

Thermo Scientific Finntip® Sterile and Finntip Filter Sterile – Importance of Guaranteed Purity

Finntips are manufactured using high-quality raw materials and the latest molding techniques. They are designed using our extensive knowledge of liquid handling. Modern automated production facilities and decades of expertise allow us to produce uniformly smooth, hydrophobic surfaces on the inside and outside of our tips. This prevents liquid retention and ensures the most accurate and precise pipetting. All tips are optimized for use with Thermo Scientific Finnpiettes.

For applications demanding the highest levels of purity, we offer sterile standard tips (Finntip Sterile and Finntip Flex Sterile) and sterile filter tips (Finntip Filter Sterile and Finntip Flex Filter Sterile) free of human deoxyribonucleic acid (DNA), deoxyribonuclease (DNase), ribonuclease (RNase) and endotoxins. The Finntip Filter range of pipette tips provides protection against contamination of both the sample and pipette. The non-sealing filter minimizes the transfer of aerosols from the tip to the pipette and vice versa, ensuring the integrity of any pipetting function.

Product purity characteristics

The sterile Finntip products are certified by validation of the manufacturing process to be free of the following contaminants:

Human DNA	< 1.9x10 ⁻¹¹ g/tip
DNase	< 9.4x10 ⁻⁴ U/tip
RNase	< 6.5x10 ⁻⁸ U/tip
Endotoxins	< 0.05 EU/ml

Free of human DNA

DNA contains the genetic instructions specifying the biological development of all cellular forms of life. It is present in all cells of living organisms.

Pipette tips used for DNA applications must be free of DNA in order to prevent false results. The polymerase chain reaction (PCR), among many other applications, is highly sensitive to DNA contamination, since it detects even the smallest amounts of individual molecules.

Free of DNase

DNases are enzymes that degrade DNA into small fragments. These enzymes are not as prevalent as RNase but, nevertheless, of con-

cern.

Absence of DNases is important since the enzymes destroy DNA and thus impair applications that require undamaged DNA molecules.

Free of RNase

RNases are very powerful enzymes that degrade RNA into small fragments and therefore must not be present in applications concerning RNA. RNases are durable and heat resistant, which makes them hard to be inactivated, for example, by autoclaving or irradiation. RNases are extremely common and result in a short lifespan for any RNA that is not in a protective environment.

Free of endotoxins

Endotoxins are complex lipopolysaccharides that are part of the outer cell wall of Gram-negative bacteria, such as *E. coli*. Growing bacteria release small amounts of endotoxins, but large amounts are shedded into the environment when bacteria die and disintegrate.

In vivo endotoxins can cause a wide spectrum of reactions, such as fever, shock or severe diarrhea. All in vitro effects of endotoxins are

not known, but they may decrease tissue culture cell viability and inhibit transfection efficiency.

Sterility

Sterility means that there are no living organisms present on the surface of the product. The sterility of the pipette tips is necessary in order to ensure reliable results in most biological applications.

For sterile Finntips the Sterility Assurance Level (SAL) is 10^{-6} . This means that 1 object out of 1 000 000 is allowed to be non-sterile.

ISO 11137 outlines validation methodologies for irradiation dose setting to achieve a given SAL. These include bioburden evaluation of the tips and dose experiments to assure the correct irradiation dose. We followed this international standard to optimize the gamma irradiation dose in order to ensure the sterility of the tips.

Methods to guarantee purity

Certification of sterile Finntips has been achieved by validation of the tip manufacturing process. This validation consisted of the following phases:

Identification of contamination sources in the manufacturing process

During this identification phase the manufacturing process was split into small working steps. For each small step we questioned if anything routinely or randomly could happen that would affect the purity of the tips. For certain steps we used testing and contamination simulation tests to obtain more accurate information.

As an outcome of this, we identified as possible contamination sources the personnel, indoor air and surfaces. The most significant contamination is caused by human interaction, which means that all manual working steps are critical to the purity of the product.

Eliminating human contamination

The most effective way to eliminate contamination by humans is to minimize manual work and to use a high level of automation. Another important way to prevent human contamination is the protective dress

code and appropriate working procedures.

Standardization of the manufacturing process

The manufacturing process is standardized by keeping the production environment stable. This includes cleaning instructions and instructions for routine work. It is also important to maintain a well-trained personnel and to have a controlled change management.

Testing

After standardization of the manufacturing process, extensive validation testing of the tip lots was performed. The results of these tests confirmed that the tips were free of contaminants and that the process was indeed stable. Because it is impossible to test all the manufactured tips for purity, we use sampling in routine testing.

Follow-up actions

In addition to product testing, the amount of particles and microorganisms in the production area are monitored. These tests provide further information on the stability of the manufacturing process.

The methods used in the above described validations follow the principles stated in the international standards ISO 14971 and ISO 11137.

Test methods

Tips are flushed with sterile water that is divided into aliquots and used for testing:

RNase and DNase

RNase and DNase in the sample are detected by using fluorescent-labeled RNase and DNase substrates. A green fluorescence is emitted when the substrate is cleaved. This fluorescence was measured using a fluorometer.

Human DNA

Possible DNA in the sample is amplified by PCR using universal primers for human DNA. A semi-quantitative and -qualitative analysis of the PCR products was performed with a commercial microchip. An example of the results of this analysis is shown in Figure 1.

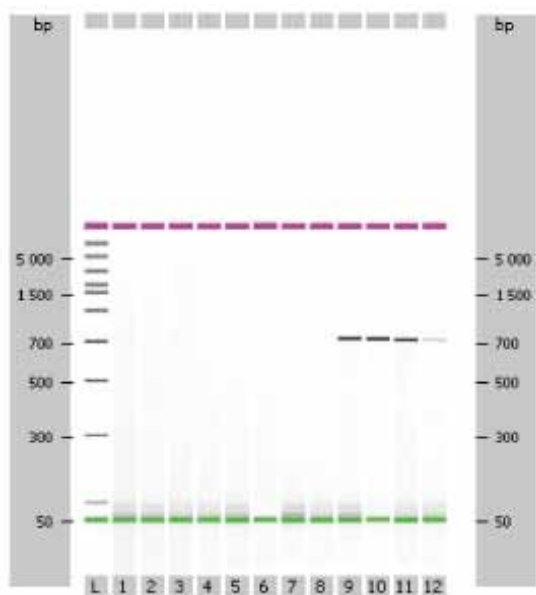


Figure 1. Picture of a gel electrophoresis run. L = DNA marker, lanes 1-9 = tip samples, and lanes 9-12 = human DNA controls. The picture shows that the samples were free of human DNA.

Endotoxins

Pipette tips are rinsed with an extracting solution for 1 h at room temperature. Endotoxins are measured from the extract using the LAL kinetic turbidometric method.

LAL is an aqueous extract of blood cells (amebocytes) from the horse shoe crab, *Limulus polyphemus*. Endotoxin triggers a cascade of enzymatic reactions, which result in an activated clotting enzyme. In the presence of bacterial endotoxins at an elevated temperature, the LAL reagent will clot after addition of the reagent. The formation of the gel clot is proportional to the concentration of the endotoxin. The gel clot method is the official test reference in the USP monograph.

References

- Standard ISO 11137:1995/2006. Sterilization of healthcare products – Requirements for validation and routine control – radiation sterilization.*
Standard ISO 14971:2007. Medical devices – Application of risk management to medical devices.

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North America: USA/Canada +1 866 984 3766

Europe: Austria +43 1 801 40 0, Belgium +32 2 482 30 30, Finland/Nordic +358 9 329 100, France +33 2 2803 2000, Germany national toll free 08001-536 376, Germany international +49 6184 90 6940, Italy +39 02 95059 1, Netherlands +31 76 571 4440, Russia/CIS +7 095 225 11 15, Spain/Portugal +34 93 223 3154, Switzerland +41 44 454 12 12, UK/Ireland +44 870 609 9203

Asia: China +86 21 6865 4588 or +86 10 5850 3588, India +91 22 5542 9494, Japan +81 45 453 9220, Other Asian countries +852 2885 4613

Countries not listed: +49 6184 90 6940 or +33 2 2803 2000

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