A History of Sterile Filtration

Maik W. Jornitz

Sterilizing Grade Filter Company History

1845 **FICK** - First synthetic membrane, Synthetic membranes based on Nitrocellulose had been produced since 1845, however a major problem with these membranes was reproducibility , consequently there use was almost zero, as they could not be guaranteed to work accurately.

1918 **ZSIGMONDY & BACHMANN** - In 1918 Professor Richard Zsigmondy and DR. Bachmann began to develop, at Goettingen University in Northern Germany, a method by which it was possible to manufacture membrane filters with a consistent and reproducible porosity. Small scale production took place and by 1925 membranes were being made on a laboratory scale. Dr. Zsigmondy sterilized culture media using Cellulose Nitrate, developed a method of interfering with a polymers molecules.

1927 **SARTORIUS** - In 1927 a company known as "Membran Filter Gesellschaft" was founded by Florenz Sartorius to commercially produce membrane filters. They made membranes using the Zsigmondy technique for studying bacteria. Initially sales took place within Germany and the production process was patented to offer a degree of protection around the rest of the world. However following the end of world war 2 the technology to produce membrane filters fell unto allied hands. Sartorius began production following a rebuilding program on the facility in 1951.

1942 **Dr. MULLER** - Used membranes for examining contaminated water

1952 **MILLIPORE CORP.**- Founded producing membranes from Zsigmondy technology. In the process market they have a very good range of products in the micro electronic industry, as well as a popular range of filters for the pharmaceutical industry.

1959 **PALL CORP. -** Founded by Dr. David Pall. First company to invent the pleated process filter device.

1963 **GELMAN** - Founded by Charles Gelman, sold Sartorius membrane in USA prior to production of their own products.

1965 **SCHLEICHER & SCHUELL** - Produced membrane for Sartorius for a short period, before producing their own membrane. Particularly known for Nitro-Cellulose blotting

1969 **GENERAL ELECTRIC** - Dr. Spurry produced a plastic membrane

1976 **AMF CUNO** - Produced truly synthetic membrane

1979 **AKZO** - Dutch Company, produced synthetic membrane

1980 **BRUNSWICK CORP.** - Produced synthetic polymer

1984 **DOMNICK HUNTER** - British company, entered membrane market in UK mainly with air Treatment systems

.

The History of Sterilizing Grade Membrane Filtration

Nobel price winner Richard Zsigmondy invented in 1918 membrane filters, which found their commercial use within the pharmaceutical industry in the 1930´s as flat filter device, mainly 293 mm discs and in the 1970´s as pleated filter cartridges. In the late 60's when *Pseudomonas diminuta* (now *Brevundimons diminuta)* penetrated 0.45 µm rated filters,

the standard of sterilizing grade filter definitions changed to 0.2 micron. These filters have to retain 10^7 per cm² *B. diminuta* according to HIMA (1982), now ASTM 838-38 (1988). Since this time, appropriate process validation received a higher focus than pore size ratings.

The first pleated filter devices were resin bonded, which changed in the 80's to polymeric melt weld and in the late 80's to ultrasonic welding, which increased the robustness of the weld and reduced the thermal stress to the membrane. Ultrasonic welding is now a standard procedure with very high reliability.

In the early pleated device filter design, single layer membranes were the main utilized membrane configuration. Since single layer filters did not show sufficient total throughput, heterogeneous double layer membrane configuration appeared in the early 80's. These filter devices utilize a filter membrane with a larger pore size over a 0.2 µm filter membrane and therefore gain higher total throughput due to fractionate retention. In the late 80's asymmetric membranes made their entry and became more refined in the mid 90's. These membrane structures added to the total throughput.

Asymmetric Polyethersulfon membranes achieved rising popularity in the late 90's and since 2000 19 of 20 launched sterilizing grade filters contain Polyethersulfon membranes. The next generation of filters in the 2000 gained new pleating designs and technologies which created the current performance standards. The total throughput tripled since the 90's and the flow rate quadrupled, all the same dimensional ratio of the filter cartridges of the 90's but with enhanced membrane and prefiltration fleece technologies.

Early pleated devices also had a high level of leachables, as wetting agents or softeners had to be used to be able to pleat the filter membrane or to perform an integrity test. With new polymer technologies, filter surface are now treated in different ways, either the hydrophilizing agent is chemically bonded or e-beam fixed. These filters have a minimal amount of extractables.