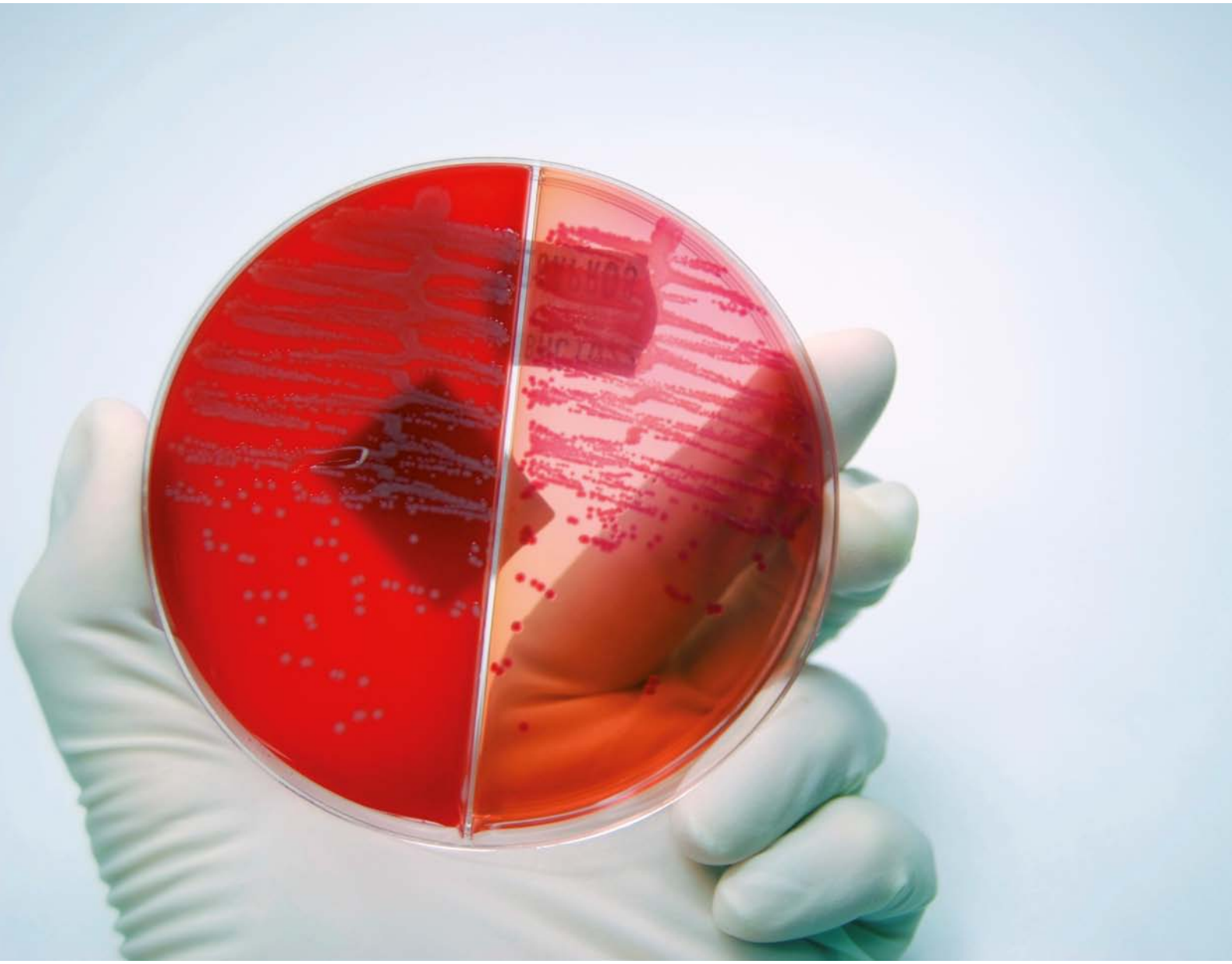


Pharmaceutical Biotechnology

Downstream processing with centrifuges and package units from GEA Westfalia Separator

Quality in its Purest Form

Downstream processing technology

Aseptic process management, optimum cleaning capability, closed product handling, reliable compliance with GMP requirements, gentle product treatment, efficient recovery of active ingredients and reliable scale-up – the requirements of pharmaceutical biotechnology are high. With separators designed specifically for this sector, GEA Westfalia Separator Group stands for reliable compliance with these requirements.

GEA Westfalia Separator Group built the first centrifuge in Oelde, Westphalia in 1893. Since then, the company has been instrumental in the advancement of mechanical separation technology. Today, it is a key technology in the recovery of active pharmaceutical ingredients with substantial potential for optimising production processes and products. A critical factor underlying the success of the company in pharmaceutical biotechnology is its ability to swiftly translate new developments into marketable processes and systems which fully meet the complex requirements of biotechnological processes. The basis for this is decades of experience in the construction and production of separators for the pharmaceutical industry, picking up on new research findings and the implementation of the latest design and production processes. Using this approach, GEA Westfalia Separator Group has developed numerous innovative improvements to separating processes and brought them to market world-wide by applying first-class engineering.

Efficient, reliable and economical

GEA Westfalia Separator Group supports new developments in the branch from the outset through continuous cooperation with universities, research institutes and industry. In this way, a rapid and individual response to current customer needs is assured at all times. With stand-alone machines or package units which guarantee a high yield of valuable substances and which operate trouble-free, efficiently, reliably and economically throughout a long service life. Convince yourself!

Enzymes

Process acceleration with biocatalysts

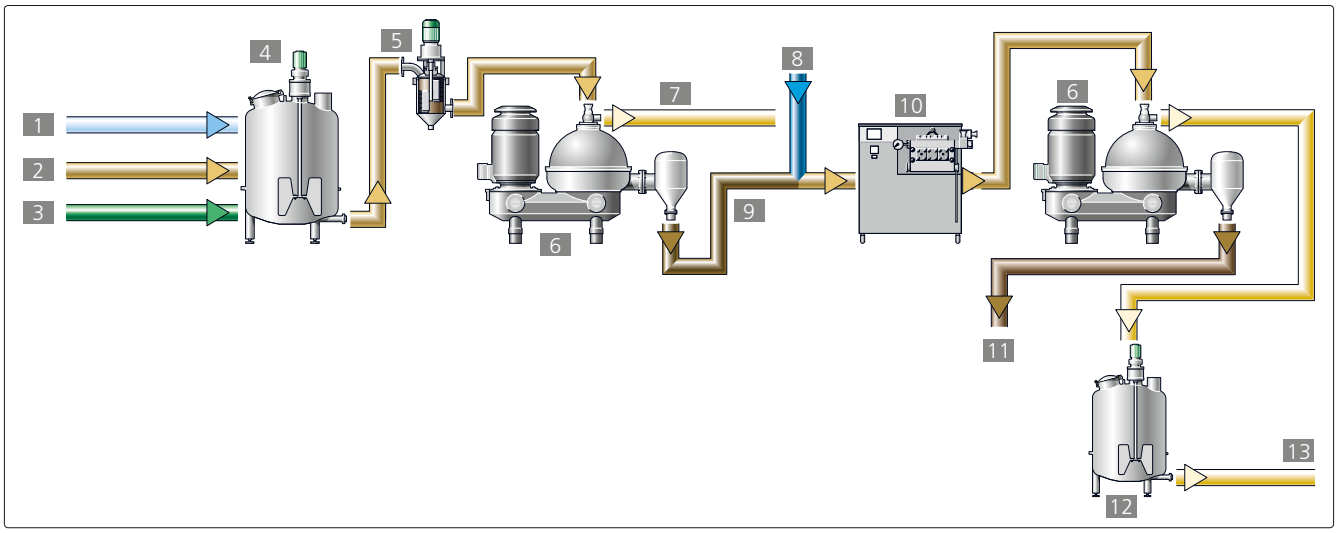
Enzymes are complex organic protein compounds located in every living cell, where they are produced. They accelerate organic processes such as the breakdown of starch, protein, fat or sugar as catalysts, i. e. without being expended themselves. These valuable proteins are known to industry as esteemed helpers. The separators and decanters from GEA Westfalia Separator Group ensure that the intracellular and extracellular enzymes are separated undamaged and in high concentrations.

Production of intracellular enzymes

Glucose isomerase is an example of an enzyme which converts glucose into fructose and is highly significant in the starch industry. The enzyme is produced and remains in the cells of the employed micro-organisms. To process it, the liquid phase of the fermentation broth is separated by centrifuging after fermentation. The concentrated microorganisms are treated further after centrifuging. The cell walls are broken down. Depending on the consistency of the suspension, it is diluted before the cell fragments are separated by continuously operating separators.

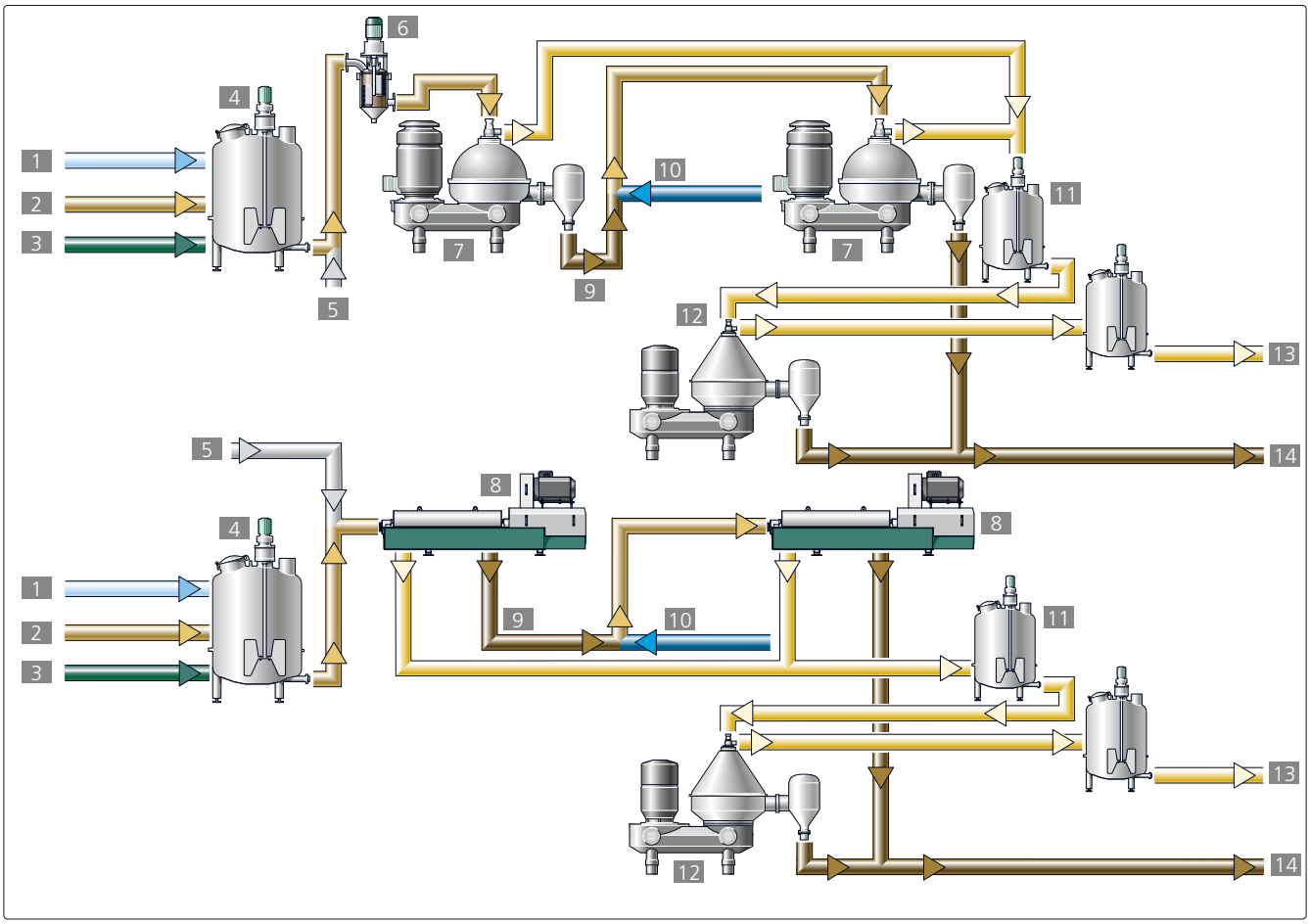
Production of extracellular enzymes

Separators and decanters from GEA Westfalia Separator Group are predestined for the optimum treatment of washing powder enzymes. Carefully purified and sterilised air is injected into a fermenter equipped with an agitator. The air bubbles are distributed in the nutrient solution, which is composed of carbohydrates, protein, growth agents and nutrients. This is sterilised, heated to an optimum temperature and then inoculated with the purified culture of a nonpathogenic microorganism. The microorganisms nourish themselves by converting the substances and simultaneously produce the enzymes. These are then excreted to the fermentation broth. After fermentation, the microorganisms are separated by adding a flocculent and centrifuging with separators and decanters. Succeeding stages of washing and polishing with centrifuges further increase the yield and the purity of the enzymes.



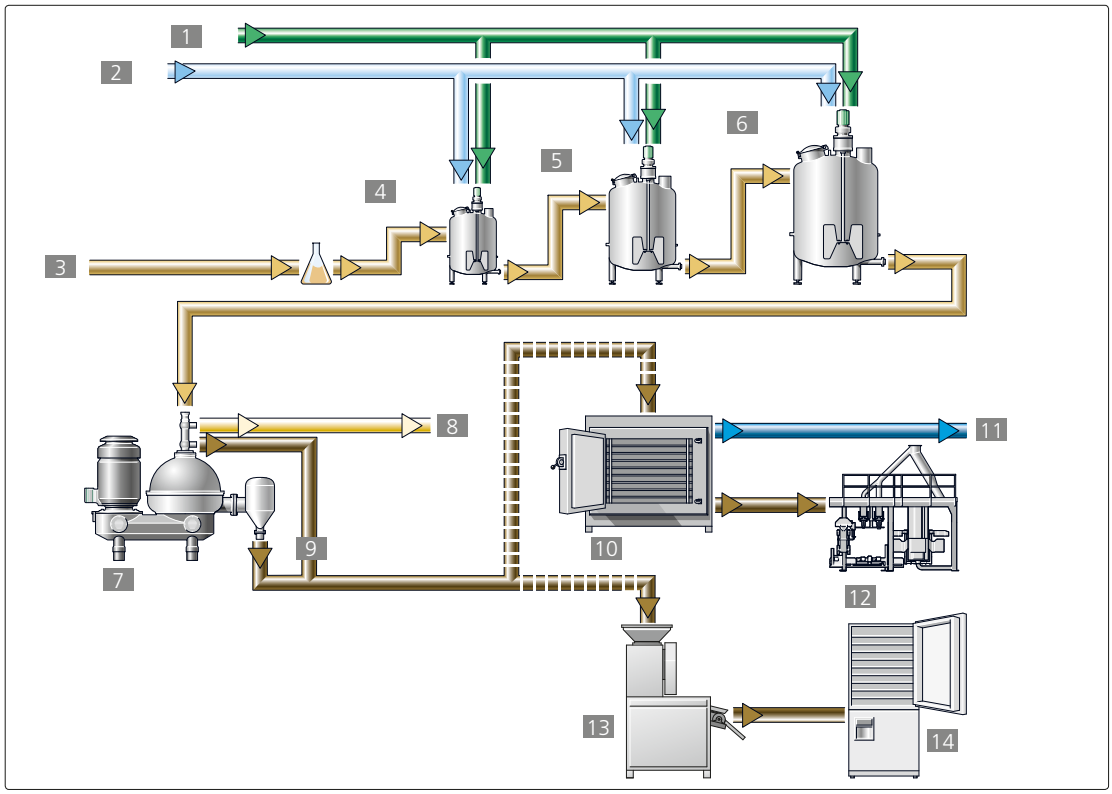
1 Aeration
2 Microorganism
3 Substrate
4 Fermentation
5 Rotary brush strainer
6 Separator
7 Liquid (waste)
8 Water/buffer (washing liquid)
9 Biomass
10 Cell disruption
11 Cell debris to disposal
12 Intracellular liquid
13 Further processing

Intracellular enzymes



1 Aeration
2 Microorganism
3 Substrate
4 Fermentation
5 Flocculents
6 Rotary brush strainer
7 Separator
8 Decanter
9 Biomass
10 Water/buffer (washing liquid)
11 Extracellular liquid
12 Polishing
13 Extracellular liquid for further processing
14 Biomass to disposal

Extracellular enzymes



1 Nutrient solution
2 Aeration
3 Freeze-dried starter cultures
4 Seed fermenter
5 Pre-fermenter
6 Main fermenter
7 Nozzle separator
8 Waste
9 Concentrate
10 Freeze drier
11 Water (waste)
12 Packaging
13 Pelletizer
14 Cold store

Microbial Food Cultures

Microbial food cultures can be subdivided into starter cultures and probiotic products; they are used in many segments of the food industry.

Starter cultures are now an established part of the food, medical product and animal feed industries. They are responsible for predictable and reproducible product quality and thus for controllable production processes. Probiotic products are also becoming more and more important, mainly as a result of their beneficial health characteristics. Sterilisable separators are becoming more and more important for recovering such products; they can be used in a variety of ways and enable the yield and vitality of the cultures to be enhanced.

Cultivation, processing, harvesting

The production of starter cultures can be divided into two sections. After cultivation in fermenters, the bacteria must be processed and separated from the fermentation solution. This consists of the nurtured lactobacilli and the remainder of the nutrient solution including the produced lactic acid. Firstly, the micro-organisms are separated and concentrated

from the liquid phase. Nozzle and self-cleaning disc separators in steam-sterilised design are available for this step of the process. The concentrated lactobacilli then pass to a freeze drier. Finally, the cultures are packaged under oxygen exclusion and stored at low temperatures. This retains their activity for months before they are processed, e. g. as "live cultures" in probiotic yoghurts.

Sterility and careful treatment

The careful treatment of the living microorganisms, sterility and a high separation efficiency are prerequisite to the economical, reliable and efficient processing. The separators from GEA Westfalia Separator Group employed in this production process are therefore equipped with hydrohermetic product feed systems which minimise the shear forces when the product enters the bowl and therefore guarantee the high vitality of the cells.

Vaccines

Protection against germs

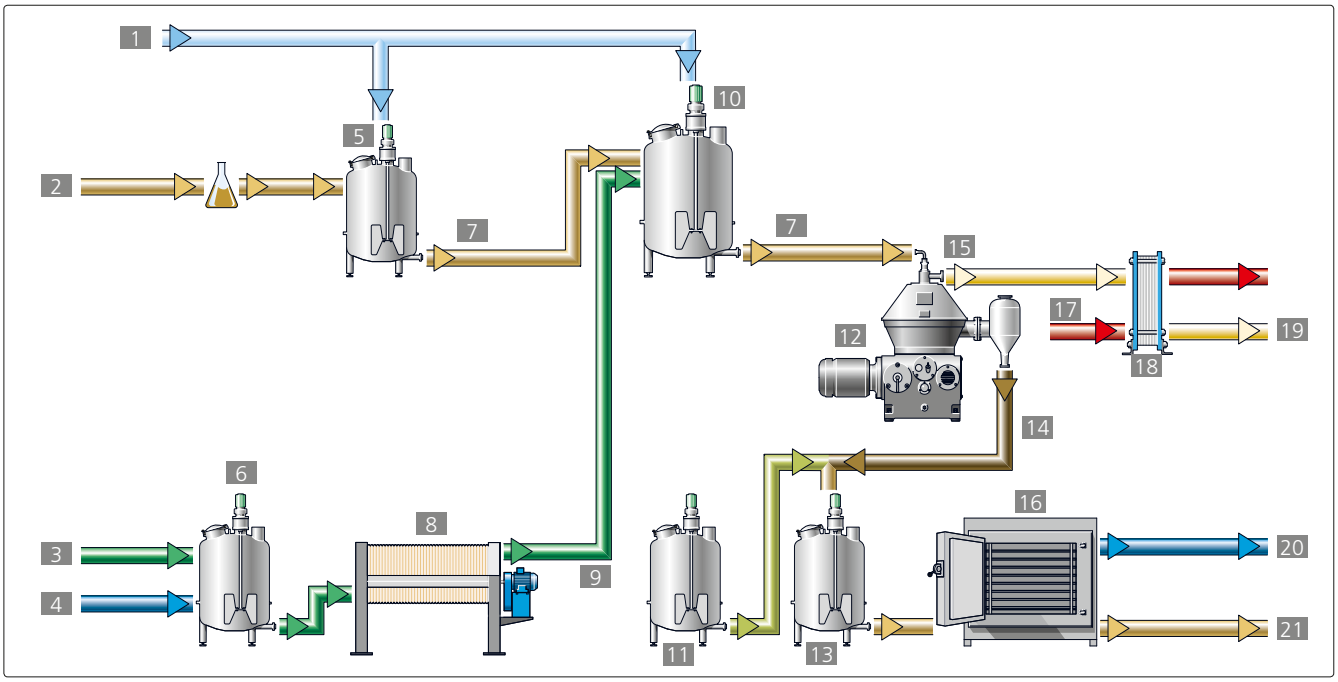
Vaccines are medicines which immunise human or animal organisms against diseases. The organism to be protected is repeatedly exposed to small quantities of antigens (vaccines) or antibodies in the form of a serum. This achieves immunity.

Live vaccines

One means is therapy with live vaccines. These are germs with weakened virulence or closely related to pathogenic germs and are therefore antigens, but without the pathogenic effects. They are bred from less pathogenic mutations of virulent germs, which are suitable for the production of vaccines.

Process of vaccine manufacturing

When a suitable virus strain has been chosen, it is isolated in ampoules and stored at -192 °C in liquid nitrogen. Breeding is then conducted starting with the pre-fermenter and continuing in the main fermenter. The fermentation process is supplemented by a nutrient solution. The nutrients are dissolved in the nutrient tank and added to the fermentation process after filtration. The cells are then separated from the clear phase by centrifuging. The raw vaccines pass into the mixing vessel, where their immunogenity is increased by the addition of adjuvants, stabilisers and preservatives.



1 Aeration
2 Starter culture
3 Dried nutrients
4 Water
5 Pre-fermenter
6 Nutrient tank
7 Virus culture
8 Filter press
9 Nutrient solution
10 Main fermenter
11 Additives
12 Separator
13 Mixing tank
14 Raw vaccine
15 Liquid
16 Freeze dryer
17 Steam
18 Continuous sterilizer
19 Effluent
20 Water (waste)
21 Vaccine

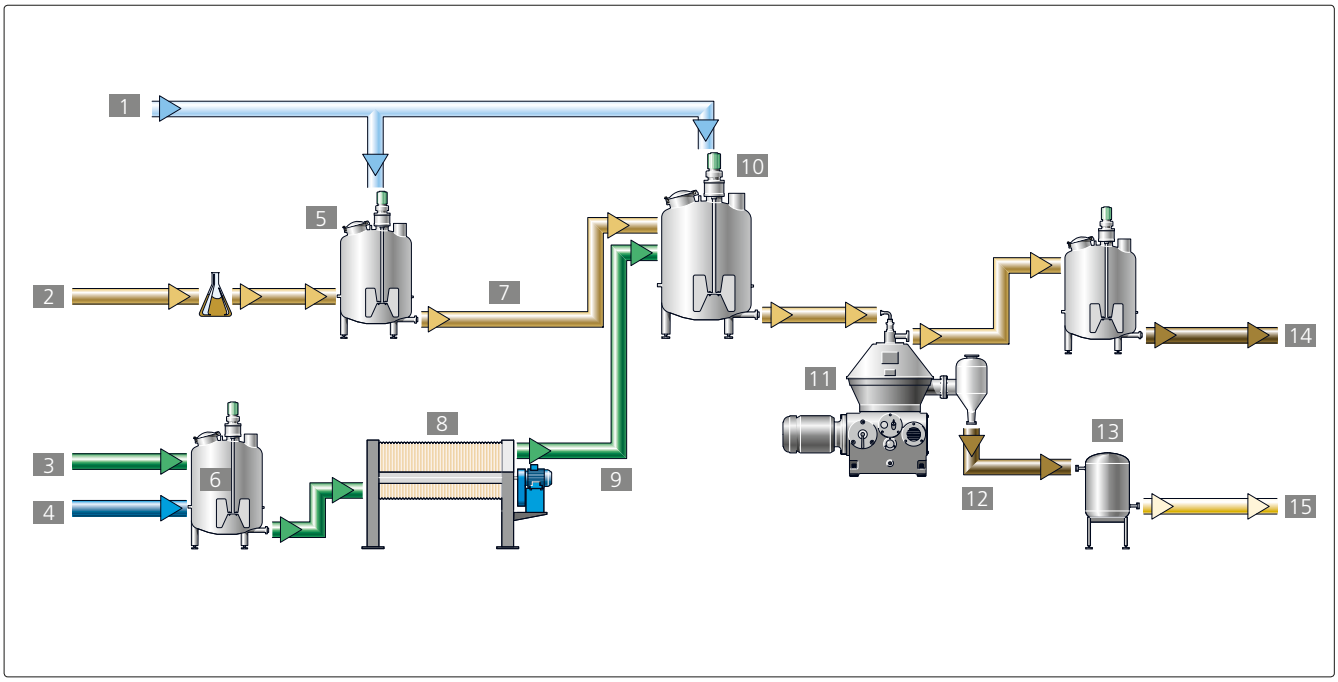
Live vaccines

- Measles
- Mumps
- Rubella
- Yellow fever
- Chickenpox
- BCG (= tuberculosis vaccine)
- Typhus
- Human rotaviruses
- Whooping cough (pertussis)

Non-live vaccines

In serum therapy, the infected organism is supplied with the sera produced with the antibodies of immunised individuals. Sera are gained by multiplying bacteria in a suitable nutrient solution. The serum produced during fermentation is excreted by the cells into the fermentation solution. The serum is isolated by separating the biomass in centrifuges and by further stages of processing in the clarification phase.

An aseptic process is essential in the production of vaccines and sera.



1 Aeration
2 Starter culture
3 Dried nutrients
4 Water
5 Pre-fermenter
6 Nutrient tank
7 Virus culture
8 Filter press
9 Nutrient solution
10 Main fermenter
11 Separator
12 Biomass
13 Killing tank
14 Serum for further production
15 Biomass to disposal

Non-Live vaccines

- Influenza
- Cholera
- Bubonic plague
- Hepatitis A or hepatitis B
- Whooping cough (pertussis)
- Tetanus
- Diphtheria
- Pneumococcal bug

Hormones / Insulin

Separation technology for human medicine

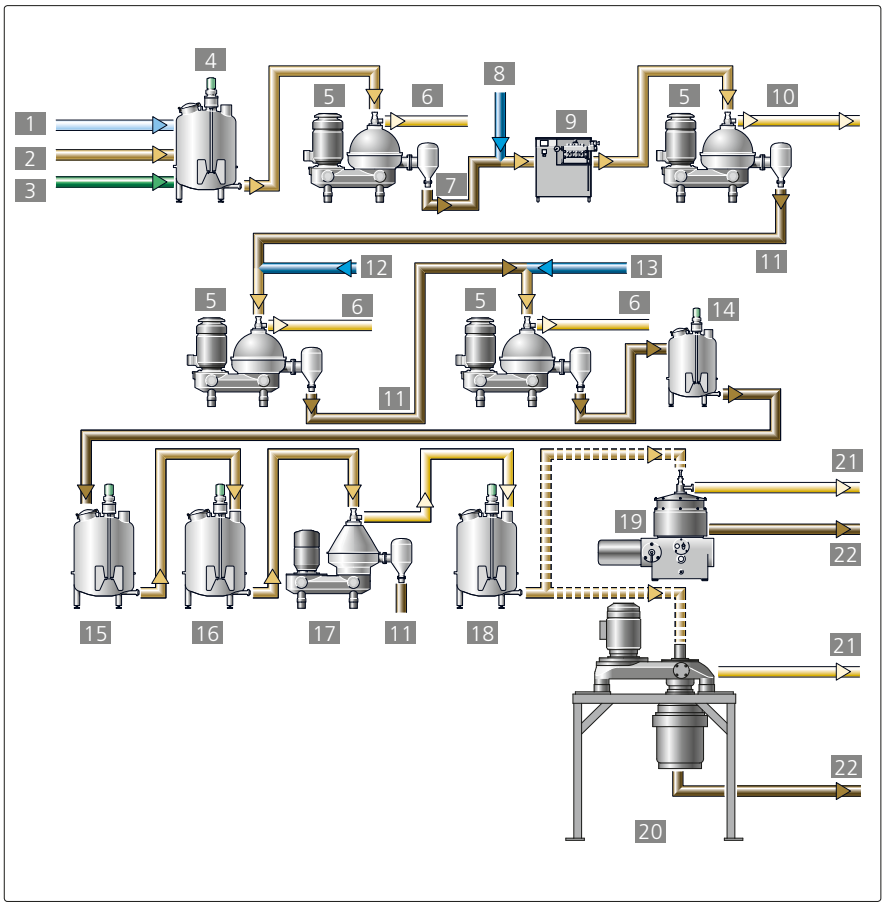
Hormones are chemical messengers which have a regulating effect on the metabolism and organ activity. In collaboration with the nervous system, they co-ordinate all bodily functions. A complicated control mechanism ensures a harmonic interaction of the bodily functions. The separation technology of GEA Westfalia Separator Group plays an important part in the production of hormones, e. g. insulin.

Diabetes

Diabetes is a metabolic disorder. Diabetics can no longer adequately utilise glucose, which is conveyed by the blood to all cells of the body. The hormone insulin has a key function in this. Amongst other functions, it operates as a "door opener" for glucose molecules when they enter cells. Around 150 million people worldwide now suffer from this metabolic disorder. They must inject supplementary insulin daily to prevent serious cardiovascular or renal diseases.

In the service of human medicine

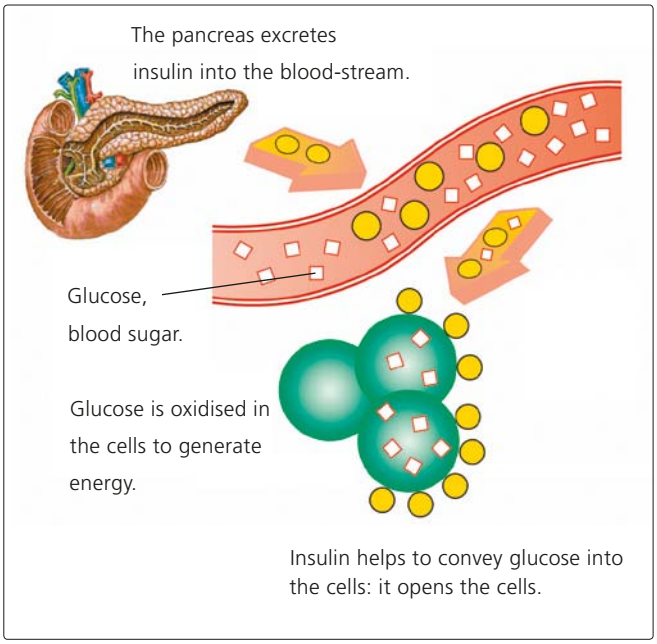
Separators from GEA Westfalia Separator Group play an important part in the production process. Nozzle separators operate in the depicted process, in which the solid material is extracted continuously in a constant concentration. The biosynthetic production of human insulin is conducted by bacteria or yeasts. After fermentation, or the conversion of the chemical raw materials by the micro-organisms, the biomass is extracted by a nozzle separator. In further stages, the active ingredient is washed and concentrated. GEA Westfalia Separator Group machines are also employed in the succeeding crystallisation stages, for example GEA Westfalia Separator **hy**con and chamber separators.

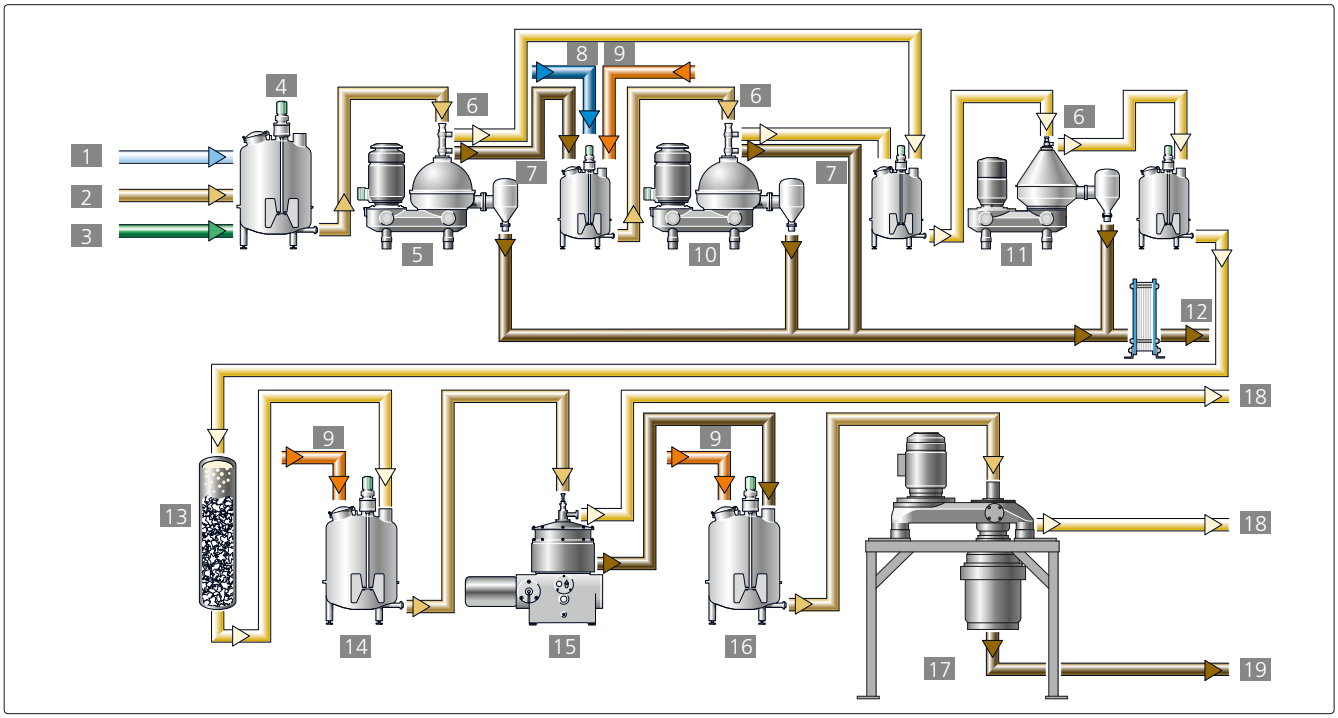


Example insulin based on E.Coli

1 Aeration
2 Microorganism
3 Substrate
4 Fermentation
5 Nozzle separator
6 Liquid (waste)
7 Biomass
8 Water / buffer (washing liquid)
9 Cell disruption
10 Cellular liquid with cell debris (waste)
11 Solids
12 Water / buffer
13 Washing liquid
14 Inclusion bodies
15 Protein folding
16 Precipitation of foreign proteins
17 Separator
18 Crystallization of insulin
19 Chamber bowl centrifuge
20 **hy**con
21 Clear phase to waste
22 Insulin crystals to freeze dryer

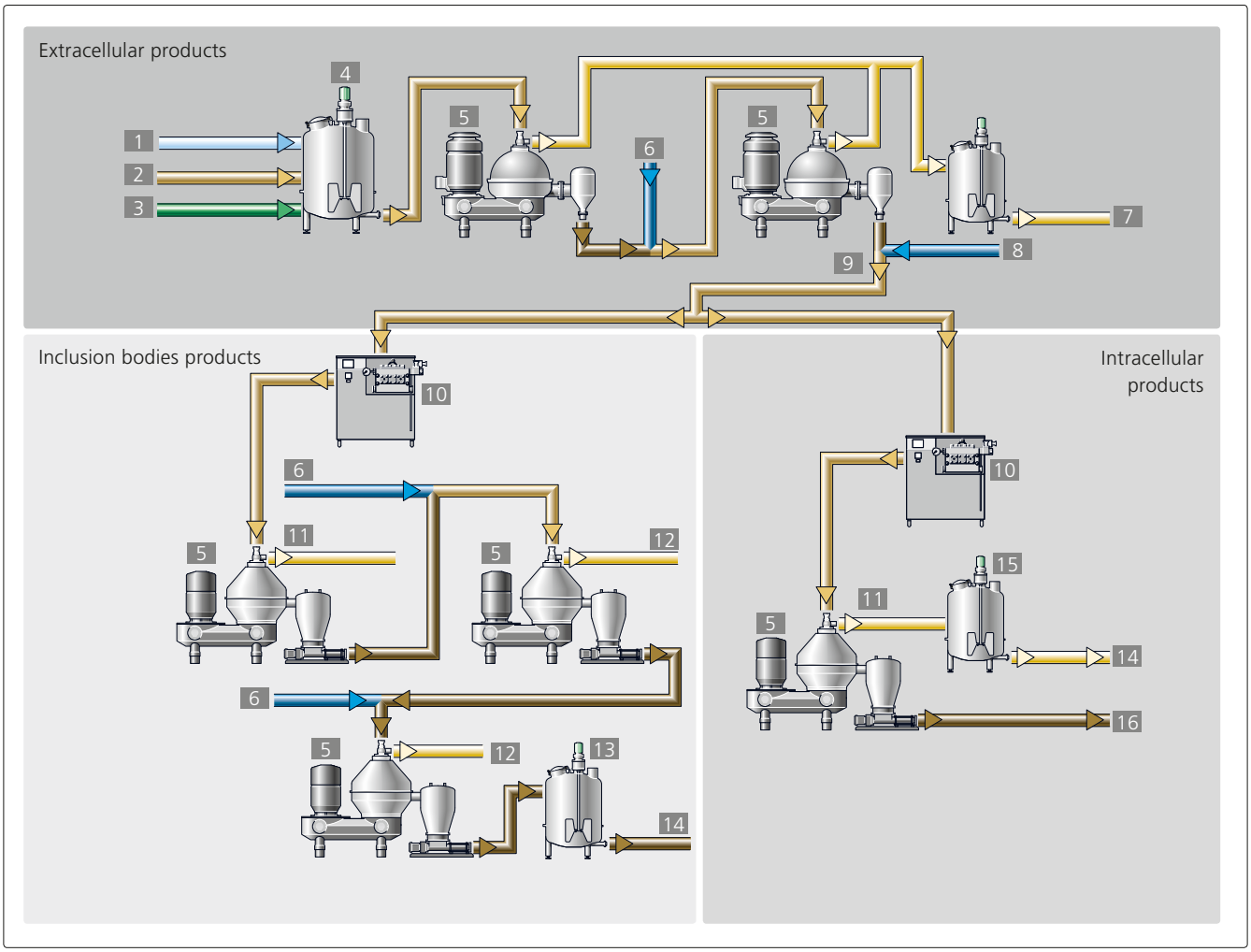
How sugar metabolism works





1 Aeration
2 Microorganism
3 Substrate
4 Fermentation
5 1st stage nozzle separator
6 Clear phase
7 Concentrate
8 Water
9 Additive
10 2nd stage nozzle separator
11 Polishing separator
12 To waste
13 Chromatography column
14 1st stage crystallization
15 Chamber bowl centrifuge
16 2nd stage crystallization
17 **hy**con
18 Clear phase to waste
19 Insulin crystals to freeze dryer

Example insulin based on yeast



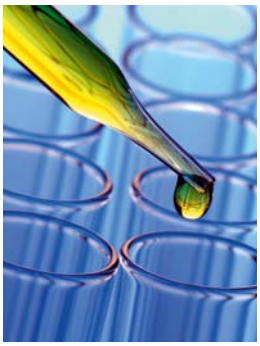
1 Aeration
2 Microorganism
3 Substrate
4 Fermentation
5 Separator
6 Water / buffer (washing liquid)
7 Extracellular liquid containing soluble protein
8 Water / buffer
9 Biomass
10 Cell disruption
11 Cellular liquid with cell debris (waste)
12 Liquid (waste)
13 Inclusion bodies
14 Further processing
15 Intracellular liquid
16 Solids to disposal

Pharmaceutical Proteins

Genetically modified bioproducts

Biotechnological processes can be characterised as processes employing genetically modified micro-organisms. These are able to produce biological products which they would never have created in their natural form. The modified DNA chain and therefore the genetically manipulated heredity factor is multiplied by fermentation of the micro-organisms. The DNA chain with the modified gene and the substances which it produces develop simultaneously. The desired cell products may be contained intra or extracellularly.






Extracellular products

After fermentation, the micro-organisms are extracted by continuously operating separators. To increase the yield, the solid material is washed and extracted again by centrifuging. The clarified phases of the two stages are mixed and fed to further stages of the process. All material streams leaving this enclosed process must be sterilised at at least 121 °C. To keep the process as simple as possible, the biomass is killed directly after fermentation in the fermenter either by heat or by chemical methods. Completely enclosed, steam sterilised centrifuges are employed in this process and can be connected to the other equipment in a sterile manner.

Intracellular products and inclusion bodies

In intracellular processes, it is differentiated whether the desired product is contained in the intracellular liquid or in so-called inclusion bodies. In contrast to extracellular bioproduction, the clarified phase leaves the process here and the biomass is processed. The washed and concentrated biomass is homogenised, i.e. the cells are broken down and the intracellular liquid and the inclusion bodies are released. These are separated from the cell fragments, washed and concentrated in further stages of the process by centrifuges from GEA Westfalia Separator Group. For intracellular products gained from the cell liquid, the solids are extracted by continuously operating separators.

Mammalian Cell Cultures

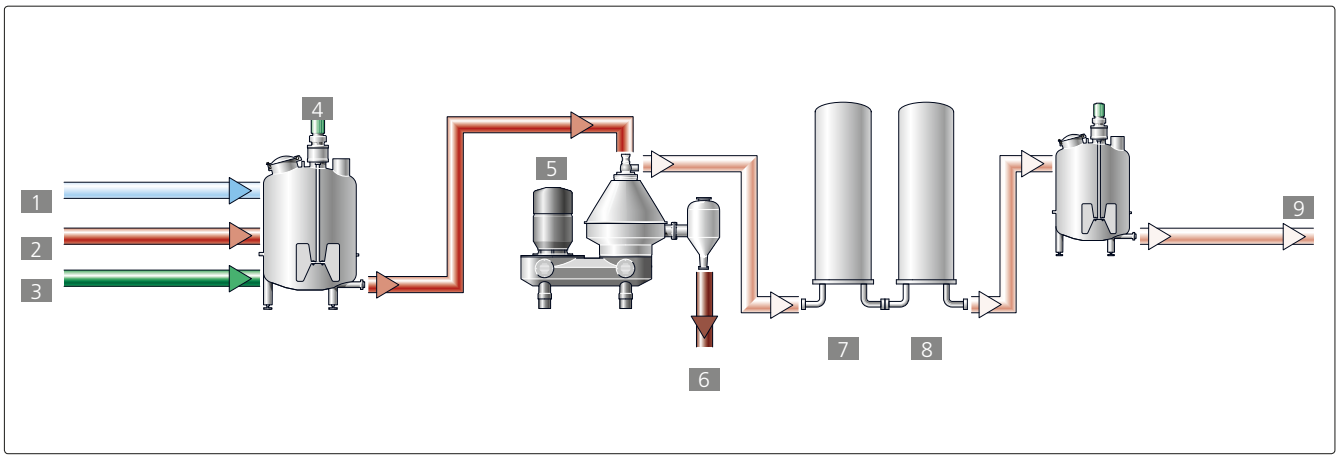
Cultures of the future

The cultivation of mammalian cell cultures is becoming increasingly interesting for the pharmaceutical industry. With these cells, proteins can be produced in their effective form (quartiary structure). In comparison with production by micro-organisms (bacteria / yeasts), downstream stages of the process can be substantially reduced. In addition, risks such as infections in the production of human proteins can be avoided.

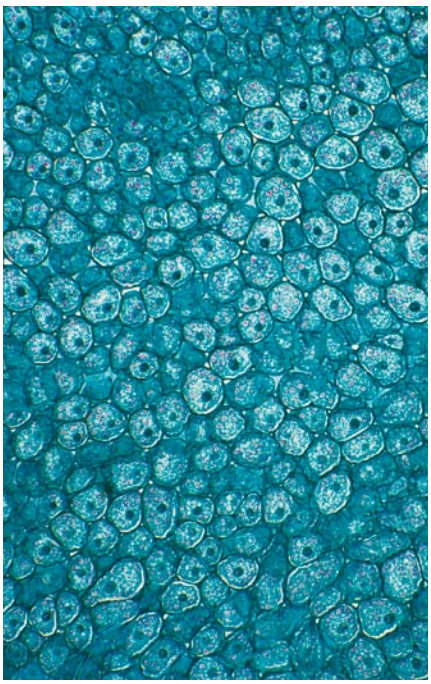
Optimisation of the production process

In this process, particular attention must be paid to the effects of extraneous influences such as the shear forces on the behaviour and productivity of the cells. Due to this circumstance, the machines were optimised to reduce the shear forces on the cells. This process is therefore gaining significance for industry.

The "hydrohermetic inlet" developed by GEA Westfalia Separator Group reduces the shear forces to a minimum. This has been tested and published in cooperation with the University of Bielefeld. Typical cell cultures which are processed are CHO, BHK, hybridoma and insect cells.



1 Aeration
2 Microorganism
3 Substrate
4 Fermentation
5 Separator
6 Solids to disposal
7 Depth filtration
8 Microfiltration
9 Protein solution for further processing



Human Blood Plasma Fractionation

Progress with blood

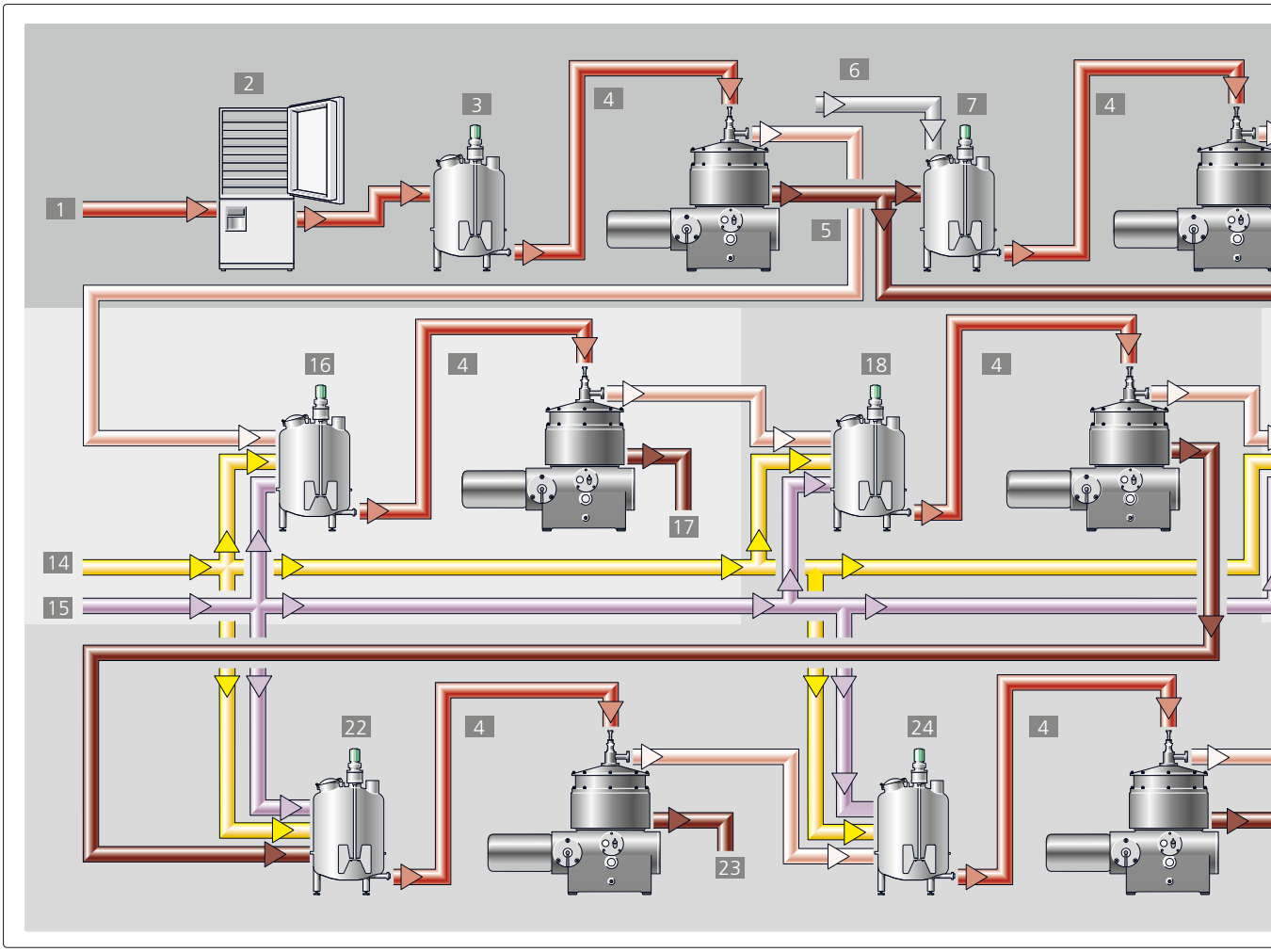
Blood is a special liquid. Is there actually anything more valuable? The basis of all human life is also the foundation for a globally operating industry. Whereas state institutions and aid organisations generally use and pass on whole blood, many industrial companies have specialised in fractionation. Therapy with blood components to explicitly combat numerous illnesses long ago developed from simple blood transfusions.

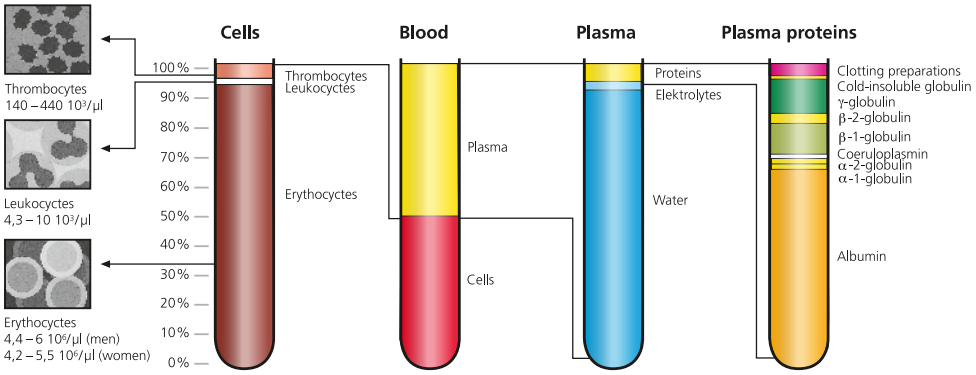
Valuable: plasma proteins

Fractionation is the separation of the proteins in the plasma phase by physical and chemical processes. They are based on changes in the three parameters temperature, alcohol concentration and pH value, which affect the solubility of the proteins in water. Human blood consists of a red phase and the clear plasma phase. The red phase, about 40 percent of the blood, is separated by special centrifuges in the donor bag. The plasma is deep frozen after extraction and is processed by fractionation equipment. Only about 5 percent of the plasma consists of the valuable components, which must be fractionated. The remainder is water and electrolytes.

Therapy with blood components

Many valuable substances can be extracted from the proteins. The cryoprecipitate, the clotting preparation "Factor VIII concentrate" and the prothrombin complex (PPSB) can be gained from the fresh plasma straight after thawing. The remaining plasma then passes to the ethanol fractionation by the Cohn process, where the individual fractions such as fibrinogen, gamma globulin, aplha and beta globulin and albumin



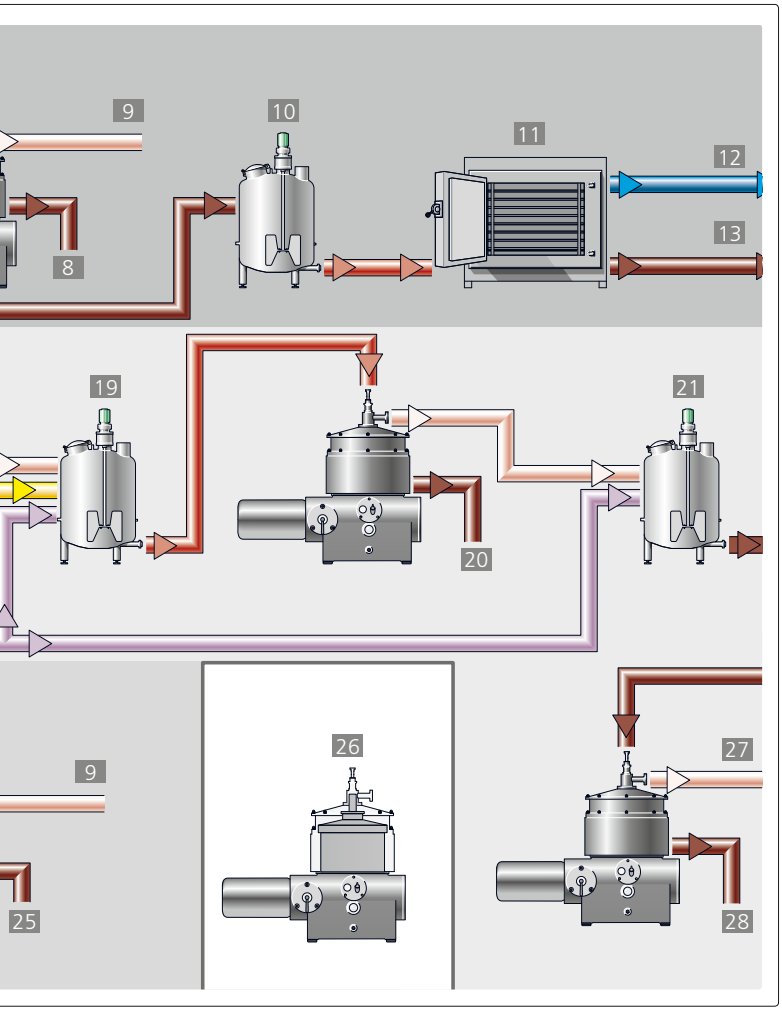


are precipitated. The plasma protein particles are used to prevent and treat bleeding, to control bleeding during operations, for various infectious diseases, for protein deficiency, malnutrition and to increase the proportion of blood plasma. After fractionation, the proteins are treated by various specific methods before they are available for clinical purposes.

Demands on the separating technology

Fractionation by the Cohn process is conducted by reliable separators with cooled bowls and housings. The maintenance of a temperature range of -3 to -6 °C is important for the process. Chamber separators of type BKB are employed for this purpose.

The separators of the latest generation are self-cleaning separators of the GEA Westfalia Separator **hy**con type (BSH 30), with which manual handling of the solids is no longer necessary (see page 28).



1 Collecting of plasma
2 Cold store
3 Thawing (temp. appr. 0 °C)
4 Protein concentration
5 Solids
6 Buffer
7 Washing (temp.appr. 0 °C)
8 Factor VIII concentrate
9 Liquid (waste)
10 Re-suspension with buffer (temp. appr. 0 °C)
11 Freeze drying
12 Water (waste)
13 Cryo precipitate
14 Alcohol
15 Regulation
16 Protein precipitation (Alcohol content = 8%, temp. = -3 °C, pH = 7.3
17 Fraction I (Fibrinogen)
18 Protein precipitation (Alcohol content = 25%, temp. = -5 °C, pH = 6.8
19 Protein precipitation (Alcohol content = 40%, temp. = -5 °C, pH = 5.9
20 Fraction IV (α- and β- Globulin to disposal)
21 Protein precipitation (Alcohol content = 40%, temp. = -5 °C, pH = 4.8
22 Protein precipitation (Alcohol content = 8%, temp. = -5 °C, pH = 5.1
23 Fraction III (α- Globulin to disposal)
24 Protein precipitation (Alcohol content = 25%, temp. = -6.5 °C, pH = 7.3
25 Fraction II (γ- Globulin)
26 All separators/bowls cooled with alcohol/water of 20 °C
27 Liquid phase to waste
28 Fraction V (Albumin)

Good Manufacturing Practice

GMP stands for "Good Manufacturing Practice". The rules specify that the quality of a product cannot be assured exclusively by a final inspection. Specific measures before, during and after production are required. The focus is on the detailed documentation of each relevant production stage or test being carried out.

All relevant departments are incorporated in the GMP team

The GMP documents can therefore quickly assume a volume of 400 to 800 pages. Suppliers without GMP experience enter this "collection of materials" into production, manufacture and then attempt to put together the required documents. However, a better solution is if the supplier works in line with GMP right from the very beginning. GEA Westfalia Separator Group has set up a separate GMP group comprising specialists from all relevant departments; ranging from project management, design, production, plant construction, measuring and regulating technology, right through to quality assurance and acceptance. The aim of the project is to reduce the amount of qualification work for the customer and also to implement his specifications as effectively as possible in project processing.

Documentation standards cover almost 100 percent of GMP requirements

A documentation standard that is consistent with GMP has been developed as a major module in this respect, and has been continuously improved in cooperation with the customer. This documentation standard now covers almost 100 percent of GMP requirements. Individual customer requirements can be quickly and easily implemented as a result of the "open" documentation structure. Flexibility is therefore a strong point of the documentation.

Documented qualification for pharmaceutical machinery

As stipulated by GMP and other rules, the qualification and validation of pharmaceutical machinery have a high priority. Qualification designates the documented proof of the execution and functionality of a machine. Validation refers to the reproducible, reliable setting of the processes. In this, it is particularly important to work with qualification plans and documents approved by the user. Within the machine qualification, GEA Westfalia Separator Group can execute the design qualification (DQ), installation qualification (IQ) and operating qualification (OQ) in the course of the FAT. If requested, the OQ can be conducted in the course of the SAT, with support at the first production.

Additional profit by way of synergy effects

Most of the qualification work, which is normally the responsibility of the client, is provided by GEA Westfalia Separator Group as a service. The structured procedure at GEA Westfalia Separator Group provides major advantages for the future operator: it considerably reduces the amount of qualification work and also benefits from numerous synergy effects.

Separators for Pharmaceutical Biotechnology

Machines for all applications

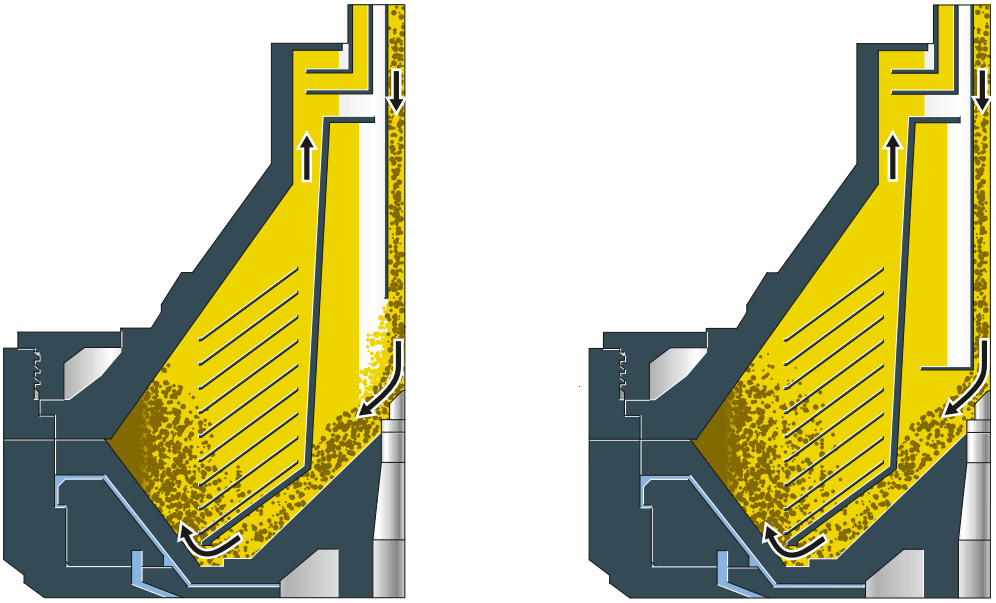
GEA Westfalia Separator Group offers an extensive selection of separators for biotechnology with varying production capacities and designs, from the smallest nozzle separator with GEA Westfalia Separator **viscon**® technolgy right up to the largest steam-sterilizable centrifuge in the world – the CFE 300.

Machine type	Product throughput (depending on the product and process in l/h)	Applications
Self-cleaning separators		
FSC 6* / PSC 6	100 – 200	Mammalian cell cultures, microbial food cultures, enzymes, pharmaceutical proteins, hormones
FSC 15* / PSC 15	250 – 500	
FSC 20* / PSC 20	500 – 1000	
FSE 80* / PSE 80	1500 – 3000	
FSE 170* / PSE 170	3000 – 6000	
FSE 300* / PSE 300	5000 – 15.000	
Steam-sterilized, self-cleaning separators		
CSC 6	100 – 200	Aseptic processes, vaccines and sera, mammalian cell cultures, microbial food cultures, pharmaceutical proteins, hormones/insulin
CSC 15	250 – 500	
CSC 20	500 – 1000	
CSE 80	1500 – 3000	
CSE 100	1800 – 3700	
CSE 170	3000 – 6000	
Steam-sterilized separators with **viscon**® nozzles		
CFC 15	300 – 600	Aseptic processes, microbial food cultures, enzymes, pharmaceutical proteins, hormones/insulin
CFA 65	3000 – 6000	
Steam-sterilized separators with nozzles		
CFD 130	3000 – 8000	Aseptic processes, microbial food cultures, mammalian cell cultures
CFE 300	10.000 – 20.000	
Chamber separators		
PKB 25	300 – 600	Hormones/insulin, pharmaceutical proteins
PKB 45	500 – 1000	
BKB 28	300 – 600	Human blood plasma fractionation
BKB 45	500 – 1000	
Hyperconcentrators – **hy**con		
PSH 30	500 – 1500	Aseptic processes, hormones/insulin, pharmaceutical proteins
CSH 30	500 – 1500	
BSH 30	500 – 1500	Aseptic processes, human blood plasma fractionation
Solid wall disc separators		
FTC 1*	30 – 60	Research establishments, labs
Self-cleaning separators		
Pathfinder PSC 1 / PSC 5 / PSC 8*	15 – 300	Research establishments, labs
FSD 1*	20 – 50	Research establishments, labs

* This design will be offered without polished surfaces and documentation.

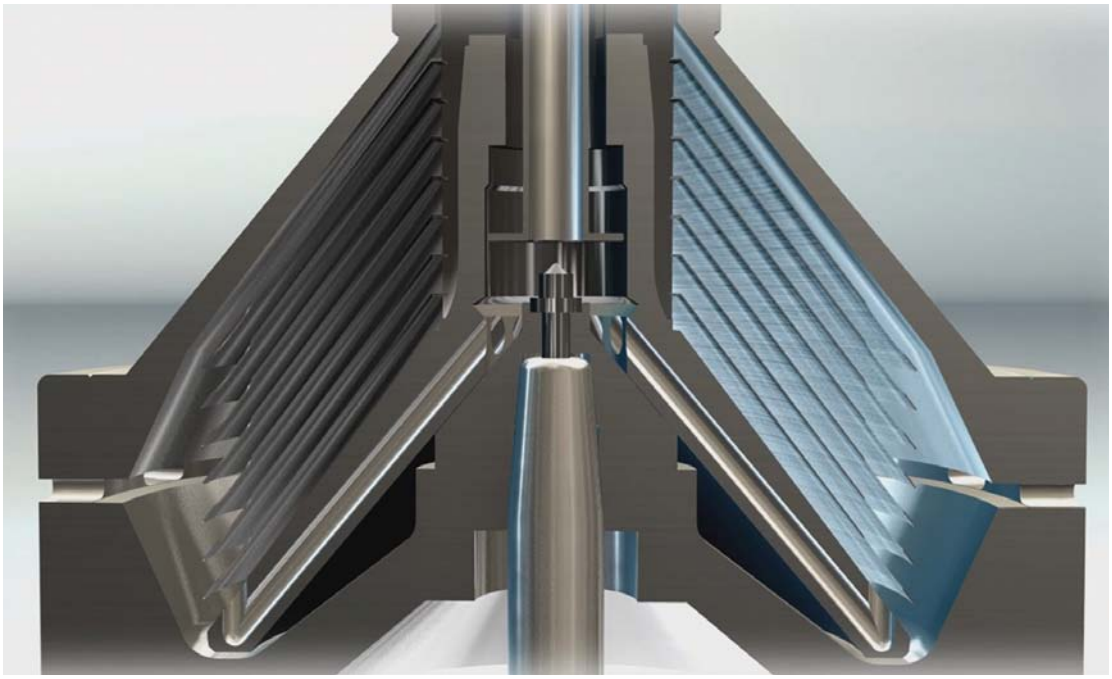
Hydrohermetic Inlet

Gentle product feed



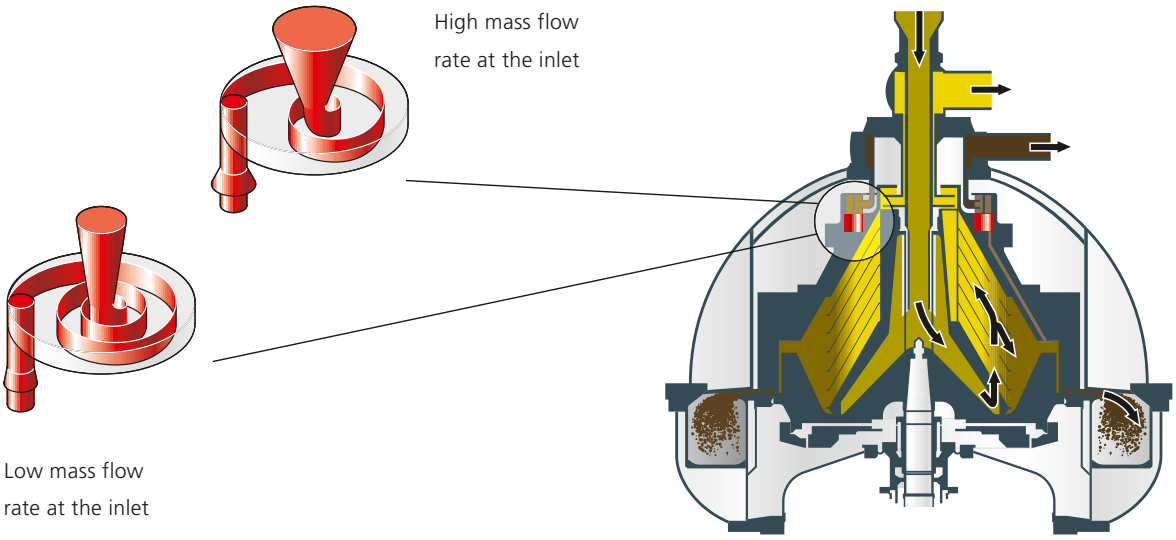
Gentle and careful handling of the product is extremely important in biotechnology to achieve a high degree of vitality and protein activity and to minimise changes. To feed all fluid products carefully into the rotating bowl, all separators from GEA Westfalia Separator Group for the pharmaceutical sector are equipped with a hydrohermetic inlet.

This inlet system prevents shear forces when the product enters the bowl. The product is introduced beneath the level of the liquid. It allows the level of the liquid to reach the axis of rotation, beneath which the product is gently introduced into the filled bowl and accelerated. The hydrohermetic inlet, developed and patented by GEA Westfalia Separator Group, has been successfully tested on mammalian cell cultures and published by the University of Bielefeld.

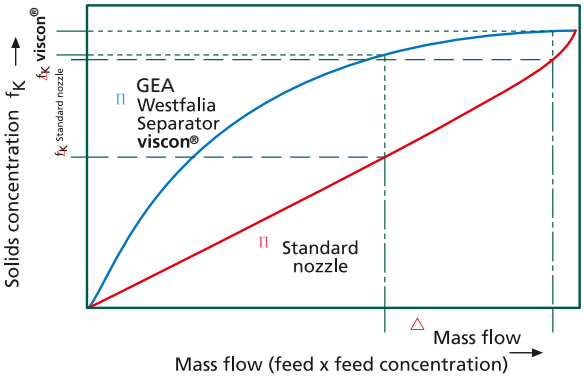


GEA Westfalia Separator **viscon**®

Gentle discharge of solids – no problem



Great advances have been made in recent years in the field of centrifuging for concentration with nozzle separators. With the development of the viscosity-controlled nozzle (viscon®), the inconvenient adjustment of the separator parameters (ejection time) to changing inlet conditions has become unnecessary. This achieves constant solid discharge concentrations. The nozzle separators represent the state-of-the-art in the field of the treatment of microbial food cultures, hormones, pharmaceutical proteins etc, last but not least due to viscon®.

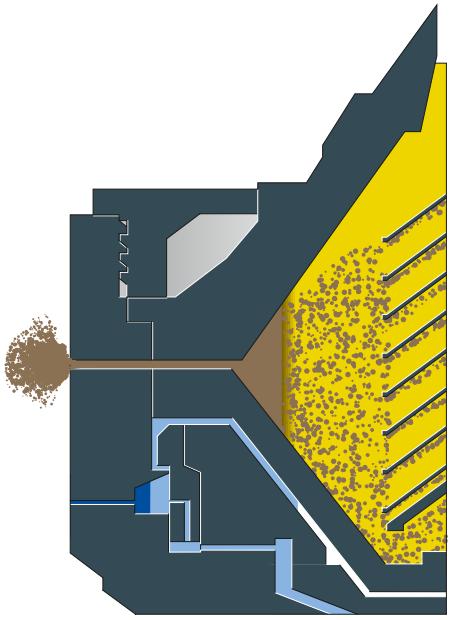


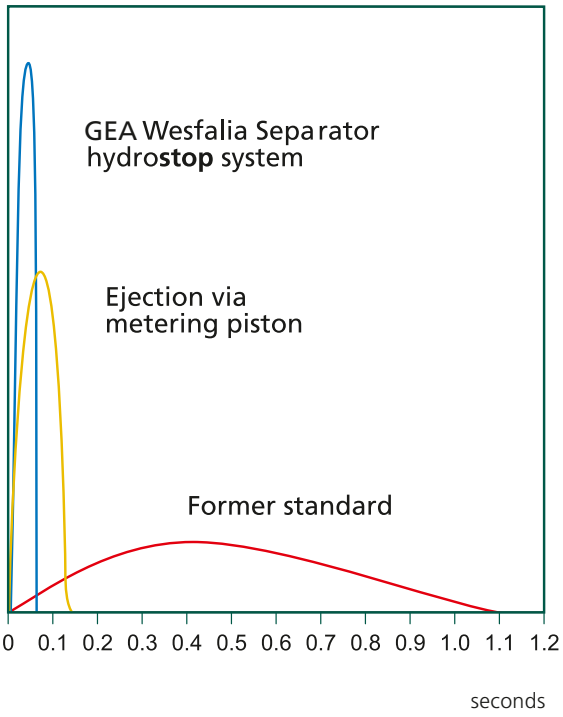
Increased survival rate

In contrast to conventional nozzle separators, the nozzles of the **viscon**® system are not located at the edge of the bowl, but at a smaller circumference in the bowl top. Pressures of up to 250 bar prevail at the periphery of the bowl, whereas the pressures are substantially lower at the centre of the bowl. This means that the separated cells are subjected to much lower shear forces. The introduction through the hydrohermetic inlet and the discharge through the **viscon**® nozzles increase the activity of the separated cells. The result: the end product is more valuable and can be employed more economically.

Ejection with
GEA Westfalia Separator hydrostop

Extremely fast, precise and flexible



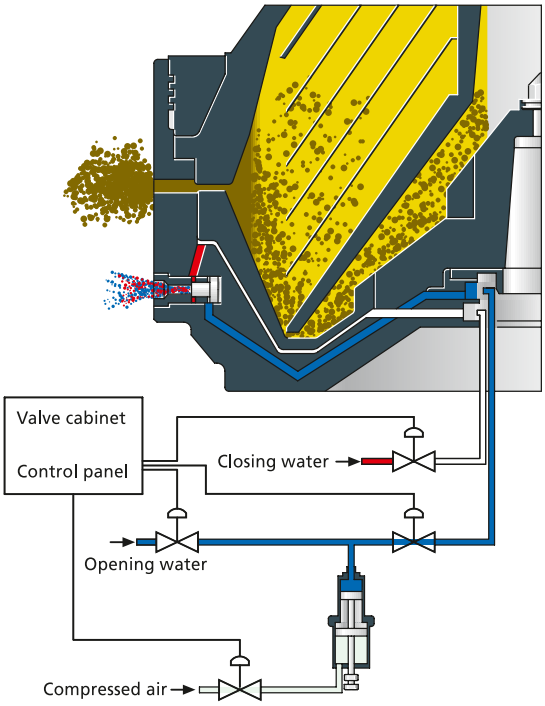


With the hydrostop** system, GEA Westfalia Separator Group has provided an ejection system which can be adjusted precisely and reproducibly to specific requirements with regard to the concentration of solids. This patented ejection system makes it possible to optimise the ejection sequence to the shortest time. The hydro**stop** system reduces the actual ejection time to less than 1/10 of a second and allows partial ejection every thirty seconds.**

Extremely precise even with the smallest volumes
The great disadvantage of older ejection systems was that they were substantially slower and less precise. The volume and thereby the concentration of the solids fluctuated widely. No form of control was possible. The hydro**stop** system ensures that even small volumes from 1.5 to 2 litres can be ejected reproducibly with an error margin of less than 10 percent. This innovative technology allows precise, fast ejection and therefore substantially increased and higher quality yields.

Ejection with Metering Pistons

Precisely metered discharge volumes



The fundamental idea of the control system is to inject a precisely metered volume of opening water with a metering system for partial ejection. Precise ejected quantities can be achieved in this way. The advantage in comparison with the hydrostop** system is the low required operating water pressure of just 1.5 bar.**

In the pharmaceutical industry, high-purity water from ring systems is often employed as the operating water. Pressures of 1.5 to 2 bar usually prevail here. For this reason, separators from GEA Westfalia Separator Group with pneumatically-operated external metering pistons have a proven track record. The volume of opening water can be varied with an adjusting screw. The metering device is filled with water through the inlet valve. Compressed air is then injected through the valve into the lower chamber of the metering device. After the opening water valve has been operated, the air pressure applied to the piston of the metering device injects the adjusted volume of water into the opening chamber. The air pressure for the metering device should be 4 – 4.5 bar. A pressure converter installed in the metering device ensures correct ejection, overcoming the resistance of the piping, valve and injection chamber.

Steam Sterilising – SIP Cleaning Capability – CIP

Securely sterile and clean

In some processes, e.g. in the production of vaccines and sera, a strictly aseptic process is required. The separator must not only be easy to clean, but is also a part of a sterile, completely closed system. Apart from guaranteeing the agreed performance parameters, GEA Westfalia Separator Group also grants a so-called sterile guarantee on the employed sterile separators.

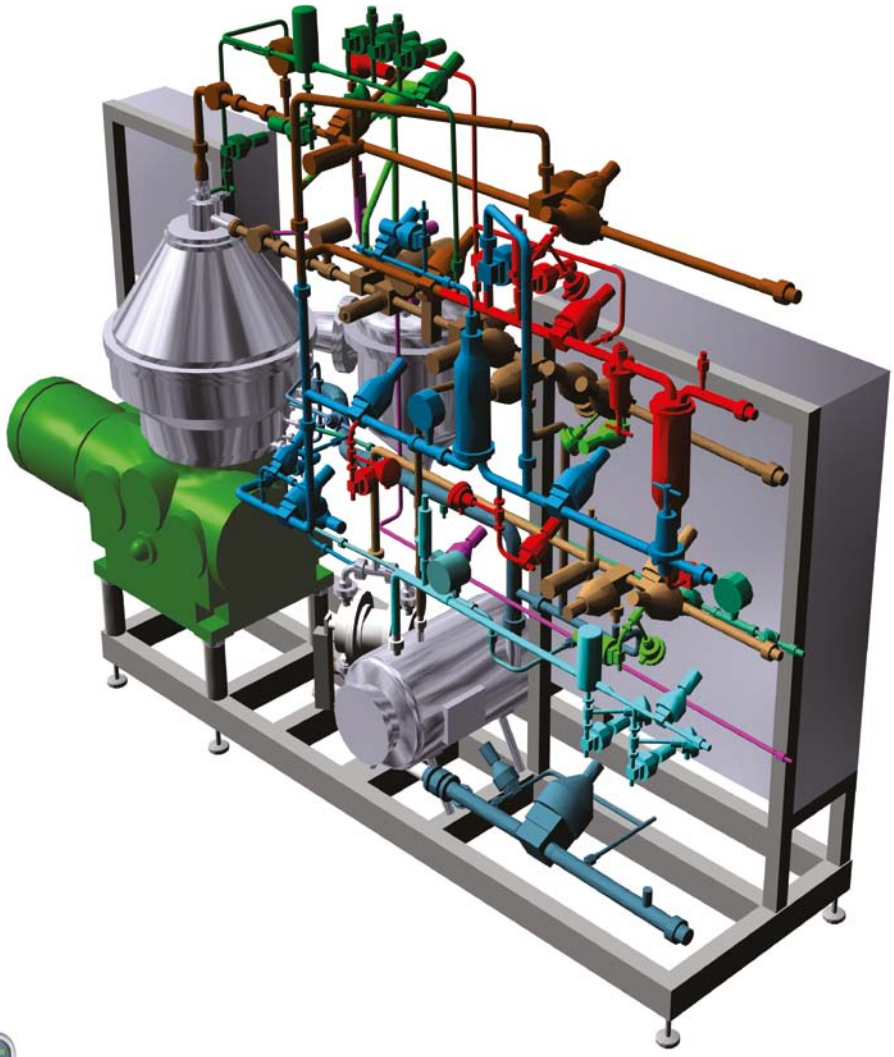
A validation of the sterilising capability of a separator package unit according to the FDA specifications (Food and Drug Administration) was tested successfully and certified by the "Gesellschaft für biotechnologische Forschung" (GBF) in Brunswick. This concept has proven favourable in more than 600 steam-sterilised separators installed world-wide.

Sterile with steam

SIP (Sterilisation-in-place), for example, this applies to our self-cleaning disc separators with hydrohermetic inlets in a special steam-sterilised design. Sterilising is conducted with the separator stopped with hot steam under pressure at a temperature of over 121 °C. The sterilising period is dependent on the type of bacteria and the cell count. After sterilising, the separator is filled with sterile air for cooling and blanketing until the next production run. Sterilisation prevents cross-contamination of different fermentation products which are processed by the same separator. It also prevents toxic bacteria or living germs from escaping to the exterior and endangering people (biocontainment). This has also been proven and published by the UCL (University of London).

Absolutely clean with CIP

Chemical CIP cleaning (CIP = cleaning-in-place) cleans process lines without the need to dismantle or open individual machines. Apart from hot water, 2 percent sodium hydroxide solution at a temperature of up to 80 °C is used as the cleaning liquid. This is circulated until all organic sediments have been dissolved. 0.5 percent nitric acid solution at a temperature of up to 80 °C is used to dissolve anorganic sediments. The last stage of the CIP chain is rinsing with high-purity water.



Good design

Apart from the specified steps of cleaning, a good machine design is very important. This particularly includes a good draining capability, the prevention of dead spaces, easily cleaned, smooth surfaces and an optimum wetting of the surfaces in contact with the product by the CIP media. GEA Westfalia Separator Group achieves this by installing spray nozzles at different points in the separator and ensuring the wetting by an uranine test, the employment of separators and system components with little dead space such as laser-welded spacers and diaphragm valves, surface roughness of Ra ≤ 0.8 µm or better and a minimum pipe inclination of < 2 percent.

Automatically safe

GEA Westfalia Separator Group not only supplies centrifuges, but also fully automatic CIP systems. The cleaning cycle is controlled by a programmable logic controller. The program sequence for cleaning can be adapted according to the local requirements. The volume of cleaning agents is metered by the installed pumps. A conductivity sensor adjusts and monitors the concentrations of the media in the respective cleaning circulation systems.

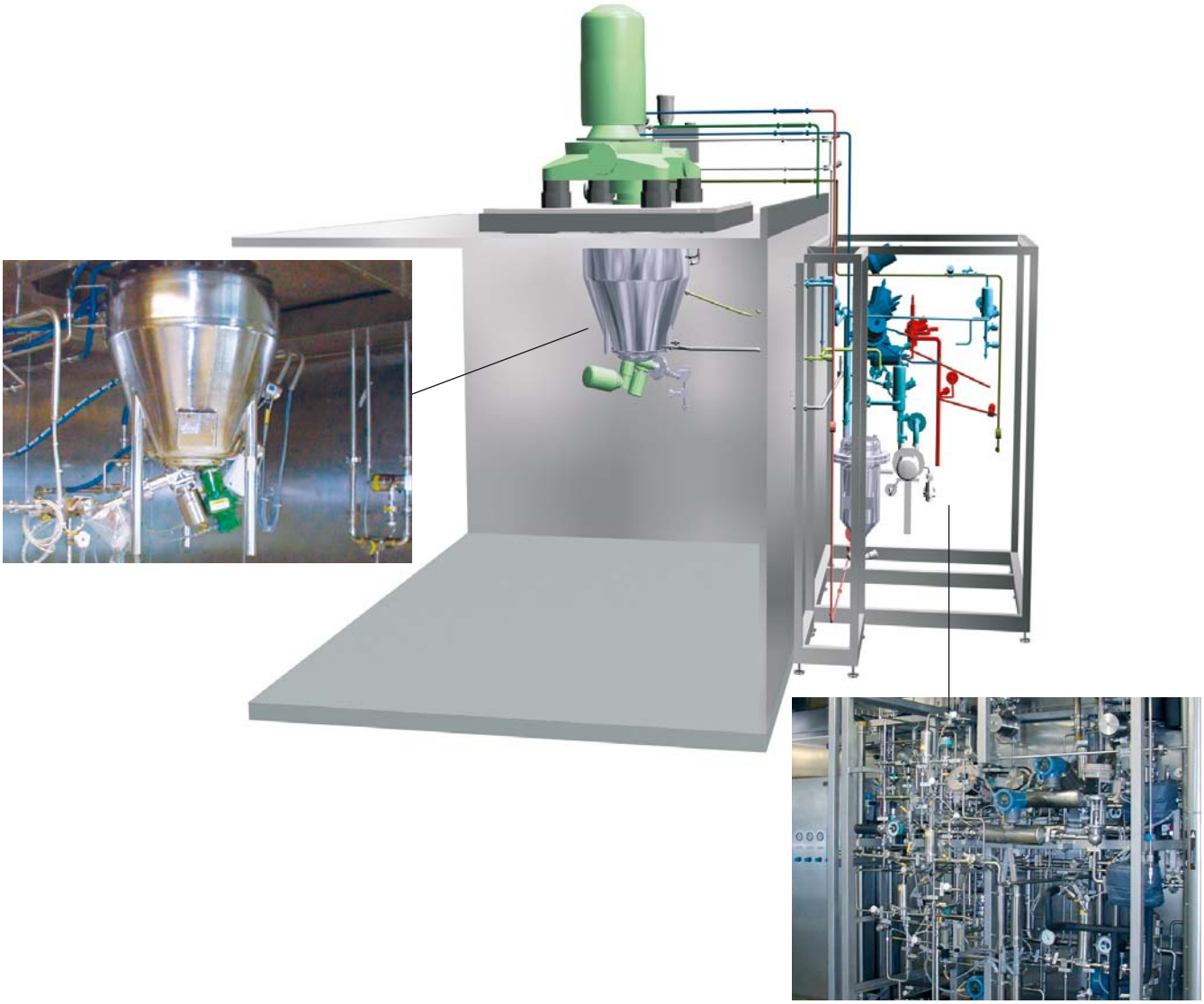
GEA Westfalia Separator **hy**con

Design for clean room applications

When separators are installed in clean rooms, special attention must be paid that no particles are emitted to the surroundings and that the machinery can be easily cleaned. At GEA Westfalia Separator Group, this is achieved by direct frequency converter drives (no centrifugal friction clutches), stainless steel control cabinets and the integration of machine components such as pilot valves and pressure reducing valves in a valve cabinet. The latest development by GEA Westfalia Separator Group is the design as a two-room concept with hycon.

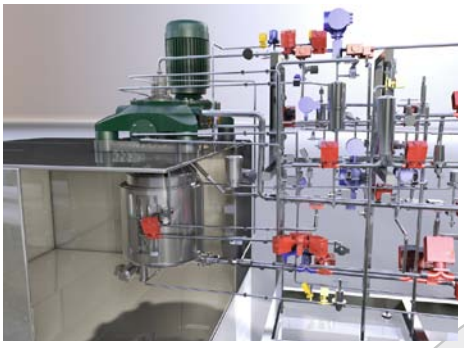
Two-room concept

To achieve a sterile process, the drive section (drive system and motor) and the process room (bowl and solids discharge) are sealed hermetically from each other by gas-lubricated slide ring seals. The design is such that the respective components are located apart from each other. This so-called two-room concept is implemented by the suspended bowl and solids discharge in the clean room. This precludes contamination of the process room by the drive equipment.



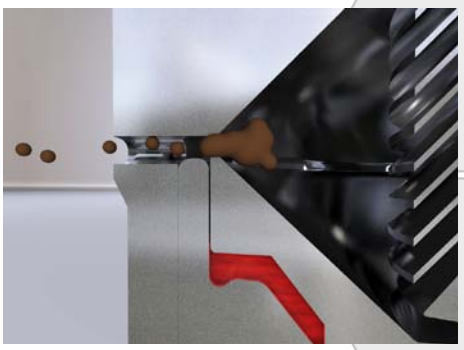
Economical clean room conditions

The **hy**con achieves the highest concentrations of solids in an aseptic process. It unifies the advantages of chamber separators and self-cleaning separators, thereby completely fulfilling the high requirements of the pharmaceutical industry. The hermetic isolation of the product-contacting and the mechanical sections allows the user to create economical clean room conditions. A sterile process is also achieved by a fully closed, steam-sterilised system. The required careful handling of the product is conducted by the hermetic inlet and the gentle draining of the bowl at reduced speed. To achieve a high quality of the end product, the sanitary equipment of the process room is executed in the highest surface quality. Due to the suspended vessel concept, solids handling adapted by the customer is possible. This new centrifuge system ensures a consistently high product quality under economical operating conditions.



Two-room concept

Cooling with liquid nitrogen

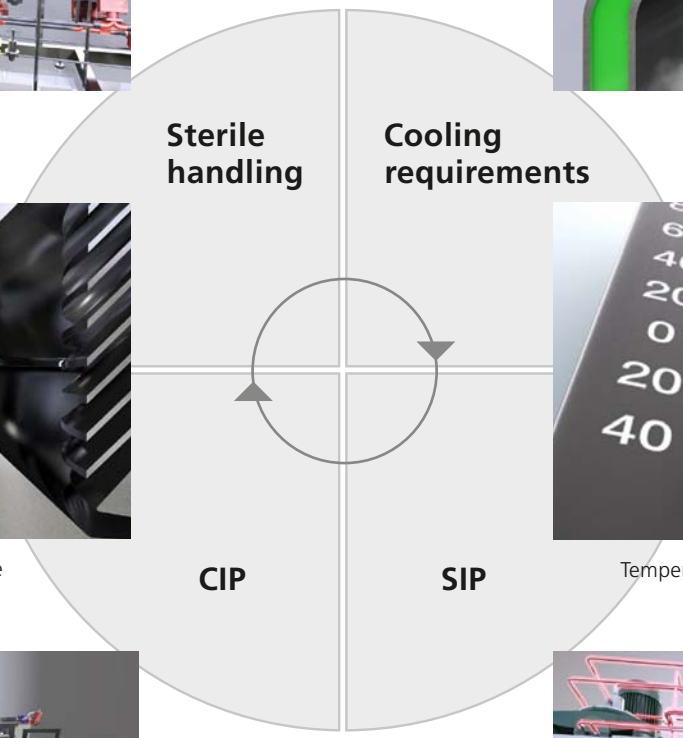


Pneumatically controlled discharge

Temperature range +135 °C (SIP) / -29 °C

Cleaning-in-place

Sterilisation-in-place



Special Separators for Low-Temperature Applications

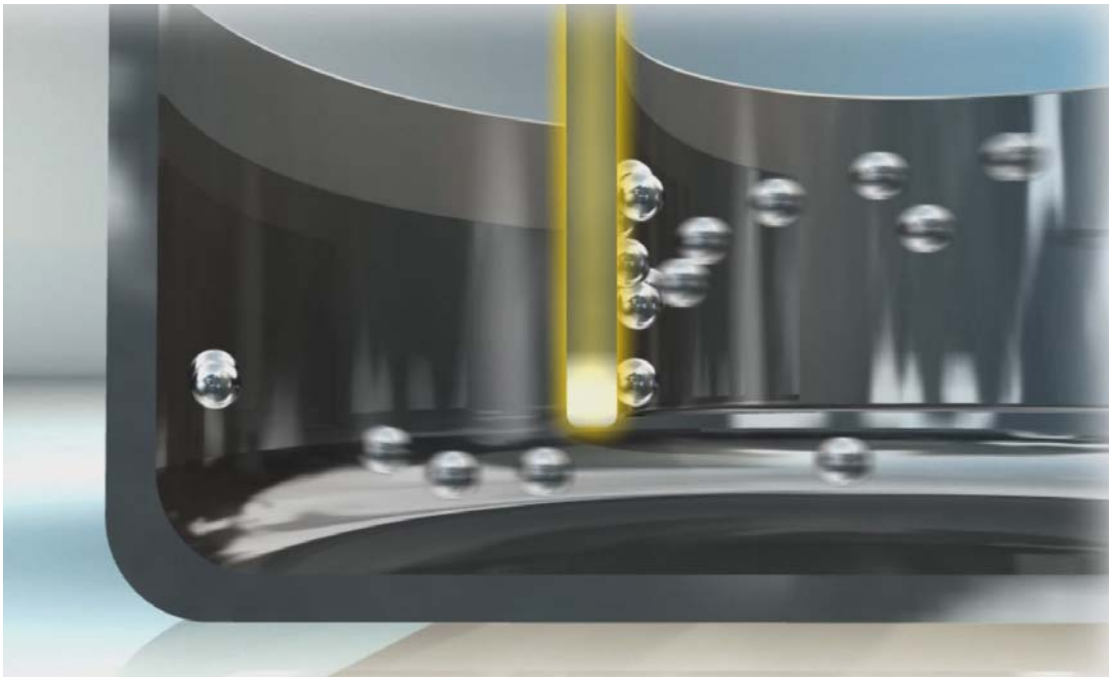
Always keep cool

In certain processes, the temperature of the product must not rise or may rise only slightly, for example in human blood plasma fractionation using the Cohn process. This process is characterised by the successive precipitation of different blood proteins in the negative temperature range. In the development of the chamber separator for this process, the dissipation of the individual amounts of heat created in the separator was examined and new cooling methods were employed. This experience has also been applied in the new development of the GEA Westfalia Separator hycon.

Chamber centrifuges: hundreds in operation

Fractionation by the Cohn process is executed by reliable, cooled chamber centrifuges. These BKB separators operate in performance ranges from 60 to 1000 l/h. They have long become established world-wide and have proved their worth in over 400 sold machines for human blood plasma fractionation. The compliance with a narrow temperature range of -3 to -6 °C is important for the process. In the clarifying separators of series BKB, this is achieved by triple cooling: a direct bowl cooling which extracts the heat created by air friction at the

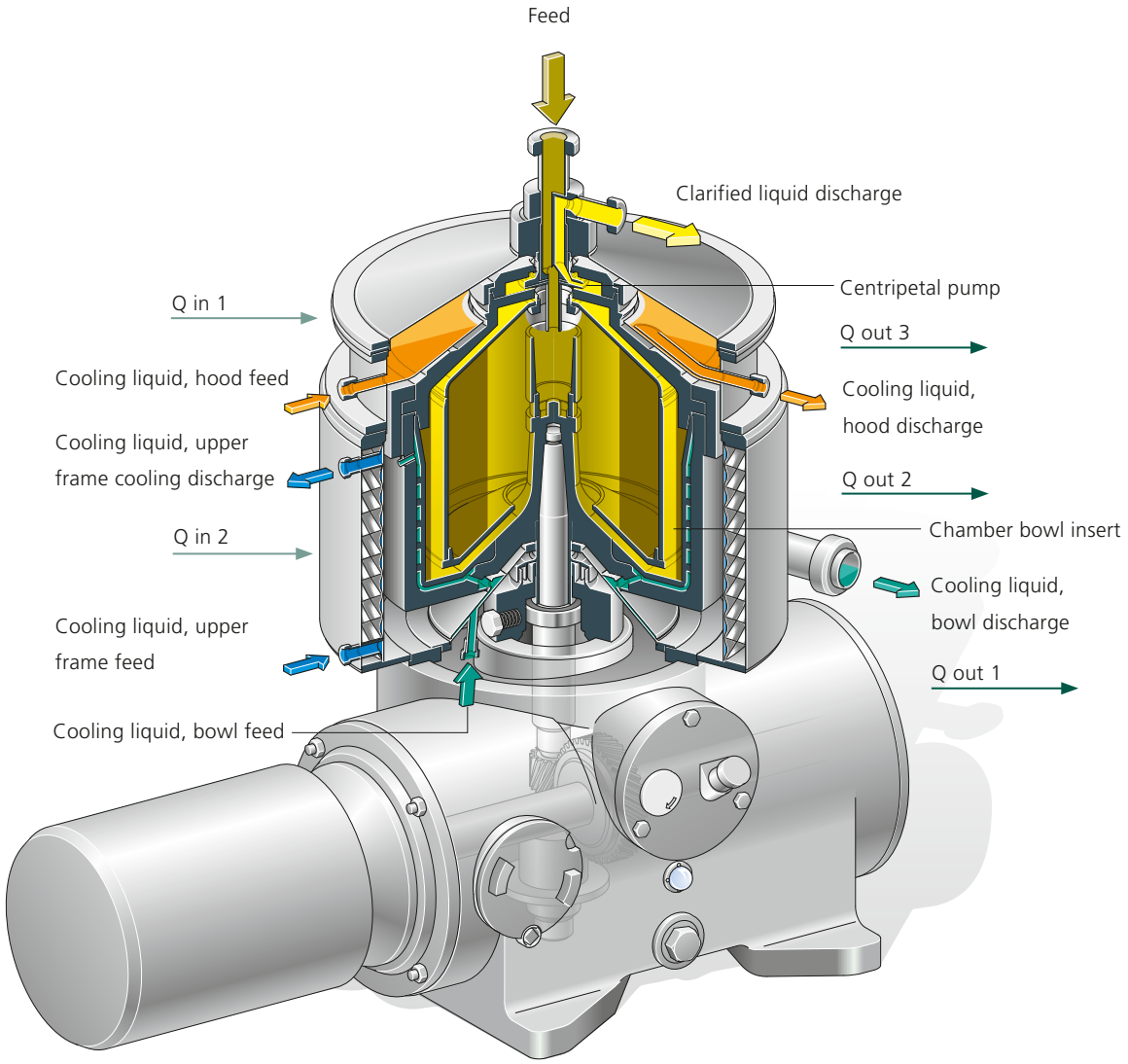
outer bowl, an upper frame cooling which extracts the heat of the cooling medium from the bowl and a hood cooling, which extracts the heat from the bowl top and the lock ring. The cooling solution introduced into the cooling chambers has a temperature of up to -20 °C, so that the outer surfaces of the separators are completely iced during operation. With this system, a controlled product temperature can be achieved with a tolerance of +/- 0.3 °C.

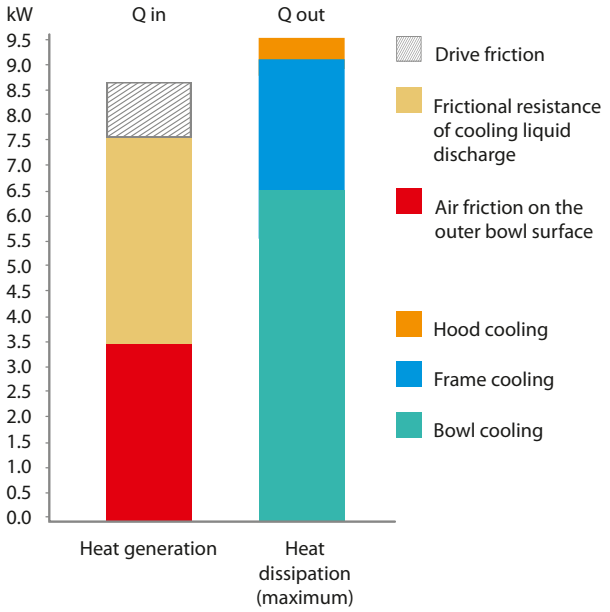


Thermal balance under control

The bowl schematic shows the main effective flows of heat. Q in 1 is the amount of heat introduced into the bowl by the air friction at the outer surface of the bowl. Q in 2 is the braking effect on the bowl caused by the inflow and outflow of the cooling liquid. Q out 1 is the amount of heat extracted by the bowl cooling. Q out 2 is the amount of heat extracted by the frame cooling and Q out 3 is the amount of heat extracted by the hood cooling. The bar diagram shows the results of measurements in a separator type BKB 28 with a 11 kW (9.3 kW) motor. The heat balances were calculated under constant conditions. The left bar shows the main amounts of introduced heat. The right bar indicates the amounts of heat which can be extracted at the lowest temperature of the cooling medium (-20 °C). It can be seen that controlled product temperatures can be adjusted and that cooling can even be achieved under certain conditions with this type of separator.

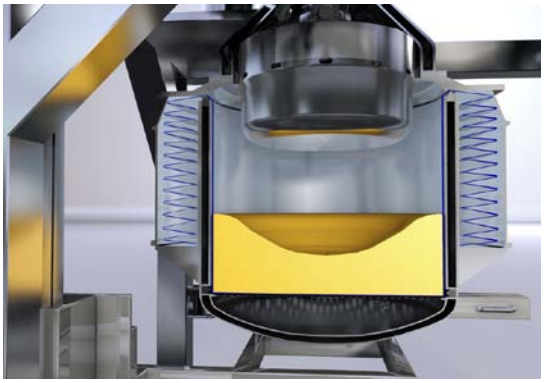
Similar heat balances can also be realized with the hyperconcentrator through targeted implementation of these findings in the conceptual design of the **hy**con.





GEA Westfalia Separator hycon: the latest centrifuge technology

The latest tendency in human blood plasma fractionation is the closed handling of the solids. A good example of this is the hyperconcentrator **hy**con with the two-room concept. It fulfils the highest sanitary and hygiene requirements of a machine built to GMP. A special feature for low-temperature applications, such as human blood plasma fractionation, is the liquid nitrogen cooling of the bowl. Apart from the bowl cooling, the hood and solids container cooling ensure adequate heat extraction. It is also possible to eject the solids into so-called endless bags for further processing.



We live our values.

Excellence • Passion • Integrity • Responsibility • GEA-versity

GEA Group is a global engineering company with multi-billion euro sales and operations in more than 50 countries. Founded in 1881, the company is one of the largest providers of innovative equipment and process technology. GEA Group is listed in the STOXX® Europe 600 Index.

GEA Mechanical Equipment

GEA Westfalia Separator Group GmbH

Werner-Habig-Straße 1, 59302 Oelde, Germany
Phone: +49 2522 77-0, Fax: +49 2522 77-2828
www.gea.com

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