindrical glass or plastic containers with simply flanged alu-caps with or without plastic cover (FLIP-OFF), pilfer-proof caps, press-on plugs or screw caps (with proper equipment).

5 Cartoning Machine

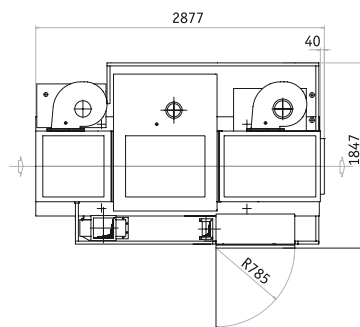
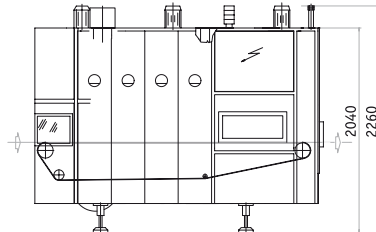
With speeds up to 400 cartons per minute Promatic cartoners deliver optimum performance and versatility. In combination with the Promatic case packers, this is the perfect solution for secondary packaging.

Packaging - Processing
Bid on Equipment
 1-847-683-7720
www.bid-on-equipment.com

T 800 H3C4



T 600 H1C1



Key Technical Data

	T 600 H1C1	T 600 H2C2	T 800 H2C3	T 800 H3C4
Length, in mm	2.870	3.750	4.500	5.770
Sterilizing area length, in mm	1.030	1.550	1.550	2.190
Cooling area length, in mm	1.005	1.360	2.110	2.720
Width, in mm	1.820	1.820	2.270	2.270
Infeed conveyor belt width, in mm	550	550	850	850
Output and Speed	depending on vial/ampoule dimensions, glass type and weight of vial/ampoule			
Air aspirated from environment, in Nmc/h	670	670	1.000	1.000
Air ejected through the chimney, in Nmc/h	600 – 1.750	600 – 1.750	600 – 1.750	600 – 1.750
Cooling water at 15°C, in L/h	1.255	1.537	2.792	3.074
Installed power, in kW	46.4	51	58	87
Net weight, in kg	2.240	2.670	4.300	5.060

Pharmaceutical expertise

Romaco Macofar has built its reputation in over 30 years of outstanding performance, with over 1.800 installations worldwide and an exceptional record in service and support. Macofar is a recognized global

supplier of capsule fillers, liquid fillers, powder microdosing machines, powder macrodosing machines, aseptic liquid fillers, vial and ampoules washing machines as well as sterilization tunnels.

Macofar is the expert partner to assist any pharmaceutical company in the process of installing a new aseptic filling line, from feasibility study to validation. Our Romaco Macofar team is looking forward to the next challenge.

Romaco
Macofar

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