

Normal flow filtration glossary



Absolute filtration

Total retention of target particles of a given size, generally under a well-defined test or operational protocol.

Absolute rating

A filter value that expresses the smallest particle that will be completely retained under a standard test method (with attendant experimental uncertainty) consistent with the filter's application.

Absorption

Taking up of matter within other matter, such as a sponge drawing in water, or a liquid taking up a gas; reversible.

Adsorption

The binding of molecules to a surface as a result of a chemical or physio-electric interaction between the membrane surface and the molecule.

Air diffusion rate

The rate at which air diffuses through the wetted pores of a membrane at a given differential pressure. Measuring the air diffusion rate is a method used to check the integrity of a membrane filter.

Air flow

The amount of air that flows through a filter; related to contamination, differential pressure, filter area and filter porosity. In membrane separations, generally expressed as l/minute/cm² at a given pressure.

Aseptic filtration

Filtration whose object is effluent free of pathogenic microorganisms. Sterilizing filters (that is, those with 0.2 and 0.1 µm rating) are validated against the standard challenge organism, *Brevun-dimonas diminuta* (previously know as *Pseudomonas diminuta*), under controlled laboratory conditions based on ASTM standard methodology. The FDA Guidelines on Aseptic Processing define a sterilizing grade filter as: "A filter which, when challenged with the microorganism *Pseudomonas diminuta* at a minimum concentration of 10⁷ organisms per cm² of filter surface, will produce a sterile effluent."

Asymmetric membrane

A membrane that is made such that the pore size increases through the membrane matrix.

Atmospheric pressure

Pressure at any point in an atmosphere attributable solely to the weight of the atmospheric gases at that point. Expressed as 1 barg, approximately 75 cm of mercury (14.7 lbs/in²) at sea level.

Autoclave, autoclavability

An autoclave is a device that uses saturated steam at a specified pressure over time to kill microorganisms and thus achieve sanitization or sterilization. Because many materials change properties when exposed to moisture, heat, and pressure, products destined for this process must be specially engineered for autoclavability. A sterilizing grade air filter is required to maintain sterility during air inrush after autoclaving.

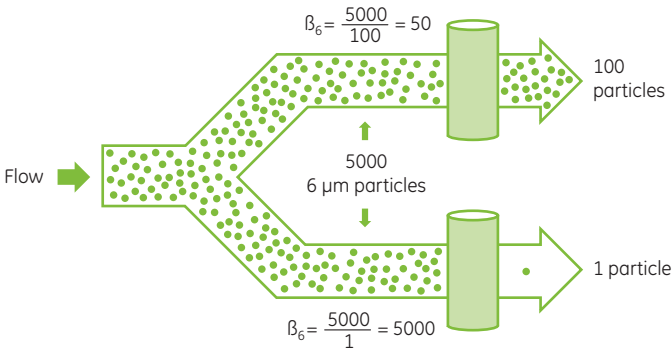
Back flushing, backwash

Reversing the permeate flow to mechanically clean the membrane.

Beta rating, beta ratio

A standard method of rating a filter's ability to remove particles. It is defined as follows:

$$\beta_n = \frac{\# \text{ particles } \geq n \text{ microns in}}{\# \text{ particles } \geq n \text{ microns in}}$$



Binding

The process by which some components in a feed solution adhere to the membrane. Binding can be desirable in some instances, but often, as in the case of protein binding during sterile filtration, can result in a loss of valuable product.

Biosafety tests

A class of tests that determine whether a filter's materials of construction can induce systemic toxicity, skin irritation, sensitization reaction, or other biological responses. These tests are often completed by labs *in vivo* or *in vitro*. For example, United States Pharmacopoeia XXVII Class VI Plastics Test involves both the implantation and extraction of drug product contact surfaces to demonstrate that these materials are not toxic to various mammalian cells.

Blanketing

The use of nitrogen or other inert gas to hold a tank such that product is not exposed to atmospheric air. Hydrophobic filter cartridges are typically used for blanketing.

Blinded

When a filter is "blinded," it means that particles have filled the pores, and the flow through the filter from the feed side to the permeate side is reduced or stopped.

Blow down

The act of draining a system or of introducing constituents into a reactor through the use of gas at a positive pressure. Care must be exercised to prevent pressures above the maximum operating pressure.

Bubble point

The minimum pressure required to overcome the capillary forces and surface tension of a liquid in a fully-wetted membrane filter. The bubble point value is determined by observing when bubbles first begin to emerge on the permeate side or downstream side of a fully-wetted membrane filter when pressurized with a gas on the feed (upstream) side of the membrane filter.

Bubble point test

The test procedure for determining the bubble point of the largest pores in a microfiltration membrane.

Capillary

A tube with a very thin lumen, by analogy with the smallest vessels in the human circulatory and lymphatic systems. In filtration, descriptive of the pores in a membrane.

Cartridge or cartridge filter

A filtration or separations device having a membrane encapsulated within a housing. The housing normally has feed and permeate ports and, in the case of cross flow filters, a retentate port. All of these ports may be used to control the flow parameters of fluid into and out of the housing and through the membrane.

Cell harvesting

The process of concentrating (dewatering) the cell mass after fermentation. Cell slurries in excess of 70% wet cell weight are achievable. The cells may also be washed to prepare them for further processing, such as freezing or lysing. Unlike clarification processing, with cell harvesting the cells are the target material.

Centrifugation

From centrifuge, a rotating device for separating liquids of different specific gravities; the act of using a centrifuge to separate substances.

Chemical compatibility

The ability of the components of a filter to resist chemicals that can influence the filter's performance. For example, some chemicals could cause the filter to shed particles, swell, or dissolve filter components. Repeatable performance requires that filters are resistant to all the chemicals they are exposed to at a given concentration, temperature, and total exposure time.

Clean-in-place (CIP)

The process of cleaning a filtration device without removing it from its filtration system.

Clogging

Blockage of filter pores by solids in the process of being removed by the filter; generally results in increased differential pressure.

Composite membrane

A membrane that is made up of two or more layers that are usually chemically or structurally different.

Cutoff

See Molecular weight cutoff (MWCO) and nominal molecular weight cutoff (NMWC).

Delta P, ΔP

In filtration, the pressure drop across the membrane. See Pressure drop.

Depth filter

A thick filter that captures contaminants within its pore structure using entrapment and adsorption.

Differential pressure

In cross flow filtration, the pressure drop along the membrane between the feed (inlet) port and the retentate (outlet) port.

Differential pressure gauge

Instrumentation capable of showing or recording differential pressure readings between two points.

Diffusion

Movement of gas molecules caused by a concentration gradient.

Diocetyl Phthalate (DOP) test

Test for evaluation of filtration efficacy that counts the number of controlled-size, 3 μm particles (diocetyl phthalate aerosol) entering and emerging from a filter.

According to ASTM:D2986-71), a HEPA (High Efficiency Particulate Air) filter must retain at least 99.97% of 0.3 μm DOP droplets. Particles of 0.3 μm were chosen because for many air filters, this size is the most difficult to retain.

Direct flow filtration

Filtration process where the entire feed stream flows through the filter's media. Also called normal flow filtration or dead-ended filtration.

Downstream processing

Starting with a feed stream free of cells and cell debris, the purification sequences involving chromatography and membrane separations to achieve final product purity.

Drain

Connection on a filter, generally fitted with a valve, at a low point to allow outflow of liquid.

Drain valve

A device for controlling the flow of material in a filter housing, generally at the lowest point.

Effective area, effective filtration area, EFA

In a membrane separations device, the active area of the membrane exposed to flow. It represents the area available for filtration, not the total area of material used to make the filter, some of which is occluded by seals, joints, and so on.

Effluent

Fluid that has passed through a filter. Opposite of affluent.

Element

A filter element consists of filter media and any hardware and supporting materials, installed as a single unit. Examples: filter cartridge, filter capsule.

Endotoxin

The outer cell wall of gram-negative bacteria, also known as lipopolysaccharides (LPS) and pyrogens.

Ethylene oxide sterilization (EtO)

A sterilization process still common for biomedical products, in which product is subjected to steam and highly toxic ethylene oxide gas. Because many materials change properties when exposed to moisture and EtO byproducts, products destined for this process must be specially engineered for EtO sterilization.

Expendables

Filter cartridges, elements and other media that require periodic replacement to maintain filtration efficacy. Expendables are additional to basic initial equipment or system hardware and piping configurations.

Extractables

Substances that may dissolve or leach from a membrane device during filtration and contaminate the process solution. For example, the leachates might include wetting agents in the membrane, membrane cleaning solutions, or substances from the materials used to encase the membrane.

Feed

Material or solution that is introduced into a membrane separations system.

Filter

A device used to separate a liquid or gas from another liquid or gas; or to remove solid contaminate from a liquid or gas. The latter meaning is the most common in the industry. Types include membrane, centrifuge, baffle, pre-coat, leaf, edge, plate and frame, cyclone and replaceable filter.

Filterability

Descriptive term expressing the ease or difficulty of filtering.

Filter area

The surface area of filter media inside a separations device.

Filter efficiency

Filter efficiency represents the percentage of a given size particle removed from the fluid by the filter.

Filter press

A filtration device typically consisting of carrier plates fitted with filter media or pads and clamped in series. The pads may contain absorbents. Also, "plate-and-frame" filter.

Filtrate

Also called *permeate* or *effluent*. The portion of the process fluid that passes through the membrane.

Filtration

The act of removing particles (normally solids) from a substance (generally fluids). These particles can be valuable products, or contaminants.

Flowpath length, nominal flowpath length

The total length that a feed solution travels from inlet to outlet. Flowpath length is an important parameter to consider when doing any process development, system design, or scale-up or scale-down experiments. The flowpath length and other fluid channel geometries, such as lumen diameter or channel height, can affect the fluid dynamics of the system and will directly affect pump requirements and differential pressure of the filtration step.

Fouling

A buildup of material on the membrane surface that reduces the filtration rate. This material is not redeposited in the bulk stream by higher shear rates.

Gamma sterilization

A type of sterilization process accomplished by bombarding the object to be sterilized with electron beam, x-ray, ^{60}Co or ^{137}Cs irradiators. All generate forms of gamma rays, radiant energy at short wavelength (0.1 nm or less). The governing standard is ISO 11137—Sterilization of Healthcare Products—Requirements for Validation and Routine Control—Radiation Sterilization. Because some product materials can be adversely affected by gamma radiation, objects destined for gamma sterilization must be engineered specifically for this process.

Gel layer

During the filtration process, the thin layer of particles or molecules that may build up at the membrane surface. It is also referred to as the *concentration polarization* layer. Higher TMP can be the result of an increase in the thickness of the gel layer. Gel layer formation can negatively impact the filtration process by reducing flux and inhibiting passage through the membrane. Operating at a higher shear rate may reduce the thickness of the gel layer.

Housing

A mechanical structure that surrounds and supports the membrane or filter element. The housing normally has feed, retentate, and permeate ports that direct the flow of process fluids into and out of the filter assembly.

Hydrophilic

Filters that wet out easily with water and work well with aqueous solutions.

Hydrophobic

Filters that do not wet out easily with water but typically do wet out easily with nonpolar solvents such as alcohol. Once wetted, many aqueous solutions can be processed in a hydrophobic filter.

Inlet air

Air drawn or injected into a system, typically into a fermentor or reactor. Inlet air generally requires a hydrophobic filter element to ensure sterility.

Inlet pressure

The pressure of a fluid at the feed port of a separations device.

Integrity testing

The evaluation of the completeness of sealing on the filter medium between affluent and effluent and of the homogeneity of filter membrane pore size. Reveals internal leakage and/or oversize pores or torn membrane. Test protocols to evaluate integrity include bubble point, diffusive flow, and water intrusion.

Maximum differential pressure

Value of the greatest differential pressure a filter can withstand without collapse or failure.

Maximum operating pressure

Value of the greatest allowable pressure in a system, generally lower than the maximum pressure of any of the components, as a safety factor.

Media exchange

A filtration step used to exchange one type of media for an alternative type of media during an aseptic cell culture separation.

Media migration

Media migration occurs when solid components of a filter (particles, adhesives, etc.) break free of the filter and enter the process solution.

Medium (media)

The component of a separations device that actually filters the process solution. For example, the membrane in a cartridge or membrane cassette.

Membrane

A thin layer of a highly engineered material with controlled pore size used to separate particulates, biological matter, and molecules from a solution.

Membrane recovery

The degree to which the original performance of a membrane can be restored by cleaning.

Microfiltration

The process of removing particles from a liquid by passing it through a porous membrane under pressure. Microfiltration usually refers to removing submicron-size particles.

Micron (micrometer, μm)

One one-millionth of one meter. The average human eye can discern particles as small as $\sim 40 \mu\text{m}$.

Microporous membrane

A thin, porous film or hollow fiber having pores ranging from 0.1 to 10 μm . Cross flow microfilters typically range from 0.1 to 1 μm .

Molecular weight

Mass of one molecule of a nonionic substance in atomic mass units.

Molecular weight cutoff (MWCO)

The size designation in Daltons (Da) for ultrafiltration membranes. Typically measured as the molecular weight of a globular protein that is 90% retained by the membrane. No industry standard exists; hence the MWCO ratings of different manufacturers are not always comparable.

Nanofiltration

Separation processes targeted for solutes having molecular weights from 500 to 1000 Da. *See* Molecular weight cutoff (MWCO).

Nominal filter rating

A rating that indicates the percentage of particles of a specific size or molecules of a specific molecular weight that will be removed by a filter. No industry standard exists; hence the ratings from manufacturer to manufacturer are not always comparable.

Non-woven

In filter material, fibers in a random array, as opposed to woven, where a more or less regular, interlaced network of fibers is created, as in cloth.

Nominal molecular weight cutoff (NMWC)

In ultrafiltration, the molecular weight size of a protein or other solute (in Daltons) that will be retained to 90% by the membrane. *See* Molecular weight cutoff.

Normalized water permeability (NWP)

The water flux temperature corrected to a standardized temperature.

Off-gassing

Generation of gases during fermentation and/or reaction processes.

Particle size distribution

The dispersion of particle sizes (number or weight fraction) in a fluid.

pH

Negative logarithm of the hydronium ion (H_3O^+) concentration in an aqueous solution. Indicates the acidity or alkalinity of a substance.

Pleating

Folding flat sheet filter media to increase the surface area that can be fitted into a given separations device, generally used in dead-ended filtration.

Pore size distribution

The range of pore sizes in a membrane. The tighter the pore size distribution, the better control one has over the filtration process.

Pores

The open spaces in a filter membrane; also, a small, interconnecting passage through the membrane. The removal rating of a membrane is dependent on the (irregular) path and size of the membrane's pores.

Porosity

A measurement of the open space in a membrane. The higher the membrane porosity, the more pores there are, hence, a higher flow rate is anticipated.

Pre-coat

In a filter system, a material introduced to coat the surface, forming a build-up or cake that enhances filtration.

Prefilter

A device installed before—upstream from—the main filtration process, generally to remove large solids that might prematurely clog the primary filter.

Prefiltration

The act of using a prefilter to remove large particles prior to final filtration.

Pressure, absolute

Gauge pressure plus 1 barg (14.7 psig).

Pressure, atmospheric

Pressure at any point in an atmosphere attributable solely to the weight of the atmospheric gases at that point. Expressed as 1 barg, approximately 75 cm of mercury (14.7 lbs/in²) at sea level.

Pressure drop

The difference in pressure between two points.

psig

(English system) Pounds per square inch, a unit of pressure.

1 psig = 6.78 kPa = 70.05 grams per square centimeter.

Pyrogen

A substance that produces a fever within a warm-blooded animal when injected into the bloodstream. Filtration materials of construction that come in contact with injectable liquids must meet pyrogenicity standards and be non-pyrogenic.

Pyrogenicity

The tendency of a substance to raise body temperature in a warm-blooded animal when injected into the bloodstream. Filtration materials intended for the processing of injectable liquids must meet pyrogenicity standards and be classified as non-pyrogenic. The Limulus Amoebocyte Lysate (LAL) test is a standard test for pyrogenicity.

Residence time

The time required for an incremental unit of feed solution to pass through a separations device.

Retention

The ability of a separations device to retain an entity of a given size.

Sanitization

A cleaning process that destroys most living microorganisms.

Screen or membrane filter

Filter that works by size exclusion (sieving) via a regular porous matrix.

Separation

Dividing a liquid or gas feed stream into separate components.

Sieving

Removal of particulates from a feed stream as a result of entrapment within the depth of the membrane pore structure.

Size exclusion

Mechanism for removing particulates from a feed stream based strictly on the size of the particles. Retained particulates are held back because they are larger than the pore opening.

Solute

An ionic or organic compound dissolved in a solvent; for example, the sugar in a cup of coffee is a solute.

Steam-in-place (SIP)

The process of sterilizing a device, such as a hollow fiber cartridge, with steam, without removing the device from the separations system.

Sterile

Devoid of living microbial organisms and/or toxins generated by living organisms; defined formally by USP or AAMI sterility requirements.

Sterilization

A process that removes/destroys all microorganisms from a solution or a filtration system. See Autoclave, Ethylene oxide (EtO) sterilization, Gamma sterilization.

Surface filter

A filter in which particles larger than the pores are retained on the surface of the filter.

Surfactant

A surface-active or wetting agent that in solution reduces the surface tension of a liquid, or reduces interfacial tension between a liquid and another liquid or a liquid and a solid. Filters coated with surfactant may be easier to wet out than otherwise, but the surfactant may combine with filtered liquid as an undesirable extractable, thus making the use of surfactants undesirable. Also, molecules with split solubility, with one portion soluble in water, and the other in oil.

Thermal stability

The ability of a membrane and filtering device to maintain its performance during and after exposure to excursions of temperature, such as the elevated temperatures experienced during autoclaving or steam sterilization.

Throughput

(1) The volume of solution that will pass through a separations device before the filtrate output drops to an unacceptable level.

(2) The rate at which a separations system will generate filtrate. In a business sense, throughput can be a constraint on the rate at which product is made available for sale.

Titer reduction

The measurement of a filter's ability to remove microbes or viruses from a fluid.

Turbidity

A measure of relative liquid clarity. Measurements are based on the amount of light transmitted in straight lines through a sample. The more light that is scattered by fine solids or colloids, the less clear (and more turbid) the solution. Often reported in nephelometric turbidity units (NTU).

Upstream

The feed side of a separations process.

Upstream processing

Cellular separations including: cell lysates, cell harvesting, clarification, and cell culture perfusion.

Viscosity

A measurement of a fluid's resistance to shear. A slow-flowing liquid such as gear oil, has a higher viscosity than a free-flowing liquid such as water. In a given separations process, higher-viscosity fluids are operated at a lower flow rate through a cartridge than lower viscosity fluids.

Void volume

The combined volume of all filter pores, interstices, passages, and the like. Indicates, in general, the solids or contaminant holding capacity of filter cartridges.

Volumetric flow rate

The rate of flow of a substance through the determination of the volume it occupies, usually at standard atmosphere in cubic centimeters/cubic inches or cubic meters/cubic feet.

Wetting

In a hydrophobic membrane, the process of filling pores with water. Alcohol can be used as a wetting solution, or high pressure can drive air out.

Yield

The amount of particulates or molecules of interest (product) that can be recovered from the cross flow filtration process; also referred to as *recovery*.

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