Measurement of HEPA filter performance using the dispersed oil particle (DOP) aerosol test for leak detection in filter installations

2nd Edition

April 2008

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This test protocol is supplementary to Quality Assurance of Aseptic Preparation Services, Fourth edition, Edited by Alison M Beaney, Pharmaceutical Press, 2006

1. Introduction

The test is used to detect leaks in HEPA (high efficiency particulate air) filters in their operational conditions. The test is intended to test the filter, seals, housing and terminal ductwork and, in addition to testing filter integrity, ensures that all air entering the controlled environment passes through the HEPA filtration system.

The test method used is that described in BS EN 14644-3:2005 "Cleanrooms and associated controlled environments – Part 3: Test methods" and in PD6609:2007, "Environmental cleanliness in enclosed spaces – Guide to in situ high efficiency filter leak testing" an explanatory supplement to BS EN 14644-3:2005. In this test an aerosol is dispersed upstream of the filter and the downstream face and seals of the filter are scanned for leaks.

The purpose of HEPA filters in cleanrooms, controlled environments, workstations and cabinets is to control particles and microbes so that environmental standards can be maintained and the particulate and microbiological challenge to processing is minimised. HEPA filters may also be used to provide operator protection in safety cabinets.

Analysts involved in this area of testing must be trained in and familiar with the following:

- The requirements of BS EN ISO 14644-3 (B.6)
- The requirements of PD6609:2007.
- Correct use of the photometer and aerosol generator used.
- Current GMP requirements.
- Good clean-room practice.

2. Equipment

2.1 An aerosol generator capable of generating a polydisperse aerosol of the test oil.

BS EN ISO 14644-3 specifies a number of test oils. Shell Ondina EL is the test oil normally used in the UK Other test oils are used in the USA, for example Durasyn 164, which is a poly-alpha olefin with a viscosity of 4 centistokes. Contractors operating in both the UK and the USA may choose to use this oil or similar.

The distribution of particles in the aerosol is described in BS EN ISO 14644-3 (B.6.6.2) and further explained in PD 6609:2007 at 3.2 which states "BS EN ISO 14644-3:2005 considers that the mass median particle size of the test aerosol should be between 0.5µm and 0.7 µm with a geometric standard deviation of up to 1.7. This is a size distribution typical of that produced by a Laskin nozzle.

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However, it is known that the mass median particle diameter of particles produced by a thermal generator is likely to be below the size suggested by BS EN ISO 14644-3:2005 and closer to the most penetrating particle size (MPPS) of high efficiency filters. It is therefore likely that more leaks will be found when a thermal generator is used, but this is not considered a disadvantage."

The upstream aerosol challenge should be between 20 mg/m^3 (µg/l) and 80 mg/m^3 (µg/l). It should be homogeneous and remain uniform from the start to the finish of each individual test. The generator must have sufficient output to ensure that an adequate upstream concentration can be achieved in the installation under test.

The aerosol generator should be serviced and tested annually, using an aerosol photometer that has been calibrated for the oil being used in the generator, and a certificate obtained to certify that it is performing in accordance with the manufacturer's specification. Full calibration is unnecessary and very expensive.

2.2 A photometer capable of estimation of mass concentration of airborne particles of the aerosol described in 2.1 with an accuracy of better than $\pm$5% over a range of 0.001% to 100% of the test aerosol.

The photometer should have a minimum threshold sensitivity of 0.00002 mg/m^3 (µg/l)* (so as to register a penetration of 0.001% against the minimum upstream challenge of 20 mg/m^3 (µg/l)) and be capable of measuring the maximum aerosol challenge concentration of 80 mg/m^3 (µg/l) of aerosol. A linear photometer is preferable to a logarithmic photometer because it is capable of indicating % penetration directly and is more likely to meet the threshold sensitivity requirement. Logarithmic photometers should not be used to test for penetrations less than 0.01%, as they do not meet the required threshold sensitivity. They are no longer manufactured.

The photometer should be serviced and calibrated annually with an aerosol of the test oil that is normally used, and a calibration certificate obtained.

3. Pre test conditions

The test is performed with the installation in its operational condition at its designed airflow rate, in a balanced condition with any pre-filters removed. The refrigeration, heating and humidification circuits of the plant (if fitted) must be turned off prior to testing to avoid attenuation of the aerosol challenge. Diffusers must be removed from filters before scanning to enable adequate access to the filter face, housing and seals.

Note: Pre-filters may be left in place and refrigeration, heating and humidification circuits left on if the aerosol is introduced into the duct downstream of these components. If testing is performed in this way, the aerosol is likely to be introduced after the fan, necessitating the use of an aerosol injection pump to overcome the pressure in the system. The length of ductwork between the introduction of the

* This threshold sensitivity is lower (more sensitive) than in BS EN ISO 14644-3 so that the photometer can detect penetrations down to 0.001%. (BS EN ISO 14644-3 states "Designated leaks are deemed to have occurred where a reading greater than 0.01% of the upstream challenge aerosol concentration. Alternative acceptance criteria may be agreed between the customer and the supplier.")

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aerosol and the filters will be reduced and this may adversely affect mixing of the aerosol with the air stream.

4. Aerosol injection

The aerosol is injected upstream of the filter sufficiently far upstream to ensure adequate mixing of the aerosol and air stream and ensure even distribution over the filter face. This is typically 15-20 duct diameters upstream. An aerosol injection pump may be required to inject aerosol into pressurised parts of the system. The ports used for introducing and measuring the aerosol concentration must be capable of being effectively sealed when not in use. Where the required mixing distance of 15 – 20 duct diameters cannot be achieved, the aerosol should be introduced using a distribution system such as sparge pipes. This is known as distributing the aerosol at the point of injection.

Suitable ports should be fitted to the air handling plant to enable introduction of an adequate level of aerosol challenge upstream of the filters. Each filter terminal should also be fitted with a re-sealable sample port to enable the upstream aerosol concentration to be measured. In cases where an upstream sample point has not been included in the design of the equipment or where the equipment has been installed in such a way that the sample point is not accessible, then an appropriate sample point must be fitted before testing can start.

5. Upstream aerosol concentration

The up stream concentration of aerosol must be in the range 20 – 80 mg/m^3 (µg/l), measured as close as possible to, and preferably no more than 50mm upstream of the filter. If more than one filter is served by the ductwork, distribution in branches of the ducting may not be uniform. For this reason it is essential that upstream concentration is measured at each filter.

6. Upstream measurement of aerosol concentration

The upstream aerosol concentration is adjusted until it is in the range of 20 – 80 mg/m^3 (µg/l). This should be checked over a short period of time to establish that it is a stable concentration. Care should be taken not to measure high concentrations of aerosol over long periods of time as this may saturate the optical cell in the photometer. When a stable reading in the specified range has been achieved, the concentration should be recorded. The upstream concentration can be used subsequently to calculate percentage penetration when the downstream measurement has been made. Alternatively the linear photometer may be operated in the percentage penetration mode using the upstream concentration as a 100% reference reading. The downstream reading is then shown as the percentage penetration.

The upstream concentration should be checked and recorded at the end of each test to confirm that it is the same as at the start.

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7. Downstream measurements of aerosol concentration

Scanning is performed with a suitable fishtail probe attached to the photometer inlet tubing. After setting the photometer as described in 6 the filter face should be scanned in overlapping scans approximately 30mm from the filter face at a rate derived from the formula in BS EN ISO 14644-3:2005 (B.6.2.5), which says that the scan rate should be approximately 15/Wp cm/s, where Wp is the probe dimension perpendicular to the scan direction. If the probe is 3 cm wide, the scan rate is 5 cm/s. The filter seal and any exposed parts of the housing and ductwork should also be scanned. In order to facilitate proper scanning any diffusers fitted must be removed to enable access.

When testing for leaks between a HEPA filter and its housing, the leak may be into a recess or 'dead zone' where there is no natural airflow. The concentration of the challenge aerosol is likely to build up in this 'dead zone'. Therefore, when a high reading is indicated in such a situation, the photometer probe should be held in the same spot until the accumulated challenge aerosol has been cleared by the air drawn into the probe (which is typically at a rate of 28 litres/min) and a steady reading obtained. This steady reading is the one that should be used to determine whether the leak is within the specified limits. Alternatively the 'dead zone' may be flushed with a source of HEPA-filtered air to clear the accumulated aerosol until a steady reading is obtained.

8. Leak integrity of facility

The aerosol generator and photometer may also be used to check for leaks into the controlled environment from surrounding non-controlled areas at the same or different static pressures. These leaks may be through construction joints, service conduits, light fittings and other fittings, and may be caused by induction or by pressurisation of ceiling and other voids. A suitable test is described in BS EN ISO 14644-3:2005: B.13 - Containment leak test.

It is recommended that the facility is inspected annually for potential leaks and the leak test is carried out where appropriate.

9. Limits

Limits to be used for aerosol penetration in filter installations and facilities are:

> EU GMP Grades A & B environments – maximum penetration = 0.001%
> EU GMP Grades C & D environments – maximum penetration = 0.01%
>
> Leak integrity of facility – BS EN ISO 14644-3:2005: B.13 gives the limit for leaks into the controlled environment as 0.01% maximum penetration. It may however be difficult to measure the concentration of the upstream challenge in this test, in which case it becomes a leak detection test.

A leak shall be deemed to have occurred if a steady repeatable reading on the photometer at any point exceeds the maximum penetration value.

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10. Reporting of results

A report is prepared and contains at least the following information: -

- Name and address of the laboratory performing the test and analyst ID
- Unique laboratory reference number
- Name and location of client and contact person
- Filter or cabinet ID and location
- Date of the test and date report completed
- The upstream aerosol concentration
- The maximum downstream concentration detected
- Result of testing including a statement to indicate pass or fail
- Signature of person approving the report

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APPENDICES

APPENDIX 1. Grades of filters used in controlled environments

Filter manufacturers use BS EN 1822-1:1998 to classify filters by their Overall Efficiency against the MPPS (most penetrating particle size). The MPPS is normally between 0.1 and 0.3µm. The following table shows the BS EN 1822-1:1998 classification: -

Grade	Overall % Efficiency @ MPPS	Local % Penetration @ MPPS
H10	85	-
H11	95	-
H12	99.5	-
H13	99.95	0.25
H14	99.995	0.025
U15	99.9995	0.0025
U16	99.99995	0.00025
U17	99.999995	0.0001

Although maximum Local Values for % Penetration are given in the above table (summarised from BS EN 1822-1:1998), these are too high for pharmaceutical applications and the standard provides for lower values to be agreed. Purchase specifications for HEPA filters should therefore include a requirement for the filter manufacturer to carry out a DOP scan test, as described in this protocol, to the required local penetration. The following HEPA filter specifications have been found to provide suitable particulate and microbial levels in EU GMP environments:

EU GMP Grades A & B – H14 with 0.001% maximum DOP penetration
EU GMP Grades C & D – H13 with 0.01%maximum DOP penetration

APPENDIX 2. Filter casings

Filters should be supplied with a suitable casing to support the filter medium. This casing is preferably metal. Casings made of wooden materials such as MDF or chipboard are not recommended.

APPENDIX 3. Repairs

Repairs to the HEPA filter medium are not permitted, however temporary repairs may be acceptable as emergency short term measures as long as no more than approximately 5% of the filter face area is covered. For filters used in more critical unidirectional airflow applications, the area of repair should never be so great as to affect the uniformity of airflow.

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APPENDIX 4. Witnessing of filter integrity tests

Personnel involved in witnessing filter tests should check the following:

- The photometer and aerosol generator should be in good condition and within their respective calibration and certification periods.
- The aerosol should be introduced into the air handling plant sufficiently far upstream of the filters to ensure mixing, usually 20 duct diameters upstream from the filters. If this is not possible there should be an alternative mixing system such as sparge pipes.
- The upstream aerosol concentration should be in the range 20µg/l to 80µg/l. This must be measured with the photometer adjusted to the settings determined during calibration. The photometer may be adjusted AFTER it has been established that the upstream concentration is in the prescribed range to use the measured value as 100% for calculation of % penetration.
- The upstream concentration of aerosol should be checked and recorded at each filter at the start and finish of each test.
- The filter and seals should be scanned carefully and slowly, recording any leaks detected.
- Leaks through the filter seals may be resolved by careful adjustment of the clamping bolts by suitably trained staff.

NOTE: Upon publication of BS EN ISO 14644-3, PD 6609:2000 and all parts of BS 5295:1989 were withdrawn. PD 6609:2007 is supplementary to BS EN ISO 14644-3.

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Acknowledgements

The authors would like to acknowledge the help and advice received from John Neiger (Clean room Consultant and Technical Writer) and Neil Stephenson (Technical Director, DOP Solutions Limited) in the preparation of this document.

Prepared by Philip Hunt and the Microbiology Protocols Group, a working group of the NHS Pharmaceutical Quality Assurance Committee.
April 2008.

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