The Microclean BIG BLUE Cleanroom Handbook

Written by Neil Clayton | Tim Eaton

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Introduction

The first Microncleanan Handbook was published in 1981 and was revised and re-issued ten years later as the 'New Microncleanan Handbook to Good Cleanroom Clothing Practice'. Over 10,000 copies have been distributed internationally.

The **'Microncleanan Big Blue Cleanroom Handbook'** is the latest edition and has been completely re-written to provide an up-to-date resource for anyone involved with any aspect of contamination control systems and controlled environments.

It is produced by Microncleanan - a group of companies operating internationally that in the early stages of cleanroom technology pioneered the development of contamination control clothing and cleanroom garment decontamination and that has since expanded to provide a wide range of contamination control products and services.

Much of the information provided in this book is therefore based on practical experience gained in operating our own cleanrooms and in supplying services to a wide range of industries throughout the world, each with their own specific contamination control requirements and challenges.

The **'Microncleanan Big Blue Cleanroom Handbook'** is divided into self-contained sections which provide the reader with readily available and practical information on specific topics. It is hoped that this will be of benefit in helping to address the technical and financial problems routinely posed by complex contamination control requirements.

We would welcome any comments and can be contacted by email at: **bigblue@microncleanan.co.uk**

About the authors

Neil Clayton trained as a Biomedical Scientist and worked in Medical Microbiology for 10 years before moving to Science Education. He has worked for Microncleanan since 1991 in a variety of Technical, Commercial and Training roles.

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We would also like to thank Microncleanan staff for their help, comments and suggestions during the writing of The Big Blue Cleanroom Handbook.

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1.0 The Cleanroom Environment

1.1 A Brief History of Cleanroom Development

The increasing complexity and precision of some manufactured products has led to the requirement for contamination control techniques and associated systems.

The potential for damage to complex products by environmental contaminants, introduced during manufacture, was first identified as a significant problem during the Second World War. It was realised that the cleanliness of the manufacturing environment had to be improved to prevent damage to and malfunction of precision products such as airplane bombsights.

Development of nuclear, chemical and biological weapons also required the control of very small particles and the High Efficiency Particulate Air filter (HEPA filter) was developed to meet this need.

The HEPA filter was fundamental to the first industrial cleanrooms which were constructed in the 1950s, supplying clean air to the manufacturing areas and achieving low airborne contamination levels for the manufacture of precision components such as missile gyroscopes. These early types of cleanroom were non-unidirectional airflow (or turbulent airflow) cleanrooms.

Early cleanroom manufacturing

The development of controlled production environments into the modern cleanroom concept was accelerated by the space race in the 1960s.

The photograph shows the first Horizontal Laminar Flow Bench owned by the United States Air Force (Circa 1962). Dr Philip R. Austin is seen carrying out experiments to determine how cleanroom clothing affected operations within the workbench. Photograph reproduced with the kind permission of Dr. Philip R. Austin.

Rocket engines were found to have failed when liquid oxygen release valves jammed due to contamination by microscopic dust particles during assembly and space project-engineers are credited with the development of unidirectional airflow cleanrooms (often referred to as laminar airflow) as a solution to this major problem.

This new approach to contamination control provided an airborne cleanliness level that was over 1000 times cleaner than that achievable with the earlier non-unidirectional airflow cleanroom and continues to provide a major method of contamination control to this day.

The rapid global development of microelectronics and ever decreasing circuit geometry has led to the introduction of very large cleanroom manufacturing sites with emphasis on the control of sub-micron size particulate, electrostatic and chemical contaminants.

Developments in modern health-care products have led to the global use of very closely-controlled and regulated Pharmaceutical and Biomedical cleanroom manufacturing facilities.

Health-care cleanrooms not only provide control of environmental particulates and fibres but also have additional emphasis on the monitoring and control of microbiological contamination.

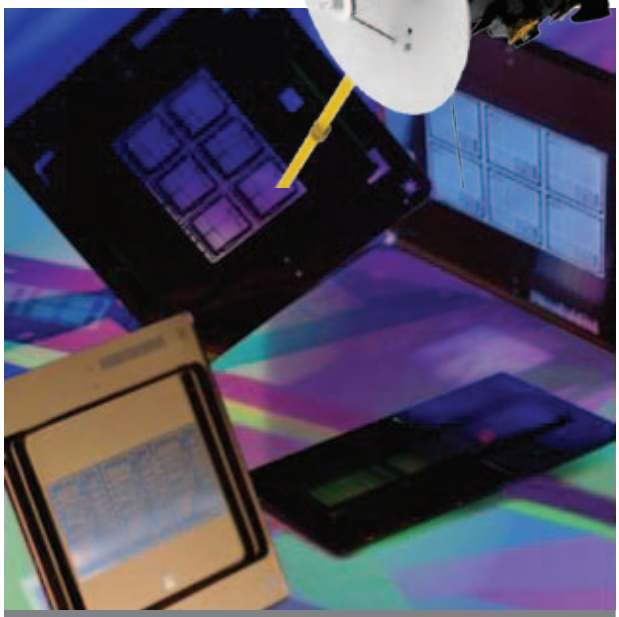
These types of facilities have incorporated the aseptic techniques and sterilisation processes, developed since the early 1900s within hospital operating theatres, into industrial cleanrooms.

Standard procedures include the use of protective garments for personnel and the sterilisation of critical components prior to transfer into the cleanroom areas. Specialised working techniques and manipulations, such as avoiding working directly above any cleanroom products, became the established operational procedures.

Cleanrooms are now widely used throughout the modern world for the manufacture of a vast range of products, such as electronics and semiconductor devices, nanotechnology products, medicines, medical devices, paint and surface finishes, optical devices, food and drinks.

Cleanroom manufactured industrial products

Cleanroom manufactured space and communication products



Cleanroom manufactured microelectronic products.
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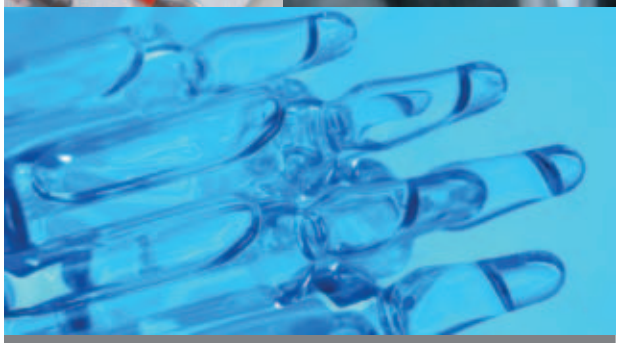


Cleanroom manufactured medical products

Throughout the period of cleanroom development various National and International Standards, Guidelines, Test Methods and Recommended Practices have been introduced and subsequently updated and these are discussed in Section 2.0 *Cleanroom Classifications and Standards.*

1.2
Cleanroom Design and Construction

A cleanroom is designed, constructed and maintained to provide a production environment which minimises the potential for damaging contamination of product. The type of product and the degree of control required to protect the product are therefore the most critical factors in determining cleanroom specifications. In general, simple room shapes allow for the most effective airflow patterns and facilitate effective cleaning and so to meet these requirements, most cleanrooms are box-shaped without overhanging obstructions.

A cleanroom works by controlling the introduction and entry of particles into the room and also controls the generation and retention of particles within the room. High volumes of filtered air are supplied to the cleanroom to dilute and remove contamination and to pressurise it to prevent the entry of less clean air from adjacent dirtier areas. The cleanroom is constructed with materials that do not themselves generate particles and can be readily cleaned to remove deposited contamination. Personnel who enter the cleanroom are a great source of particle contamination and are required to wear appropriate cleanroom clothing to minimise this risk. (The effect of people and the use of contamination control clothing are discussed in detail in Sections *3.0 Contamination Control and Staff* and *4.0 Reusable Contamination Control Clothing*.)

Control of environmental factors such as temperature and relative humidity may also be required.

Non-filtered air varies greatly from location to location and also varies over the course of time.

This occurs because a vast quantity of particulate matter, from many sources and of varying sizes, is generated by natural events and human activity and most of these particles are invisible to the unaided eye.

Collectively, airborne particulate material is often referred to as *'dust'* and as microscopic particles remain suspended in air, or fall only slowly under gravity, they can travel great distances.

Airborne particles

Airborne particulate matter is composed of two distinct types:
a) Inert particles and fibres which can be damaging to products either physically or chemically.
b) Micro-organisms, also know as viable particles.

Micro-organisms not only compromise product by physical and chemical damage but also present a unique threat to biomedical products by their ability to grow and multiply. This may lead to products being contaminated by harmful exotoxins and endotoxins, such as pyrogens, which can remain active even if the viable micro-organisms are destroyed.

Particles of concern to precision manufacturing facilities usually range in size from approximately 50 micrometres (microns) down to sub micron *'superfine'* particles and HEPA filters and ULPA filters (Ultra Low Particulate Air filter) are used as the principle control method of these airborne contaminants.

The number and type of filters used will therefore be a critical factor in the cleanroom design and an increase in air filtration will produce a reduction in airborne particulate.
Put simply; **More filtration = Less contamination**

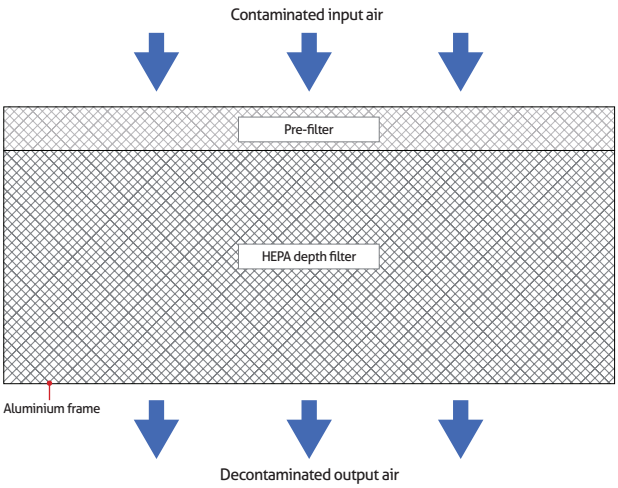


Diagram of HEPA Filter

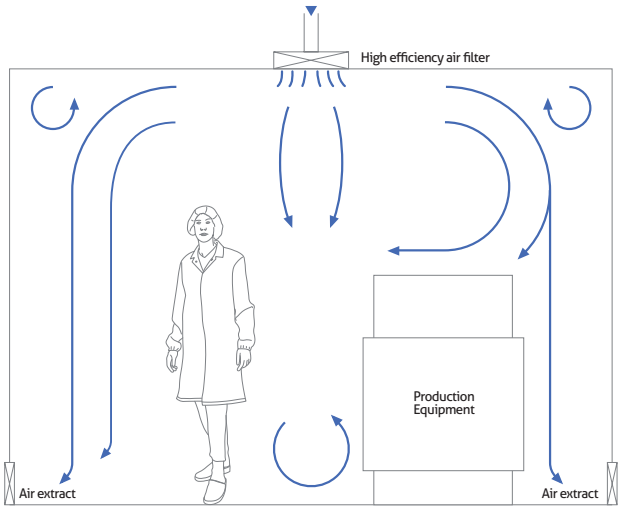
Airflow

The rate of airflow through the filters and through the cleanroom is also a significant factor in removing particles generated within the room with a greater number of air changes producing higher cleanliness levels and so this too is determined by the degree of contamination control required.

Non-unidirectional or Turbulent Airflow

Non-unidirectional airflow cleanrooms work by mixing and diluting the contamination generated within the cleanroom with filtered supply air.

The filtered air is normally supplied at ceiling level and extracted via ducts at low level located around the cleanroom, or it may simply escape through the door gaps to the adjacent areas. In general, the higher the rate of supply air and the better the mixing within the cleanroom, the higher the attained airborne cleanliness levels. The number of room air change rates per hour (ACH) is often measured to provide some information relating to the airborne cleanliness levels. This type of cleanroom provides a basic level of contamination control suitable for a number of less critical activities such as the manufacture of pneumatic equipment, optical components, basic wound dressings, or circuit assembly.

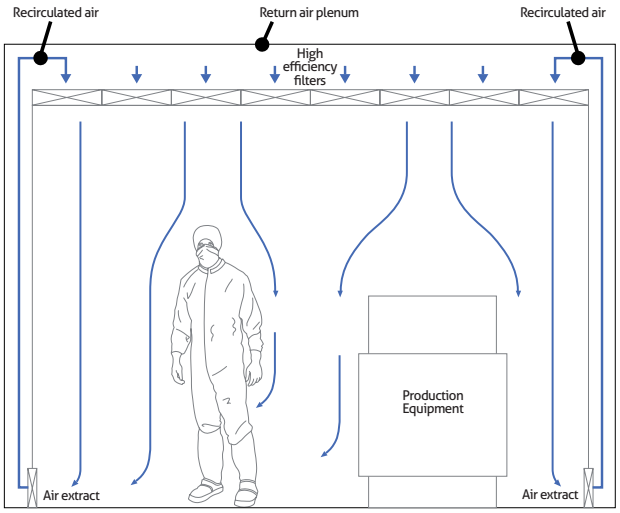


Non-directional or turbulent airflow cleanroom

In many facilities however more stringent control is required and unidirectional airflow is used.

Unidirectional Airflow

Unidirectional (or laminar) airflow is achieved by constructing the room so that the air supply is from a complete coverage of HEPA filters. Air from the filters passes through the room in a continuous one-way airstream at a uniform velocity.



Unidirectional airflow cleanroom

This airflow provides a 'piston' of air that flows down through the room, effectively removing particulate material generated within the area through room extract vents and by re-circulation through the filters via return air plenums incorporated into the cleanroom structure. Air re-circulated in this way typically makes up around 80% of air within the room with the remainder being made up of fresh air.

Unidirectional flow gives a continuous purging effect which can be improved by increasing the velocity of airflow; often measured as the number of air changes per hour (ACH) in the cleanroom. In general, the higher the airflow velocity, the better the airborne operational cleanliness levels.

Unidirectional airflow is most commonly arranged to pass from ceiling mounted filters to floor-level return-air plenums and the most effective flow is achieved by incorporating a perforated floor providing unidirectional flow right through the full height of the cleanroom. This configuration is referred to as vertical unidirectional airflow and contaminants being liberated into the room are purged downwards and out by this flow.

For some production processes however it is preferable to have airflow which purges the cleanroom horizontally and this is achieved by wall-mounting the filters and siting the return air ducts in the opposite wall.
This airflow across the room produces a horizontal unidirectional airflow cleanroom.

Unidirectional airflow cleanrooms are used for the manufacture of products requiring the highest level of contamination control such as injectable medicines and integrated circuits.

Horizontal unidirectional airflow cleanroom

Vertical unidirectional airflow cleanroom

Product and People Flow

When contemplating design of a new cleanroom or modification to existing facilities, product flow and people flow are of major importance.

Many products will require multiple components and process stages and the workflow should provide the most efficient production route whilst ensuring that the different production stages are carried out with appropriate levels of contamination control.
This will often mean considering the removal of component packaging or containers, primary preparation stages, final manufacture or assembly, primary packaging, labelling and final packaging.

For any grade of cleanroom best practice advocates a single process flow of product, with entry at one end and exit of finished product from the opposite end of the facility. This helps to manage the various stages of the process and to control component segregation and the risk of cross contamination. Separate entrances to segregate personnel from components are recommended with separate exits for finished product.

Staff numbers and activities must be carefully considered as they will have the most significant effect on the in-use cleanroom contamination levels and the people effects are discussed in more detail in Sections *3.0 Contamination Control and Staff* and *4.0 Reusable Contamination Control Clothing*.

The number and type of changing rooms required will be a critical factor in cleanroom design with several consecutive changing rooms, each at an increased level of contamination control, providing the highest standard.

For a high grade cleanroom manufacturing operation, personnel entry into the cleanroom area would typically utilise a two or three stage entry system.

The first stage would be to change from normal clothing into dedicated plant attire. Further entry into the cleanroom area would involve the application of specialist cleanroom garments which have been decontaminated by a cleanroom garment decontamination plant and may also have been sterilised.

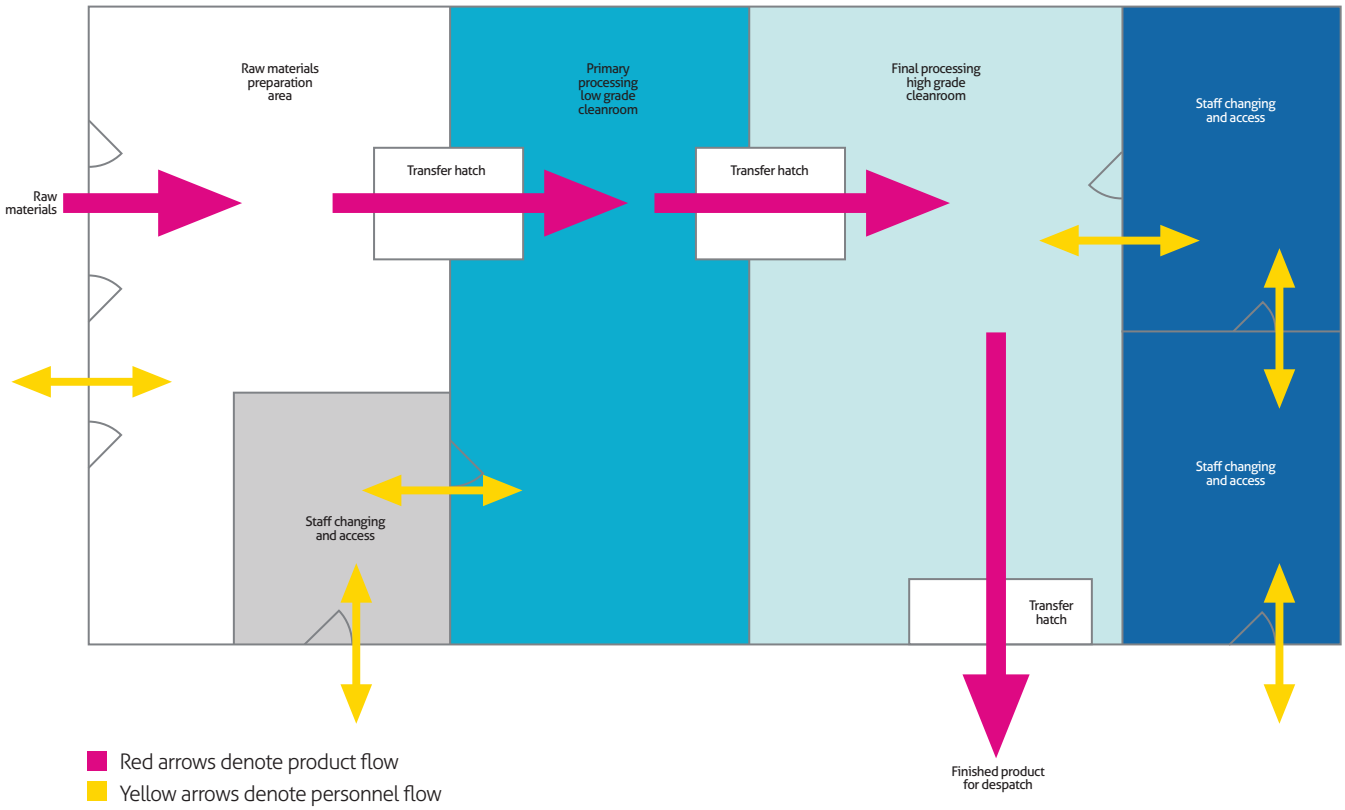


Diagram showing product and personnel flow in a typical cleanroom manufacturing process.

1.3
Materials, Fixtures, Fittings and Construction - Points to Consider

Selection of cleanroom construction and materials will depend on the level and type of contamination control required, speed of construction, lifespan and cost.

Cleanroom areas can be quickly and inexpensively constructed using various systems such as PVC strip curtains, softwall enclosures or portable structures. Modular rooms can be constructed within existing structures or complete design and build can be undertaken.

For any cleanroom where control of microbiological contamination is the main requirement all materials of construction and cleanroom surfaces must be smooth, impervious, non shedding, durable and laid to an even surface. Surfaces need to be readily cleanable, resistant to cleanroom disinfectants and not contribute any cleanroom contamination. All joints must be airtight and well sealed and horizontal surfaces should be avoided to reduce the accumulation of contamination.

As angular corners are difficult to clean effectively the interface of the floors, walls and ceilings needs careful consideration and the use of coved and rounded corners is usual.

Cleanroom Wall and Ceiling Interfaces

Common materials of construction for walls, floors and ceilings include sheet vinyl, epoxy screed, terrazzo (epoxy resin binder) epoxy paint on plaster, glass reinforced plastic, plastic-coated metal, stainless steel, powder coated steel with suitable enamelled paint and other synthetic materials such as *'Trespa'*, and *'Melamine'*.

Cleanroom wall and ceiling interfaces with coved and rounded corners

Floors that are subject to wetting may need to have a slip-resistant finish and other areas that are subject to heavy equipment and abrasion may require especially durable materials.

If ESD (electro-static discharge) control is important then materials must be used which will facilitate this requirement. This may require electrically conductive materials and fittings such as earthing points and conductive flooring together with additional equipment such as ceiling mounted de-ionisers.

Communication to personnel within the cleanroom is an essential requirement. Any intercom system should be of hygienic design, flush-mounted and easily cleanable. Window-mounted speech panels are also used but conventional telephones should be avoided in high grade areas as they are difficult to clean and require significant handling,

Where possible cleanroom windows should be non-opening, flush-fitting and double-glazed and any sills need to be steeply sloped. The windows need to be pressure tested to withstand the room differential pressures and should provide good visual access to permit supervision and observation of cleanroom activities.

Cleanroom window with rounded corners

Hatches and entrance doors are an important mechanism for the transfer into the cleanroom of staff, consumables and components and for the exit of finished product and waste.

Doors should not be opened simultaneously and should be controlled by an interlock system with visual and or audible alarms to alert personnel of loss of pressure or the simultaneous opening of both sets of doors.

Drains and sinks are normally excluded from aseptic cleanroom areas due to their high risk of contamination from water borne organisms.

Open drains should not be used in cleanroom areas where water is required. If drains are fitted to equipment such as washing or cleaning units air breaks are utilised between the outlet pipe and the drain to prevent back siphoning of soiled water.

Services

Where possible, all services should be run outside the cleanroom with minimal equipment or pipework inside the cleanroom. This reduces cleaning problems and allows maintenance activities to be completed without entering the cleanroom.

It is bad practice to run water and steam pipes directly above the cleanroom in case they develop leaks that can then seep into the cleanroom below. Welded pipe joints are more hygienic and the preferred choice, especially for water systems.

Cleanroom lighting should be flush fitting with the ceiling to aid cleaning and be fitted to permit the changing of defective tubes from above the cleanroom, thus preventing unnecessary cleanroom maintenance activities.

Cleanroom plant room

Wherever possible, plant rooms should not be included into the cleanroom but accommodated in an adjacent area and the services piped in or supplied accordingly. This minimises cleanroom disruption and enables easy access for maintenance activities.

Furniture and equipment provided must also meet contamination control requirements and stainless steel is often used to manufacture these items.

Stainless steel cleanroom equipment

Stainless steel cleanroom equipment
Image courtesy of Medical & Scientific Structures

Cleanroom barrier isolator. Image courtesy of Bioquell UK Ltd

Any non-shedding materials may be used however as long as they are not producing or harbouring particulate contaminants and can be easily cleaned.

For safety and compliance monitoring continuous particle monitoring systems may be required for high grade cleanrooms together with the use of CCTV.

Health and Safety issues must also be addressed and especially the provision for fire detection and emergency exits for cleanroom staff.

Specialist cleanroom construction and equipment companies provide a valuable source of information and services to suit all applications and requirements.

1.4 Barrier Isolators, Laminar Airflow Cabinets and Biological Safety Cabinets

Barrier Isolator

A barrier isolator is an enclosed space supplied with filtered air which provides effective isolation of its interior from the surrounding environment.

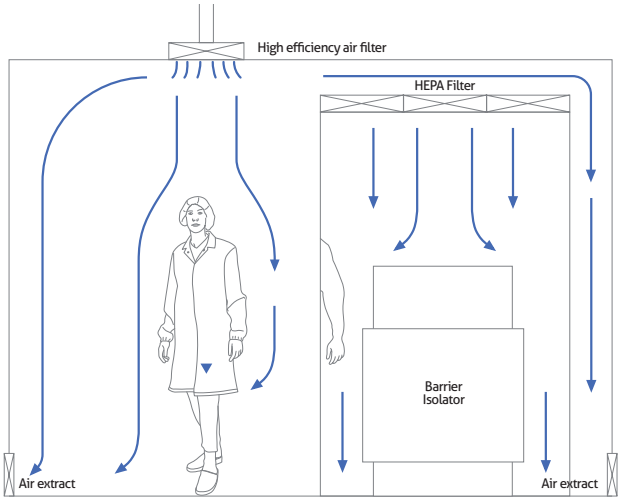
This means that by installing a barrier isolator, cleanroom conditions can be obtained within a contained workspace.

Barrier isolators (also called a unidirectional airflow workstation) provide a controlled environment with work occurring inside a closed, pressurised cabinet accessible only via sealed gloves that reach into the work area.

It is common to find a low-grade unidirectional or non unidirectional airflow cleanroom in which there is also a unidirectional airflow workstation. The workstation provides a working zone of high environmental control, or 'critical' area where open product or components are manipulated or processed. The lower grade controlled background environment helps to minimise the transfer of contamination into the critical area.

Many different types of Isolator are produced with different configurations of docking device which allow components, materials and products to be transferred in and out of the Isolator.

Isolators are frequently used for aseptic compounding of drug products and can often be internally sterilised e.g. using hydrogen peroxide vapour.



Barrier isolator inside a low grade cleanroom

Laminar Airflow Cabinet

Laminar air flow cabinets (often called LAF or clean benches) are designed to create a particle-free working environment usually within a classified cleanroom.

Air is taken through a filtration system comprised of a pre-filter and one or more HEPA filters and then exhausted across a work surface in a laminar or unidirectional air stream.

The laminar flow cabinet creates a very clean zone for many manufacturing operations in the medical, electronic and industrial sectors.

Laminar airflow cabinet

Laminar flow enclosures can also be made to any size and are commonly used to provide increased contamination control zones over local areas of large automated operations e.g. the aseptic filling zone for ampoule manufacture.

Biological Safety Cabinets

Biological safety cabinets are used to provide primary containment when using potentially infectious or harmful materials e.g. cytotoxic drugs. There are three types.

Class I

An open-front negative pressure cabinet where the exhaust air from the cabinet is filtered by HEPA filter.

Class II

An open-fronted ventilated cabinet with a HEPA-filtered, recirculated airflow within the work space. The exhaust air from the cabinet is also HEPA filtered.

Class III

A totally enclosed ventilated cabinet of gas-tight construction. Operations within the Class III cabinet are conducted through attached rubber gloves.

Supply air is drawn into the cabinet through HEPA filters and the exhaust air is passed through two HEPA filters before discharge outside of the production area.

SECTION

2.0

Cleanroom Classifications & Standards

2.1 Cleanroom Particulate Standards and Classifications

A Brief History

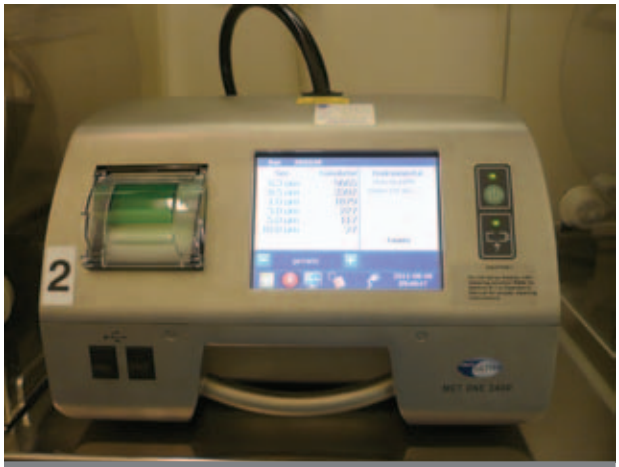
As cleanroom technology was established it became necessary for standards to be produced which would enable users to specify and monitor the levels of contamination control required for particular manufacturing operations.

Introduction of standards allowed manufacturers to understand the effects of different cleanliness levels on product contamination and this in turn led to the development of new and improved cleanroom systems. The use of clear standards also allowed customers for cleanroom products to agree and confirm conditions of product manufacture and provided assurance on the levels of contamination control maintained throughout the production process.

The first cleanroom standard was US Air Force Technical Order 00-25-203 which was written in 1961. The USAF built many cleanrooms throughout the world and initially air sampling was achieved using membrane filters which were then read under a microscope and recorded as particles at the 5µm particle size.

Royco instruments, working with the Armour Foundation, then produced the first vacuum tube particle counter, using a white light source, with channel sizes ranging from 0.3µm to 10µm. The wavelength of white light is in the range 0.3µm to 0.4µm and so particle counts at this size were not very accurate and because of this limitation 0.5µm was chosen as the smallest reliable channel. These two particle threshold limits are stated in a number of current cleanroom standards, particularly those associated with healthcare activities.

Particle counters were installed in the USAF cleanrooms all over the world and subsequently the particle size distributions were determined from hundreds of samplings within the cleanrooms.



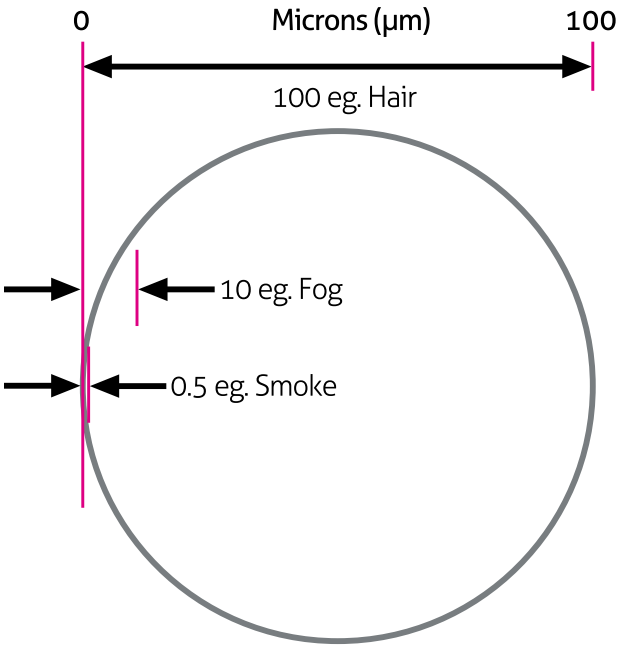
Electronic particle counter

High values and low values were recorded and the data was averaged and used in TO 00-25-203 to specify USAF cleanroom airborne cleanliness conditions for particles 0.5µm/ft^3 at class 1,000 and class 10,000. Laminar (unidirectional) airflow benches and cleanrooms were then developed and USAF class 100 was additionally defined and included in the standard. Word of TO 00-25-203 spread and industry started specifying cleanrooms for civilian applications. Eventually TO 00-25-203 was moulded into a new document - Federal Standard 209[ref1] which was published in 1963.

As cleanroom technology came to be used internationally countries throughout the world also produced their own National standards and these included British Standard 5295[ref2] in the UK.

Particulate Classifications

Airborne cleanliness levels are determined by counting the number of particles, at a defined threshold diameter, in a determined volume. The unit of measure of such particles is the micrometre (µm) or micron and 1 µm is a millionth (1×10^{-6}) of a metre. Typically, the smallest visible particle on a surface is approximately 50µm in diameter, fog particles are 10µm in diameter and a human hair has a diameter of approximately 100µm.



Relative particle sizes

Federal Standard 209

The first available and most readily understood standard was Federal Standard 209 (1963) which recorded cleanliness levels by considering the number of particles ≥0.5 µm per ft^3. This simple classification system, with some appropriate types of cleanroom operations, is shown below.

Federal Standard 209 (1963) Cleanroom Classification System

FS209 (1963) Classification	**1**	**10**	**100**	**1000**	**10000**	**100000**
No. of Particles/ft3 ≥0.5µm	1	10	100	1000	10000	100000
Cleanroom Manufacturing Operations	Integrated Circuit	Semi conductor	Injectable medicines	High quality optical equipment, Gyroscopes	High grade gearing, precision pneumatic equipment	General optical work, assembly of electronic equipment

Several changes to FS 209 were made over the years and the final version FS209E, utilised metric nomenclature i.e. particles per m^3 ($1\ m^3 = 35.2\ ft^3$). Consequently, 100 particles per ft^3 became 3520 particles per m^3.

With the rapid increase in the global use of cleanrooms for the production of pharmaceutical products and microelectronic devices the requirement for an agreed international standard became apparent and International Standard ISO 14644[ref 3] was developed.

ISO 14644 contains nine separate parts with ISO14644-1 published in 1999 followed by ISO 14644-2 in 2000. The issue of the first two parts enabled National standards to be replaced with the new International standard and Federal Standard 209E was withdrawn in November 2001.

The nine separate parts of ISO 14644 are shown below

ISO 14644-1:	Classification of air cleanliness
ISO 14644-2:	Specifications for testing and monitoring to prove continued compliance with ISO 14644-1
ISO 14644-3:	Test Methods
ISO 14644-4:	Design, Construction, and Start-up
ISO 14644-5:	Operations
ISO 14644-6:	Vocabulary
ISO 14644-7:	Separative devices (clean air hoods, gloveboxes, isolators and mini environments
ISO 14644-8:	Classification of airborne molecular contamination
ISO 14644-9:	Classification of surface particle cleanliness

The whole standard provides a comprehensive source of information and specifications for all aspects of cleanroom design, construction, classification, operation and monitoring.

ISO 14644 allows the user to specify the particle size to be counted and to calculate the ISO classification from the number of particles measured.

This differs in its approach from the original National standards which specified specific particles sizes to be counted.

The standard also requires the ISO classification to be described as 'at rest' or 'in use' to differentiate between the performance of the room as built and the contamination levels which exist whilst manufacturing operations are taking place.

Using ISO 14644-1cleanrooms are classified as ISO Class 1 to ISO Class 9.

ISO 14644-1 airborne particulate classes for cleanrooms and clean zones at the particle sizes given

ISO Classification Number	Maximum concentration limits (particles/m³ of air) for particles equal to and larger than the considered sizes shown below					
	0.1µm	**0.2µm**	**0.3µm**	**0.5µm**	**1µm**	**5µm**
ISO 1	10	2				
ISO 2	100	24	10	4		
ISO 3	1,000	237	102	35	8	
ISO 4	10,000	2,370	1,020	352	83	
ISO 5	100,000	23,700	10,200	3,520	832	29
ISO 6	1,000,000	237,000	102,000	35,200	8,320	293
ISO 7				352,000	83,200	2,930
ISO 8				3,520,000	832,000	29,300
ISO 9				35,200,000	8,320,000	293,000

The ISO Cleanroom Classification number compared to the Federal Standard 209 and British Standard 5295 (both now deleted) is shown below.

Table showing relationship between cleanroom standards

ISO Classification Number	US FED 209E (D)	BS 5295
ISO 1		
ISO 2		
ISO 3	M1.5 (1)	'C'
ISO 4	M2.5 (10)	'D'
ISO 5	M3.5 (100)	'E' or 'F'
ISO 6	M4.5 (1,000)	'G' or 'H'
ISO 7	M5.5 (10,000)	'J'
ISO 8	M6.5 (100,000)	'K'
ISO 9		

2.2 Cleanroom Microbiological Classifications and Standards

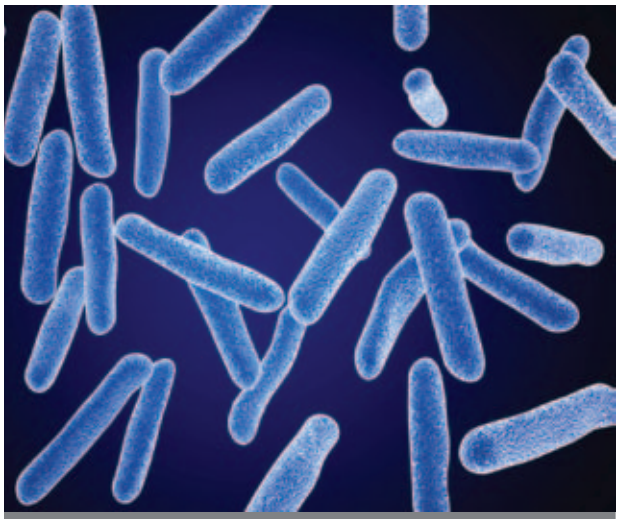
A Brief History

Early cleanroom development was concerned with the control of all contaminating particles and no differentiation was made between inert, non-living particles and viable particles such as bacteria and fungi and this was the basis of all cleanroom standards. This approach is completely appropriate for the manufacture of non-medicinal products as product damage is caused purely by the physical presence of a particle.

The use of cleanroom technology was rapidly adopted however as an excellent environment for the production of medicinal and other bio-medical products. These products are used within living systems and so are especially vulnerable to contamination by the inclusion of viable particles (micro-organisms).

In Pharmaceutical manufacture contamination control technologies were found to be especially beneficial in the production of medicinal products which cannot be sterilised after production, requiring aseptic techniques to produce safe, contamination-free products.

In order to estimate the levels of viable particles present and to establish the control levels required, microbiological monitoring systems were introduced into these manufacturing areas.



Magnified image of bacterial cells

The MHRA (Medicines and Healthcare products Regulatory Agency) Rules and Guidance for Pharmaceutical Manufacturers and Distributors [ref 4]

This important publication is also know as "the Orange Guide" and was first published in 1971. It provides information on the pharmaceutical regulations, directives and guidance for the manufacture and distribution of medicinal products in the European Union. Part of the guide deals with the classification of different manufacturing environments and assigns grades A, B, C, D.

These classifications combine a particulate standard, based on particulate sizes of ≥0.5 µm and ≥5µm and recommended microbiological limits. The microbiological limits are based on active air sampling, settle plate, contact plate and operator glove print test methods.

The table below shows the 'Orange guide' GMP Grades and limits for microbiological contamination.

MHRA recommended limits for microbial contamination (a)

Grade	air sample cfu/m³	settle plate (diam. 90mm) cfu/4 hours (b)	contact plate (diam. 55mm) cfu/plate	glove print 5 fingers cfu/glove
A	<1	<1	<1	<1
B	10	5	5	5
C	100	50	25	-
D	200	100	50	-

Notes: (a) These are average values
(b) Individual settle plates may be exposed for less than 4 hours.
cfu = colony forming unit

Table reprinted with the permission of MHRA.

The US aseptic processing guide is a further source of information.

ISO 14698 [ref 5] - Cleanrooms and associated controlled environments - Biocontamination control

This International standard was published in 2003 and is in 2 parts:

Part 1 General principles and methods.
Part 2 Evaluation and interpretation of data.

ISO 14698 does not suggest specific microbiological levels associated with cleanroom classifications but instead gives comprehensive information on establishing and maintaining a rigorous and meaningful microbiological test programme.

Recording and interpretation of results, the setting of action, alert and target levels and trending of data for assessment are also discussed in detail.

2.3 ESD Requirements and Standards

Control of electro-static discharge (ESD) is critical in any manufacturing area where products may be damaged by static discharge or where a fire risk is present. High-grade surface finishing operations may also require ESD control.

Fabrication of electronic devices and the assembly of medical devices are the main cleanroom manufacturing operations which most often consider this hazard.

ESD controlled area

BS EN 61340 [ref 6] - Protection of electronic devices from electrostatic phenomena, gives details of how to create an ESD protected area of manufacture (EPA). It contains guidance on the requirements for anti-static clothing including garments for cleanroom use.

BS 6524 [ref 7] British standard method for the determination of the surface resistivity of a textile fabric.

ESD testing of cleanroom clothing

This method is appropriate for the testing of all cleanroom clothing which has anti-static properties.

The RP gives details of the Helmke drum test which may be used to determine the particle emission rate from cleanroom clothing and as such can be used as a process measure for garments which have been processed by a cleanroom decontamination plant.

Helmke drum test on garment

2.4 IEST-RP-CC003 [ref 8]

The Institute of Environmental Sciences and Technology Contamination Control Division have produced a Recommended Practice 003. This is currently published as IEST-RP-CC003.3 Garment System Considerations for Cleanrooms and Other Controlled Environments.

This document addresses the gowning of personnel as an important aspect of cleanroom contamination control and gives guidance on the selection, specification, maintenance and testing of clothing for use in aseptic and non-aseptic cleanroom conditions.

Garment cleanliness classifications are described for Category I, II and III and are shown below.

IEST-RP-CC003 Garment cleanliness classifications

Category	Garment Type	0.3µm particles and larger/min	0.5µm particles and larger/min
I	I Frock	<1700	<1000
I	1 Coverall	<2000	<1200
I	3 Hoods	<780	<450
II	I Frock	1700 to 17000	1000 to 10000
II	1 Coverall	2000 to 20000	1200 to 12000
II	3 Hoods	780 to 7800	450 to 4500
III	I Frock	17000 to 170000	10000 to 100000
III	1 Coverall	20000 to 200000	12000 to 120000
III	3 Hoods	7800 to 78000	4500 to 45000

A test method is also described which may be used to determine the penetration of microbes through cleanroom fabrics.

2.5 ASTM F51/00 [ref 9]

The American Society for Testing and Materials (ASTM) method F51/00 covers the determination of detachable particulate contaminants 5 micrometres (µm) or larger in and on the fabric of cleanroom garments.

As this is a microscopic test method, fibres are separately identified and defined as particles longer than 100 µm and with a length-to-width ratio exceeding 10:1.

ASTM F51/00 particulate test, removal of particles and microscopic evaluation

Garment classifications for decontaminated garments are given for Class A, B, C, D, and E.

This test method may be used as a process measure to determine the cleanliness of garments processed by a cleanroom decontamination plant.

Garment cleanliness classifications given by ASTM F51/00 are shown below.

ASTM F51/00 Garment cleanliness classifications

Class	Maximum particles 5µm or greater/ 0.1m² fabric	Maximum fibres/ o.1m² fabric
A	999	10
B	4999	25
C	9999	50
D	14999	125
E	25000	175

Table reprinted with the permission of ASTM International.

2.6

BS EN 14065:2002 [ref 10] Textiles - Laundry Processed Textiles - Biocontamination Control System

The standard provides the basis for a management system for effective biocontamination control in laundries, particularly those serving end-users such as food processing and healthcare. The standard has been developed using the principles of a Risk Analysis and Biocontamination Control (RABC) system which is closely analogous to Hazard Analysis Critical Control Point (HACCP) systems.

SECTION

3.0 Contamination Control and Staff

3.1 The Effect of Staff

A correctly designed and functioning cleanroom is extremely efficient in controlling contamination when at rest. In most operational instances however people are required to be present in the room to carry out production processes.

Cleanroom production

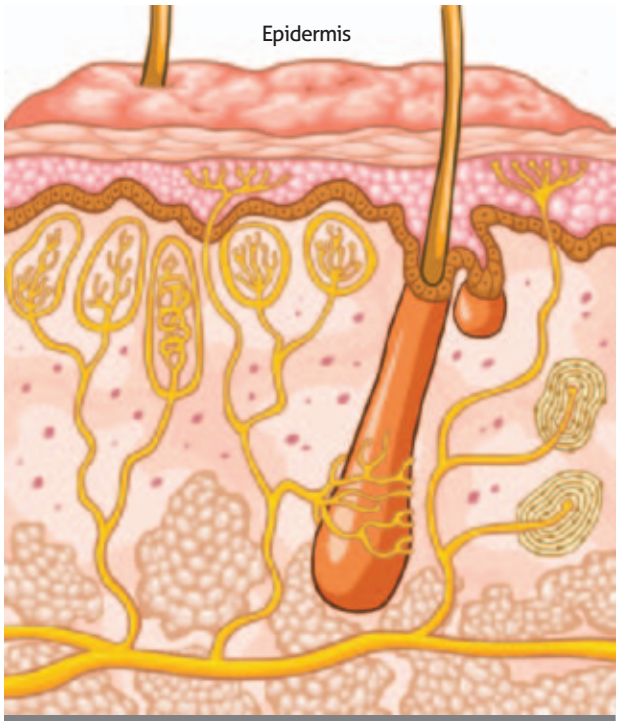
The presence of staff poses a major contamination control challenge to the cleanroom as people produce large numbers of both inert and viable particles with 80% of the contamination found within most operational cleanrooms estimated to be produced by the occupants.

This "people contamination" comes from two main sources.

The first and major source of particulate comes from the skin which is the largest organ of the body, with a surface area of around 1.5m^2.

Its two main layers are the epidermis (outer layer) and dermis (inner layer) and part of the normal physiological function of the skin is to continuously shed the surface layer in a process know as desquamation. Everyday, each person sheds their epithelial skin layer of approximately 10^9 skin cells.

In this process the dead, dry cells of the epidermis form skin scales which break off and leave the body surface, especially when rubbed or abraded by clothing.
This skin debris leaving the body may be individual cells or large rafts of cells, typically 5 to 60 micrometres in size.

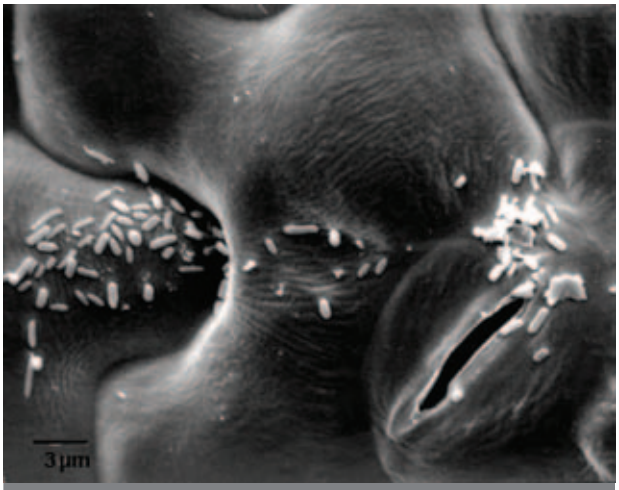


Cross sectional diagram of human skin

The cell fragments may be further broken down into much smaller particles by abrasion with clothing, the rubbing together of skin surfaces and break-down caused by movement in air currents.

The normal microbial skin flora, which may include potential pathogens such as *Staphylococcus aureus*, will also be present on this cell debris and viable micro-organisms will leave the body surface as a consequence of desquamation. Most micro-organisms found in cleanrooms are found in the air, rafted on particles of skin.

A healthy male can disperse to the air approximately 1000 bacterial cells per minute during active exercise with an average of around 200 cells per minute, females generally disperse less.



Micro-organisms on skin cells

Normal human physiology will therefore continuously produce significant quantities of both inert and viable particles; however age, health, activity and clothing will all have an influence on total dispersion.

The temperature differential between the wearer and environment also has a large impact on the actual number of particles liberated from the body into the cleanroom.

Normal room temperature is around 20°C and normal body temperature 37°C, this temperature difference generates warm-air convection currents which rise from the body surface into the cooler room air.
These rising convection currents carry with them large numbers of particles into the room air which disperse and normally fall by gravity (although in a unidirectional flow area the particles are purged from the room by the moving, filtered air-flow).

Physical activity also plays a significant role in particle dispersion and increased activity generates and liberates more particles. This effect often leads to restrictions on types of movement and staff activity within high grade cleanrooms.

Cleanroom clothing, including gloves and masks, are used to reduce the contamination being dispersed from the people wearing them. Cleanroom garments together with mask, goggles and gloves, providing full skin coverage for the wearer, will reduce the rate of microbial dispersion by a factor of approximately 20.

However when wearing high grade cleanroom clothing and moving slowly a cleanroom operator may still disperse approximately 1 x 10^5 particles > 0.5 µm per minute, 30,000 particles > 5.0 µm per minute and up to 15 microbe carrying particles per minute into the cleanroom.

If the same operator was wearing lower grade cleanroom garments, such as a cleanroom smock or laboratory coat, the rate of dispersion into the cleanroom could increase 10 fold.


High grade cleanroom clothing

Saliva contains a large number of micro-organisms and typically has a count of 10^7 bacteria per ml. Personnel can emit as many as 40,000 microbe carrying particles in a single sneeze. Well fitted face-masks are used to control this contamination risk.

Particle emissions during sneezing

The second source of particulate and fibre contamination introduced by staff comes from contaminants associated with the individual such as personal clothing, cosmetics, jewellery, hygiene and lifestyle.

Non-cleanroom clothing (often referred to as 'street clothing') is manufactured from fabrics designed to be comfortable, fashionable and functional. There is rarely a requirement to limit the production of particles or fibres from this type of clothing however, and non-cleanroom garments usually produce large numbers of both. This means that specialised low linting-barrier fabrics must be worn as an alternative to street clothing to eliminate this contamination control risk.

The frequency of cleaning and the cleaning methods used by staff for their clothing will vary considerably, adding additional loss of control for the cleanroom operator.

The design and fit of personal clothing will also have an effect on the shedding and dispersion of particles from the wearer. Tight abrasive clothing will generate more skin particles and garments with wide openings e.g. around the neck, will allow more particulate to escape.

Street clothing will also be contaminated by materials picked up during use and these will probably include fibres and particles from furniture, pets, vehicles, smoke etc.

Street clothing

For example a simple morning walk with a pet dog along a busy street will result in contamination of the wearer from a wide range of both viable and inert particles and fibres.

Without controls normal clothing can easily become a major source of clean area contamination, and the use of specially designed and constructed cleanroom clothing has been developed to control and minimise these contamination problems.

Many cosmetics produce particulate contamination and cleanroom staff are normally subjected to restrictions on the use of these products.

The wearing of jewellery also presents various problems and the loss of jewellery or metal fragments can seriously affect many cleanroom products and electronic components are especially sensitive to these contaminants.

Jewellery items also allow a build-up of dirt and micro-organisms and are difficult to clean effectively and may puncture or otherwise damage staff equipment e.g. cleanroom gloves.

These sources of contamination normally result in restrictions on the wearing of jewellery in cleanrooms however, where an item cannot be removed, it is usually covered with adhesive tape. Spectacles can also present a problem and it may be necessary to cover these with cleanroom goggles.

In lower grade clean areas where hoods and face masks are not required beards and moustaches may have to be covered and long hair controlled by hair nets and snoods.

Product handling in cleanroom.
Image courtesy of Photronics UK Ltd.

Cross contamination by staff can also occur through touching, sneezing and coughing with both inert particulate and viable micro-organisms being transferred to cleanroom clothing, surfaces and products.

Documented staff training in appropriate cleanroom behaviour together with a clear policy on reporting and assessing minor illness is usually required to reduce these contamination risks.

3.2 Entry and Exit Procedures

Entry and exit procedures should be developed to enable staff to enter a clean area in an efficient and timely manner without compromising the integrity of the cleanroom.

For a low grade cleanroom this may mean a simple one-stage change with staff donning perhaps a cleanroom coat, hat and overshoes in a single changing area attached to the production cleanroom.

Simple changing room

High grade cleanrooms used for aseptic pharmaceutical manufacturing will normally require entry through 2 or 3 separate changing areas, each at a higher classification than the first and with the third changing area at an equivalent classification to the production cleanroom.

High grade changing area

Staff entering such a facility are likely to need to remove all their street clothing and put on cleanroom undergarments as well as full cleanroom outer garments of coverall, boots, hood, mask, gloves and face cover e.g. goggles.

As the emphasis is on the control of micro-organisms exacting changing procedures will be required to minimise cross-contamination of the garments and this will be more critical than speed of entry.

For a microelectronics manufacturer large numbers of staff may need to quickly access the cleanroom but still require full cleanroom hood, suit, boots and mask. As these garments are likely to be changed on a weekly basis then clean air cabinets will be required for storage in the changing areas.

A check on the ESD performance of the clothing may be required on entry.

Grounding test station entry test

These variations in contamination control requirements together with the physical layout of the building mean that cleanroom entry procedures must be tailored to each application.

When designing a staff entry system the following key elements should always be considered;

a) *What degree of contamination control is required in the production area to be accessed?*

b) *What contaminants pose the main threat to the products being manufactured e.g. fibres, viable microbes, superfine particles, static discharge?*

c) *How many staff need to pass through the entry areas and do they need to be able to enter quickly?*

d) *Are separate male and female changing areas required?*

e) *How much storage is required for personal possessions and cleanroom clothing and where can it be conveniently sited?*

f) *If hand washing and hand sanitisation is required how and where can this be achieved?*

Exit procedures will also be required and in any areas where garments are not changed on entry, and so not discarded on exit, suitable storage points must be provided for each staff garment set.

Containers for used garments and disposable items must be provided and clearly identified and should be sited so that they do not increase the risk of cross contamination with clean items.

Emergency exit e.g. in the event of a fire alarm must also be planned.

3.3 Changing Areas

Changing areas are a key part of any contamination control facility and should be built and maintained to the same standard of construction as the cleanroom production area itself. This allows efficient cleaning and decontamination to take place in areas likely to receive periodic high levels of contamination from the staff passing through.


Well designed changing area.
Image courtesy of Medical & Scientific Structures

Whenever possible the changing rooms should be large enough to easily accommodate not only the staff but also the garment storage and discard equipment which may take up considerable space.

Simple stainless steel garment storage pegs

Basic garment storage and discard lockers

The changing areas should be maintained at positive air pressure and where several consecutive changing rooms are used in sequence e.g. a three stage change, then a pressure cascade should be maintained from the production area down through the changing areas. For multiple changing areas it is also usual to incorporate a system to alert staff if the adjacent room door is open e.g. a traffic light system.

Traffic lights above doors

As staff progress through a changing room they are donning cleanroom clothing and this normally includes some type of footwear.

Step-over benches are used to provide physical separation between the areas of floor where non-cleanroom footwear and cleanroom footwear is being used, with the cleanroom footwear being put on whilst the staff member is seated on the bench.

Vinyl step-over bench

These benches are often fixed but if the changing area is also used to allow transport of large items into the production area then the step-over bench may need to allow for this.

Mirrors are usually provided to allow staff to check their garments before entry to the cleanroom and contamination control mats are sometimes used to reduce floor contamination at critical points.

Hand washing facilities may be required but are normally confined to the lowest grade changing area with hand sanitisation often provided by alcohol hand-sanitiser dispensers.

Dispenser for alcohol hand sanitiser

3.4 Gowning Techniques and Changing Procedures

All gowning techniques and changing procedures should be kept as simple as possible whilst still maintaining the level of contamination control required by the production process.

Staff are required to use the gowning techniques several times each day and significant production time can be lost in large production areas if unhelpful protocols are introduced.

Unnecessarily complicated changing procedures can also lead to staff shortcutting the system increasing the risk of contamination.

If very strict and detailed changing procedures are required then staff will need comprehensive training and practice in gowning and will often be required to pass a formal assessment before being allowed into the production areas.

Thoughtful siting of changing equipment such as personal lockers, garment dispensers and hand sanitisers can add significantly to the ease and efficiency of the gowning procedure and mapping the flow of personnel through the system can assist in this.

Packaging and presentation of the cleanroom garments will also be a factor in developing area procedures with either individual garment sets provided for each wearer or a pool of sizes available for selection.

Occasional visitors to the production areas will also need to be considered and their requirements incorporated into the changing procedures

Types of garment and garment fastenings will also affect gowning techniques, a simple centre zip coat being easier to put on effectively than full cleanroom clothing incorporating undergarments, dedicated footwear, hood, boots, mask, goggles and gloves.

Typical cleanroom undergarments

If cleanroom undergarments are used it will be necessary to determine where these can be worn within the plant and many cleanroom manufacturing operations require staff to change into dedicated undergarments on entry to the building, only removing them on exit to outside.

Where multi-stage changing systems are required each changing area will need to be considered individually and specific gowning procedures will be required for each changing room.

Each cleanroom production facility is unique and it will therefore develop its own specific gowning techniques and changing procedures based on the contamination control requirements and plant layout.

As a general rule however changing procedures for each area should always indicate;

a) What garments should be worn.
b) Where garments may be worn.
c) In what order the garments should be put on.
d) How garments should be worn and fastened.
e) The requirements for hand sanitisation.

Staff changing procedures can be usefully displayed as posters in each area with visual guidance on the gowning techniques required.

Visual guidance for changing areas

3.5 Training Requirements

Staff training is a key contamination control measure for all cleanroom production units. Specific training will depend on the type of production and the degree of contamination control required however the following basic training should be provided for any staff working in controlled areas;

a) *The theory and requirements of contamination control systems and associated standards.*
b) *The effect of people on controlled areas.*
c) *Cleanroom clothing – purpose and function.*
d) *Gowning, entry and exit procedures.*

Additionally training in GMP, basic microbiology, effects of ESD and cleanroom cleaning may also be beneficial. Internal and external courses together with training from suppliers can provide various options and most benefit is usually obtained when courses are related to the specific working area and procedures of the trainees.

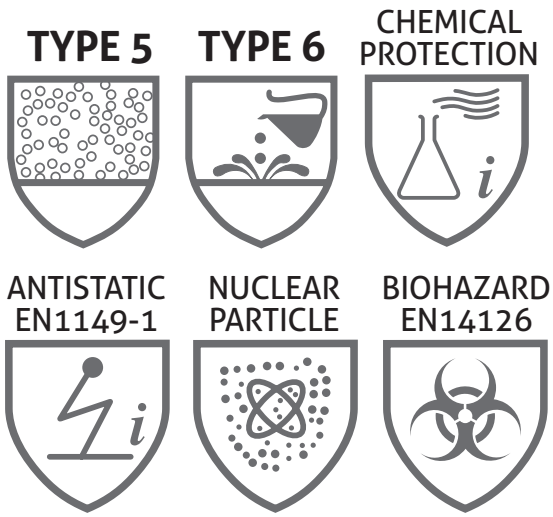
Staff training

For high grade cleanrooms staff are usually required to successfully complete a full and documented training programme and to pass a validation of gowning competence before being authorised to enter controlled areas. Individual staff training should be reviewed and repeated on a scheduled basis, usually annually.

3.6 Garment Systems and Changing Frequency

The level of contamination control required in the production area will largely determine the cleanroom clothing system to be used.

Cleanroom clothing acts as a mobile filter for the wearer and the basic rule is that more cover = more contamination control, however the use of more clothing layers will result in an increase in clothing costs and the time taken for gowning to access clean areas. For some production processes it may also be necessary to consider special requirements for cleanroom clothing e.g. chemical resistance, flame retardancy or water repellency.



Clothing protection symbols

The frequency of change of cleanroom clothing is also critical to effective control and different approaches have been adopted by bio-pharmaceutical and general industrial cleanrooms, reflecting the specific requirement for the control of viable contaminants in bio-pharmaceutical production.

In high grade bio-pharmaceutical cleanrooms it is usual to change outer garments on entry to the cleanroom with undergarments being changed daily. If goggles or captive footwear are in use then these are usually retained and sanitised on a regular basis.

For lower grade areas a daily change of outer garments and undergarments is usually appropriate.

In general industrial cleanrooms, including high grade areas producing microelectronic components, a weekly change of outer clothing is common with a daily change of items such as launderable masks, gloves and cleanroom socks if these are being used.

As these garments are retained for several days then they must be stored in conditions which minimise contamination and this is often achieved by using hanging space flushed with filtered air.

Some published guidance is available and The Institute of Environmental Sciences and Technology, Contamination Control Division, have produced a useful Recommended Practice; IEST-RP-CC003.3[ref 1]

This document addresses the gowning of personnel as an important aspect of cleanroom contamination control and gives guidance on the selection, specification, maintenance and testing of clothing for use in aseptic and non-aseptic cleanroom conditions.

It provides recommendations on the types of clothing appropriate for different ISO 14644-1[ref 2] classified areas and recommends change frequencies for these areas, as shown in the table below.

The MHRA publication Rules and Guidance for Pharmaceutical Manufacturers and Distributors [ref 3] also provides guidance on the type of clothing systems expected in pharmaceutical manufacture.

IEST-RP-CC003.3 clothing recommendations at different ISO classifications

Apparel Type	ISO 14644-1 Air Cleanliness Class						
	8 and 7	6	5	5 Aseptic	4	3	2 and 1
Inner suit	AS	AS	R	AS	R	R	R
Hair cover	R	R	R	R	R	R	AS
Woven gloves	AS	AS	AS	NR	NR	NR	NR
Barrier gloves	AS	AS	AS	R	R	R	R
Facial cover	AS	AS	R	R	R	R	AS
Hood	AS	AS	R	R	R	R	AS
Powered headgear	AS	AS	AS	AS	AS	AS	R
Frock	R	AS	AS	NR	N	NR	NR
Coverall	AS	R	R	R	R	R	R
Two piece suit	AS	AS	AS	NR	NR	NR	NR
Shoe cover	R	AS	AS	NR	NR	NR	NR
Boot	AS	R	R	R	R	R	R
Special footwear	AS	AS	AS	AS	AS	AS	AS
Frequency of change	2 per week	3 per week	Daily	Per entry	Per entry	Per entry	Per entry

Key: R = Recommended, NR = Not Recommended, AS = Application Specific.

Regulatory bodies, customer requirements and current industry practices will all provide guidance on the garment system and change frequency required for a particular manufacturing operation. Cleanroom clothing suppliers will also be able to provide advice and technical specifications on the various clothing products and options available.

These are discussed in further detail in Section 4.0 *Reusable Contamination Control Clothing*.

SECTION

4.0

Reusable Contamination Control Clothing

Contamination control clothing

4.1 Reusable Cleanroom Clothing - the Three Principal Requirements

Reusable cleanroom clothing has three principal requirements.

1. Reusable cleanroom clothing must act as an effective contamination control measure appropriate to the area where the clothing is in use. The clothing must control the loss of particulate from the wearer and additionally not itself provide a source of particulate or fibre contamination. Control of electro-static discharge (ESD) may also be an additional key requirement.

2. Reusable cleanroom clothing must be comfortable and practical for the wearer whilst providing a cost-effective contamination control solution for the specified manufacturing operation.

3. The environmental impact of reusable cleanroom clothing must be as low as possible throughout its life cycle.

These three requirements together form the basis of all processes involved with the manufacture, use and processing of cleanroom clothing.

4.2
Cleanroom Fabrics

Fabrics for cleanroom use

Barrier fabrics have been developed and continuously improved since the introduction of contamination control techniques in the 1960s.

Many different manufacturers of technical fabrics throughout the world have invested large amounts of time, effort and resource to produce the very effective contamination control textiles which are currently available.

The fabrics which have been developed for use in contamination control clothing are of 3 basic types.

a) *Woven.*
b) *Laminated.*
c) *Non-woven (which are largely used in disposable items and discussed in Section 5.0 - Disposable Contamination Control Clothing).*

Woven fabrics

Fabric weaving is one of the oldest human technologies dating back to at least 5000 BC. It consists of lacing together long vertical yarns (the warp) with horizontal yarns (the weft) to produce a sheet of fabric which may then be cut and joined to produce textile items.

Yarns, Fibres and Filaments

The yarns of many woven fabrics are produced by twisting together short staple fibres to form a continuous cohesive thread. A single yarn being called a single ply. These single plies may then be combined to form thicker yarns which become the weaver's warp and weft, woven together to produce the finished fabric

A common example of a class of fabrics produced in this way are the polyester and cotton mixtures, often called 'polycottons', extensively used in the manufacture of a whole range of textile items including clothing.

The choice and blend of materials used for the yarn, together with the type and tightness of the weave, influence the look, feel, comfort and strength of the final fabric and almost endless variations are possible, producing the astonishing range of woven fabrics we see daily.

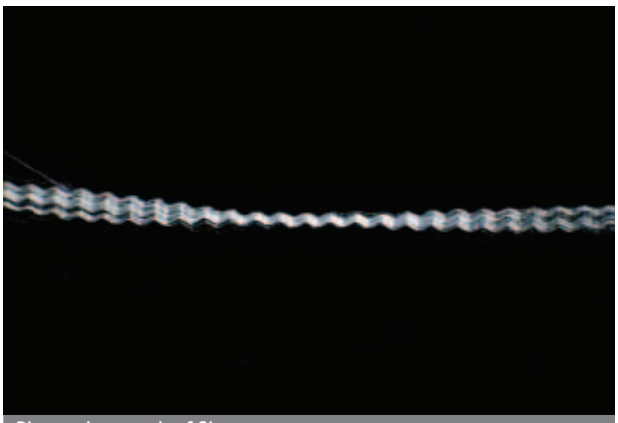
Fabric manufacture

Weaving produces effective contamination control textiles but achieving the unusual requirements of these fabrics requires special techniques.

Standard yarns, produced by twisting together short staple fibres, are not suitable for cleanroom fabrics. With fabrics constructed in this way, fibre ends, protruding from the yarn, are constantly broken off during normal wear resulting in both fibres and small particles being shed into the environment.

Photomicrograph of staple yarn

Contamination control fabrics therefore require the use of filament yarn. These consist of very long continuous fibres twisted or simply grouped together to form the yarn. The filaments are produced in a single smooth strand and their continuous nature means that no ends protrude from the woven fabric surface and so the possibility of fibre and particle liberation from the fabric is greatly reduced. Silk is a naturally occurring filament and man-made filament yarns include extruded polyesters.



Photomicrograph of filament yarn

The filaments and yarns also lie very closely together and this allows fabric to be produced with a tight, smooth, consistent finish.

Filaments can be extruded in different diameters and these can give the final fabric different characteristics such as appearance, feel and performance.
It is also possible to texturise the yarn to produce a less smooth surface finish to the fabric and a different feel against the skin.

Polyesters
The principle materials used to manufacture cleanroom woven fabrics are polyesters, a category of polymers which contain the ester functional group in their main chain.

Polyesters have been shown to produce very stable fabrics capable of withstanding repeated wear and wash cycles and are incorporated into polycottons for this reason.

Sterilisation by gamma irradiation and autoclaving will accelerate fabric deterioration but polyester fabrics still have an acceptable life expectancy of around 50 gamma sterilisation cycles at min 25 kGy.

Polyesters will dye successfully, are rarely allergenic and are readily accepted by most wearers. The material does not absorb moisture in the same way as many natural fibres and is readily available and competitively priced.

In addition polyesters are also used to make a wide range of items as diverse as bottles, films, and canoes and this gives a route to re-cycling at the end of useful garment life.

These factors mean that currently most re-usable contamination control fabrics are woven from 100% filament polyester.

Weave
The weave used to manufacture contamination control fabric is critical in producing the desired filtration and wearer comfort characteristics.

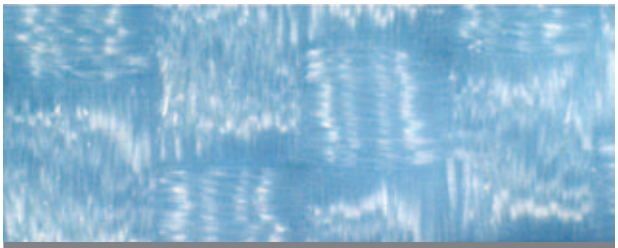
As a consequence of the weaving process holes occur in the fabric where the warp and weft yarns cross. The size of these holes in the fabric, often referred to as fabric pores, determine the rate at which particulate, air and water vapour will pass through.

For non-cleanroom garments this usually means that the fabric is woven with a loose weave and large pores which produces a soft, breathable material. This allows the wearer to quickly lose heat and moisture vapour and maintain a comfortable environment within the clothing resulting in maximum wearer comfort.

Photomicrograph of polycotton fabric

For contamination control fabrics this presents a problem as the larger the pore size the more the fabric can "breathe" but at the same time increasing pore size allows more particulate to escape from the wearer and reduces the barrier properties of the clothing.

Cleanroom fabric is therefore a compromise, the weave selected to produce a fabric pore size which gives an acceptable level of wearer comfort whilst still acting as an effective particle barrier.



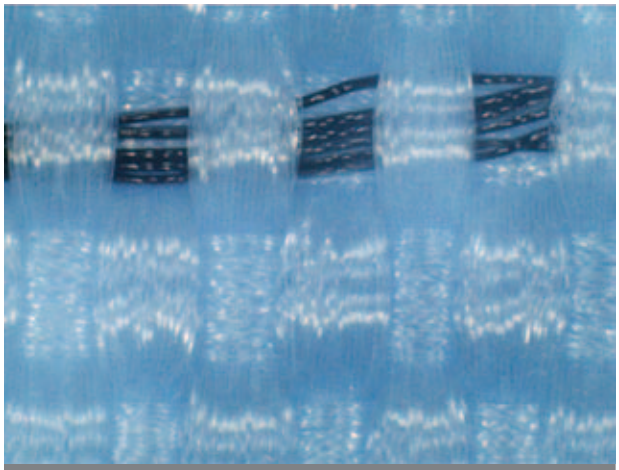
Photomicrograph of cleanroom fabric

Tightly woven cleanroom fabrics must therefore have small fabric pores which are consistent throughout the material.

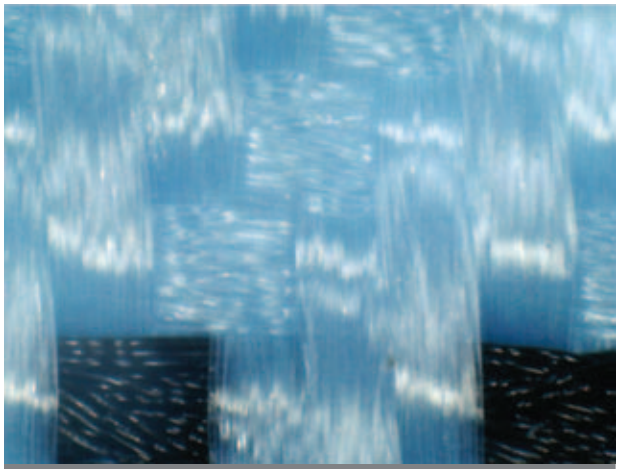
As a guide polycotton fabric will have a pore size of around 65 micrometres and a cleanroom polyester fabric will have a pore size of approximately 18 micrometres. (See section 4.6 for details of test methods)

Magnified images of fabric reveal that woven cleanroom fabric is not a thin, flat layer but that it has complex three dimensional structures with the pores passing from one fabric face to the other rather like tunnels. This three-dimensional structure gives a depth-filtration effect and increases the likelihood of particle entrapment whilst allowing both heat and moisture vapour to pass through.

Plain, twill and satin weaves can also be used to produce different fabric characteristics and appearance. In the manufacture of different contamination control fabrics both plain and twill weave have been used and both types of fabrics are used effectively in the full range of cleanrooms.



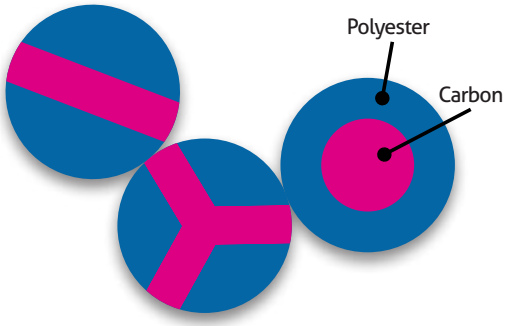
Photomicrograph of plain weave cleanroom fabric with ESD yarn



Photomicrograph of twill weave cleanroom fabric with ESD yarn

Conductive yarns for Electro Static Discharge (ESD) Control

The majority of woven cleanroom fabrics also have a conductive fibre incorporated into the fabric during the weaving process to help in the control of ESD. These fibres are often visible as a black stripe or grid.
The conductive fibres can be made in a variety of ways with the conductive material, usually a carbon compound, embedded into a polyester base.



Carbon encapsulated in polyester producing different configurations of conductive yarns

Triboelectric charging is a phenomenon which most people experience from time to time when a significant static charge builds up on their clothing, often due to rubbing together synthetic fibres.

Once the potential is high enough and a route to earth becomes available the charge can dissipate violently and the electric shock sometimes experienced when applying a key to a car lock is a common example of this effect. As well as being uncomfortable the discharge of high voltage sparks in this way can cause a fire hazard and can also cause extensive damage to microcircuits, which may not be immediately evident.

During use static electrical charge accumulates in this way on cleanroom garments made from synthetic fibres and migrates to the conductive yarns.

This charge may then be dissipated by the conductive yarns being grounded to earth or by corona discharge into the air.

In production areas where control of static electricity is a key element of the contamination control requirement care is taken to ensure that the charge on the garment passes safely to earth and this is often achieved by the use of conducting straps or flooring.

In the very highest level of control it is useful to have all the individual fabric panels of a garment electrically connected together and each part of the garment set connected to the next e.g. hood to coverall, coverall to boots, so that charge being generated on any part of the clothing can be quickly conducted to earth.

Calendering

After manufacture the surface of the fabric can be finished by passing through heated rollers at high pressure in a process known as calendering. This melts and flattens the surface and closes the fabric pores slightly. (Ceramic Terylene was a calendered material adopted for early cleanroom use which was originally developed for workers in the ceramic industry who needed to be protected from the fine dust in their working environment).

Over time, repeated high-temperature laundry processing relaxes the fabric and the calendering effect is lost. If the calendering process is not very carefully controlled it can also lead to local overheating and damage, eventually causing the surface of the fabric to breakdown. These factors mean calendering is now rarely used as a finish for contamination control fabric.

Laminated fabrics

Laminated fabrics are constructed by bonding together different layers, often a woven and non-woven combination. There can be two or more layers.

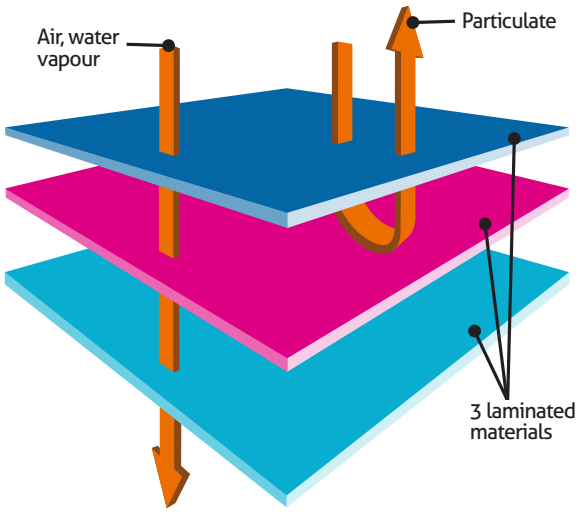


Diagram of fabric laminated from 3 layers

A membrane containing pores of known size is commonly used as part of the laminate construction. PTFE is a commonly used membrane material and laminated fabrics of this type have become popular in the manufacture of rain-proof clothing.

The pores in the membrane are normally less than I micrometre in size and so act as a very effective particle barrier whilst still allowing air and moisture vapour to pass through.

By laminating a coating or membrane to a cleanroom filament fabric very effective control of particulate can be achieved in high grade cleanroom operations whilst still giving acceptable wearer comfort.

These types of fabric can also be used when a waterproof cleanroom garment is required although this will also require additional stages in garment manufacturing such as seam taping.

Air cannot easily pass through contamination control fabrics however and any cleanroom garment must have tight fitting closures at the garment openings e.g. neck, to produce an effective seal and prevent particles being pumped out by the movement of air trapped inside the garment.

Laminated fabrics cannot be washed and dried by a cleanroom laundry at high temperature and so it is not possible to achieve thermal disinfection. These fabrics will also break down or de-laminate with repeated sterilisation cycles by autoclave or gamma irradiation. Laminated contamination control fabrics are more expensive than other types of fabric and although very effective have not been widely used in cleanroom manufacture with the exception of some high-grade microelectronics areas.

4.3 Cleanroom Clothing Design and Construction

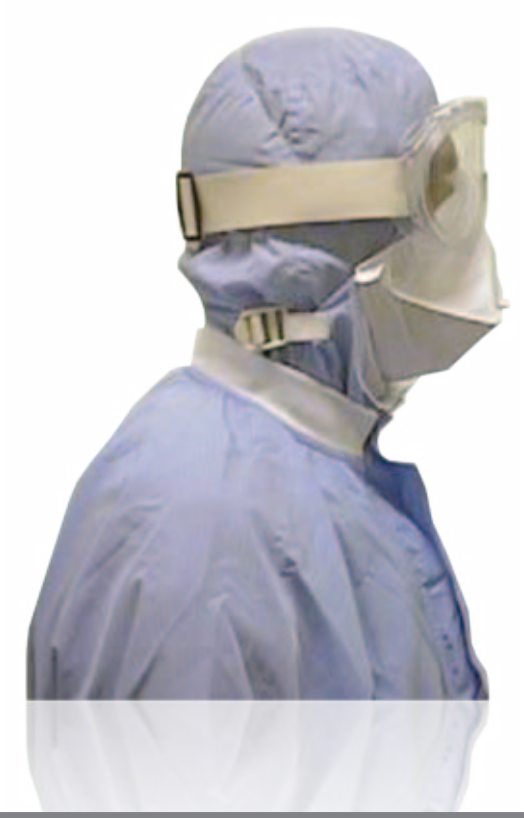
Design

Cleanroom clothing has two basic design requirements;

1) *To act as an effective contamination control barrier and not itself be a source of contamination.*
2) *To be as comfortable and practical as possible.*

These requirements have led to the development of several basic styles of reusable cleanroom clothing.
Cleanroom undersuits and general clean-area wear.
Cleanroom coats.
Cleanroom coveralls.
Cleanroom captive shoes and overboots.
Cleanroom hats and hoods.

Simplicity of design is preferred with emphasis on good fit to the neck, wrists, ankles and face to reduce particle loss from these openings.



Close fitting cleanroom clothing

Personal adjustment to these closures is usually achieved by studs allowing a degree of variation to suit individual wearers. Garments should be designed and fitted to allow ease of movement, especially during gowning, and unisex styles in a range of sizes are the normal choice.

Pockets are not normally an option but loops and open pouches can be provided to accommodate pens, badges and small tools which may be required by some staff. Garment earthing studs, electrically interconnected garment fabric panels and interconnected garment wearer sets may also be required for ESD sensitive applications.

Construction
Specialised manufacturing techniques must be employed when constructing contamination control clothing. These methods are more complicated than those used to manufacture normal workwear but are required to minimise the possibility of contamination occurring from the garment itself.

1) Sealed edge fabric panels.
Fabric panels are cut using a controlled and graded pattern before being sewn together to manufacture the garment. The edges of the panels are sealed before sewing begins and this ensures that no fibre break-out occurs within the enclosed seams.

2) Fully enclosed seams.
All seams are totally enclosed using a double stitching technique. This method encapsulates all the cut and sealed edges of the fabric and is in sharp contrast to overlocked seams used for most garment construction.


Double stitched garment seam construction

3) Sewing thread.
All sewing thread used is silicone-free continuous filament polyester. Normal sewing threads are not suitable as they are manufactured from short staple filaments which can produce fibres and particles.

4.4 Cleanroom Clothing Fixtures and Fittings

Tapes, zips, studs and buckles are used to adjust and fasten cleanroom garments whilst various compounds are used for cleanroom shoe and boot soles. Elasticated cuffing materials are often used for the wrist closure of coats and coveralls. (Velcro is not routinely used as it can easily snag and also holds fibres and particles).

These fixtures and fittings come in a variety of materials, colours and patterns, however any materials used must not be a source of particulate and fibres and must be able to withstand repeated wear and decontamination. When sterilisation of the garments by autoclave or gamma irradiation is an additional requirement then any fixtures and fittings should not be deformed or broken down by these processes.

Electrically conductive tapes, studs and sole materials may also be a special requirement for ESD controlled areas.

Clear data showing the performance of all garment fixtures and fittings will be available from the garment supplier.

4.5 Special Cleanroom Garment and Fabric Requirements

Cleanrooms are used to produce a very wide range of products and the emphasis of contamination control can range from the control of surface finish, removal of micro-organisms or control of electro-static discharge (ESD).

These varied requirements mean that many different manufacturing processes are employed and some of these will pose unusual contamination control risks and problems.

Special cleanroom fabrics have been developed which help to solve these specific problems.

Water repellent fabric
Cleanroom fabrics can be used which will stop the penetration of water droplets produced as a spray. These fabrics are often referred to as spray resistant, water resistant or shower proof and are not waterproof. The fabric finish used to provide this protection does not significantly affect the other performance characteristics of the fabric.

Waterproof fabrics
Waterproof fabrics are able to resist the penetration of significant volumes of water falling onto the fabric surface and the degree of water resistance is measured by the height of the column of water which can be suspended above the fabric before water seeps through.

Laminated fabrics are especially useful for this application and normally provide a degree of breathablity to maintain wearer comfort.
(Note ; If waterproof garments are required then taped seams and waterproof closures such as zips must also be used during manufacture).

Chemical resistance
Cleanroom fabrics which can protect the wearer from chemical splashes are produced and fabric information will be available to indicate the level and type of protection afforded.

It is recommended that when protection is required against specific production chemicals controlled laboratory testing is carried out to ensure that the fabric will perform effectively with the specified chemicals. Garment suppliers will be able to arrange these tests.

Flame retardancy
In some instances flame retardant garments or additional protective layers e.g. arm guards, may be required to protect the wearer from sources of heat. Cleanroom compatible fabrics are available to meet this need.

Anti-microbial fabric
Several different anti-microbial materials have been developed for cleanroom clothing and applied as a surface finish or incorporated into the fabric yarn. These may be useful in reducing the build up of micro-organisms on cleanroom garments worn over an extended period of several days and especially if the clothing is damp or wet for a significant time. Issues concerning the introduction of anti-microbial chemicals into the cleanroom and skin-contact with the wearer must be considered.

Electro-static discharge (ESD)
Control of ESD is of particular significance in cleanrooms where fire and explosion risks are present or where ESD sensitive components are being manufactured. Different levels of control are required and section 2.3 - ESD requirements and standards, gives details of the current guidance.

The great majority of cleanroom fabrics incorporate an electro-conductive yarn (as outlined in section 4.2), as a grid or stripe into the weave and this provides basic ESD control.

When higher levels of control are required then specially constructed garments must be used which achieve conductivity between individual garment fabric panels and between the separate garments in the wearer set e.g. coverall, hood and boots. This is usually achieved by incorporating conductive materials into the garment during manufacture.

These type of clothing systems are usually permanently earthed during use either by earth straps or through conductive flooring. Sleeve-to-sleeve and point-to-point testing will be required throughout garment life to ensure the garment ESD system is functioning correctly.

Point to point ESD test on cleanroom garment

Special designs
Unusual designs of contamination control garments or equipment covers may be needed. Cleanroom clothing manufacturers will be able to advise on the best approach to produce individual tailor-made items.

This can be especially useful for production machinery and equipment where items such as parts bins or production robots may need to be covered to reduce contamination.

4.6 Fabric Test Methods

Testing contamination control fabrics
In order to assess the suitability of fabrics for different contamination control systems it is necessary to test a range of performance characteristics both of the material itself and also of garments constructed from the fabric.

A variety of standard tests can be used to assess factors affecting contamination control and wearer comfort and to give a direct comparison of different fabrics.

The following list gives examples of useful test methods; however, different National Standards and tests are used by different fabric manufacturers.

It is therefore recommended that when selecting cleanroom fabrics, samples are subjected to the same test methods, preferably carried out by the same test house at the same time, to obtain directly comparable results.

Fabric pore size
BS 3321 [ref 1] Method for measurement of the equivalent pore size of fabrics.

The bubble point test is used to establish the size of the pores which pass through the fabric from one side to the other. Pore size results from the tightness and accuracy of the weave.

Decreasing pore size gives greater particle hold out and therefore better filtration but also decreases the ability of the fabric to transmit air and water vapour and therefore reduces wearer comfort.

For a filament polyester fabric the pore diameter will typically be around 18 micrometres or less.

As a comparison a polycotton fabric will have a pore size of approximately 65 micrometres.

Particle holdout efficiency
British Textile Technology Group (BTTG) Particle Barrier Efficiency (Shirley method 22) [ref 2].

A direct particle challenge test is used to estimate the number of particles of different sizes filtered out by the fabric.

The fabric is subjected to an airstream containing a known number of particles with a range of sizes. The number of particles passing through the material is measured and the percentage of particles filtered out by the fabric can be calculated. This is reported for each particle size as a percentage holdout.

A typical woven high-grade filament fabric and polycotton will produce the following results.

Particle size range (micrometres)	% holdout Filament fabric	% holdout Polycotton
0.2 - 0.3	50	14
0.3 - 0.5	85	22
0.5 - 1.0	92	27
1.0 - 3.0	92	32
3.0 - 5.0	92	32

Dry linting propensity
BS 6909 [ref 3] 1988. Method for generation and counting of the airborne linting propensity of fabrics in the dry state.

This test examines the numbers of particles generated by the fabric itself whilst undergoing a standard flexing under mild abrasion.

Water vapour permeability
ASTM E96 [ref 4]. Standard test methods for water vapour transmission of materials

This test is used to establish the rate at which water vapour will pass through the fabric and is measured in grams per square metre of test fabric per hour. A high-grade barrier fabric will typically give a result of 20 grams per square metre of fabric per hour. Polycotton fabric will be approximately 28 grams per square metre of fabric per hour.

This test gives an indication of garment comfort as the faster moisture vapour can disperse from the skin surface the more comfortable the wearer feels.

Air permeability
BS EN ISO 9237 [ref 5]. Textiles. Determination of the permeability of fabrics to air

This test method is used to assess the rate at which air can pass through the fabric and gives a further indication of wearer comfort.

The results are obtained in litres of air per square metre of test fabric per second at 0.98 mb pressure differential.

A typical result for a woven filament barrier fabric would be about 45 litres of air per square metre of test fabric per second and for polycotton approximately 170 litres of air / square metre of test fabric per second.

If air can pass easily through the fabric then the body temperature of the wearer is more readily adjusted resulting in a more comfortable garment.

Static dissipation behaviour
BS EN 1149 [ref 6]. Protective clothing: Electrostatic properties. Test method for measurement of surface resistivity.

Gives details of tests to investigate the electro-static dissipative properties of fabrics.

Abrasion resistance
BS EN 530 [ref 7]. Abrasion resistance of protective clothing material.

This test gives an indication of the likely wear characteristics of the fabric over time.

4.7 Body Box Test

One of the best methods to study the types and numbers of particles dispersed from personnel is to utilise a body box or a dispersal chamber. This can be utilised to study the effectiveness of various types of cleanroom garments. Dispersal rates under varying conditions of movement can be assessed and the body box can also be used to investigate if any particular individual is an abnormally high generator of contamination.

IEST-RP-CC003.3 [ref 8] gives full details of a recommended particle dispersion test procedure.

The picture overleaf shows a typical body box, consisting of a metal framed glass booth, approximately 0.75m x 0.70m x 2.5m that can be accessed via the door at the front. A variable fan, located above the chamber, provides a constant stream of air, via a HEPA filter, into the chamber.

Typically air is supplied at just over 700 l/min, and balanced by the removal of air by a high-volume bacterial sampler operating at 700 l/min, and an airborne particle counter operating at 2.83 l/min (1ft^3/min), at the sampling port at the rear base of the unit. A slight positive pressure is maintained inside the chamber to ensure that no contamination enters the chamber from outside which can be checked by observation of the exhaust port flaps at the adjacent side of the base.

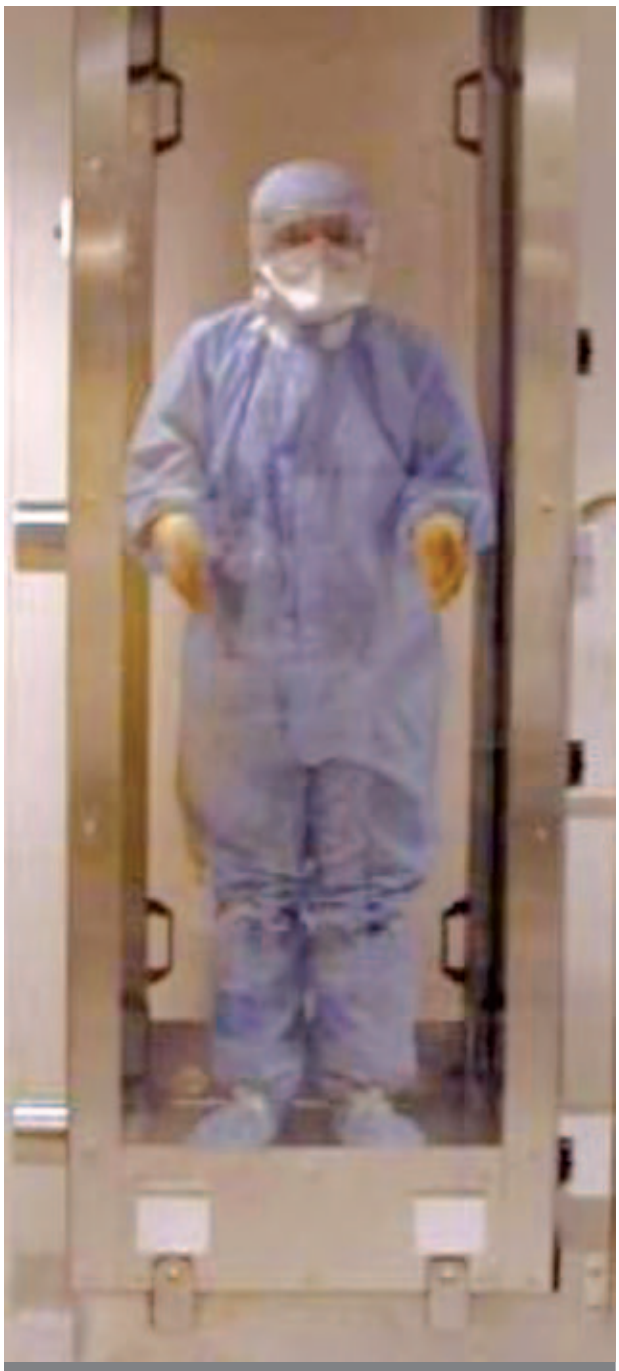
The subject enters the chamber wearing the required clothing and is usually requested to march to the beat of a visible metronome. After a period of about 1 minute, the bacterial air sampler is switched on for a defined period and the microbe carrying particles (MCPs) deposited onto microbial media plates are subsequently incubated and then the bacterial colonies counted.

The particle counter simultaneously records the total particle concentrations during the exercise.

Whyte [ref 9] used a similar body box to test 55 people (30 females and 25 males) wearing basic cleanroom garments, manufactured from woven polyester fabric, which had a pore diameter of 25µm. A coverall was worn and its trouser bottoms were covered by knee-length boots.

Disposable latex gloves, disposable mask and woven polyester hood, were also worn, leaving only the eye area uncovered.

The graph shows the dispersion rate per minute of MCPs, particles ≥0.5µm, and ≥5µm, obtained from the 55 people wearing cleanroom garments. The counts on the left are from females, and those on the right are males.



Test subject in a body box

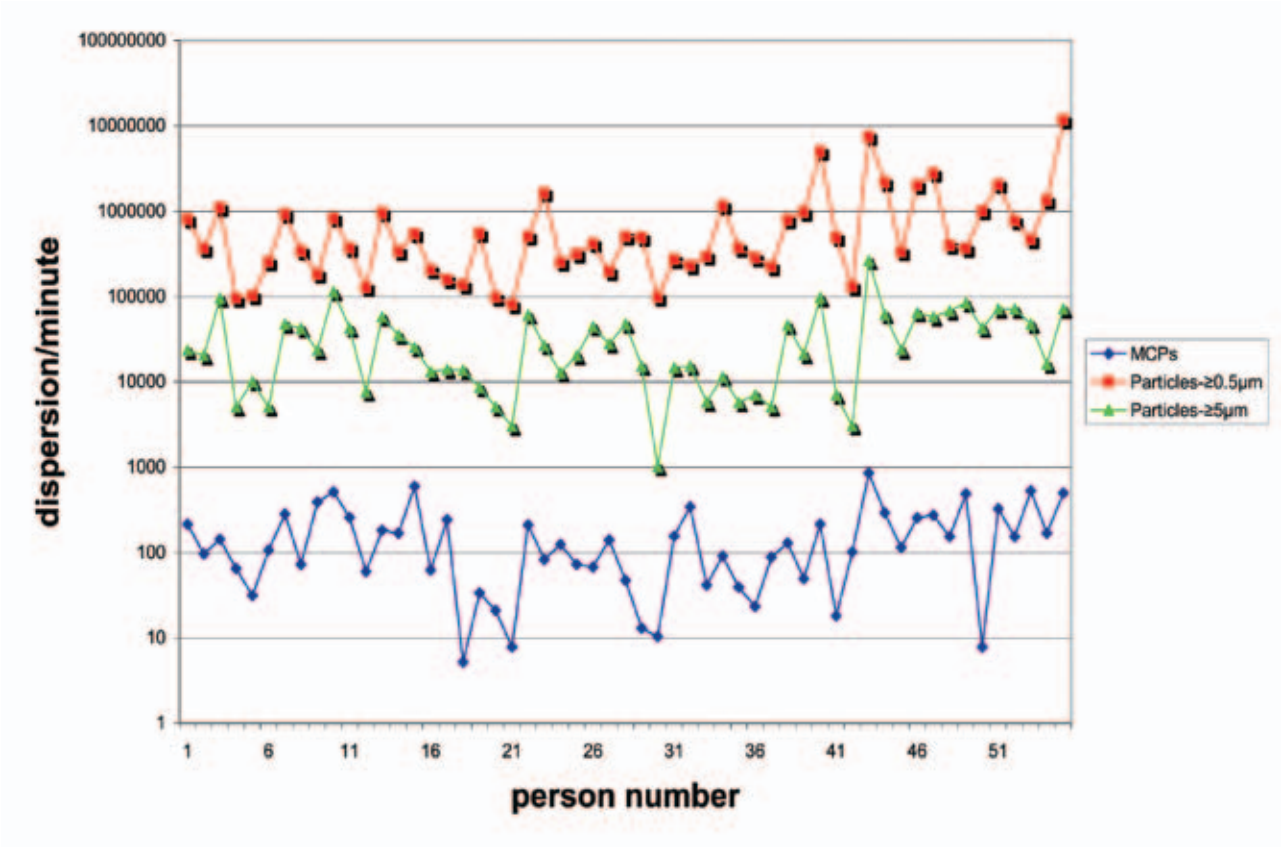
Each person was marching to the beat of a metronome (1 beat/s), while swinging one arm, and then the other, up to their shoulder. Large variations in airborne dispersion from people were apparent, and the rates of dispersion of MCPs, particles ≥0.5µm, and ≥5.0µm were interlinked i.e. high dispersers of one type of particle would disperse high rates of particles of the other two

types, and vice versa. It has been demonstrated that the reduction in the dispersion of MCPs and particles by the use of cleanroom garments was determined by the tightness of the weave of the cloth, and the design of the garments. The more occlusive the fabric and garments, the greater the reduction in airborne dispersion, and more larger particles would be retained than smaller particles.

The relative dispersion from males and females was also studied.

It was found that men dispersed greater numbers of MCPs and particles. (It is well established that males disperse more MCPs than females).

The ratios of the number of particles dispersed of ≥0.5 µm and ≥5.0 µm diameter, to the number of MCPs, was found to be 5800 and 210 for the cleanroom garments tested. These ratios will vary depending on the personnel tested, the design of the clothing, the type of clothing fabric, and whether the fabric was new, unwashed and unsterilised.



MCPs and particles from 55 people wearing cleanroom garments. (30 females and 25 males)

4.8
Cleanroom Undergarments

The clothing worn beneath the outer cleanroom garments is of considerable importance in controlling the contamination released into the cleanroom.

If normal street clothes are worn under outer cleanroom clothing then these garments will have great variation in fabric type and soiling levels.

Body box testing shows that particles are released through the cleanroom garments and a proportion of any contaminants released will be from the undergarments.

It is therefore essential that in high grade cleanrooms undergarments are used and are manufactured from a fabric that does not itself shed large numbers of particles or fibres. The undergarment layer will also provide additional filtration for the wearer thus reducing the particulate challenge to the outer garments and the cleanroom.

As these garments are worn next to the skin, fabrics must be used which provide a high level of wearer comfort. Fabrics with a soft "feel" and the ability to wick moisture away from the skin will usually be most acceptable.

Fabrics which are dark in colour and non see-through are preferred.

When control of electro-static dissipation (ESD) is a key area for contamination control then an undergarment fabric with ESD properties is required.

Cleanroom undergarments are usually a two piece set of tunic and trouser (sometimes called PJs – pyjamas) and loose, comfortable-fitting styles are needed.

Elasticated trouser ankles prevent dragging on the floor and the tunic is usually short sleeved. A long sleeved tunic provides a more effective barrier to the release of skin particulates; however, the cuffs can become wet during hand washing and produce a source of microbial contamination.

Cleanroom undergarment set

SECTION

5.0 Disposable Contamination Control Clothing

This section describes the materials, manufacture, characteristics and testing of disposable cleanroom clothing. Other disposable cleanroom items, such as cleaning wipes, are discussed in Section 7.0 *Cleanroom Cleaning Methods, Equipment and Cleanroom Ancillaries.*

Guidance on the selection and purchasing of cleanroom disposables for specific manufacturing environments is provided in Section 9.0 *Planning, Sourcing and Optimising Cleanroom Consumables Supply.*

5.1 Disposable Clothing

In the majority of cases cleanroom clothing is manufactured from re-usable cleanroom fabrics which can be processed, decontaminated and worn many times and Section 4.0 *Reusable Contamination Control Clothing*, and 6.0 *Cleanroom Garment and Consumables Decontamination - Plant and Process* give full details of these garments and decontamination systems.
In some applications however it is appropriate to consider disposable clothing items, which although generally low comfort and high cost, are available in a wide range of options and are simply disposed of after use.

Suitable applications for disposable cleanroom clothing may include the following:

For use in remote or difficult to access locations.

When very low numbers of cleanroom garments are required.

When cleanroom clothing is worn infrequently.

When heavy staining with oils, greases, paints and inks would make decontamination of reusable clothing impossible.

Where garments may be contaminated with harmful biological, chemical or radioactive substances.

As disposable clothing for staff during the cleaning and commissioning phases of new builds.

For use as a back-up for re-useable garments; especially to accommodate visitors, contractors and new starters.

When it is necessary to have cleanroom clothing which is also required to act as Personal Protective Equipment (PPE) for the wearer and to be CE marked. This is often the case for bulk active pharmaceutical ingredient (API) manufacturing when specific chemical repellency is needed.

To provide the best contamination control option e.g. cleanroom gloves.

Non-woven fabrics

The fabrics used to produce disposable cleanroom garments are not produced by a weaving process and are therefore referred to as non-woven fabrics.

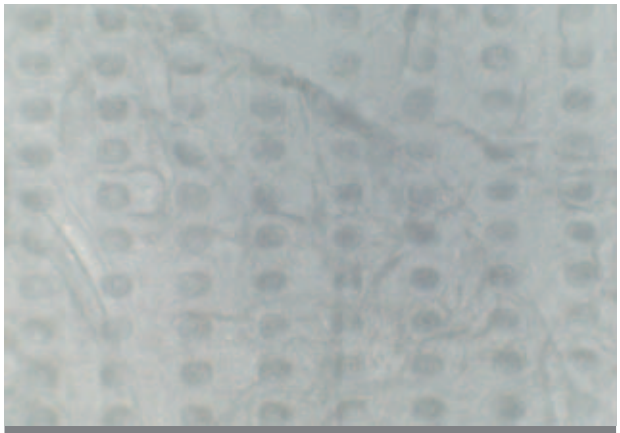
Non-woven contamination control fabric

Non-woven fabrics are produced using spunlaid techniques from plastic polymers such as Polypropylene, Nylon and Polyester.

Filaments of the material are extruded then drawn and laid on a moving screen, called a web former, to form a filament web

The filament web can be made into a finished fabric by the application of heat and pressure without the need for additional binding agents.

Fabrics produced in this way are usually referred to as spunbonded non-woven fabrics.



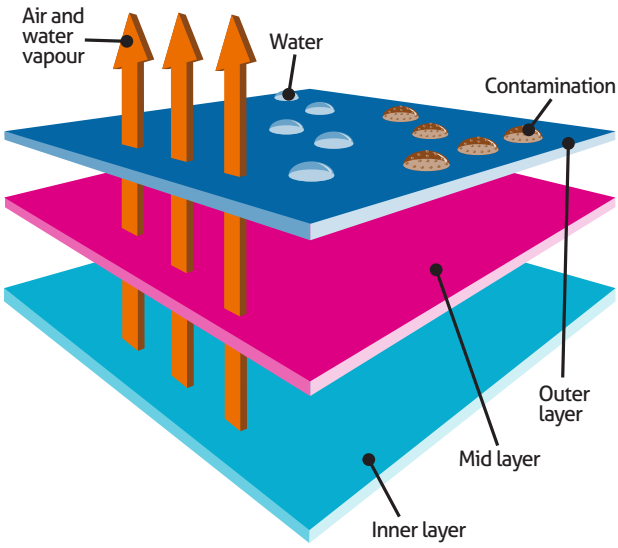
Photomicrograph of non-woven fabric

Variations in the method of producing the filaments have been developed to produce non-woven fabrics with different characteristics.

Meltblown non-wovens are produced by using a spunlaid technique which extrudes and draws molten polymer resins with heated, high velocity air to form much finer filaments. The filaments are again cooled and collected as a web onto a web former before being made into a finished fabric.

Flashspun fabrics are produced by a further variation of spunlaid technology; a solution of polymer and solvent is extruded under conditions which produce rapid solvent evaporation; this causes the extruded filaments to split further into a highly intricate and fine web which is again collected onto a web former before being made into the final fabric.

Laminated non-woven fabrics are also available and produced from layers of different materials glued together to produce different characteristics of strength and permeability.



L aminated 3 layer non-woven fabric

There are many different types and brands of non-wovens available but the most commonly recognised brand is TYVEK™ which is a registered trademark (DuPont).

Disposable clothing for use as Personal Protective Equipment (PPE)

When a risk assessment has identified that a specific cleanroom task requires the use of PPE then disposable garments which are CE marked to confirm suitability for the task must be chosen. The clothing must also be compatible with the contamination control requirements of the area of use.

European directives [ref 1] require that all PPE must be certified according to category I, II or III.

Category I clothing is identified as simple design with minor risk which can be identified by the user. Garments are labelled with a CE mark only.

Category II describes all PPE except those in category I or III. Garments are labelled with a CE mark only.

Category III garments are identified as complex design and intended to protect the wearer from risk of serious or fatal injury which may not be identified by the wearer in sufficient time. Category III garments are labelled with the CE-mark plus a four digit code of the relevant notified body.

Category III garment CE label

In addition the garment type indicates the kind of protection offered by protective clothing as defined by European Standards [ref 2].
Category III PPE includes six Types
Type 1 - Gas-tight clothing
Type 2 - Non gas-tight clothing
Type 3 - Protection against pressurised liquid chemicals
Type 4 - Protection against liquid aerosols
Type 5 - Protection against airborne solid particulate chemicals
Type 6 - Limited protection against mist

It is important to note that if disposable garments are required for PPE then advice must be obtained from a Health and Safety professional to confirm the correct choice of clothing.

When disposing of contaminated items after use, safe and acceptable disposal procedures must be identified and used.

5.2 Bodywear

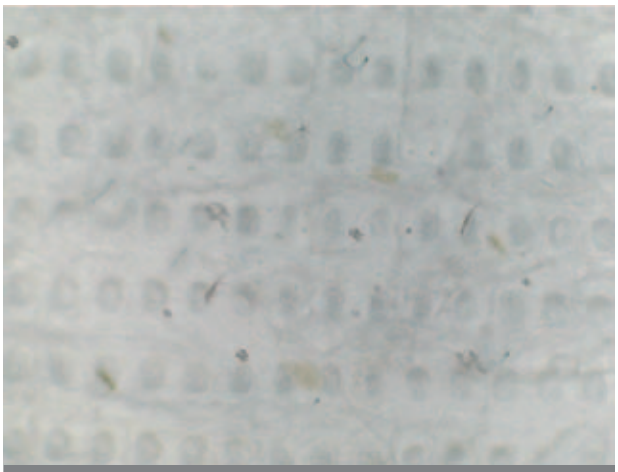
Non-woven fabrics can be used for the manufacture of all types of products and this is reflected in the large number of disposable garment styles and ranges which are available. White is the usual colour for cleanroom disposable garments, however other colours are also available.

Non-woven contamination control clothing

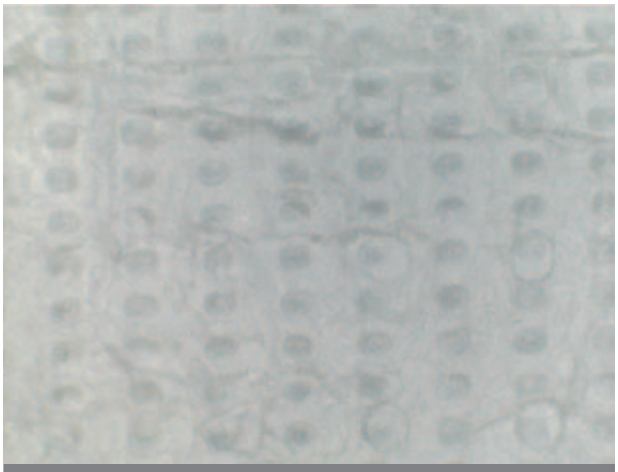
When selecting disposable clothing for use in a controlled environment it is important to select a non-woven fabric which has the appropriate filtration requirements and low shedding characteristics. Seam construction varies considerably and care must be taken to ensure that the manufacturing method does not allow particles to escape from the garment via this route. Fixtures and fittings such as thread, studs and elastic must also be compatible with the cleanroom.

Many disposable clothing items are sold direct from the producer without any cleaning or decontamination process following manufacture. Such garments are completely unsuitable for cleanroom use as they are likely to be heavily contaminated with particulates and fibres from the manufacturing process and may also be a significant source of bacterial and fungal spores.

When disposable garments are required for cleanroom use it is therefore necessary to ensure that the clothing has been effectively cleaned, decontaminated, packed in a cleanroom environment and if required sterilised before use.



Photomicrograph of unprocessed non-woven garment showing surface contamination



Photomicrograph of processed, decontaminated non-woven garment surface

The type of non-woven material used and the standard of manufacture, finishing, packing and sterilisation will all have considerable impact on the final cost of the garment.

When ESD (electro-static discharge) control is required then disposable garments which incorporate ESD control properties must be selected. ESD control is often achieved by the use of sewn-in conductive tapes or conductive fabric finishes and full data on garment static dissipation properties will be provided by the supplier.

Coat

Centre fastening, lancer and "Howie" style coats are all produced with zip or stud fastenings. Different pockets, cuff closure, fastening options and colours are available.

Non-woven cleanroom coat

Top and Trouser
Two piece bodywear, comprising a separate top and trouser, can be obtained in a range of styles.

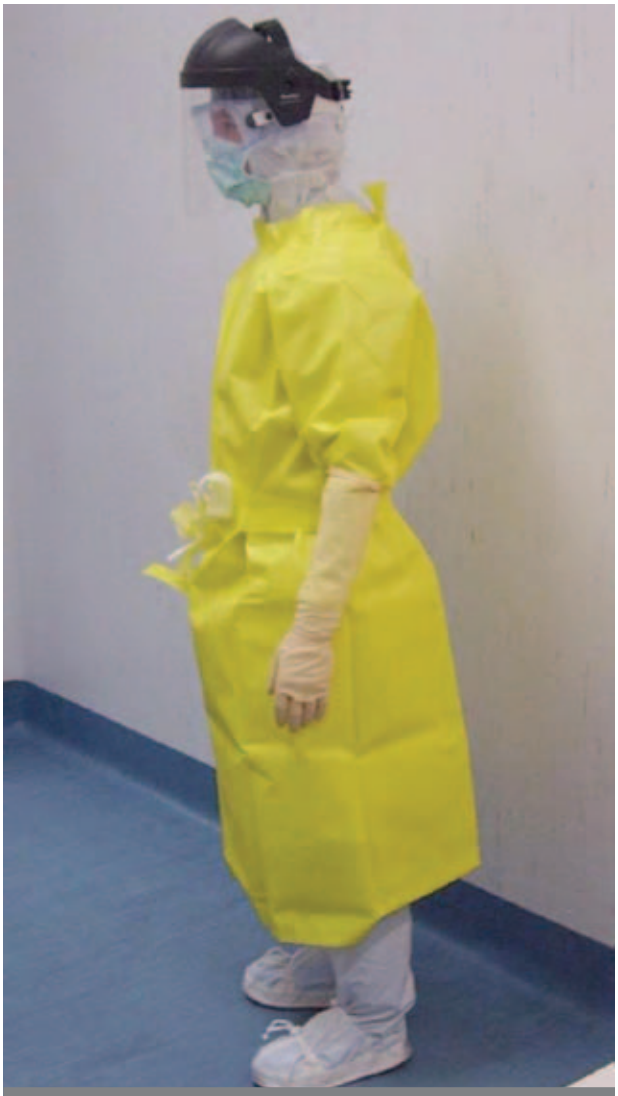
Coverall
Disposable coveralls are probably the most commonly used disposable cleanroom body garment.
A number of styles are available from the basic centre zip coverall to coveralls with incorporated hood and those with integral hood and overshoes (often called a "Bunnysuit")

Non-woven cleanroom 'Bunnysuit'

Where a high level of control is required a disposable cleanroom coverall, complemented with disposable overboots, latex gloves, mask and goggles is appropriate.

One piece non-woven coverall with overboots, gloves, mask and goggles

Apron
Disposable aprons may be worn to protect re-usable cleanroom garments from excessive wear or contamination from stains or liquids. They may also be required as PPE to protect the wearer from chemical or biological hazards. Aprons can be obtained in a variety of styles and materials to suit the specific application.



Disposable apron, complemented with gauntlets and face visor, worn to protect the wearer from chemical hazards

5.3 Headwear

Head coverings are worn to achieve three contamination control objectives;

- *To contain hair and prevent loss of hair into the controlled environment.*
- *To contain droplets produced from the nose and mouth.*
- *To control the dispersion of skin particles from the head.*

Control of hair and skin particles

Head and facial hair can pose a threat to any controlled environment and some controlled manufacturing environments are especially sensitive to hair contamination e.g. tablet manufacture and high grade surface finishing.

Hair is composed mainly of the protein keratin and the diameter of human hair can vary from approximately 30 to 180µm, the average being approximately 100 µm, with the length varying from a few mm to many cm. Because of its location on the body surface and its contact with the skin it can be contaminated with a range of non-viable particles and micro-organisms. Hair grooming products may also be present on the hair surface.

A range of hair control clothing options are available for cleanroom use.

The most basic control is provided by hair net, mob hats and beard snoods.

Mob hat

Beard snood

These are usually disposable items made of a non-woven material. Different strengths and densities of fabric are available and identified by the weight in g/m^2.

These items are normally secured by elastic fastenings which can be single or double strength and must be large enough to enclose all head or beard hair.
Mob hats and beard snoods are not usually supplied cleaned and decontaminated as they are used as a primary control in direct contact with the hair. They can be supplied in a range of colours which can be useful when such items are dedicated to different controlled areas, the colour readily identifying a particular zone and helping to control the area of use.

Disposable mob hats may be used without additional headwear in low grade manufacturing areas, however when higher levels of contamination control are required then it is usual to wear a mob hat underneath an additional covering such as a full cleanroom hood which will give the best control of not only hair but also of skin particulates and micro-organisms dispersed from the head.

Disposable cleanroom hoods of various styles, manufactured from non-woven fabrics are readily available. They can be supplied as decontaminated, sterile or non-sterile.

When very high levels of control are needed then visors, visor masks or goggles can be used to contain loss of hair from the eyebrows and eyelashes and additionally give protection against the dispersion of particles from the skin of the upper face.

Disposable visors or visor masks do not form a seal against the face and therefore provide a limited degree of contamination control however they may be required as PPE to protect the wearer from splashes of product or disinfection solutions.

Goggles which are specified for contamination control purposes seal against the face and overlap the hood and mask , providing full facial coverage to give the best control of both facial hair and skin.

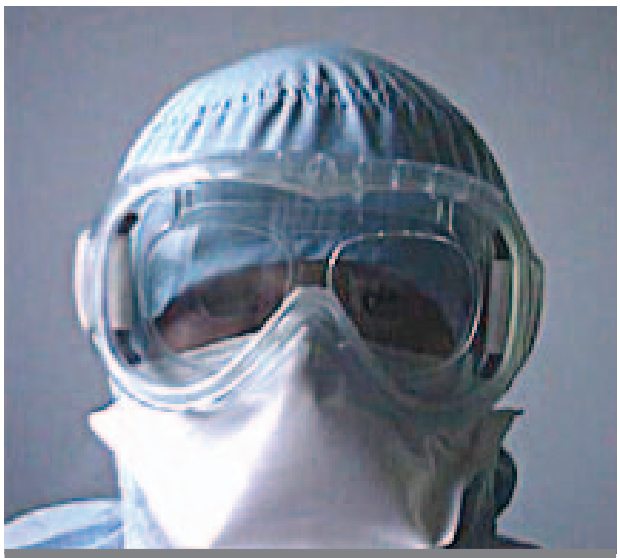
If the goggles are also required to protect the wearer then suitable PPE goggles must be selected.
Cleanroom goggles are available as single use disposable items but more usually are retained by a specified wearer and sanitised between use, typically by wipe down with sterile IPA or IMS. They may be sterilised by gamma irradiation, steam (autoclave) or ethylene oxide (ETO).

A comfortable fit is usually achieved with a soft PVC surround with a broad, adjustable elasticated head strap preferably made from food grade rubber or nitrile and fitted with high grade non-misting lenses to allow undistorted vision. The lenses typically would be manufactured from polycarbonate to reduce the risk of breakage.

Typical cleanroom goggles

Some form of ventilation of the goggles is normally required to prevent excessive condensation forming during use. Typically this may take the form of a series of ventilation holes, or adjustable vents, designed to prevent a direct transfer route into the cleanroom and fitted on the upper (forehead) side of the goggles to ensure contamination isn't transferred by gravity from holes on the underside.

Designs are available to accommodate staff who require prescription spectacles. Cleanroom goggles are available which fit over spectacles or alternatively prescription lenses can be fitted inside.



Cleanroom goggles with prescription lens inserts fitted

Cleanroom goggles used with the operator's normal glasses

Cleanroom masks are chosen when it is necessary to protect the production environment from droplets of saliva and mucus generated by the cleanroom staff. When a mask is required to protect the wearer from chemical or particulate inhalation hazards then the correct PPE must be used.

Typically saliva contains 10^7 micro-organisms per millilitre and droplets are dispersed from the mouth and nose by sneezing, coughing or talking and each droplet may contain hundreds of micro-organisms. These droplets are relatively large in size with an average diameter of approximately 50µm and will therefore be readily deposited onto surfaces and not remain suspended in the surrounding air. As these droplets are large particles even the most basic masks have high retention efficiencies of >95%.

Masks have been used by Medical Professionals for many years especially during surgical procedures. Masks were originally worn to reduce the number of airborne micro-organisms near open wounds and thus reduce post operative infections. More recently surgical masks have also been seen as a way to protect the wearer from cross-infection and are often used in conjunction with a face shield to help protect against blood borne infective agents.

Surgical mask

Surgical masks have been adopted by cleanroom industries and are extensively used in highly controlled manufacturing environments because of their filtration properties.

Masks are usually composed of several layers of non-woven materials often polypropylene or polyester. The layers may be moisture absorbent next to the mouth and nose so producing a more comfortable mask.

Masks can be tested to show their effectiveness in several ways;

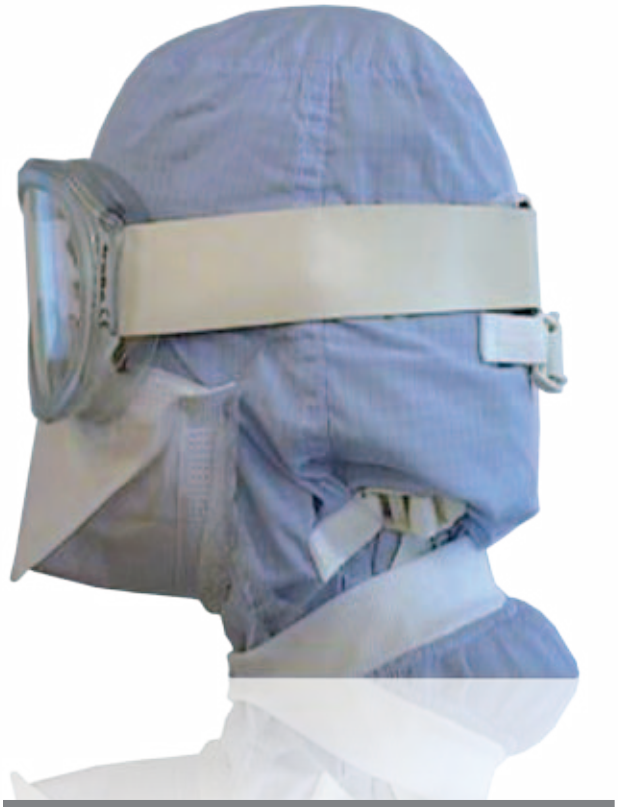
- *PFE (Particulate Filtration Efficiency) measures the percentage efficiency at which the face mask filters particulate matter.*
- *BFE (Bacterial Filtration Efficiency) measures the percentage efficiency at which the face mask filters out bacteria.*
- *Delta P (Delta pressure) is the pressure drop across a facemask, the higher the Delta P the more difficult the mask is to breathe through and the more likely it is that breath will pass around the mask rather than through it.*
- *Tests for skin irritation and sensitisation can also be carried out to ensure that the masks do not produce skin problems when worn for long periods.*

Masks must fully cover the nose and mouth and so a mouldable metal nose band is incorporated into the mask to allow the wearer to fold the mask into position and produce an effective seal.

Disposable masks are held in position by ear loops or ties which fasten or clip behind the head.

Flat folded masks are regularly used however in many cleanrooms one of the key requirements is to ensure that the mouth and lips do not contact the mask material. If this happens, the mask may become wet and is then more likely to tear, providing a direct pathway for contamination into the controlled area.

To prevent this problem cone shaped or 'duck bill' masks can be worn which stand clear of the wearer's mouth.



"Duck bill "mask worn with goggles and hood

Blue or white masks are commonly selected but other colours are available.

Disposable cleanroom masks can be supplied in single or multiple packs and may be sterile or non-sterile.

Face veils provide an alternative to masks and are clipped or studded to the inside of a cleanroom hood. These veils are usually re-usable items but single use disposable veils can be obtained if required.

5.4 Handwear

Gloves

Cleanroom gloves are a critical element of contamination control. Most manufacturing operations will require hand contact with equipment or materials giving high potential for direct (primary) or secondary contamination or cross-contamination of product.

Cleanroom gloves in use.
Image courtesy of Photronics UK Ltd.

Cleanroom gloves must therefore provide an effective protective barrier to stop skin particles and viable organisms from the hands contaminating the cleanroom.

A punctured glove provides a potential route of microbial contamination and in critical operations such as aseptic manipulations the commonly adopted measure to control this risk is for operating personnel to wear two pairs of gloves [ref 3].

Gloves must also be a comfortable fit for the wearer and have good flexibility and sensitivity to allow precision operations to be carried out.

In some instances the gloves will also have to act as protection for the wearer and be classified as PPE and for some drug manufacturing operations patient protection standards must also be addressed.

When control of electro-static discharge (ESD) is a key element of contamination control then gloves must be used which meet this requirement.

ESD cleanroom gloves. Image courtesy of Asiatic Fiber Corp

Re-usable gloves which can be cleaned and decontaminated are available however the great majority of gloves used in controlled environments are single use disposable items.

Materials

Disposable gloves for cleanroom use can be manufactured from a range of materials with different properties.

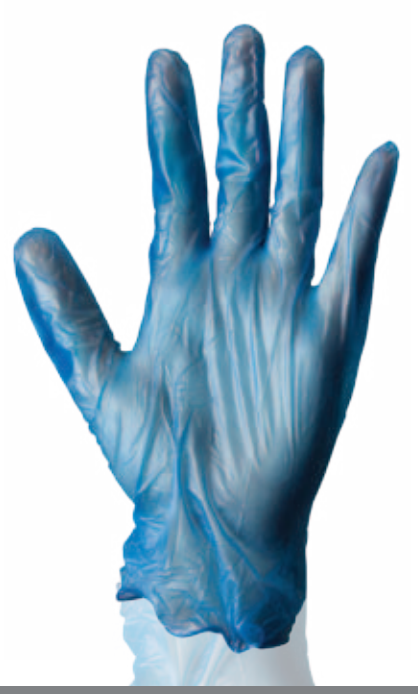
Latex is natural rubber which has very good stretch and flexibility and is resistant to wear and tear. Protein allergens may be present however and these can cause allergic reactions in sensitised individuals.

Latex cleanroom glove

Nitrile rubber is a synthetic material manufactured from various proprietary compounds; it is very similar to latex and has good resistance to wear and tear. No protein allergens are present.

Nitrile cleanroom glove

PVC (Polyvinyl Chloride) gloves provide protection against many water-soluble chemicals. PVC is resistant to wear and tear but has limited stretch and flexibility. No protein allergens are present.



PVC cleanroom glove

Butyl rubber gloves are air and water tight and can provide wearer protection against strong acids. They have limited stretch and flexibility.

Butyl cleanroom glove

Categories, standards and test methods
Contamination control requirements dictate that cleanroom gloves must provide an effective barrier against the viable and non-viable particles lost from the hands. The gloves may also need to protect the wearer from chemical or biological contaminants present in the production environment and in addition the gloves may have to comply with patient protection standards. Various standards and test methods have been developed to assess the performance and suitability of different gloves for these different requirements.

The following terms are often used to identify different glove characteristics.

Penetration *- the passage of chemicals and micro-organisms through the glove.*

Degradation *- the rate of loss of glove integrity following chemical exposure.*

Diffusion, Permeation and Desorption *- all describe the movement of molecules through the glove.*

Acceptance quality limit *(AQL) a statistically valid sampling procedure giving a numerical indication of the conformance of a product batch tested for a particular characteristic. The lower the AQL the higher the level of conformance to the test pass limits.*

For pharmaceutical and the medical industries, this is a particularly important parameter for glove leaks or pin holing. Typically, surgeon's gloves are supplied with an AQL of 1.5%. The generally accepted method of testing latex gloves for leaks is detailed in European Standard, EN455 Part 1 [ref 4]. This test involves securing the glove around the circumference of the bead to hold it in an open position prior to filling with 1000ml of water and then observing for leaks. Some glove manufacturers have purpose built testing machines which automatically fill gloves that have been loaded onto a moving carousel with the correct volume of water and present them for inspection as the next glove is filled with water. This is useful if a large quantity of gloves are to be tested.


Automated glove leak testing machine

Gloves to protect the wearer
When gloves are required to protect the wearer and are acting as personal protective equipment (PPE) it is necessary to select a suitable risk category of glove.

Three categories of gloves are identified according to their design and the risks associated with the intended use;

- *Category I gloves are identified as simple design with minor risk which can be identified by the user and are labelled with a CE mark only.*
- *Category II describes all gloves except those in category I or III. Labelled with a CE mark only.*
- *Category III gloves are identified as complex design and intended to protect the wearer from risk of serious or fatal injury which may not be identified by the wearer in sufficient time. Category III gloves are labelled with the CE-mark plus a four digit code of the relevant notified body.*

CE
0123

Category III glove marking

In addition gloves may also be classified under the Medical Device Directive (MDD) as a Class 1 product when patient safety requires this classification.

Two standards are commonly used to test cleanroom gloves.

- *BS EN 420:2003* [ref 5] *Protective gloves. General requirements and test methods*

This covers general factors such as sizing, dexterity and leachable proteins.

- *BS EN 374:2003* [ref 6] *Protective gloves against chemicals and micro-organisms*
  Part 2 Determination of resistance to penetration
  Part 3 Determination of resistance to permeation by chemicals

These tests include air and liquid leak tests and chemical permeation tests and are used to determine the effectiveness of category II and III gloves.

Tests may also be carried out using The Institute of Environmental Sciences and Technology recommended practice IEST-RP-CC005.3 [ref 7] - Gloves and fingercots used in cleanrooms and other controlled environments. This describes procedures for testing and evaluating gloves and finger cots for use in controlled environments. Tests are provided for determining cleanliness, physical and chemical integrity, and other relevant properties. Guidelines are also provided to assist users in the proper selection of gloves or finger cots.

Whenever gloves are required as PPE e.g. for the preparation of cytotoxic drugs, a Health and Safety specialist must be involved in all aspects of risk assessment, product evaluation and selection.

Glove design and presentation

There is a very large range of glove styles and presentations available.
Options include;

- *Size range*
- *Handed or ambidextrous*
- *Different cuff lengths*
- *Smooth or texture finish*
- *Different colours*
- *Powder free or powdered (not usually appropriate for cleanroom use)*
- *Bulk packed or individually packed*
- *Sterile or non-sterile*
- *Anti-static*

Boxed ambidextrous disposable gloves


A variety of different glove packs

The final selection of the appropriate glove for a specific application will depend on the contamination control system, the cleanroom garment styles, gowning technique, wearer comfort and safety.

Section 9.0 Planning, sourcing and optimising cleanroom consumables supply provides advice on specifying and selecting the correct glove to meet the requirements of specific operations.

Oversleeves and finger cots

Oversleeves may be worn to give additional protection to the lower arm and are a tube of material which is elasticated at each end drawn over the cleanroom garment sleeve.

Disposable oversleeve

Oversleeves may be produced in a variety of non woven or plastic materials and are often used to protect the inner re-usable garment from significant permanent staining, to stop moisture penetration or provide chemical protection.

Where there is a heat risk non-flammable oversleeves may be used to protect the wearer.

Disposable finger cots

Finger cots are usually made from the same materials as cleanroom gloves and provide primary or additional protection for the fingertips.

5.5 Footwear

Most cleanroom footwear is re-usable. This includes dedicated cleanroom clogs and shoes together with woven fabric overboots and shoes which are cleaned and decontaminated with other re-usable cleanroom clothing.

Single use disposable overboots and overshoes are also used and are manufactured using non-woven materials. They are available in a range of sizes with different fastenings and sole materials. They may be supplied cleaned and decontaminated, sterile or non-sterile with various packing options.

Lightweight plastic disposable overshoes are often required and these are usually manufactured from basic cross linked polyethylene (CPE).

They are normally blue, bulk packed, non-sterile and are not decontaminated after manufacture.

Disposable plastic overshoes

Plastic overshoes are available in different thicknesses of material and the lighter 4.5g/m^2 shoes are only suitable for short periods of use e.g. as a changing area shoe cover.

If more prolonged use is required then the heavier 8.0g/m^2 weight is needed to withstand wear without perforating.

Operator slipping, particularly on smooth or wet cleanroom surfaces can be an issue with this type of footwear and needs to be carefully considered.

Disposable overshoes which incorporate an ESD tape can be selected when control of static electrical discharge is important.

Disposable cleanroom socks are also available and can incorporate anti-bacterial and ESD properties.

ESD cleanroom sock. Image courtesy of Asiatic Fiber Corp

SECTION

6.0

Decontamination of Cleanroom Garments and Consumables

6.1 Purpose and Function

Most cleanroom manufacturing operations require staff to be present in controlled areas. The staff will undertake a variety of tasks and may be working in cleanrooms with a wide range of classifications.

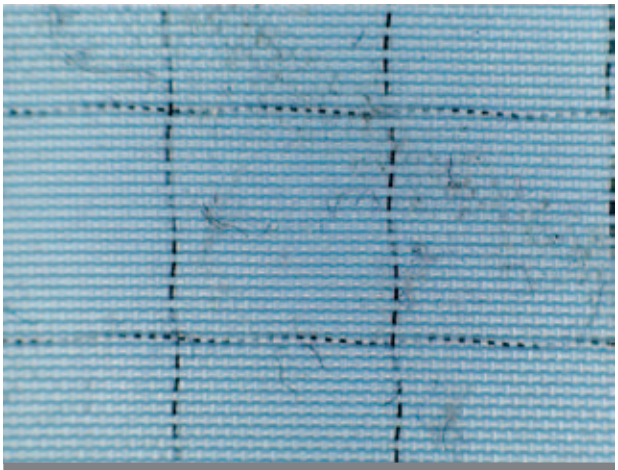
As part of the contamination control systems, staff will be equipped with cleanroom clothing which is suitable for the task and for the contamination control requirements.

The clothing will usually have disposable elements such as gloves and masks but the majority of the clothing will be reusable as these garments provide the most efficient, cost-effective and environmentally friendly option.

Contamination control clothing

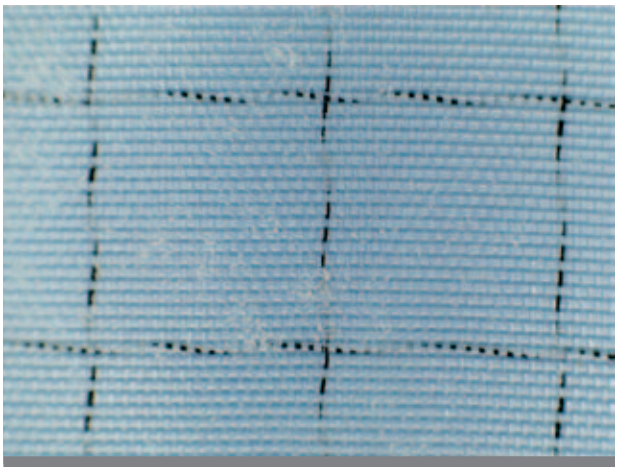
Cleanroom clothing (and other textile items) are manufactured from fabrics which act as a filter for the wearer and do not themselves produce significant contaminants. (This is discussed in detail in Section 4.0 *Reusable Contamination Control Clothing*).

Once the garments have been worn however, the clothing becomes contaminated by fibres, particulate and micro-organisms which have been shed by the wearer and which become trapped by the fabric, especially on the garment inner surface.



Photomicrograph of fibre and particulate contamination on cleanroom garment

Cleanroom clothing may also be contaminated during use by materials from within the production area. These contaminants may be powders or liquids and are usually present on the outside of the garment.



Photomicrograph of powder contamination on cleanroom garment

For the cleanroom to operate efficiently staff must have easy access to clean, decontaminated cleanroom garments which are fit-for-purpose and presented in a way which allows changing procedures to be followed effectively.

Various non-clothing items such as equipment covers, cleanroom mops and cleanroom wipes may also be required and these too will require processing by a cleanroom decontamination process.

Decontaminated cleanroom mop

The cleanroom decontamination plant is responsible for the supply of these key services to the cleanroom manufacturing operations.

Cleanroom decontamination plant

The six major stages listed below summarise the key elements of cleanroom garment and consumables decontamination operations and although only clothing is discussed the same approach is applicable for all other processed items.

1 .Cleaning
The removal of soiling and stains to provide visually clean, dry, odourless garments.

2. Disinfection and sterilisation
The production of cleanroom garments with a very low bio-burden and the addition of a further sterilisation treatment when sterile clothing is required.

3. Particulate decontamination
The removal of particulate and fibre contamination from the garments to leave only a very small residual number of particles and fibres.

4. Checking and inspection
Comprehensive inspection and checking of every item to ensure that there is no damage which would subsequently compromise the contamination control systems.

5. Packing, labelling and presentation
Folding, labelling and packaging of the garments following processing.

6. Process control systems
Use of control systems and associated monitoring methods for all critical aspects of the cleanroom decontamination process to ensure consistency of process and product quality.

6.2 Cleanroom Garment and Consumables Decontamination Plant - Layout and Contamination Control Requirements

Diagram 1 shows the basic elements of a cleanroom decontamination plant, and the general material flow.

The facility will have a dedicated entrance for personnel where staff will change into cleanroom clothing that is consistent with the cleanroom cleanliness classification level, prior to entry into the processing cleanroom. The garment processing cleanroom will be at a higher differential pressure than the adjacent staff changing and secondary packaging area. This helps to prevent the ingress of both viable and non-viable particulate from these areas. The cleanliness classification level of the cleanroom will be determined by the requirements of the materials being processed in the cleanroom.

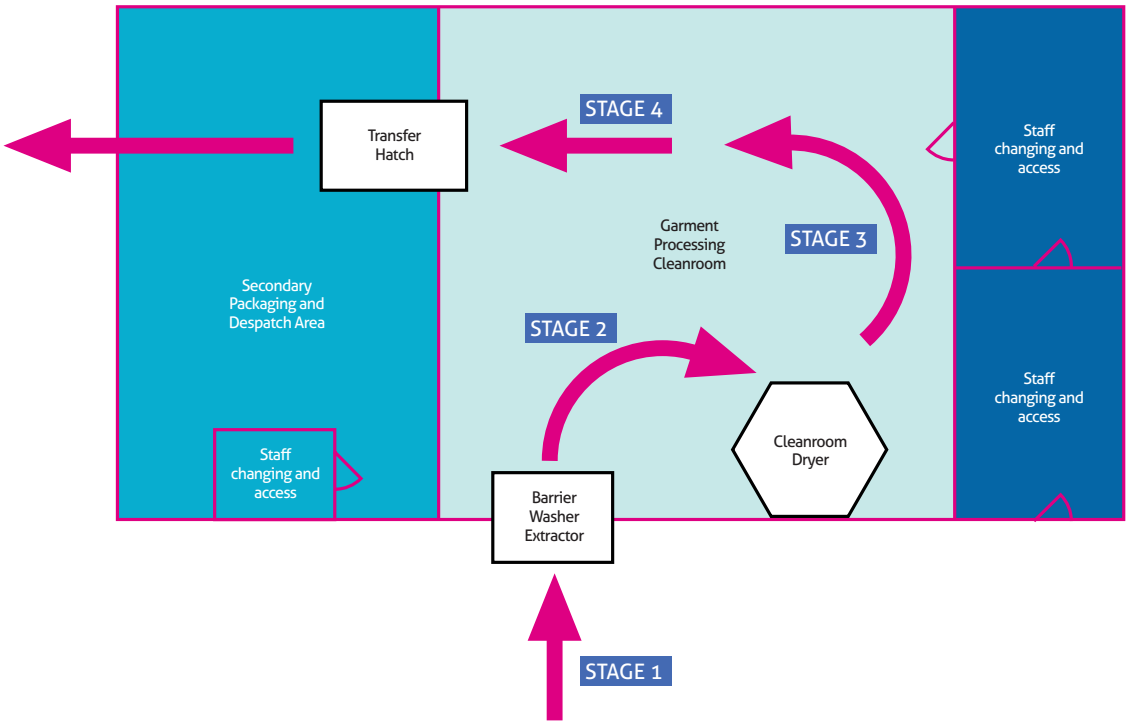


Diagram 1. Plan of typical decontamination plant

The secondary packing area is likely to be of a less stringent classification due to the nature of the activities undertaken in it.

Stage 1.
Contaminated items are loaded into a barrier washer-extractor unit from a non cleanroom area. When the cycle has been successfully completed, the decontaminated load is unloaded into the cleanroom area.

Barrier washer-extractor machines are designed to wash and centrifuge items held within a rotating drum. The entry and exit doors are interlocked so that only one door can be opened at a time and the exit door remains locked until the decontamination cycle has been successfully completed. The washer-extractor therefore acts as a pass-through barrier in the cleanroom wall allowing soiled items to be placed within the machine on the outside and clean, disinfected items to be removed from the machine directly from inside the processing cleanroom.

Barrier washer extractor exit (unloading) door


Barrier washer extractor machines incorporated into the cleanroom wall to act as a pass-through barrier into the processing cleanroom

Stage 2.
The decontaminated garments are then loaded into the cleanroom dryer from the cleanroom. The dryer has the same cleanliness levels as the processing cleanroom in which it is sited.

Drying of the processed items in this unit is achieved with hot, filtered air; the hot airstream enters the unit via an appropriate grade of filter and is exhausted to atmosphere out of the cleanroom.

This filtered airflow prevents recontamination of the load and also helps to remove any remaining particles and fibres during the drying operation.

Items for use in high grade cleanrooms are usually dried using a tumble dryer.

Cleanroom tumble dryer in operation

Garments for use in lower grade cleanroom areas may be dried using a tunnel finisher. In this type of process garments are placed on hangers and pass through a chamber which is supplied with hot, filtered air.

Tunnel finisher

Stage 3.
The decontaminated and dry garments are unloaded into the processing cleanroom where they will be inspected, folded, packed and sealed into an appropriate primary protective wrapper.

Cleanroom clothing being folded ready for packaging

Decontaminated cleanroom garment in primary packaging

Stage 4.
The primarily protected items are then transferred into a less controlled area, normally connected to the cleanroom by an air-lock pass-through hatch, for secondary packaging and assembly for delivery to the customer.

Fully processed and packed items for despatch

Cleanroom decontamination plant classification
Each cleanroom manufacturing operation will specify a clothing policy and cleanliness levels appropriate for their contamination control plan.

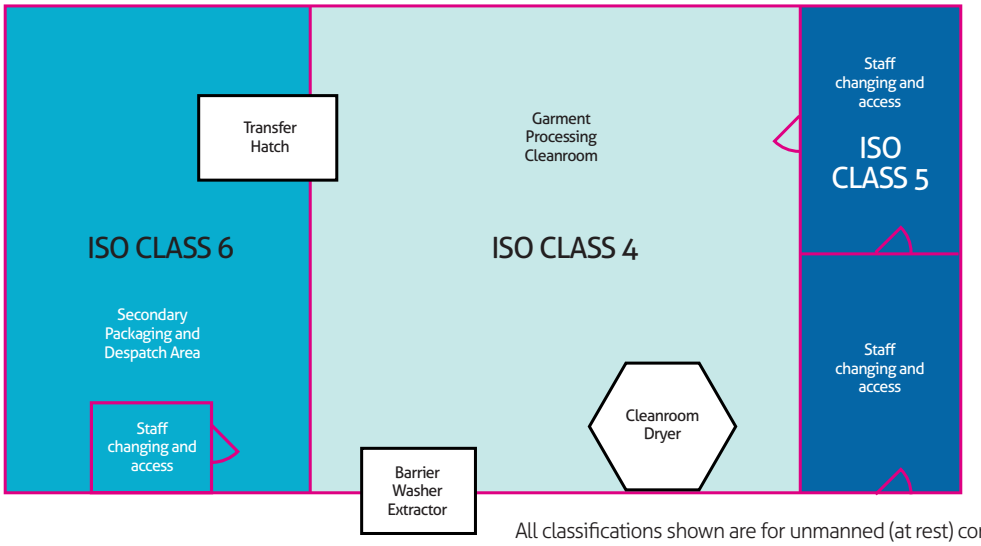
As the cleanroom cleanliness levels become more stringent, so do the operating costs and it is clearly inefficient to use cleanroom clothing and consumables which have been processed through a high grade cleanroom decontamination plant in a low grade manufacturing area. Conversely it would be completely unacceptable to provide items for use in a high grade environment that have been decontaminated in a low grade cleanroom.

To meet different contamination control requirements various classifications of cleanroom decontamination plant are available, however as each cleanroom operation is unique it is not always possible to exactly match the production area cleanliness classifications with those of a decontamination plant.

A professional cleanroom decontamination plant operator will be able to offer a range of processing options and will work closely with the end user to agree the most technically appropriate and cost effective service.

Any decontamination plant must be validated and monitored to confirm the cleanliness classification level. ISO standard 14644-1 [ref 1] defines the various cleanroom cleanliness levels, the lower the ISO classification number, the more stringent the cleanliness level. The ISO cleanliness classifications, measured by particulate monitoring within the cleanroom, can be stated either when the cleanroom is not occupied (at rest) or when it is occupied and functioning (in use). The cleanroom staff and activity associated with production will produce particulates and so the in use ISO classification will normally be higher than the at rest ISO classification for the same room.

Diagram 2 shows the ISO classifications (at rest) which would be required for a decontamination plant producing products for use in a range of high grade cleanrooms.



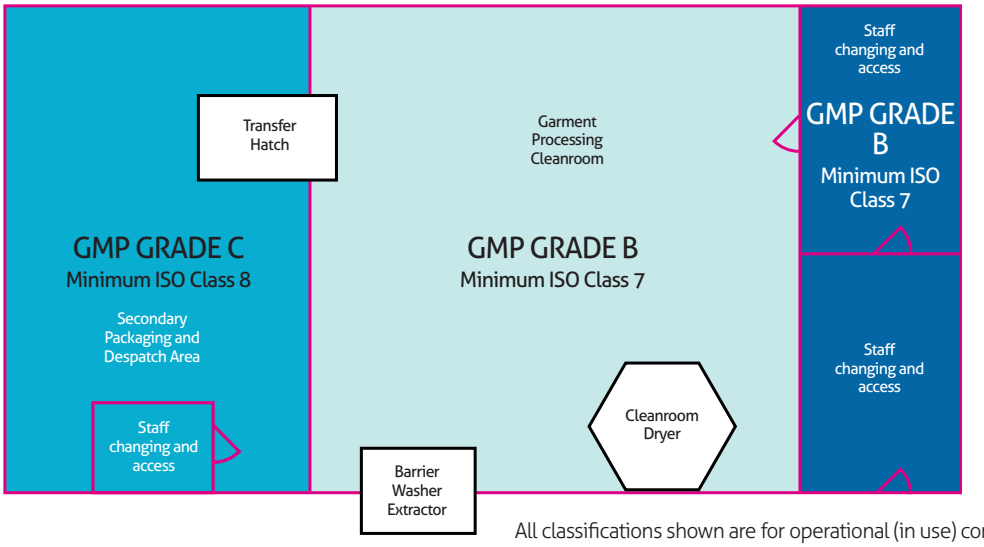
All classifications shown are for unmanned (at rest) conditions

Diagram 2. Example cleanroom garment and consumables decontamination plant cleanliness classifications

Diagrams 3, 4 and 5 show examples of operational, (in use) classifications for different garment and consumables decontamination plants together with examples of the types of manufacturing operations they could supply. The GMP EU grades [ref 2] shown are obtained by monitoring the microbiological levels within the cleanroom during use.

The garment particulate classifications normally achieved by these grades of processing facility are also shown.

(Section 2.0 *Cleanroom Classifications and Standards* provides more detailed information on the relevant standards).



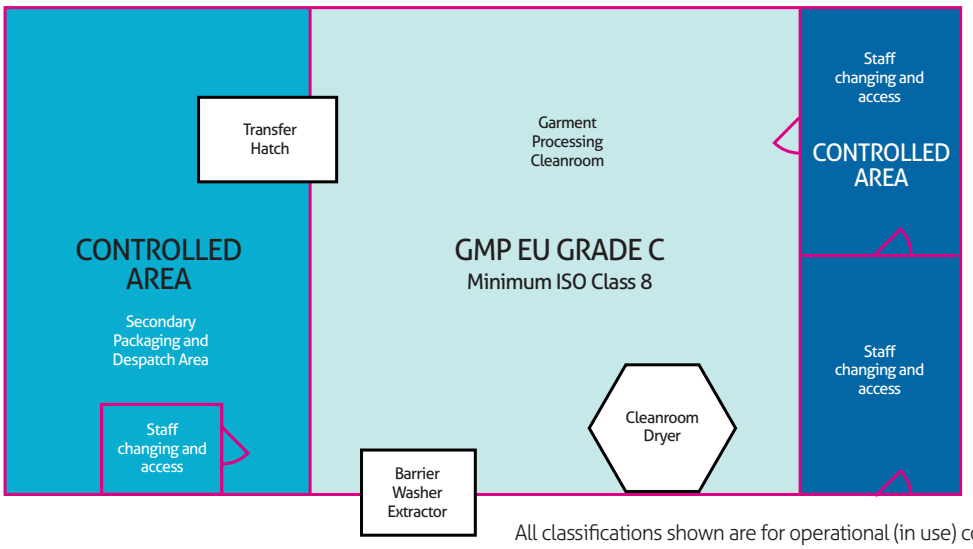
All classifications shown are for operational (in use) conditions

Diagram 3. Example cleanroom garment and consumables decontamination plant cleanliness classifications

The decontamination plant classifications shown in diagram 3 would be suitable for processing cleanroom garments and equipment for use in high grade Bioscience and Pharmaceutical manufacturing operations where control of viable microbiological contaminants is paramount.

This would include aseptic manufacture, vaccine production, blood products and other biological preparations.

The garment particulate and fibre classification following processing and packaging in this environment would be IEST-RP-CC003 [ref 3] class I and ASTM F51/00 [ref 4] Class A.



All classifications shown are for operational (in use) conditions

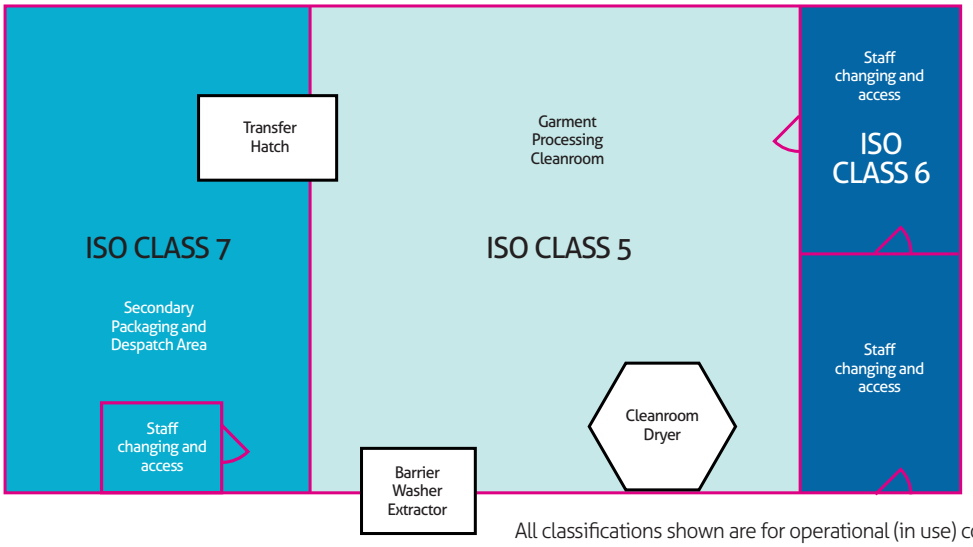
Diagram 4. Example cleanroom garment and consumables decontamination plant cleanliness classifications

The cleanroom classifications shown in diagram 4 would be suitable for the processing of cleanroom clothing and equipment for use in the outer areas of high grade Bioscience and Pharmaceutical cleanrooms and for cleanroom undergarments.

It would also be appropriate for clothing used in barrier isolator manufacturing, tabletting operations, basic wound care and medical device production.

For non-biological manufacturing this grade of cleanroom decontamination plant would be suitable for electronic circuitry and optical products production, surface finishing and high care food manufacturing facilities.

The garment particulate and fibre classification following processing and packaging in this environment would be IEST-RP-CC003 [ref 3] class II or III and ASTM F51/00 [ref 4] Class B or C.



All classifications shown are for operational (in use) conditions

Diagram 5. Example cleanroom garment and consumables decontamination plant cleanliness classifications

The cleanroom classifications shown in diagram 5 would be suitable for the processing of cleanroom clothing and equipment for use in high grade micro-electronics manufacturing and precision engineering with strong emphasis on the control of fine particulate, chemicals and ESD.

Examples of operations which would utilise this type of cleanroom decontamination plant are waferfab plants, microelectronics assembly, critical space engineering, optical engineering and weapons manufacture.

The garment particulate and fibre classification following processing and packaging in this environment would be IEST-RP-CC003 [ref 3] class I and ASTM F51/00 [ref 4] Class A.

6.3 Cleanroom Decontamination Plant Cleaning Process

The cleaning process used by the decontamination plant is designed to remove visible stains, odours and other contaminants so that the garment is returned to the wearer in a visually clean and dry condition. Garments used in high grade cleanroom manufacturing are not usually subjected to significant soiling or wear but for some operations such as medical device manufacture, tablet production and surface finishing, cleanroom garments may become soiled with a range of contaminants including ink, paint, powders and sealants.

If it is suspected that items for decontamination could be contaminated with harmful materials then the cleanroom decontamination plant must be informed prior to garment handling and processing.

Soiling may be removed using either a solvent (dry-clean) or wet-wash (water based) process.

Solvent processes may be used for the removal of paints, heavy oil and grease; however the solvent systems used pose a variety of particulate, chemical, microbiological, safety and environmental problems and so are rarely used for cleanroom product decontamination. Water based methods are therefore the usual choice for cleanroom product cleaning.

For a low grade cleanroom decontamination operation potable water is used, for high grade processing however, the water quality is usually improved e.g. by filtration or reverse osmosis (RO), to ensure a consistent and low bio-burden with low dissolved solids.

Water based processes may be used for the removal of all types of soiling and different cleaning requirements are addressed by selecting the appropriate chemicals, washing machine action, temperature and process time. By varying these parameters it is possible to remove soiling and reduce most staining to an acceptable level; however some materials, such as indelible printing ink, may be difficult to remove.

Following cleaning the items are dried using either a tumble dryer or tunnel finisher. Tumble dryers are used in high grade cleanroom decontamination with measured loads of damp items being mechanically tumbled in hot filtered air.

The tumble drier is kept under positive pressure and fed with heated, filtered air which is exhausted to atmosphere after passing through the machine.

A tunnel dryer operates by passing hanging garments continuously through a hot air chamber fed with heated, filtered air, exhausted to atmosphere and this type of drying may be used for processing low grade cleanroom garments.

6.4 Disinfection and Sterilisation

General principles

Simple definitions of the terms disinfection (sanitisation) and sterilisation are;

- *Disinfection; to clean in order to destroy or prevent the growth of disease-carrying micro-organisms.*
- *Sterilisation; the procedure of making some object free of live bacteria or other micro-organisms.*

The cleaning process used by the decontamination plant removes and kills micro-organisms. The mechanical action of the washer extractor, together with the use of process chemicals, physically removes and suspends micro-organisms, many of which are damaged or killed by chemical action.

Part of the cleaning cycle is very likely to be at high temperature which will kill or damage most vegetative microbes.

The subsequent drying process further reduces the small number of surviving micro-organisms by desiccation and so the process greatly reduces the number and type of microbes (the bioburden) on the cleaned item.

All processing takes place in a controlled cleanroom environment and this ensures that the chance of re-contamination of the product by staff or from the environment is reduced to a minimum.

Items cleaned, dried and packed by a cleanroom decontamination plant will therefore be effectively disinfected and have a very low bioburden.

Thermal disinfection

During the Victorian era heat was recognised as the main method for textile disinfection and *'Steam Laundry'* employed boiling for all items.

Victorian steam laundry

Effective cleaning can be achieved at low temperature using modern wash chemicals and most domestic washing machines operate at 30ºC to 40ºC however this low temperature does not achieve disinfection and higher temperatures are required.

Guidance for the thermal disinfection of textiles has been provided in the UK by the Department of Health publication HSG (95)18 [ref 5]: Hospital laundry arrangements for used and infected linen, which stipulates that consistent and acceptable disinfection can be achieved if the temperature of the wash load is held at 65ºC for 10 minutes or 71ºC for 3 minutes and this has become accepted practice for the disinfection of textiles.

Fungal and bacterial spores are not killed by these temperatures however.

Use of a high water-temperature as a disinfecting stage has several advantages.

Water can be easily heated by a variety of means which do not contaminate the water with particulate or chemicals.

Water temperature can be easily monitored using simple and easily validated temperature sensors and software.

The mechanical action of the washing machine gives rapid and consistent mixing of the contents.
Any textile items submerged in the water are quickly raised to the water temperature evenly across all contact surfaces.

The high wash temperature increases soil removal and cleaning, reducing the requirement for chemicals.

Drying

To achieve drying the textile item is raised to a minimum of 100ºC and the majority of residual vegetative organisms, but not fungal or bacterial spores, will be killed by desiccation during this process.

Cleanroom handling and packing
Once items have passed through the disinfection stages all further processes are designed to minimise the possibility of recontamination of product by the staff, from the production environment or process equipment. All items are therefore handled, sorted and sealed in primary packaging within the main manufacturing cleanroom before being transferred to dispatch areas.

Disinfection Process Summary
Production of cleanroom garments and consumables with a consistent and very low bioburden therefore has several interlinked process stages;

- *Mechanical removal or damage to micro-organisms by the wash process.*
- *Destruction or damage to micro-organisms by the process chemicals.*
- *Thermal disinfection from high temperature wash.*
- *Use of biologically controlled process water to prevent re-contamination.*
- *Desiccation of micro-organisms during drying.*
- *Cleanroom processing of disinfected items to prevent re-contamination.*
- *Cleanroom application of sealed protective packaging to prevent re-contamination.*

Non-thermal disinfection methods
Chemical biocides may be added to the wash cycle. The correct dilution and distribution throughout the entire wash load together with an adequate contact time is necessary to achieve satisfactory disinfection of all items being treated. These parameters are more difficult to control and monitor within the washer extractor than temperature and it is therefore difficult to easily confirm effective disinfection of each item within each load.

Residual biocide may be retained on the fabric surface and give additional antimicrobial benefit during use. However residual chemical on the clothing may pose a contamination risk to wearers (especially on garments in contact with the skin), to the cleanroom environment and to the products being manufactured.

Chemical disinfection is usually only used therefore when materials will be damaged by thermal disinfection temperatures e.g. laminated fabrics.

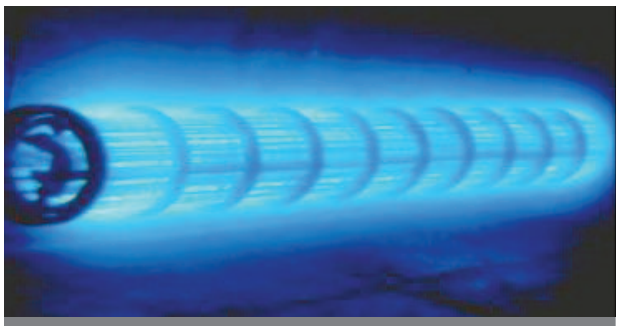
Disinfection can be achieved at low temperature using ozone wash systems which saturate the process water with highly oxidizing ozone (O_3) molecules.
Small purpose-built washing machines are available which incorporate ozone injection systems with good reported results. In full size cleanroom washer extractors however producing and maintaining adequate levels of ozone throughout the wash load is very difficult to achieve and monitor. This technology is therefore currently not considered to be reliable for large scale cleanroom decontamination plant use.

Sterilisation
Gamma irradiation
For some high grade bio-medical and pharmaceutical manufacturing procedures a further sterilisation process is required for garments or consumables following production and packing by the decontamination plant.

A sterile product is accurately defined as an item with a sterility assurance level (SAL) of 10^{-6}. This means that there is a theoretical chance that if 1 million organisms were present on the product before the sterilisation process, 1 viable organism could remain after the process.

Cleanroom processed items presented for sterilisation by the decontamination plant will have only a very few organisms present which means that effectively no viable organisms (including fungal and bacterial spores) remain after sterilisation.

Sterility is usually achieved for textile items by gamma irradiation using a minimum irradiation dose of 25kGy.


Gamma irradiation

The process is highly automated and controlled [ref 6] with annual dose validations proving the effectiveness of the process for each product type. Additionally each sterilisation batch is monitored to measure the gamma dose throughout the product and a certificate of irradiation is issued to confirm that the minimum gamma dose has been received. Detex labels, which change colour from yellow to red on exposure to ionising radiation, are often applied to products and provide a quick visual confirmation of sterilisation.

Irradiated and unirradiated detex labels

Sterilisation is usually carried out by a specialist sub-contractor employed by the decontamination plant. Gamma sterilisation is an effective method for producing sterile textile products for cleanroom use however the process physically damages fabrics over a prolonged period and will reduce the useful life of the sterilised products.

Cleanroom fabric showing discolouration following repeated decontamination and gamma irradiation sterilisation cycles

Autoclave

Autoclaving uses pressurised steam to sterilise items packed within a chamber, typically at a temperature of 121ºC. To be effective the steam must contact all surfaces to be sterilised and so steam permeable packaging is needed for any bagged items. The time required for sterilisation will vary with the product type and loading density and is usually validated using physical, chemical or biological sterility indicators placed within the load.


Industrial autoclave. Image courtesy of Baxter Healthcare Ltd

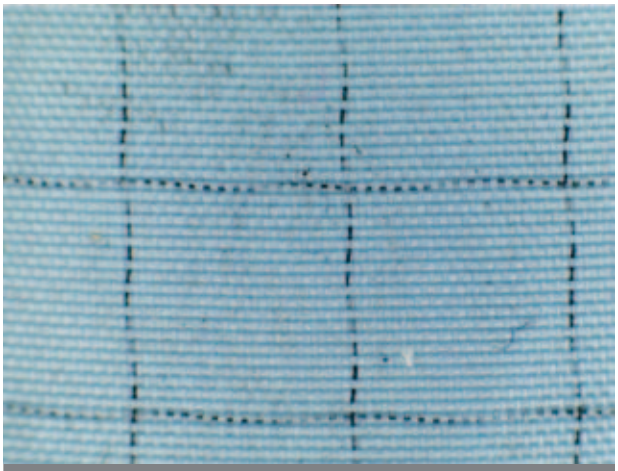
This method of sterilisation is often used when cleanroom garments must be sterilised after use, and before transport to the garment decontamination plant, in order to control a biological hazard e.g. when the clothing has been used in a virus culture area in vaccine manufacture.

Steam sterilisation causes heat-set creasing in polyester fabrics and shortens garment life.

6.5
Particulate and Fibre Decontamination

The decontamination plant must remove fibres and fine particulate from the processed items in addition to achieving visual cleanliness and disinfection.

Low shedding cleanroom fabrics are used to reduce the number of particles and fibres being produced by the items themselves and so the main requirement for the decontamination plant is to remove contamination which has been deposited on the surface during manufacture or use.



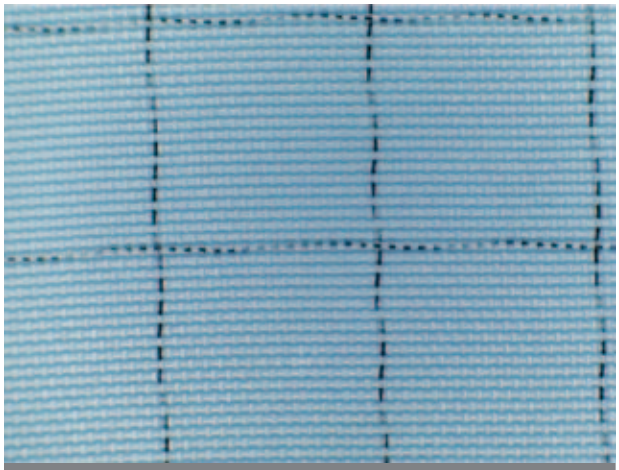
Photomicrograph of contamination on a cleanroom garment following use

A cleanroom decontamination cycle will remove contaminants as part of the cleaning process and particles and fibres of all types will be removed during the wash cycle. Use of purified water reduces the possibility of re-deposition of particulate onto the processed items.

After the washing stage all operations are carried out in a controlled cleanroom, again reducing the possibility of recontamination.

The final stage of particulate removal occurs during drying when the processed items are agitated in a fast flowing stream of heated, filtered air.

Particulate adhering to the fabric surface is lost as the fabric dries and is carried away by the airflow.



Photomicrograph of decontaminated cleanroom garment

Following the drying stage the clean, dry, decontaminated items are packed within a cleanroom environment in non-shedding packaging to again reduce any risk of particulate and fibre re-contamination.

Confirmatory checks are carried out to show that the decontaminated items have achieved the particulate cleanliness level required. These will usually be either the Helmke drum test as detailed in IEST-RP-CC003.3 [ref 3] or the ASTM F51/00 [ref 4] microscopic test. (See Section 2.0 *Cleanroom Classifications and Standards* for further details).

Sequence of photos showing ASTM F51/00 particulate and fibre test.
1. Preparing the equipment. 2. Placing the test garment on the test frame. 3. Taking a vacuum sample onto a filter. 4. Fibre counting.
5. Particle counting.

6.6
Product Inspection and Conformance Checks

The physical integrity of fabric items is a critical aspect of contamination control.

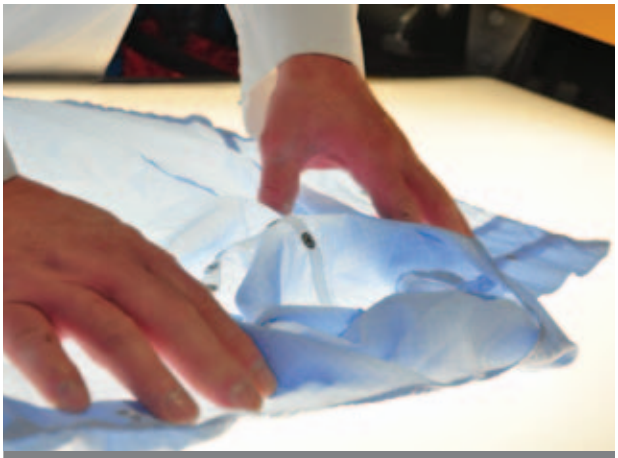
Damaged mops, wipes or equipment covers can shed large numbers of particles and fibres and damaged cleanroom clothing may also allow the escape of particulate from the wearer.

The ESD (electro-static discharge) properties may also deteriorate and this can cause damage to products by static discharge.

For all decontaminated items it is therefore necessary to have clear and comprehensive inspection and test procedures to ensure that all products are suitable for purpose.

Visual inspection is carried out to detect physical damage such as holes or tears. Checks are also required on fixtures and fittings such as zips, studs and tapes, the sole material of boots and shoes must be checked for damage or cracks.

For re-cycled items, such as cleanroom clothing, the fabric must be inspected to check that it has not deteriorated significantly and remains in an effective and acceptable condition.



Inspection of garments for physical damage

When ESD control is a key requirement then standard electrical conductivity tests [ref 7] are required to confirm that fabric and garment conductivity are still functioning at the required level.

ESD garment test

Fabric wear is influenced by many factors including the type of manufacturing operation in which it is used, the number of decontamination processes received and any sterilisation cycles.

This variability means that as well as a visual inspection it is often necessary to validate an acceptable garment life for a particular process and to remove the item at the pre-determined maximum number of wear and process cycles regardless of its physical appearance.

If an item fails to achieve the minimum standard set by the various conformance procedures it must be removed from cleanroom use and either repaired or replaced.

6.7 Labelling, Packaging and Presentation

Single use items such as wipes or disposable garments are not usually individually marked and product packaging provides all relevant information.

Fully labelled cleanroom wipes

Reusable items which undergo repeated use and cleanroom decontamination cycles are individually labelled.

Labelling of cleanroom items is required for various purposes;

- *To individually identify the item.*
- *To track the location of the item.*
- *To monitor the process count of re-cycled items.*
- *To provide process and expiry date information.*
- *To visually identify sterilised items.*
- *To identify items with user-specific information.*
- *To meet corporate identity requirements.*

Each individual item is identified with either a barcode or a transponder which can be read at any point by a suitable electronic reader.

Garment transponder

Garment barcode

Information gathered in this way can be managed in a database to provide information such as location, number of process cycles and number of sterilisation cycles.

In order to identify the item visually, printed labels are produced which may be sewn onto the fabric or sealed on with adhesive.

Direct printing onto the fabric can be achieved using sublimatic ink transfer and this allows the application of any design or colour and is especially effective for the application of corporate logos or to provide information such as department of use.

Examples of sublimatic printing on cleanroom garment

Process labels, such as process batch number, expiry date and sterilisation indicator labels (detex labels), are normally applied to the primary packaging and are clearly visible at the final point of use.

Packaging and presentation

The packaging and presentation of cleanroom decontaminated products is dependent on the type of product and the cleanroom in which it will be used.

Primary packaging is product specific, for example;

1. *Sterile alcohol-impregnated cleanroom wipes require primary packaging which will completely contain the alcohol impregnant and be physically strong enough to contain the wipes but also allow easy access to the contents. It must remain unchanged by gamma irradiation or VHP gassing, be effectively cleaned by wiping and readily accept product labels.*

2. *Cleanroom clothing for low classification areas requires primary packaging which will contain the garment and provide a protective barrier to prevent re-contamination. It may need to be cleaned by wiping with alcohol and will need to accept process labels. The material needs to be transparent to allow the clothing and its labels to be visible to the wearer and must be easy to open.*

Packed cleanroom wipes

Packed cleanroom mop

Packed cleanroom garment

Secondary packaging consists of additional layers which can be removed in stages when the product is being used and for high grade cleanroom operations up to 4 packaging layers may be required.

Presentation of cleanroom clothing and consumable products can also be tailored to individual needs. For example specific folding of garments may be needed to match prescribed and validated gowning procedures or a variation on the number and type of packaged cleanroom wipes or mops may be requested by the end user.

6.8 Process Monitoring, Controls and Records

The cleanroom decontamination plant provides a critical service to manufacturing operations. Failure of correct garment supply can lead to shut-down of the operation or contamination of the product resulting in serious financial loss.

When patient safety is a risk then the potential for harm caused through a contamination control failure is even higher.

For this reason the decontamination plant must be monitored and controlled to provide evidence and assurance that all operations are robust and products within specification. This is usually accomplished within the framework of a recognised and accredited QMS (quality management system).

Monitoring and control systems are broadly based around two operational areas;

1. *Process and engineering controls*
2. *Cleanroom and product controls*

Process and engineering controls

Cleanroom decontamination operations require the use of industrial processing machinery and purified water systems.

These machines require regular maintenance to provide uninterrupted and consistent operation and a planned preventative maintenance (PPM) schedule is required with accurate PPM records retained for reference.

The wash and dry cycles are critical process points providing cleaning, disinfection, particle removal and drying. Control, monitoring and batch process information are therefore required for these stages.

SCADA (supervisory control and data acquisition) systems are used to achieve this degree of control and data collection.

The SCADA system will monitor critical parameters such as wash temperature, process time and conductivity. The drying cycle will also be monitored and the SCADA system can be used to adjust the process time according to the moisture content of each load.

Alarm states will be set for all critical stages and failure to meet the specified parameter will result in an immediate alarm and automatic halt of the process. All key data, including any out of specification alarms, will be captured and stored for future reference.

SCADA process monitoring

Cleanroom and product controls

Testing is required to ensure that the decontamination plant cleanroom is operating effectively and within specification.

The unmanned (at rest) cleanroom will be tested and validated on a regular basis by validation engineers using the methodology specified in ISO 14644 [ref 1].

Further particulate monitoring will be carried out during decontamination operations to give an indication of the contamination levels present during operational (in use) conditions.

Pressure monitors will be in place to continuously monitor and record cleanroom overpressure.

Cleanroom pressure monitoring

If control of viable particles is required then the decontamination plant cleanroom will be monitored during use for microbiological contaminants and the test methods recommended in the MHRA Rules and Guidance for Pharmaceutical Manufacturers and Distributors [ref 2] are usually adopted.

Microbiological testing

The purified water system will also be monitored for its physical characteristics and microbiological loading.

Particulate and fibre tests will be carried out on sample processed textiles to confirm acceptable decontamination of products using either the Helmke drum test, IEST-RP-CC003.3 [ref 3] or the ASTM F51/00 [ref 4] microscopic test.

When an additional sterilisation stage is required the process will be validated, monitored and certified by the sterilisation contractor. Microbiological sterility testing may also be carried out on finished product to confirm that the process is effective.

Cleanroom decontamination plant operations will be controlled by a documented system covering all aspects of the process.

This will include all critical areas such as staff training, changing procedures, access controls, cleaning procedures, records, validation and change control.

Records

Monitoring and control systems operated by the decontamination plant produce a variety of results and records. These results are used to provide confirmation that the plant is producing products which meet the agreed specification and are suitable for cleanroom use. The records are also available for inspection during investigations, for example if there is a potential contamination issue either at the decontamination plant or the end user.

6.9
Cleanroom Decontamination Plant Audits

Customers for decontaminated products will audit their key cleanroom suppliers, including decontamination facilities, to ensure that the services provided meet the needs of their contamination control systems and regulatory requirements.

The exact format of these audits will depend on the organisation involved but a minimum audit checklist will include the following;

1. *Profile and organisational structure of the clothing and consumables decontamination company.*
2. *Cleanroom design, layout, classifications and validation.*
3. *Water systems and water specifications.*
4. *Product and people flow.*
5. *Process controls and monitoring.*
6. *Batch records.*
7. *Quality Management System (QMS) including accreditations, document control, standard operating procedures, deviation reporting and investigation, change control, validation.*
8. *Staff training and training records.*
9. *Garment particulate testing and results.*
10. *Microbiological monitoring programme and results.*
11. *Calibration and records.*
12. *Engineering maintenance.*
13. *Disaster recovery plans.*

When sterile products are required then the sterilisation process will also need to be audited.

Audits are an essential element of contamination control and also provide an excellent forum for the exchange of ideas and information of benefit to both customer and supplier.

6.10
Special Customer Requirements

Cleanroom decontaminated garments and consumables are used in a wide variety of manufacturing operations. Each manufacturer will use the principles of contamination control to protect their product but each location and process will have different requirements.

Cleanroom decontamination plants offer a range of standard products which are designed to meet the majority of customer needs, however, if a particular operation requires a unique product or service the cleanroom decontamination plant will be able to work with the customer to develop the best and most cost-effective solution.

Cleanroom production of wipes

Examples of special products and services are;

1. *The cleaning and decontamination of medical device components.*
2. *Packing and sterilisation of equipment packs.*
3. *Specific impregnants on wipes and mops.*
4. *User specific garment design.*
5. *Machine and equipment covers.*
6. *Unusual fabric requirements.*
7. *Additional microbiological or particulate testing.*
8. *Special validation exercises.*

In addition new fabrics, products and processes are being continuously developed by the cleanroom garment and consumables decontamination industry to match the expanding global use of cleanroom technology.

Compliance 100® Micronclean syringes

SECTION

7.0

Cleanroom Cleaning - Methods and Equipment

Sections 7.1, 7.2 and 7.3 discuss the reasons for cleaning and the basic elements of a cleaning system. The later sections give further details of cleaning products, methods and materials.

7.1 Contamination Control and the Requirement for Cleaning

A large amount of time, energy and money is usually expended on the design and development of contamination control facilities.

Once the cleanroom is operational an equal emphasis is required to establish and maintain consistent ongoing control and the cleaning system is a key element of this process.

Cleaning can sometimes be regarded as a secondary function and may also be seen as an easy target for cost reduction exercises. However without an efficient cleaning programme the whole cleanroom facility is at real risk of failure as contamination can quickly build up and be transferred to the product.

The cleanroom air filtration system effectively controls the ingress of airborne fibres and particulate into the cleanroom, however this does not mean that the area will remain free from contamination during use. Both the cleanroom staff and the production process will introduce a range of contaminants during manufacturing operations.

Cleanroom clothing is low shedding and acts to filter the viable and non-viable particulate being lost by the wearer. Although very effective in greatly reducing the contamination from staff not all fibres or particles are contained within the garments and a significant amount of contamination will still be dispersed into the cleanroom by the occupants and their clothing. Many of the larger particles will settle by gravity onto horizontal surfaces in the cleanroom.

The smaller particles may be more widely dispersed before similarly settling onto cleanroom surfaces. Static electrical charges generated by cleanroom equipment and activities will also increase attraction and adhesion of fine particulate.

Staff access to the cleanrooms will be through changing areas and these locations will become contaminated during gowning procedures. Contamination may also be transferred between areas with floors being particularly vulnerable as dirt can be transferred into a cleanroom by foot.

Re-usable cleanroom garments are extensively packaged to protect the garments from contamination during transport and storage, the outer layers of packaging will become contaminated and the opening and removal of packaging and the packaging material itself all produce contamination.

Removal and disposal of cleanroom clothing will also generate significant particulate.

Transfer of equipment and materials into the cleanroom will be strictly controlled but the transfer operation, including removal of packaging, will also produce contamination.

As part of the production process staff will be required to operate equipment and handle different materials. Touching and contacting may contaminate gloves and other surfaces on the cleanroom gowns and may create a cross-contamination risk to other items and work surfaces.

The production machinery and process may also produce fibres and particulate and some operations may produce vapour or droplets which can be deposited onto surfaces leaving contaminating residues.

A fully-operational cleanroom may therefore become contaminated by a range of materials.

These can be usefully considered as either large visible contaminants such as discarded packaging or visible liquid droplets, or as microscopic particulates and fibres of approximately 50µm or less which are not visible in normal light.

When the concentrations of such small particles build up and become visible the cleanroom surface cleanliness levels have been grossly violated. For cleanrooms utilised by the healthcare industry, the cleanroom surfaces must also be disinfected to kill any viable contamination that may be present.

Removal of visible contamination requires good housekeeping and effective basic cleaning techniques. Removal of microscopic contamination is achieved using specialised cleanroom cleaning materials and procedures.

7.2 Cleanroom Cleaning - General Considerations

Visible contaminants in the cleanroom can be controlled by basic cleaning and housekeeping methods.

Very large contaminants such as discarded packaging or cleanroom disposables can be placed in a disposal bag and carried from the area. Disposal containers should be placed in areas where they can be frequently emptied. Reusable cleanroom clothing can be removed and placed in designated containers for collection and reprocessing. These containers should not be large enough to allow several days of discarded items to accumulate and should be emptied using a technique which minimises dispersion of particulate into controlled areas.

Large visible particulates and fibres are quickly deposited by gravity and so are normally found on horizontal surfaces. This material can be readily removed using cleanroom compatible vacuum cleaning, the material being lifted from the surface by the airflow and collected for disposal.

Microscopic contaminants, containing both viable and non-viable particles range from approximately 50µm down to <1µm in size and are affected much less by gravity. This material will be deposited on horizontal surfaces but will also become attached to walls, ceilings and equipment. The cleanroom airflow (vertical or horizontal unidirectional airflow or turbulent flow) will also affect the distribution and deposition of these particulates.

All surfaces in a cleanroom should be as smooth as possible with minimal sharp corners as rough surfaces and inaccessible angles are more likely to hold fine particles making them difficult to remove.

Microscopic particles and fibres on cleanroom surfaces may be attached by physical, chemical and electrical forces the main force being the physical intermolecular force known as London-van der Waals. Particles of this small size cannot be removed by dry vacuum cleaning as this method has insufficient energy to overcome these adhesive forces.

This material must be dislodged by direct physical contact and this is usually achieved by mopping or wiping. The material from which these mopping or wiping products are made will affect their particle removal efficiency - the greater the contact area the better the removal effect.

Particle removal is significantly improved if a liquid is used to aid the process which allows some of the particle to surface bonding to be broken. Suitable cleaning liquids not only increase the physical removal efficiency but may also dissolve or suspend the contaminants.

Water, surfactants or solvents may all be used in this way to dampen wipes and mops and improve particle removal. Wet cleanroom compatible vacuum cleaning, which is more efficient than a dry vacuum system, may also be employed for appropriate surfaces such as large floors.

Water used for cleaning or chemical dilution should be at a purity which is acceptable in the area being cleaned and must not be a source of micro-organisms or chemical residues.

In any cleanroom cleaning programme it is therefore necessary to first remove the visible contamination before the removal of the microscopic contamination. The removal of visible contamination is sometimes referred to as "cleaning" and the subsequent removal of microscopic particles as "decontamination" and this can be a helpful distinction during staff training.

As part of the cleaning process it is often necessary to use antimicrobial chemicals which are used to kill or inactivate any micro-organisms remaining after cleaning. These are usually referred to as disinfectants or sanitisers and are available in a wide range of formulations.

ISO 14644-5 Operations [ref 1] gives limited guidance on cleanroom cleaning but the cleaning system and materials will be largely developed to suit the requirements of each cleanroom facility.

Significant factors which will influence the cleaning programme;

- *The product being manufactured*
- *The cleanliness classification(s) of the facility*
- *The requirement for microbiological control*
- *The size of the facility*
- *Hours of operation*
- *Production equipment and machinery*
- *The number of staff*
- *The types of contaminant present*
- *Health and safety requirements*
- *Availability of trained cleaning staff*
- *Cost*

The product
The product being manufactured must be protected from damaging contaminants. This may range from large fibres e.g. for optical or surface finished products to microscopic particles harmful in microelectronics manufacturing. Biomedical products will be especially damaged by viable particles.

The cleaning methods and materials chosen must help to minimise product contamination and at the same time not themselves produce any damaging effects or residues.

Cleanliness classification
The established cleanliness classifications for each area will guide the requirements of the cleaning programme. The more highly controlled areas will usually warrant the most frequent and intensive cleaning methods. Non-classified outer areas should also be included in the cleaning programme and a high standard of housekeeping and cleaning in areas adjacent to the controlled areas will assist in overall contamination control.

Microbiological control
When the cleanroom is producing biomedical products the main emphasis is on the control of micro-organisms and the highest level of control is required during aseptic manufacture.

This requirement will influence the cleaning methods and materials. Micro-organisms form part of the microscopic contamination and so great care must be taken to ensure the removal of viable organisms during this stage of cleaning.

Anti-microbial chemicals will be required as part of the cleaning process and all cleaning products and materials will be sterilised before use. Following cleaning no residues should be left on cleanroom surfaces.

Plant size
Cleanrooms vary in size from small units, perhaps containing one isolator, to very large microchip manufacturing plants. The same cleaning principles will apply whatever the size of the manufacturing operation but the scale of cleaning will be very different.

The size and type of cleaning equipment needed, purchase and storage of cleaning materials and staff requirements will all increase with larger and more complex cleanroom facilities. For a large operation the cleaning programme will be a significant cost and is likely to be managed by a dedicated team. In a small cleanroom the cleaning programme may be managed and carried out by the area production staff as part of their normal duties.

Operational hours
All staff involved in cleanroom operations have a responsibility for a "clean-as-you-go" approach. This ensures that staff are aware of the cleaning requirements and help to maintain the facility in good condition throughout production.

In addition it is preferable for the full, regular cleaning cycle to be carried out when the cleanroom is not producing product. This gives better access for the cleaning staff and their equipment without disruption to production activities. When wet cleaning is being performed surfaces may become slippery and this can pose a slip hazard especially on smooth flooring surfaces.

During cleaning operations the actions of the cleaning staff may generate temporary increases in airborne particulate which could be damaging to product being manufactured at the same time.

For these reasons it is preferable to time the cleaning programme around the operational hours.

When the production operation is continuous and cleaning must be carried out during production it is especially important to ensure that any cleaning operations are safe and do not compromise the process.

Production equipment and machinery
The presence of production machinery and equipment in the controlled area will present two issues. The equipment itself may disperse particulate or vapour into the area and so contribute contamination during operations. Removal of the contaminants produced by equipment may require specific cleaning methods and cleaning agents.

Machinery and equipment may also require cleaning both externally and internally on a regular basis and this needs to be included in the cleaning programme. Any cleaning procedures for machinery must enable the required cleaning to take place without risk to the equipment or cleaning staff. When cleaning of this type is performed a Health and Safety risk assessment is likely to be required and appropriate safety procedures must be in place and strictly followed.

Cleaning of machinery may also produce significant additional contamination of adjacent areas and this must be considered when developing the overall cleaning plan.

Staff numbers
Cleanroom staff will create particulate contamination in their area of work; more particulate will be produced with increased activity. The numbers of staff and their activity level must therefore be taken into account when assessing cleaning requirements. Contamination from discarded cleanroom disposables and clothing together with the associated packaging will also increase. It is likely therefore that as the number of operational staff increases so too will the requirement for cleaning and housekeeping.

Types of contaminant present
Particulate from cleanroom staff will be viable and non-viable particulate from lost skin fragments together with particles and fibres from clothing. These particulates will be mostly microscopic and removed by standard cleanroom cleaning techniques.

Some manufacturing operations however may produce contamination which presents a chemical, microbiological or radiation hazard. This may occur for example when cytotoxic drugs are being prepared or during virus production for vaccine manufacture. Cleaning protocols for these contaminants need to be established and all staff made aware of the procedures for cleaning and disposal of contaminated materials. Contamination may also occur which is difficult to remove. This contamination may be present in particular work stations or departments where materials such as adhesives, sealants and inks are used as part of the manufacturing process.

These types of materials will not be removed by normal cleanroom cleaning methods or products and will require special procedures to ensure they are effectively removed and that no residues remain.

Health and safety requirements
Cleaning operations will take place in enclosed cleanrooms, usually not during normal production hours and with minimum staff present.

The cleaning procedures may include the use and dilutions of different chemicals some of which may be harmful or flammable.

Cleaning staff may have to access difficult areas and work on or near electrically powered machinery. Application of solutions to smooth surfaces such as floors can generate a slip hazard. Hazardous materials may be present in the controlled areas both as contaminants and as process components. Cleaning staff may need to be equipped with items of personal protective equipment (PPE) which must be compatible with the cleanroom environment.

An example is shown below and is a battery-powered air fed hood to control the inhalation of sporicidal disinfectant solutions used during healthcare cleanroom cleaning.

Battery powered air-fed cleanroom hood

The full extent of the cleanroom cleaning requirements and associated hazards should be established when developing a cleaning system and a health and safety risk assessment carried out on all aspects of the cleaning programme to address these types of issues.

Staff availability

All cleanroom staff have responsibilities for keeping the area clean. As a minimum this involves the correct disposal of packaging, consumable items and re-usable clothing and removal of visible contamination.
A "clean-as-you-go" philosophy is usually adopted with each member of staff responsible for the general care and cleanliness of their work area and may include regular wipe down of critical surfaces.

However most cleanroom cleaning is carried out separately from production activities and undertaken by trained cleaning staff.

Staff performing these duties must be thoroughly trained in cleaning operations and also in the general rules for staff operating in the cleanroom.

Cleaning staff have a great influence on the continued successful operation of the facility and may often work unsupervised. Training should therefore include basic cleanroom technology and the requirements for GMP.

Cleaning staff must be equipped with full cleanroom clothing as well as any PPE and follow the changing procedures for each area.

When large areas require cleaning, or for special cleandowns e.g. following a new build, specialised cleanroom-cleaning contractors can provide a good alternative to in-house staff.

Cost

Once the cleaning requirement has been established it is advisable to investigate various options to obtain the best solution at the lowest cost. The total cost of a cleanroom cleaning programme is made up of a range of items including staff, cleaning materials, wastage and disposal charges.

It is often necessary to assess different cleaning materials both for their cleaning efficiency and ease of use in a specific location. For example in a cleanroom with a large surface area and low cleanliness classification it may be satisfactory to mop the floor using a mop and a two or three bucket system using concentrated cleaning agents or disinfectants diluted by staff at point of use. For cleanrooms with smaller floor area and for those with high classifications, sterile mops, pre-impregnated with a volume of RFU (ready for use) chemical, may be more cost effective.

Cleaning equipment can be purchased or leased and some items such as mops and wipes may be re-usable and require a cleaning and decontamination service. It is beneficial to discuss the full cleaning programme with specialist suppliers of cleanroom products who will be able to provide advice and information on suitable products and the most cost effective solutions.

7.3 Cleaning Plans, SOPs and Records

Once all information relevant to the cleanroom cleaning requirements has been assessed a cleaning plan should be created. The plan will provide clear information when discussing requirements with cleaning suppliers, and for developing cleaning standard operating procedures (SOPs) and a staff training programme.

Any changes to the cleanroom facility or its function must be assessed using the cleaning plan and a new revision of the plan produced when required with traceability of the changes implemented. A cleaning plan will be a useful reference when cleaning validations and re-qualifications are performed and is also essential for customer or compliance audits.

The cleaning plan will define;

- *What is to be cleaned*
- *How the cleaning will be carried out*
- *When the cleaning is to be carried out*
- *Who is responsible for cleaning*

When producing a cleaning plan the different cleanliness zones and areas of greatest risk to product should be detailed.

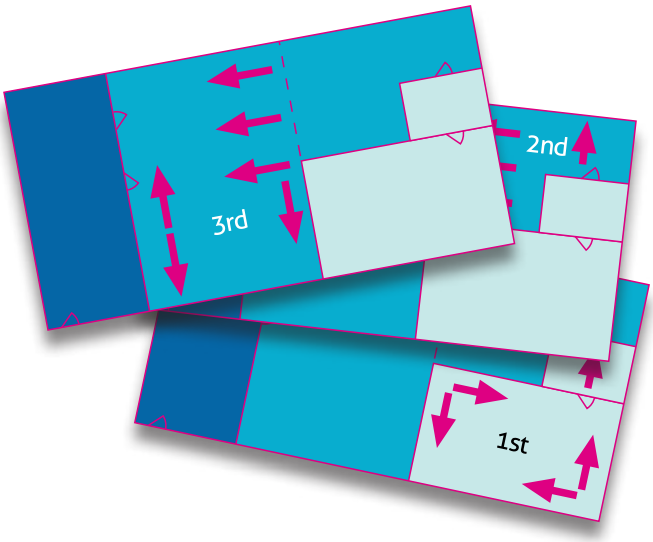
Locations of manufacturing equipment, dedicated cleaning equipment e.g. connection points for built-in vacuum system and garment issue and disposal points should be shown.

Any areas of notable hazards, first aid boxes and emergency exits must be clearly identified.
The cleaning plan will include details of the cleaning equipment and chemicals and the associated dilution and application rates specific to the production unit. The order, frequency and methods of cleaning will also be chosen to suit each unit however the following principles of cleanroom cleaning will apply to all plans.

- *Cleaning must start with the cleanest area and finish with the least clean area.*
- *Cleaning follows the air pressure cascade in a series of cleanrooms from the highest pressure to the lowest pressure.*
- *In a cleanroom cleaning starts at the point furthest from the exit and works towards the exit.*
- *Cleaning is carried out in a series of steps starting with the removal of visible contamination followed by the removal of microscopic particulate.*
- *When a chemical sanitiser is used the correct concentration, volume and surface contact time must be clearly stated.*
- *No cleaning equipment or products must be specified which will produce particulate contamination or leave harmful residues.*
- *Cleaning operations which have the potential to cause contamination e.g. emptying garment discard bins, must be identified and confined to non-critical areas.*
- *Any staff involved with cleaning must be properly trained and equipped.*
- *Any cleaning operations involving hazardous materials must be identified and all aspects of cleaning and disposal clearly described.*
- *All cleaning activities need to be appropriately recorded. The cleaning records need to be reviewed on a scheduled frequency and retained for future reference.*

For a small operation a cleaning plan may provide sufficient cleaning information. It is usually beneficial however to produce standard operating procedures (SOPs) for each cleaning task. SOPs not only provide detailed instructions for anyone performing a cleaning task but also form the basis for staff training.

Cleaning logs are completed by staff to ensure that all cleaning operations are being carried out correctly and on-time. These documents act as a check list for the cleaning staff and can also provide evidence that the cleaning procedures are being followed correctly.



A series of diagrams of the cleanroom areas to be cleaned is a clear way to develop a cleaning rationale

7.4 Vacuum Systems

Vacuum cleaning usually provides the first stage of cleanroom cleaning and is used to remove visible material from surfaces such as floors or machinery. There are two main systems used in cleanrooms and both are often used in the same facility for different tasks and areas;

- *Portable cleanroom vacuum cleaners*
- *Built-in vacuum cleaning systems*

Portable vacuum cleaners

These machines are simply plugged into an electrical supply and used by the operator in a specific location. This gives easy access to areas and allows cleaning staff to use one machine in a variety of situations and with different nozzle attachments. The cleaners are available in a wide range of sizes, types and costs including wet and dry vacuum systems. To be compatible with cleanroom use portable vacuum cleaners must be easily cleanable and no part of the machine or its attachments should produce any contamination or damage to cleanroom surfaces. Equipment with electro-static dissipation properties is available.

To control particulate dispersion from the vacuum airflow HEPA or ULPA filters are fitted to the machine. These can be attached to the motor, exhaust line or both. Whatever configuration of portable vacuum cleaner is chosen it must be compatible with the cleanroom in which it is to be used. Great care must be taken when opening and emptying these cleaners to minimise contamination to the area, the user and the machine itself. Periodic checking of the HEPA or ULPA filters is required to confirm correct operation.

Portable cleanroom vacuum cleaner

Built-in fixed vacuum cleaning systems
Central vacuum cleaning systems are extensively used in large cleanrooms with all waste removed to a remote central collection point. Vacuum tubing is connected to wall mounted ports and so no exhaust air is returned to the room.

Wet or dry systems can be installed. When designing a built-in system care should be taken to site the vacuum ports in positions which will enable staff to easily access surfaces to be cleaned without needing excessive lengths of vacuum pipe.

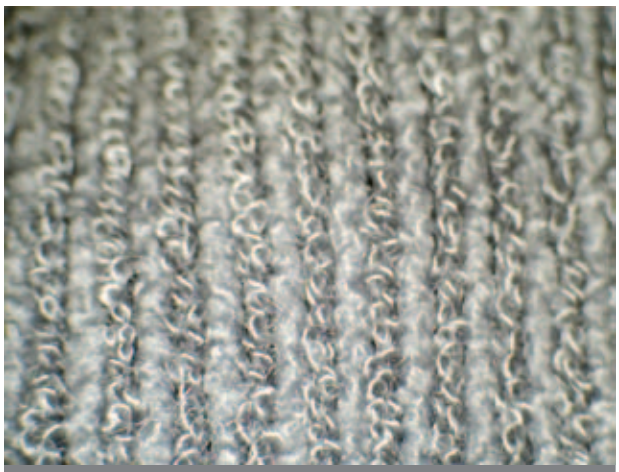
7.5 Mops

Cleanroom mops clean effectively by wiping surfaces and so can be employed to remove the invisible contamination which cannot be removed by vacuum cleaning. Mops are particularly suitable for large flat areas such as floors and walls and different designs of mop head, frame and handle are available for different cleaning operations and locations. Mops can also be used to quickly apply anti-microbial chemicals to large surfaces.

Mops should be used in long overlapping strokes so that all the surface area is covered sequentially.

The cleaning action of mopping comes from the physical drag forces applied to the particulate and removal efficiency is greatly enhanced when a wet mopping system is used. The greater the surface area of the mop in contact with the surface the better the wiping action and so any cleanroom mop should provide intimate surface contact. Mops manufactured from microfibre are especially efficient for this reason.

All materials used in the construction of the mop, the mop frame and the handle should not be a source of fibre or particulate which could contaminate the cleanroom.


Microfibre mop cleaning surface

All components should be easily cleaned, decontaminated and sterilised if necessary. The mop must also be able to withstand the abrasion from surface contact, which can be especially severe with some non-slip cleanroom flooring finishes. Disposable cleanroom mops are available but due to the high cost of disposable products re-usable mop systems are normally employed.

There are two main systems available for re-usable cleanroom mopping.

- *Impregnation and rinse bucket-system*
- *Pre-impregnated system*

Bucket system
This is the traditional mopping system modified for cleanroom use.

A bucket is used to impregnate the mop with cleaning agent and then to rinse the mop between applications.

This single bucket system has the obvious disadvantage that from the first rinse onwards the cleaning solution becomes increasingly contaminated until it is merely recontaminating the surface with each mopping. It is also possible that harmful contamination from a local area will be removed and then spread throughout a much greater area.

Single stage bucket mop system. Image courtesy of Basan UK Ltd.

Three stage bucket mop system. Image courtesy of Basan UK Ltd.

To introduce a rinse stage a two or three bucket system can be used which will also usually include a ringer to remove excess liquid from the mop. The whole system is usually mounted on a large, wheeled trolley.

For a two bucket system, bucket one is filled with the cleaning solution and the other with rinse water. The mop is impregnated with cleaning solution, wrung to remove excess liquid and applied to the floor. Once the operator decides that the mop requires rinsing it is placed in the rinse water bucket, wrung again and then re-impregnated in the cleaning solution and the cycle repeated. There will be carryover from the rinse water which gradually dilutes the cleaning agent and the rinse water becomes contaminated thus reducing its ability to clean the mop between each use.

The three bucket system adds a discard bucket. Following impregnation and use as much as possible of the contaminated liquid is removed into the discard bucket by wringing.

The mop can then be rinsed, wrung and re-impregnated with new cleaning chemical as in the two bucket system. The three bucket system has the same dilution and carryover problems as the two bucket system but they are greatly reduced by the addition of the third bucket.

Once the cleaning operation has been completed, or the cleaning agent needs replacing, the buckets must be emptied and cleaned before being stored dry. It is preferable to wipe down the equipment after use to ensure that no liquid remains which can quickly become a source of microbiological contamination.

Bucket systems are widely used for low grade areas and for cleanrooms with large floor areas and easy access. The equipment trolley is large and the buckets must be filled and emptied so adequate provision must be made for chemical and equipment storage and waste liquid disposal. It is advisable to carry out a Health and Safety risk assessment, which includes manual handling, on cleaning operations using bucket mopping systems.

Pre-impregnated system

This modern simplified mopping system was developed specifically for cleanroom cleaning and does not require buckets or wringer. In this mopping system the mop head is contained within a sealed pouch. The pouch is opened just before use and a small volume (approx. 200mls) of pre-diluted cleaning chemical added.

The mop is allowed to absorb the entire added chemical before being removed and fitted to the frame and handle. A specific square meterage of surface (usually around 20m^2) is then mopped. Once this area has been covered the mop is removed from the frame and discarded for cleaning, decontamination and re-pouching. A new mop is then used in the same way for subsequent areas.

Mops may be sourced which are packed singly or in multiples allowing several to be impregnated at one time. It is also possible to obtain mops which are already impregnated with the chosen chemical and in this case the mop only requires removal from the pouch and is then ready for use. Sterile mops are available if needed. As the mops are pre-impregnated with the correct volume of chemical to cover a specific area all the chemical is used for cleaning or disinfection and so no wasted excess chemical remains to be discarded at the end of the cleaning procedure.

This system removes the risks of cross contamination and chemical dilution present with bucket systems and the only equipment required is the mop frame, handle, mop heads, discard bag and pre-measured doses of the correct chemical. If the mop heads are supplied pre-impregnated with chemical then this further reduces the equipment needed.

As there is no handling of large volumes of chemicals the Health and Safety hazards associated with chemical dilution and the lifting of large buckets are also greatly reduced. This cleanroom mopping technique is especially suited to high grade cleanrooms and for those with restricted access.

Pre-impregnated mop system in use

7.6 Wipes and Swabs

Wipes are used in all cleanrooms as one of the main cleaning methods.

They are chiefly used to remove the invisible contamination of particles and fibres 50µm and smaller. Uses include the wiping of surfaces such as bench tops, the cleaning of small pieces of equipment such as bottles or trays, wipe down (or preparation) of items or their outer packaging before being taken into the cleanroom or isolator and glove wiping for cleanroom staff. Wipes may also be needed to absorb and pick up spillages which occur during the production process.

Wipes may be used dry but are much more efficient in removing contamination when dampened with cleaning or sanitising solutions.

In all instances wipes for cleanroom use must not introduce significant particulate or fibre contamination into the controlled areas.

In a few operations, notably surface finishing, re-usable wipes may be employed which can be re-processed by a cleanroom cleaning and decontamination plant, however the majority of cleanroom wipes are discarded after a single use.

Wipes are available in a very wide range of materials, presentations and price and so it is important to select the product which will satisfy cleaning requirements in the most efficient and cost effective manner.

The main factors to consider when comparing cleanroom wipes are;

- *Physical properties*
- *Wiper materials*
- *Wiper edge finish*
- *Wiper size, fold and packaging*
- *Wiper cleanliness and sterility*
- *Dry or pre-wetted wipes*
- *Supporting documentation*
- *Cost*

Physical properties

Wipes are made from materials which must have good surface contact so that particles can be pushed free from the surface being wiped.

Wipes must not be abrasive or cause damage to the wiped surface. Wiper materials must be able to withstand the cleaning operation without tearing or suffering surface breakdown resulting in the loss of particles and fibres from the wipe.

The wiper materials must be compatible with any chemicals with which they come into contact and not be dissolved or otherwise broken down by cleaning agents or production chemicals. In many applications the wipe should not contain materials which can be released in solution during use such as ionic chemicals or endotoxins.

Where the wipe will come into contact with hot surfaces it should have sufficient heat resistance to withstand this without damage. If control of electro-static dissipation (ESD) is a requirement the wipes must have good ESD properties.

Cleanroom wipes should have good sorption. This indicates the volume of liquid the wipe will absorb in relation to its weight and the time taken to do this. Good sorption properties will allow a wipe to quickly take up a spillage and will also enable an impregnated wipe to cover a large area without drying out.

Wiper materials

Cleanroom wipes are usually manufactured from knitted or non-woven fabrics however woven fabrics and foam material wipes are also available.

Wipes specified for use in high grade cleanroom areas are usually produced from knitted filament yarns, usually polyester or nylon, and these include those made from microfibre yarns which give increased surface contact area.

Filament polyester is low shedding and can be effectively cleaned and decontaminated before use. It will withstand sterilisation by gamma irradiation or autoclaving without damage.

Knitted fabrics are very pliable and this allows the wipe to maintain a high contact area and to be easily folded for use.

Knitted fabrics generally have high sorption properties which increase with fabric weight and this will further increase when the wipe is produced as a double layer (2-ply).

Non-woven materials are usually a combination of polyester and cellulose or polypropylene and are normally specified for use in lower grade cleanrooms, less critical wiping operations or spill control. The materials can be sterilised for aseptic area use and have good sorption.

As wipes are usually a disposable product it is preferable to use materials which can be re-cycled.

Wipe edge finish
Wiper fabric is produced in large rolls and must be cut down to produce individual wipes. The cut edges of the wipe can produce particles or fibres and to reduce this source of contamination the wiper edges can be sealed using various methods including sealing with heat or laser and heat rolled edges.

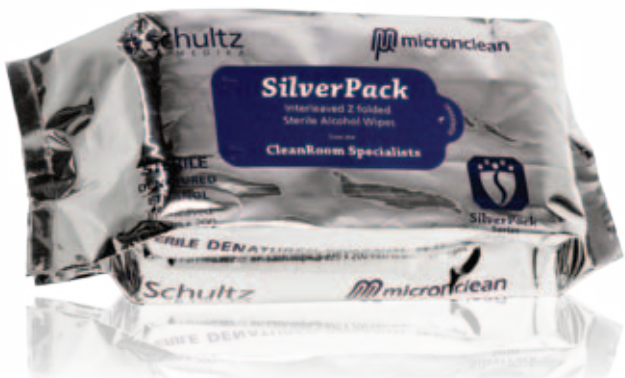
Wipe size, fold and packaging
Wipes are available in an extensive range of sizes and presentations.

They may be presented flat in a layer with each wipe being removed by the user. Wipes may also be folded so that they are interleaved and removing a wipe pulls the start of the next wipe from the pack.

Wipes can be sourced on rolls, in tubs, or in individual packs and most packaging will incorporate a re-sealing system, especially if the wipes are pre-wetted with a volatile chemical such as an alcohol or solvent.
Several layers of packaging may also be utilised to facilitate transfer into a high grade area.

Whatever packaging is employed clear and adequate labelling must be used which is not damaged by wiping with alcohol or other solvents and the packaging material must not produce significant fibre or particulate contamination during opening.

Whenever possible packaging and containers for wipes should be made from materials which can be re-cycled.



Folded, impregnated wipes

Wiper cleanliness and sterility
Knitted, woven and non-woven fabrics for wiper manufacture are produced in large industrial plants and the fabrics will become heavily contaminated with fibres, particulate, micro-organisms and chemicals from the production process. This contamination is increased when cutting the wipes to size and if they are to be used in an environment where this would present a problem, the wipes must be cleaned and decontaminated before use.

This is normally achieved using a cleanroom cleaning and decontamination plant and the process is highly successful in decontaminating woven or knitted polyester wipes. It is not possible however to decontaminate cellulose wipes in this way.

Suppliers of cleanroom wipes will be able to provide full data on particulate and fibre levels of different wipes and information on chemical contaminants such as ionic materials and endotoxins.

A wide range of sterile wipes is available and are usually required in aseptic manufacturing processes. Wipes are routinely sterilised by gamma irradiation to achieve a sterility assurance level (SAL) of 10^{-6}.

Dry or pre-wetted
Cleanroom wipes are available either dry, or pre-wetted with a cleaning or sanitising solution. All types of wipe materials can be supplied in these formats.
If wipers are to be primarily used to absorb spillages then dry wipes are used. In cleaning applications however, wiping is carried out using a liquid to dampen the wipe to improve particulate removal.

If an anti-microbial solution is used a layer of sanitising solution will also need to be deposited by the wipe to kill or inactivate micro-organisms which have not previously been removed.

A solution can be applied to a dry wipe just before use using a dispenser or spray however the chemical must be prepared in advance and will not be evenly absorbed by the whole wipe giving uneven application.

Pre-wetted wipes provide the simplest option and are dosed with a specified volume of chemical before the pack is sealed. This allows the impregnated chemical to be evenly absorbed and gives an optimum chemical loading on each wipe.

Pre-wetted wipes can be sterilised following chemical dosing so ensuring both wipe and chemical are sterile at the point of use.

When volatile chemicals are used to pre-wet wipes the packaging must be effective in stopping any chemical evaporation from the pack during storage and should also incorporate a re-sealable opening to stop loss of chemicals once the pack is opened. Sterilised wipes, pre-wetted with alcohol are used within high grade pharmaceutical cleanroom areas. For such applications, pre-wetted wipes have significant advantages over the use of similar dry wipes and alcohol discharged as an aerosol from a canister. Such canisters deliver vast quantities of alcohol particles into the cleanroom which remain airborne for extended periods of time. These particles are likely to be 'counted' by any particle counters present in the cleanroom and will consequently record artificially high levels of airborne particles [ref 2]. Additionally, such particles will be readily inhaled by personnel present within the cleanroom with significant associated health concerns.

Airborne particles generated by an aerosol delivery system

Supporting documentation

When inexpensive, non-sterile wipes are utilised for wiping operations a basic product specification is sufficient which identifies the wiper material, contamination levels and general product information on quantity and presentation. If pre-wetted wipes are being used then a materials safety data sheet (MSDS) will also be supplied.

For more highly specified wipes used in high grade areas additional documentation will be required to confirm the acceptability of the wipe before use. This will include full batch traceability for each individual wipe pouch, details of particulate and chemical contamination levels, confirmation of pouch materials, certificate of irradiation when sterility is required and colour-change detex irradiation labels on each pouch. A MSDS will be required for all impregnated wipes. Full documentation is usually supplied with each box of wipes and this may need to be included in cleanroom product batch records to satisfy regulatory requirements.

When wipes are required for critical areas the user will wish to audit the wipes production facilities and the supplier will maintain records providing full batch traceability for the whole supply chain.

Cost

Cleanroom wipes are available within a very wide price range. The material used for the wiper, edge finish, wipe size and presentation, packaging, level of cleanliness and supporting documentation all affect the final cost. Sterilisation and pre-wetting also significantly increase costs.

This means that the more highly specified and controlled the wipe the higher the cost and so it is important to ensure that the correct wipe is clearly identified for each area and each wiping operation.

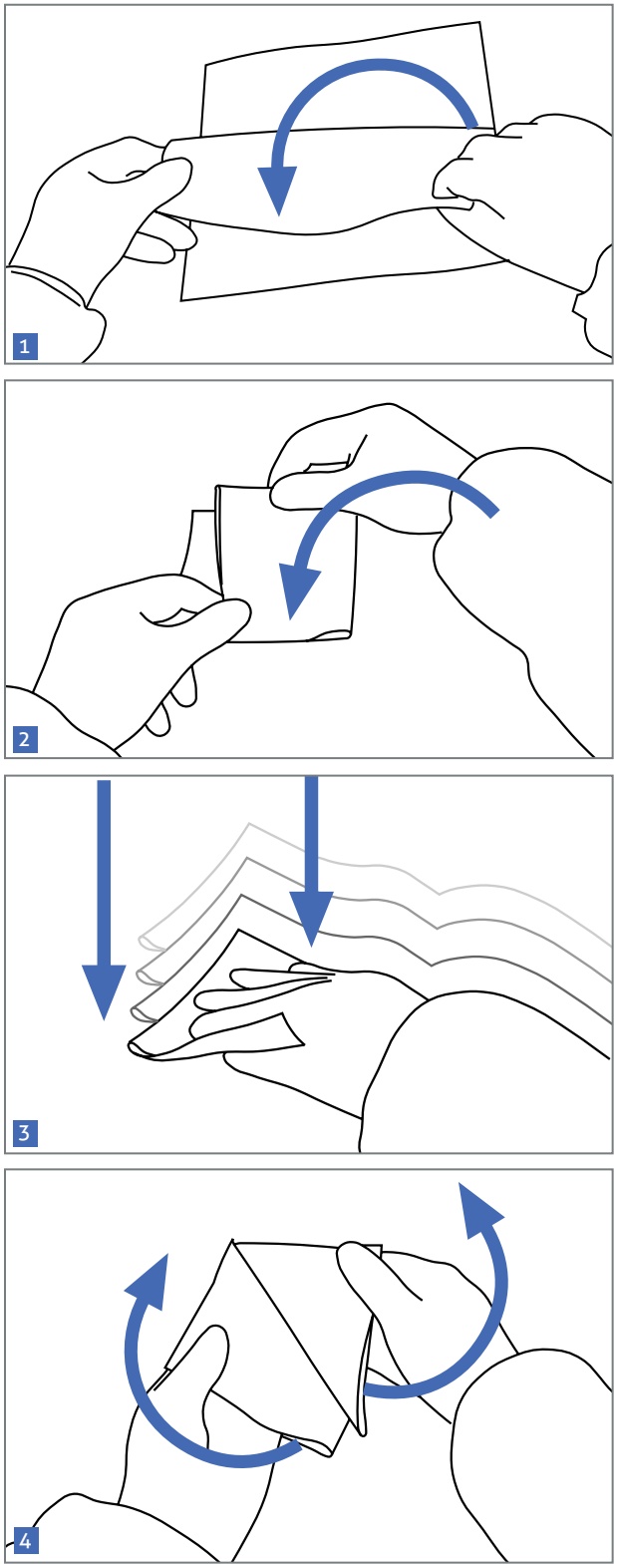
Use of wipes

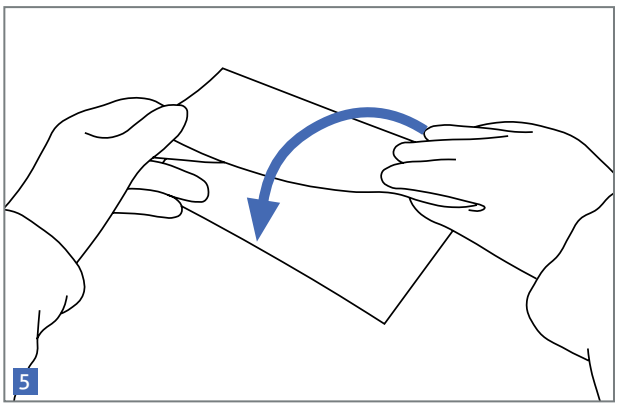
Each cleanroom cleaning plan will clearly identify the specific use of wipes however there are some useful guidelines to adopt when using wipes in any cleanroom.

- *The cleaning plan and standard operating procedures (SOPs) will indicate which wipes should be used for each cleaning application and only the specified wipe should be used. This should also be made clear to contractors or engineers who may be operating in the controlled areas.*
- *When used for absorbing spills a dry wipe is simply removed from the container and applied to the spilled liquid. Once absorbed into the wipe the wipe is discarded in a safe manner according to the area procedures. A further dry wipe should then be used to wipe over the area and remove any residual moisture.*
- *If cleaning or sanitising chemicals are to be applied to dry wipes the chemical should be dispensed onto the wipe and not onto the surface to be cleaned. This minimises the possibility of chemical aerosols contaminating the cleanroom.*
- *If pre-wetted wipes are used then care should be taken to ensure that once opened the wipes container is re-sealed between uses to stop loss of impregnant through evaporation. When pre-impregnated wipes containers have been opened and re-sealed several times it is possible that evaporation has occurred and the wipes are no longer wetted to the required level. In this case the wipes should be discarded.*

Effective packaging – validated for multiple opening and re-sealing

When using wipes to decontaminate critical areas it is good practice to fold the wipe to provide eight separate cleaning faces. The wipe should be used in single overlapping strokes with a maximum of eight passes (one for each folded face) per wipe (as shown in the sequence of illustrations 1-5 below).





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This technique will maximize particle removal and the surface area covered will depend on the size of the wipe and the quantity of liquid absorbed.

- *When wipes are being used to apply a sanitising solution care should be taken to ensure that sufficient chemical is transferred to the surface from the wipe and that it is evenly distributed. Adequate disinfection will not take place without the correct application of sanitiser.*
- *Wipes must be discarded correctly as indicated by the cleaning plan. Any wipes containing chemical residues either from spillages or chemical impregnants must be collected for safe disposal as indicated by the MSDS, Environmental and Health & Safety considerations.*

Swabs

In some instances small or inaccessible areas may require cleaning using cleanroom swabs. These are available in a range of knitted and non-woven fabrics and foams. Different designs of the swabbing tip allow a product to be selected which will satisfy most cleaning applications. Full specifications on the cleanliness and cleanroom compatibility of each product will be available from the supplier.

7.7 Chemicals for Cleaning and Disinfection

Wet vacuum cleaning, mopping and wiping are all used extensively in cleanroom cleaning. In some instances water alone is used with these methods however in most instances a chemical solution is employed to enhance cleaning efficiency or provide anti-microbial action. Whenever liquids are used for cleanroom cleaning or disinfection they should be free from contamination which could compromise the area. This means that any water used must be purified to the standard needed in the area to be cleaned. Water used for cleaning may therefore range from deionized water to water for injection (WFI) quality. Chemicals should not contain any suspended particulate and should not leave particulate residues on cleaned surfaces after evaporation.

Cleaning solutions must be effective in removing and suspending contaminants but should not damage surfaces being cleaned. Any Health and Safety issues relating to fire hazard or toxicity should be clearly understood and minimised.

For high grade pharmaceutical cleanrooms, used for the manufacture of sterile products, it is a regulatory authority requirement that the disinfectant solution to be utilised is sterile prior to use. Typically this can be achieved by preparation of the disinfection agent in controlled areas which is then piped into the cleanroom areas through sterilising grade filters and collected in sterilised containers prior to use. Alternatively, the disinfectant can be prepared aseptically, utilising sterilised equipment and irradiated disinfectant concentrates in high grade cleanroom conditions. The prepared solution may then be piped directly into the cleanroom areas without the need for a sterilising grade filter.

Cleaning chemicals

A surfactant is a chemical which lowers surface tension and improves removal of solids from cleanroom surfaces. Detergent products contain a surfactant or a mixture of surfactants but may also include other additives such as dyes or perfume.

Surfactants are classified as amphoteric, anionic, cationic and non-ionic depending on their chemical structure and detergents containing non-ionic surfactants are usually chosen for cleanroom use as they are free from electrically charged molecules. Many different proprietary detergent compounds are available and full product specifications including the MSDS will be available from the supplier.

In all instances it is recommended that a comprehensive trial is carried out on any cleaning product before it is adopted for use. This should assess not only cleaning efficiency but also compatibility with the surfaces to be cleaned, other cleaning materials and products.

Cleaning chemicals can be sourced in concentrated or ready for use (RFU) solutions and in different volumes. When large areas are being cleaned concentrated product will be most economical however dilution of the product before use will require purified water and must be carefully controlled to ensure the correct concentration is used and that no contamination is introduced. A risk assessment should also be carried out to ensure the correct PPE and equipment is supplied to staff and that a safe handling procedure is adopted. RFU products are useful when smaller areas are being cleaned or if sterile products are required with the sterilisation process taking place after the product has been dispensed into the final container.

Many chemicals are supplied at RFU concentrations in easily portable dispensing containers such as trigger sprays, making them very easy and economical to use at multiple locations.

Disinfecting chemicals

Products which have an anti-microbial action are usually known as disinfectants or sanitisers. Biostatic agents act to inhibit microbial growth whilst biocidal agents kill vegetative micro-organisms. Some bacteria and fungi produce spores which are very resistant to adverse conditions and sporicidal disinfecting agents are required to be effective against spores.

Disinfection is usually carried out as a last stage of the cleaning process and is also the principle aim when sanitising hands or 'prepping' materials being transferred into cleanrooms or isolators.

Disinfectants must be used at the correct concentration and for a sufficient time to work effectively and it is important that the chemical comes into direct contact with the micro-organisms.

There are several different types of chemicals which are used as disinfectants including alcohols, quaternary ammonium compounds (QUATS), chlorine, biguanides and phenols. All have different modes of action and varying effectiveness against different groups of micro-organisms and no one, ideal cleanroom disinfectant exists.

Many proprietary cleanroom disinfectants are a mixture of different compounds and are formulated to provide complementary modes of action and increased effectiveness.

Full information on the anti-microbial activity of disinfecting products will be available from the supplier and standard tests are employed to give an indication of the effectiveness of the product.

These include;

- *BS EN 1276* [ref 3] *Chemical disinfectants and antiseptics. Quantitative suspension test for the evaluation of bactericidal activity of chemical disinfectants and antiseptics used in food, industrial, domestic, and institutional areas. Test method and requirements*
- *CEN EN 13697* [ref 4] *Chemical disinfectants and antiseptics. Non-porous surface test for the evaluation of bactericidal and/or fungicidal activity of chemical disinfectants used in food, industrial, domestic and institutional areas*
- *BS EN 1650* [ref 5] *Chemical disinfectants and antiseptics. Quantitative suspension test for evaluation of fungicidal activity of chemical disinfectants and antiseptics used in food, industrial, domestic and institutional areas.*
- *BS EN 13704* [ref 6] *Sporicidal test. Quantitative suspension test for the evaluation of sporicidal activity of chemical disinfectants used in food, industrial, domestic and institutional areas.*

Alcohols are routinely used as disinfecting agents in cleanrooms and both filtered isopropyl alcohol (IPA) and denatured ethanol (IMS) is used as a 70% solution in purified water. These sanitisers have the benefit of rapid evaporation leaving almost no residue and are effective against a range of vegetative organisms; however they have no sporicidal activity.

Because of these properties alcohols are widely used for hand and glove sanitisation and for the wiping down of critical surfaces.

There is a theoretical risk of micro-organisms becoming resistant to a particular anti-microbial compound if it is used for an extended period. For this reason many cleanroom operations have a policy of rotating two disinfectants with different anti-microbial actions, on a regular basis.

7.8 Contamination Control Flooring and Mats

Contamination control flooring and mats are used to remove contamination from footwear and wheels at the entrance to critical areas. In this way they aid the cleaning process but themselves must be cleaned as part of the cleaning schedule.

Contamination control flooring is manufactured from polyester compounds with a high coefficient of friction. This acts to physically remove and trap particles and fibres carried on materials with which it comes into contact, normally the soles of footwear and the wheels of trolleys. The material does not therefore transfer adhesive substances to the contacted surfaces.
It can be used as mats or as covering for the whole floor and can also incorporate anti-static or anti-microbial compounds.

The flooring is cleaned using a cleanroom detergent and mopping system and the frequency of cleaning will be determined by the cleaning plan.

Contamination control mats (often called "tacky mats") consist of layers of plastic sheet coated with an adhesive. The adhesive pulls particulate and fibre from footwear and wheels contacting the mat.

Tacky mats are held in place by an adhesive backing or by a floor mounted frame.

When the top sheet is contaminated it is removed by pulling the edges into the centre so trapping the contamination and exposing a clean sheet, the removed sheet is then discarded. The individual sheets are often numbered to give an indication of use and frequency of changing is set by the cleanroom cleaning plan.

Disposable tacky mat used to control foot borne contamination

7.9 Confirming Effective Cleaning

The production and implementation of a comprehensive cleaning plan and SOPs, together with well trained staff and accurate cleaning logs, will all give confidence in the cleanroom cleaning programme.

Visual inspection of the area provides an indication of the effectiveness of general cleaning and housekeeping standards, however, additional monitoring techniques can also be employed to determine the effectiveness of the removal of invisible particles and fibres.

- *Strong visible light can be shone onto a cleaned surface at an angle of 45 degrees. This will illuminate particulate to make it visible for inspection.*
- *Ultra violet (UV) light can be used to show particulate which will fluoresce and this can be especially useful when looking for fibres.*
- *Particulate and fibre-free glass or stainless steel plates can be positioned on critical surfaces for a period and then removed for microscopic evaluation of the numbers of particles which have been deposited onto the surface and these can be cleaned using the standard techniques to evaluate removal efficiency.*
- *Cleaned surfaces can be sampled using automatic particle counting devices however these rely on vacuum removal of the particulate.*

When the emphasis is on disinfection then microbiological methods are employed and these tests are routinely carried out in GMP classified bio-medical cleanrooms to confirm levels of microbiological cleanliness. Active air sampling, settle plates, contact plates, surface swabs and finger dab sampling will all indicate the degree of control achieved by the cleanroom and the cleaning programme.

Systems which use bioluminescence to detect adenosine triphosphate (ATP), a molecule which supplies energy and is found in all cells, can be used to give an immediate indication of cellular residues left on a surface.

ATP reacts with the enzyme luciferase to produce light and a surface sample can be taken from the area to be tested and combined with the reagent. The light emitted can be measured and provide immediate feedback on cleaning efficiency. Although considered a helpful technique giving an immediate assessment of cleaning efficiency this test method is not generally considered accurate enough for high grade cleanroom areas.

SECTION

8.0

Planning, Sourcing and Optimising Cleanroom Clothing Supply

This section describes the key stages and requirements for setting up a cleanroom clothing system for re-usable items. Many of the elements discussed will also impact on the sourcing of cleanroom consumables however for clarity this is dealt with as a separate topic in Section 10.0 *Planning, Sourcing and Optimising Cleanroom Consumables Supply.*

Cleanroom clothing for different environments

8.1 Planning the Process

Cleanroom clothing is a key element of the control systems used to protect sensitive products from contamination during manufacture.

Without the correct cleanroom clothing, manufacturing units cannot operate effectively and a failure of clothing supply will lead to a complete shut down of operations. Cleanroom clothing is mainly re-usable and so the clothing will need to be collected from the wearer after use, processed by a decontamination plant and then returned to the wearer in time for re-use without deterioration of its contamination control properties.

This process must work unfailingly over the lifetime of the clothing, which will be several years, and replacement garments must be readily available in the event of garment failure

Cleanroom clothing must meet all the requirements of the Production and Quality Assurance departments; it must be acceptable to the wearer and at a cost and supply specification which will be acceptable to the Purchasing department.

The selection and sourcing of the correct cleanroom clothing programme is therefore a complex operation which benefits from a planned and well-documented approach.

The process will differ from site to site, however the following elements should always be considered when arranging cleanroom clothing supply;

- *Selecting a clothing sourcing team.*
- *New cleanroom clothing system or review of existing supply arrangements?*
- *The budget and timescale.*
- *Fabric and garment style selection process.*
- *Determining the numbers of garments required.*
- *Cleanroom clothing distribution systems.*
- *Supply options and supplier selection.*
- *Implementation and maintenance of the clothing system*

8.2 Selecting a Cleanroom Clothing Project Team

To implement an effective and cost efficient cleanroom clothing programme requires input from various sources and it is often beneficial to establish a small team with a designated team leader to undertake the task. This is especially beneficial for larger operations where it will be necessary to collect and manage a considerable amount of information and to communicate effectively both internally and with external suppliers.

For a new cleanroom clothing system or a complete clothing review the process is likely to take several months to complete and will involve significant costs. Key input will be from Purchasing, Production and Quality Assurance departments.

Additional help may also be required from company Auditors, Health and Safety representatives, cleanroom staff who will use the clothing and garment distribution staff.

It is also beneficial to start discussing requirements and options early in the process with prospective suppliers to obtain their input and advice.

8.3 New Cleanroom Clothing system or Review of Existing Supply Arrangements

When a new cleanroom production unit is being developed the provision of cleanroom clothing should be considered at an early stage.

The manufacturing operation, cleanroom classification, and contamination control emphasis will all be major considerations. The numbers of staff moving in and out of the cleanroom facility, changing procedures and staff access to cleanroom clothing are also important factors. Early specification of the cleanroom clothing system will provide adequate time to decide on the hardware required for distribution and collection, such as lockers, bins or racks, and the most appropriate fabrics, garments and decontamination services.

As there will be no existing supply arrangement the new service must be fully functioning from the production start date with all elements of the system in place.

When a production facility has an existing cleanroom clothing system it is sometimes necessary to review the supply arrangements. This may be needed for a variety of reasons such as;

1. *Purchasing department contract review procedures.*
2. *Change in Production Unit manufacturing activity.*
3. *New Regulatory or QA requirements.*
4. *Dissatisfaction with the current arrangements.*

The existing system will have both a service and financial history and this will provide the starting point for the review.

Supply contracts are likely to be in place and the contractual obligations will need to be clearly understood together with the full implications of change.

The regular review of an existing cleanroom clothing system is an excellent tool to identify areas for improved contamination control, service improvements and to provide increased cost control.

8.4 The Budget

When an existing cleanroom clothing service is in operation the current budget will already be known. If a new cleanroom clothing system is required then the costs of various options will need to be established and a budget allocated according to the choices made. There are two principle options for supply, either direct purchase of equipment, clothing and decontamination services or a managed rental programme.

For direct purchase a large initial capital outlay is required to fund the full cost of all garments, labels and distribution equipment.

Once the cleanroom clothing and equipment is in place then a variable maintenance budget will be required to cover garment replacements and additions as well as all costs associated with garment maintenance and decontamination.

When a managed rental programme is chosen the budget is fixed for an agreed period without initial capital cost and incorporates all aspects of the clothing programme including the cleanroom clothing, decontamination services, garment repair and replacement, delivery, distribution and management reports.

8.5 Timescales

Timescales are likely to be longer for a new start-up situation and also in facilities when large numbers of staff and departments are involved. Any major changes to an existing cleanroom clothing system will also require adequate time to implement.

If an existing supplier is to be replaced then cancellation of the original contract must be timed to coincide with the start of the new supply arrangement.

The initial stage is to collect basic information on the requirements of the cleanroom clothing service and to discuss these requirements with possible suppliers, obtain samples and agree garment types.

Proposals from prospective suppliers can then be obtained and reviewed and supplier audits arranged. Final discussions can then take place and once supply contracts have been agreed and contracts signed, measurement of all wearers must take place before garments can be ordered for manufacture.

Fabric supply, garment manufacture, delivery, labelling and processing by the decontamination plant prior to delivery and installation on site will then be required before the clothing can be delivered to site for use.

If new fabrics or garment styles are required then sampling, wearer trials and validation exercises will all add significantly to the overall timescale.

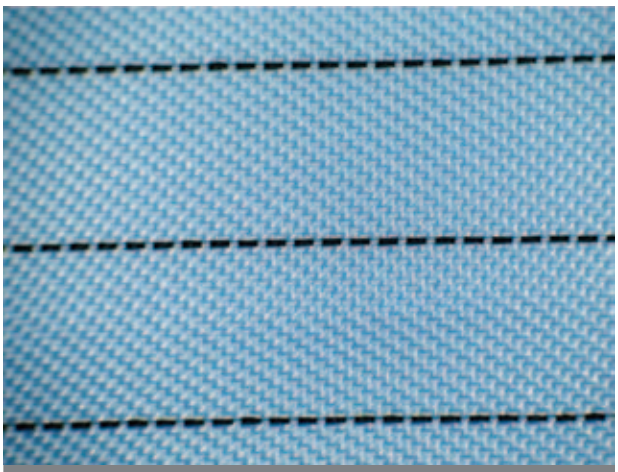
8.6 Fabric and Garment Style Selection Process

Fabrics

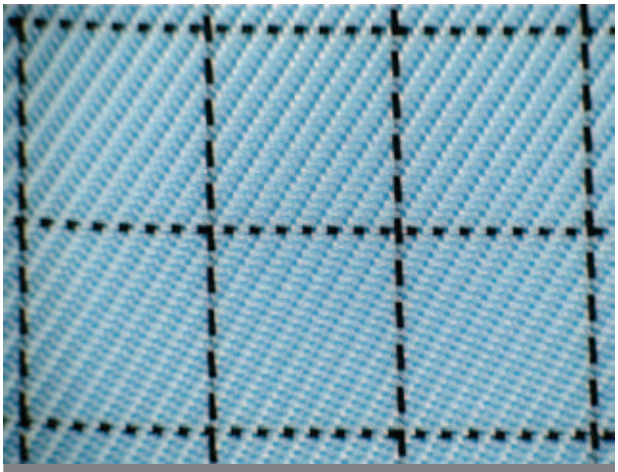
Suitable fabrics are available to meet all contamination control requirements both as outer wear and as undergarments.

Readily available fabrics will have been extensively evaluated by standard laboratory tests and used in a variety of manufacturing situations. This test data and lifecycle history provides excellent assurance that the fabric will perform well throughout the garment life. These fabrics will also be available in an established range of colours.

When special properties such as water repellency or chemical resistance are required then there will be a more limited fabric range. Technical test data will be available to demonstrate the effectiveness of the fabric, however in most instances it is beneficial to trial these fabrics in the areas of use before making the final decision.



Cleanroom fabric - filament polyester with ESD stripe



Cleanroom fabric - filament polyester with ESD grid

New fabrics can be developed for a specific end use, however this is very time consuming and expensive and is not recommended except in extreme cases where no suitable fabric exists.

Garment styles

Many cleanroom garment styles are available and all are variations on the same basic patterns, these are;

- *Coat*
- *Coverall*
- *Overboots*
- *Hood*
- *Top and trouser undergarment set*
- *Top and trouser outerwear set*

Samples of standard garments will be readily available for evaluation and trial by the garment selection team and the wearers.

Typical cleanroom undergarments

Whenever possible it is much more cost effective and efficient to select a suitable existing garment style than to design a new garment for use by a specific site. New design requires initial input from managers, wearers, clothing designers and a pattern maker, followed by production of sample garments for trial.

Once successful trials are completed (which may necessitate several stages of modifications, re-sample and re-trial) the pattern can be graded to provide the full size range and full garment sets are normally produced to be finally tested and approved. Only then can garment manufacture commence.

As the new style will be unique to the specific site additional garments, covering the complete size range, must also be ordered to be held as stock for replacements or additions.

8.7 Determining the Numbers of Garments Required

The type and numbers of cleanroom garments required to adequately supply production is one of the most critical pieces of information needed when developing an efficient cleanroom clothing service.

If the specified number of garments is too low then the flow of garments between the manufacturing unit and decontamination plant will fail resulting in garment shortages and production downtime.

If the specified number of garments is too high then this will significantly increase costs without any additional benefit.

For a small operation with only a few wearers it is relatively easy to establish the clothing requirements, however for large manufacturing sites with different departments and different standards of cleanrooms it can be difficult to obtain an accurate picture of clothing requirements.

The following check-list identifies the key areas for investigation to arrive at an accurate picture of cleanroom clothing use and will provide a helpful guide for any cleanroom clothing project team.

It is recommended that this check-list is used to collect information for each separate manufacturing unit or department.

- *Choice of garments.*
- *Clothing with special properties or decontamination requirements.*
- *Change frequency for each garment style.*
- *Number of production staff accessing the cleanroom per shift.*
- *The shift pattern in operation throughout the year.*
- *Clothing required by Engineering staff, QA staff and occasional visitors.*
- *Garment distribution and gowning system in operation.*
- *Wearer identified garments or pool stock clothing system.*
- *Sterilisation requirements both before and after use.*
- *Clothing identification for specific areas or staff.*
- *Dangerous or difficult garment contaminants.*
- *Repair options for damaged clothing.*

Choice of garments, special properties or decontamination requirements

The fabrics, garment styles and changing procedures must first be agreed by all departments.

Any requirement for garments with special properties such as water repellency, fire retardancy or ESD properties should also have been identified together with the areas in which they are to be used. Some specialised cleanroom fabrics may require unusual processing and more complex testing at the decontamination plant and this may mean more garments are required to allow more process time.

Change frequency

The frequency of garment change is one of the major factors determining garment numbers.
In some instances it may be appropriate to only change outer garments once per week with the clothing stored between use in clean areas or clean air cabinets.
In many operations however, especially biomedical and pharmaceutical production areas, it is usual to change outer clothing on each entry to the cleanroom. Daily change and twice weekly change are also commonly used.

As an example:
In a production area with 10 staff working 5 days per week, changing once per week, 10 garments will be used each week. (10 staff x 1 change)

In a production area with 10 staff working 5 days per week, accessing the cleanroom 4 times per day and changing on entry 200 garments will be used each week. (10 staff x 20 changes)

Number of production staff and shift pattern

The number of staff working in the cleanroom areas is the second major factor when establishing garment numbers.

When a single shift with unchanging staff numbers is operated throughout the year, estimating weekly garment usage is straightforward - as seen in the examples above.

With complex shift patterns and variations in production output more complicated clothing usage patterns are created. When this is the case it is necessary to obtain an accurate forecast of the maximum quantities of cleanroom clothing required to maintain production throughout the year.

This will enable the cleanroom clothing team to specify a sufficient number of garments to cover the highest level of predicted use and avoid shortages.

Engineering staff, QA staff and occasional visitors
When cleanroom equipment is used which needs routine attention, engineering staff may need to regularly enter cleanroom areas. This can lead to a significant increase in the weekly garment requirement. Other non-production personnel such as QA staff, trainers and visitors may also require cleanroom clothing for occasional use and this should be accounted for when deciding total garment numbers.

Garment distribution and gowning system
The garment distribution and gowning systems may have an impact on the number of clothing items used. Poor storage and handling can cause damage to packaging, resulting in unused clothing being removed for re-processing, reducing the number of garments available for use.

If the distribution system is erratic then staff may choose to keep their own 'personal' garment stock which can again reduce the number of garments in circulation. Incomplete collection and return of used garments for cleaning and decontamination may also lead to shortages of wearable garments.


Cleanroom garments being placed into distribution racks for use

When a strict aseptic gowning technique is required it is possible for cleanroom staff to inadvertently contaminate sterile garments during the changing procedure. This will mean that the garment set is discarded and that additional replacement garments need to be available.

Technically difficult changing procedures also need extensive training and practice to perfect and an additional supply of cleanroom clothing is required for this purpose.

Wearer identified or pool stock cleanroom clothing system
Wearer identified
If contamination control garments are required which are only to be used by one specific wearer then each wearer will need to have a complete set of garments supplied and identified to that individual. This is usually referred to as a wearer identified garment system. This option is often selected for undergarments, when the name of an individual needs to be clearly visible, if clothing is worn for several days, or if specific tasks mean that some clothing will regularly suffer significant wear or staining.

Garments can be labelled with a wearer number or with a wearer name and the garments will need to be available for collection by each wearer and this is often achieved by distribution using individual distribution lockers.

Pool stock
Cleanroom clothing may also be supplied as a circulating stock of garments with a range of sizes available for use by any suitable wearer. This system is usually referred to as a pool stock.

These garments are presented for selection according to size, usually from racking or bins.

Pool stock is often chosen to reduce the number of garments required for a large workforce and when simple styles of garments can be easily worn throughout an area without significant wear or staining. Name badges cannot be applied to garments using this system. Staff acceptance and understanding of a pool stock system needs to be established before implementation. Staff may feel that using a pool of garments may put them at risk of cross-contamination from previous wearers, however a fully validated and monitored cleanroom cleaning and decontamination process will ensure that the clothing is thoroughly disinfected and cleaned between each use with records available to illustrate this. When sterile garments are utilised then this will give staff additional confidence in the safety of a pooled garment system.


Cleanroom clothing being processed in a decontamination plant

Sterilisation requirements both before and after cleaning and decontamination
The requirement for garment sterilisation following decontamination needs to be decided and in some environments, such as virus production, it may also be necessary to sterilise cleanroom clothing after use and before return to the decontamination plant.

Sterilisation by gamma irradiation is the current best option for packed, cleaned and decontaminated clothing items. It is effective and easily controlled, however cleanroom clothing fabrics will be degraded over time by repeated irradiation processes.


Control of sterilisation by gamma irradiation

When used clothing is sterilised before return to the decontamination plant this is usually achieved by autoclaving the garments and this too increases fabric damage and so decreases garment life. (See section 6.4 for additional information).

Decreased garment life and the extra time required to sterilise garments may mean that additional clothing is needed to maintain a steady supply to production.

Clothing identification for area or staff
Some plants or departments may need to have garments labelled in a way which visibly identifies the department, the wearer, or wearer status e.g. First Aider. This requirement needs to be clearly understood by the project team and all the information for badging or labelling of clothing must be collected and checked before the clothing is ordered.

Garment labelling using sublimatic printing

Dangerous or difficult garment contaminants
In some production processes the cleanroom clothing may become contaminated with materials which could be harmful to anyone handling the item, or with materials which are especially difficult to remove e.g. paint or inks.

It is necessary to identify these types of contaminants whilst establishing a cleanroom clothing system. Many options are available to deal with these issues including different fabric types and colours, specialised cleaning methods and controlled packing and transport systems and advice on the best way to deal with these issues should be obtained from prospective suppliers.

Repair options for damaged clothing
Damaged cleanroom clothing can be repaired in a variety of ways.

Fixtures and fittings such as zips and studs can be replaced, holes can be repaired using sewn or heat sealed patches.

The level and type of repair which is acceptable to the plant or department must be determined by the cleanroom clothing team and clear guidelines agreed with the decontamination plant carrying out any repairs as part of the garment maintenance programme.

Cleanroom garment repair

8.8 Cleanroom Clothing Distribution Systems

A well planned and equipped cleanroom clothing collection and distribution system, managed by properly trained staff, will prove a great asset in the efficient operation of the cleanroom.

The clothing supply-system should enable cleanroom staff to obtain and change into decontaminated cleanroom clothing with minimal delay and contamination risk.

After wearing, contaminated clothing needs to be easily disposed of by the user and quickly dispatched to the processing plant for cleaning, decontamination and subsequent return for use.

Each cleanroom facility will have its own physical layout, cleanroom clothing system and changing procedures however the following points should be considered when establishing a system.

- *Staff responsible for the cleanroom clothing collection and distribution system.*
- *Site access, delivery point and storage for bulk clothing supplies returned from the decontamination plant.*
- *Distribution method at the point of use.*
- *Storage between use (for clothing items worn several times).*
- *Collection of soiled items and transfer to bulk collection point.*
- *Arrangements for any items contaminated with hazardous substances.*

Staff responsible for the cleanroom clothing collection and distribution system
For a small number of wearers it is useful to have a member of staff with the responsibility to oversee cleanroom clothing distribution. For larger operations with multiple wearers and departments this is a vital role.

This task can often be successfully carried out by an existing cleanroom support team, by a dedicated employee or by staff supplied and managed by the cleanroom clothing decontamination plant.

Site access, delivery point and storage for bulk clothing deliveries returned from the decontamination plant

Collection and delivery of cleanroom clothing by the decontamination plant will usually be by van. A time and location for collection of the soiled clothing and delivery of the decontaminated clothing should be agreed.

For a large facility this may include several points around the site and may entail site-specific training for the delivery driver.

When large quantities of garments are involved it may be necessary to hold them in a dedicated area before final distribution to production area changing rooms.

Bulk delivery of cleanroom clothing

When this is the case then the bulk holding area needs to be designed to separate contaminated and clean items to reduce the risk of cross-contamination. Several garment packaging layers may be required to help achieve this with layers removed during different stages of the distribution process.

Distribution method at the point of use

Cleanroom clothing needs to be readily available for the wearer in the changing areas. If a wearer identified garment system is used then each member of staff will need to have their own distribution point and this is usually achieved using named or numbered lockers.

Each wearer is assigned a locker and has sole access. Decontaminated clothing is placed in the locker by garment distribution staff so that it is available for the wearer when required. Several sets of clothing can be placed in the locker at one time.

Garment storage lockers

When cleanroom clothing is supplied as a pool stock then individual lockers are not required and the distribution staff can place clothing in bins or on racks according to garment type and size. The number of garments available needs to be periodically topped up to an adequate level and a procedure needs to be in place which ensures that stock is rotated regularly.

Storage between use
When new garments are worn on every entry to the cleanroom there is no requirement for storage between use, the garments simply being placed in the soiled collection containers on exit from the cleanroom.

If cleanroom clothing is to be used more than once it must be stored in a way which allows easy access for the wearer and which minimises the risk of cross-contamination to the wearer, the clothing or the environment.

Garments are usually stored between use within the cleanroom changing areas.

Simple pegs, individual lockers or special garment storage cabinets with their own filtered-air supply are examples of some of the storage options available.

Collection of soiled items and transfer to bulk collection point
Contaminated clothing items are discarded by the wearer after use. The collection facility for these items must be as easy to use as possible to allow the wearer to quickly and efficiently dispose of soiled garments. Overly complicated collection systems will often result in misplaced garments and eventual shortages. Simple collecting bins or boxes can be readily placed in accessible positions and garment collection lockers can also be easily accommodated in changing areas.

On a regular basis the contaminated clothing is collected and packed into bulk containers for the scheduled collection by the garment decontamination plant.


Garment transport

Arrangements for any items contaminated with hazardous substances
The risk of garments being contaminated in use with harmful chemical or biological substances will have been assessed by the cleanroom clothing team with assistance from the Health and Safety department. The type and quantity of contaminant will determine the most appropriate disposal procedure required. This may range from incineration to separate bagging and labelling. All staff involved with wear, collection, transport and decontamination of such garments should be fully aware of the procedures in place.

8.9 Supply Options and Supplier Selection

Once a clear picture of cleanroom clothing requirements is established then the cleanroom clothing project team must decide on the best supply options and the most suitable suppliers.

Whatever choices are made the full system must be in place before a cleanroom clothing programme (and therefore cleanroom production) can commence.

The principle areas for decision are;

- *Cleanroom clothing supply.*
- *Cleanroom clothing distribution equipment and staff.*
- *Cleanroom clothing cleaning and decontamination.*
- *Combined supply.*

Cleanroom clothing supply
The manufacture and supply of cleanroom clothing is arranged by many companies throughout the world. Fabrics are sourced from specialist manufacturers and supplied for make-up to contracted clothing manufacturing companies.

The fabrics and garments offered by suppliers will usually be of a standard range with full fabric and garment specifications available to confirm their suitability for cleanroom use. Samples for wearer trials will be available to test comfort and fit.

If non-standard garments are required using unique fabrics or styles then these must be developed in conjunction with the supplier and manufacturer before manufacture can commence.

When a new fabric is developed then extensive testing must be carried out by independent fabric test laboratories and this process may last for well over a year.

Development of new cleanroom clothing can therefore be a lengthy and costly process.

Direct purchase
Cleanroom clothing can be directly purchased from a supplier to match site requirements. When a new cleanroom clothing programme is being initiated a large number of clothing items will be needed with multiple new garment sets required for each wearer. This will require a high capital outlay for the direct purchase. As the garments are used replacements will be required to cover damage or loss and additional garments may be required for new wearers, especially if a dedicated wearer system is adopted. The supply of these small numbers of garments can cause problems as garment manufacturing plants operate most efficiently when producing large quantities of the same garment.

Garment rental
Cleanroom garment rental options remove many of the financing and management problems associated with direct garment purchase and are the usual choice for obtaining garment supplies.

Charges are agreed for the contract term with the clothing supplier who will source and stock and maintain garments without a capital cost to the user. Garment replacements and additions will be supplied within an agreed timescale throughout the contract period and an additional garment stock will be held by the rental company for this purpose.

Management of the cleanroom clothing manufacturing chain will be the responsibility of the rental company who will deal with fabric and garment manufacture, exchange rate variance, shipping, import and quality assurance.

Cleanroom clothing distribution equipment and staff
Distribution equipment can be tailor-made in house, purchased or rented.

Personal lockers, garment distribution lockers and collection lockers are all available from specialist suppliers in a wide range of sizes, finishes and materials. They can have various locking options and can be built into cleanroom changing areas to optimise the use of space and facilitate easy cleaning.

Cleanroom compatible bins and racking are widely available and can also be fabricated to meet individual company requirements.

If cleanroom clothing distribution staff are required then these can be directly employed or supplied as part of a full management package from the garment decontamination supplier.

Cleanroom clothing cleaning and decontamination
Full details of the cleanroom clothing decontamination plant requirements are discussed in Section 6.0. *Cleanroom Garment and Consumables Decontamination - Plant and Process* .

This process is a key service to cleanroom manufacturing and a failure of supply will lead to disruption of cleanroom operations.


Cleanroom decontamination plant packing garments

It is possible to set up an in-house laundry operating at the required cleanroom standard and with adequate controls. In most instances the capital cost, complexity and requirement for space and services means that this is not a realistic option however and a specialised external partner is usually contracted to supply this service.

As well as demonstrating full compliance with the technical and quality assurance requirements of clothing decontamination any suitable supplier will also be able to demonstrate a high level of customer service. In addition a solid trading and financial background, ethical sourcing policy and disaster recovery programme will give additional confidence in continuity of supply.

Combined supply

Many purchasing departments prefer to optimise supply by using a limited number of suppliers. This has many benefits in reducing costs for both customer and supplier and allowing higher volume purchasing resulting in reduced unit pricing.

For this reason many suppliers have developed a "one-stop-shop" service to cover all aspects of cleanroom clothing and consumables supply.

Cleanroom garment supply, distribution, staff and equipment together with full garment cleaning and decontamination services are available from single suppliers with a range of charging options incorporating both direct sale and rental.

Experienced suppliers can also provide valuable assistance in the development and implementation of a cleanroom clothing programme from fabric and garment selection through to equipment supply, staff training and system start-up.

8.10 Implementation and Maintenance of the Clothing System

Once the cleanroom clothing system has been agreed and supply routes selected contracts can be signed and purchase orders issued.

A programme must then be implemented to measure the wearers, order fabric and garments, install distribution equipment and carry out staff awareness training.

Once garments have been manufactured and delivered to the decontamination plant they can be inspected, labelled, decontaminated, packed, supplied and distributed ready for first use.

Following the initial start-up customer support staff provided by the supplier and internal staff will be required to manage and monitor the first few days of the new programme and ensure it is running smoothly.

Once fully up and running the programme should then continue to operate efficiently with periodic reporting and adjustments as required.

A good customer - supplier relationship can be enhanced and monitored by periodic audits, service level measures, defined problem reporting procedures and resolution systems.

With careful consideration of all requirements and a full appraisal of the best supply options a cost effective and wearer friendly cleanroom clothing system can be implemented which efficiently meets the contamination control needs of the manufacturing operation.

SECTION

9.0

Planning, Sourcing and Optimising Cleanroom Consumables Supply

Cleanroom manufacturing operations may need consumable products for a variety of reasons including housekeeping and cleaning, as clothing, or as items of production equipment.

Consumable products are usually single-use and disposable, and so will generate a waste-stream which will have ongoing costs associated with collection, storage and disposal activities. This issue can be easily overlooked when selecting multipacked items. If a multipack contains far more items than will be used for the procedure e.g. a cleaning procedure using impregnated wipes, then this will result in much of the consumable product being discarded unused and it will often be more cost effective to select packs containing smaller quantities with a higher unit cost but lower operational cost.

Consumable items should only be chosen therefore when no suitable re-usable alternative is available and in the most economical quantities.

Many different disposable products are available and these are discussed in detail in Section 5.0 *Disposable Contamination Control Clothing* and Section 7.0 *Cleanroom Cleaning - Methods and Equipment.*

The choice of product, cleanliness level, packaging and presentation will all affect the costs. It is very beneficial therefore to define the purpose and cleanroom compatibility requirements for each consumable item and to produce a comprehensive product specification. This will enable cost-effective products to be sourced which are fit for purpose and which meet the associated contamination control, regulatory and production requirements.

When producing documentation such as supplier agreements, validation protocols and work procedures it is essential to use product specifications rather than proprietary brand names. This will provide a greater degree of flexibility to use equivalent products which meet the required specification, without significant documentation changes.

In order to clearly establish an accurate and comprehensive specification for consumables it is helpful to have input from a range of staff. These will include those responsible for Purchasing, Production Operations, Quality Assurance and Health and Safety.

When product testing, validation and supplier audit is needed as part of the product selection process the time required to accommodate these stages should also be taken into account .

It is likely that a range of products will be needed and it will usually be most efficient and cost effective to source as many products as possible from a single supplier.

As the annual spend on consumables is likely to be a significant part of the whole cleanroom production budget a careful assessment of actual requirements can be beneficial in achieving financial and efficiency savings.

There are various methods to identify consumable products for a particular application and the simplest is to merely produce a list of currently purchased items. This is simple and quick, however no opportunities to assess product suitability, to consider alternatives or to find significant savings will be possible using this approach.

The most productive system is to use a simple assessment check-list which can be easily applied to any cleanroom consumable product.

An example check-list is shown below however it is not intended to be exhaustive and additional information may be needed in specific applications.

For a small department this type of assessment will be relatively easy; however for a larger operation, involving several production units, it will be more effective to gather the information on a departmental basis before collating the information into a total purchasing requirement.

Cleanroom consumables assessment check-list

What is the function(s) of this consumable product?
Is there a re-usable alternative?
What are the contamination control requirements of the area in which the consumable will be used?
Are there any registered regulatory authority requirements?
Are there any Health and Safety considerations?
Will the consumable item be required as PPE (personal protective equipment)?
For consumable clothing items what range of sizes is needed?
Are there any specific contamination control requirements for the product being manufactured?
What level of particulate and fibre decontamination is needed for the consumable product?
Will the consumable require ESD (electro-static discharge) properties?
Does the consumable need to be sterile?
How does the consumable need to be packed or presented to meet contamination control requirements and operating procedures?
What product conformance documentation is required?
Are there any International or National standards or test protocols against which the product must be tested?
What is the minimum shelf-life required?
How critical is this product to production continuity?
Does storage space or distribution to point-of-use present any problems or require additional equipment?
Are adequate and acceptable disposal facilities in place for the discarded consumable and its packaging?
Does the product need to be identified for use in a specific area?
Can a consumable product's design attributes be selected to improve operational efficiency or safety?
Will product trials and/or validation be required?
What quantities of the consumable product are required annually?
Are unusually large quantities of product needed at specific times to meet peak requirements?
Is there a consumables budget?
At what date should supply commence?

This check-list approach can be applied to any cleanroom consumable product including clothing, cleaning products and production items such as cleanroom paper.

Example of consumables assessment check-list in use
The following example shows how the completed check-list can be used to specify the correct product.

(It is often useful to provide this in a tabulated format with each item numbered sequentially, with adjacent spaces for the responses and an additional column to record any other comments or observations).

(Note; this example does not refer to any specific operation).

ABC pharmacy unit is manufacturing cytotoxic drug doses.

The manufacture requires aseptic technique in a Class II Biological Safety Cabinet (GMP grade A).

The departmental standard operating procedures require an inner and outer glove to be worn for this procedure.

One member of staff undertakes this work and she has a possible allergy to Latex.

A branded glove (size 7) is currently being purchased and has been in use for some time however a review of alternative products is now considered worthwhile.

ABC Pharmacy Unit

Assessment of outer glove requirements for use in cytotoxic drug production

What is the function(s) of this consumable product?
Outer glove for the aseptic manufacture of cytotoxic drugs.

Is there a re-usable alternative?
No.

What are the contamination control requirements of the area in which the consumable will be used?
Class II Biological Safety Cabinet GMP class A.

Are there any registered regulatory authority requirements?
Gloves not included in the product registration document.

Are there any health and safety considerations?
Yes - danger of skin exposure to cytotoxic drug. Possible latex allergy.

Will the consumable item by required as PPE (personal protective equipment)?
Yes - risk assessment requires the gloves to act as PPE.

For consumable clothing items - what range of sizes is needed?
Size 7.0 only.

Are there any specific contamination control requirements for the product being manufactured?
Product must be protected from particulate, microbiological and endotoxin contamination.

What level of particulate and fibre decontamination is needed for the consumable product?
Compatible with ISO 14644-1 grade 5 cleanroom, GMP class A.

Will the consumable require ESD (electro-static discharge) properties?
No.

Does the consumable need to be sterile?
Yes.

How does the consumable need to be packed or presented to meet contamination control requirements and operating procedures?
Hand specific, presented individually packed and double bagged for aseptic donning.

What product conformance documentation is required?
Certificate of irradiation, batch conformance analysis test results.

Are there any International or National standards or test protocols against which the product must be tested?
Tested in accordance with BS EN 420:2003, PPE category III product, tested in accordance with EN 374:2003 part 2 and 3, Meets or exceeds AQL level of 1.5 for pinholes, tested to show low endotoxin level (≤20 EU per pair), tested to show low particulate level. Tested to show acceptably low permeation to cytotoxic drugs.

What is the minimum shelf-life required?
Two years.

How critical is this product to production continuity?
Critical - production cannot proceed without these gloves.

Does storage space or distribution to point-of-use present any problems or require additional equipment?
No - existing adequate storage and distribution system.

Are adequate and acceptable disposal facilities in place for the discarded consumable and its packaging?
Yes - existing procedures and equipment in place for correct disposal of discarded "clean" or accidentally contaminated gloves and packaging.

Does the product need to be identified for use in a specific area?
Yes - for use in cytotoxic drug production only.

Can a consumable product's design attributes be selected to improve operational efficiency or safety?
Yes - gloves must provide easy donning and good operational dexterity. Glove must be long enough to overlap garment cuff. Colour must contrast with inner glove colour.

Will product trials and/or validation be required?
Yes - operational trial.

What quantities of the consumable product are required annually?
Approximately 3,000 pairs (gloves changed every 30 minutes).

Are unusually large quantities of product needed at specific times to meet "peak" requirements?
No, regular usage throughout year.

Is there a consumables budget?
Yes.

At what date should supply commence?
3 months supply currently in stock.

From this information a product specification can be produced for this glove.
A suggested example is shown below.

ABC Pharmacy

Consumable Product Specification # GLV-123 - powder-free cleanroom outer glove for use in cytotoxic drug production

Product	Powder-free cleanroom outer glove for use in cytotoxic drug production unit
Material	Nitrile
Size	7.0
Cuff length	30cm
Colour	White
Packaging and presentation	Hand specific, double bagged, packed as pairs for aseptic donning
Sterility	Sterile, with minimum two years shelf life
Contamination control standard	Suitable for use in ISO 14644-1 grade 5, EU GMP grade A / B environment
Glove conformance tests required	Tested in accordance with BS EN 420:2003 PPE category III product - CE marked Tested in accordance with EN 374:2003 part 2 and 3 Meets or exceeds AQL level of 1.5 for pinholes Tested to show low endotoxin level (≤20 EU per pair) Tested to demonstrate low particulate level Tested to show acceptably low permeation to cytotoxic drugs
Batch documentation	Batch conformance documentation and irradiation certificate to be supplied for each numbered batch

Requirements may change over time e.g. an alternative glove size may be required, however any changes to the generic specification can be easily accomplished using the document control procedures of a Quality Management System.

Once this assessment has been carried out for each disposable product and the product specifications produced appropriate suppliers can be contacted and the full consumables requirement discussed in detail. As well as the product specification additional information from the check-list such as annual quantities, any distribution equipment needed and timescales will all be valuable in the sourcing process.

Suppliers will wish to suggest various product options which meet the specification and it is usual for samples to be provided free-of-charge so that trials can be carried out and the products assessed by the relevant departments.

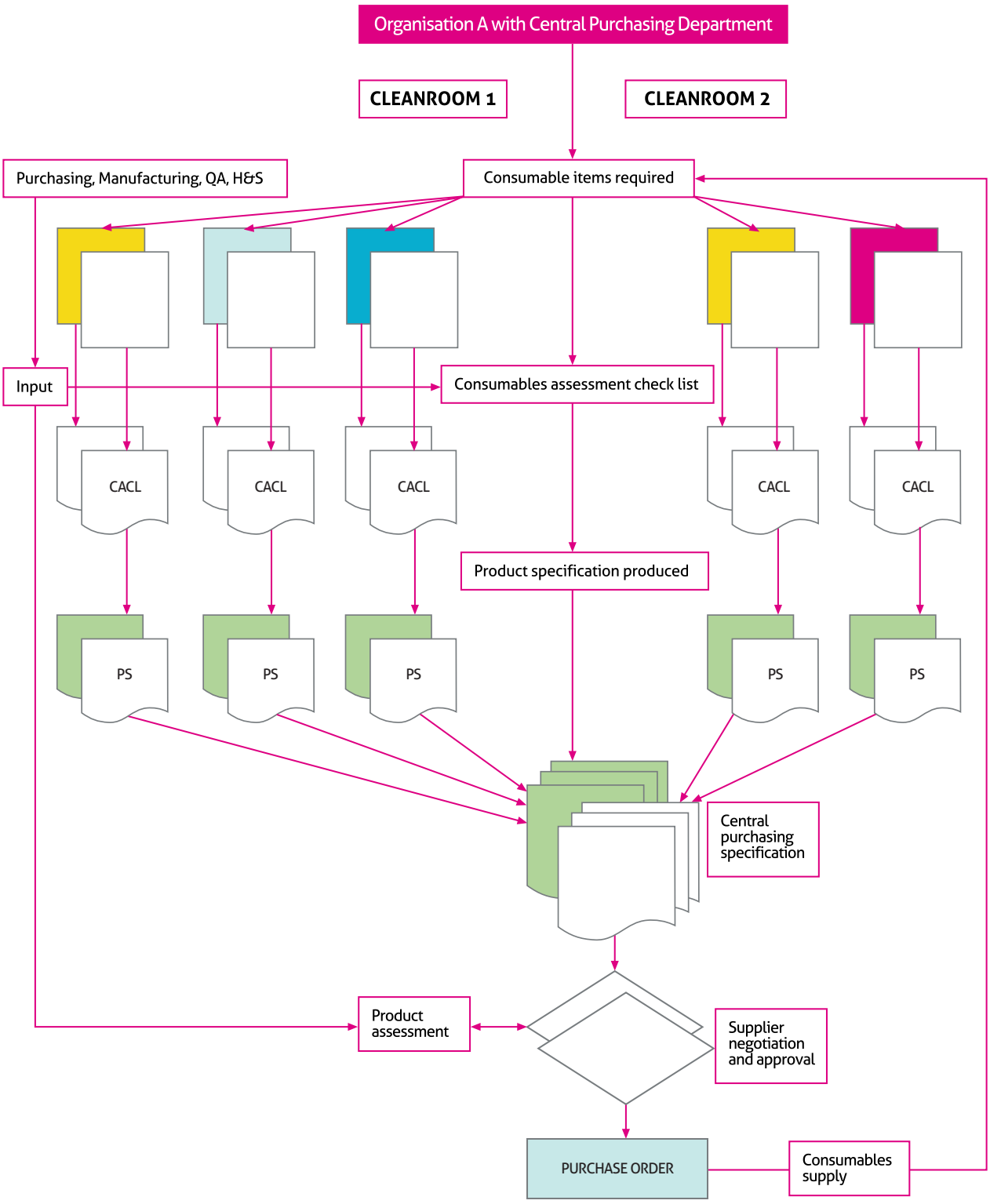
Glove samples with full supporting documentation for assessment

It is usually more cost effective to select an existing off-the-shelf product. However when no product can be sourced which meets the specification suppliers will consider developing products for a particular application. Development of unique products will increase sourcing timescales and may require a commitment to purchase significant quantities of the product

As the majority of consumable products are manufactured overseas, supply chain security, ethical sourcing policy, product stockholdings and delivery frequency will need to be assessed and this can often be accomplished during a supplier audit. Whenever possible it is usually beneficial to source all cleanroom consumable products from a one-stop-shop supplier although an alternative supplier may be needed as a back-up for critical products.

Once suitable and acceptable products have been identified the different supplier options can be assessed and supply arrangements finalised.

The flowchart shows this basic assessment and purchasing system for 5 consumable products. They are used in two separate cleanroom manufacturing operations within the same organisation, which has a central purchasing department.



Cleanroom consumables purchasing flow chart

SECTION

10.0

Acknowledgements, References, Useful Contacts and Sources of Information

Acknowledgements

The following books have been especially useful in providing valuable information for the Microncleanan Big Blue Cleanroom Handbook:

Cleanroom Technology - Fundamentals of Design Testing and Operation - W. Whyte, Second edition, Published 2010 by John Wiley & Sons Ltd.

Cleanroom Clothing Systems: People As a Contamination Source - B. Ljungqvist and B. Reinmuller, Published 2004 by PDA/DHI.

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Some photographs courtesy of Jack Grange **www.jackgrange.co.uk**

References

Section 2

1

Federal Standard 209. This standard was first published in 1963 titled "Cleanroom and Work Station Requirements, Controlled Environments". It was revised in 1966 (209A), 1973 (209B), 1987 (C), 1988 (D) and 1992 (E).

2

BS 5295 British Standard 5295:1989
The British Standard contained five parts.

Part 0 - General introduction and terms and definitions for clean rooms and clean air devices.

Part 1 - Specification for clean rooms and clean air devices.

Part 2 - Method for specifying the design, construction and commissioning of clean room and clean air devices.

Part 3 - Guide to operational procedures and disciplines applicable to clean rooms and clean air devices.

Part 4 - Specification for monitoring clean rooms and clean air devices to prove continued compliance with BS 5295

3

BS EN ISO 14644-1:1999 Cleanrooms and associated controlled environments. Classification of air cleanliness.

BS EN ISO 14644-2:2000 Cleanrooms and associated controlled environments. Specifications for testing and monitoring to prove continued compliance with ISO 14644-1.

BS EN ISO 14644-3:2005 Cleanrooms and associated controlled environments. Test Methods.

BS EN ISO 14644-4:2001 Cleanrooms and associated controlled environments. Design, Construction and Start-up.

BS EN ISO 14644-5:2004 Cleanrooms and associated controlled environments. Operations.

BS EN ISO 14644-6:2007 Cleanrooms and associated controlled environments. Vocabulary.

BS EN ISO 14644-7:2004 Cleanrooms and associated controlled environments. Separative devices (clean air hoods, gloveboxes, isolators and mini environments.

BS EN ISO 14644-8:2006 Cleanrooms and associated controlled environments. Classification of airborne molecular contamination.

BS EN ISO 14644-9 Cleanrooms and associated controlled environments. Classification of surface particle cleanliness (08/30190157 DC draft for public comment published Sept 2008).

4 The MHRA

Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007.

5

ISO 14698-1 Cleanrooms and associated controlled environments - Biocontamination control.

Part 1 General principles and methods.

ISO 14698-2 Cleanrooms and associated controlled environments - Biocontamination control.

Part 2 Evaluation and interpretation of biocontamination data.

6

BS EN 61340-5-1:2007– Electrostatics Protection of electronic devices from electrostatic phenomena. General requirements

7

BS 6524:1984 - Method for the determination of the surface resistivity of a textile fabric.

8

IEST-RP-CC003: Garment System Considerations for Cleanrooms and Other Controlled Environments.

9

ASTM F51-00 (2007) Standard Test Method for Sizing and Counting Particulate Contaminant In and On Clean Room Garments.

10

BS EN 14065:2002 Textiles - Laundry processed textiles - Biocontamination control system.

Section 3

1

IEST-RP-CC003: Garment System Considerations for Cleanrooms and Other Controlled Environments.

2

BS EN ISO 14644-1:1999 Cleanrooms and associated controlled environments. Classification of air cleanliness.

3 The MHRA

Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007.

Section 4

1
BS 3321:1986 Method for measurement of the equivalent pore size of fabrics (bubble pressure test).

2
British Textile Technology Group (BTTG) Particle Barrier Efficiency Test .

3
BS 6909:1988 Method for generation and counting of the airborne linting propensity of fabrics in the dry state.

4
ASTM E96/E96M-10 Standard test methods for water vapour transmission of materials.

5
BS EN ISO 9237:1995 Textiles. Determination of the permeability of fabrics to air.

6
BS EN 1149-1:2006 Protective clothing. Electrostatic properties. Test method for measurement of surface resistivity.

7
BS EN 530:2010 Abrasion resistance of protective clothing material. Test methods.

8
IEST-RP-CC003: Garment System Considerations for Cleanrooms and Other Controlled Environments.

9
Whyte W. Dispersion of particles and micro-organisms from people. European Journal of Parenteral and Pharmaceutical Sciences 2007; 12(2): 39-46

Section 5

1
Personal Protective Equipment Directive 89/686/EEC.

2
BS EN 943-1:2002
Protective clothing against liquid and gaseous chemicals, aerosols and solid particles. Performance requirements for ventilated and non-ventilated "gas-tight" (Type 1) and "non-gas-tight" (Type 2) chemical protective suits.

BS EN 14605:2005+A1:2009
Protective clothing against liquid chemicals. Performance requirements for clothing with liquid-tight (Type 3) or spray-tight (Type 4) connections, including items providing protection to parts of the body only.

BS EN ISO 13982-1:2004+A1:2010
Protective clothing for use against solid particulates. Performance requirements for chemical protective clothing providing protection to the full body against airborne solid particulates (Type 5).

BS EN ISO 13982-2:2004
Protective clothing for use against solid particulates. Test method of determination of inward leakage of aerosols of fine particles into suits.

BS EN 13034:2005+A1:2009
Protective clothing against liquid chemicals. Performance requirements for chemical protective clothing offering limited protective performance against liquid chemicals (Type 6).

3
Eaton T. A safe pair of hands - how secure are your gloves used for aseptically prepared pharmaceutical products? European Journal of Parenteral and Pharmaceutical Sciences 2005; 10(3): 35-42.

4
BS EN 455-1:2000. Medical gloves for single use: Requirements and testing for freedom from holes.

5
BS EN 420:2003+A1:2009 Protective gloves. General requirements and test methods.

6
BS EN 374-1:2003 Protective gloves against chemicals and micro-organisms. Terminology and performance requirements.

BS EN 374-2:2003
Protective gloves against chemicals and micro-organisms. Determination of resistance to penetration.

BS EN 374-3:2003
Protective gloves against chemicals and micro-organisms. Determination of resistance to permeation by chemicals.

7
IEST-RP-CC005: Gloves and Finger Cots Used in Cleanrooms and Other Controlled Environments.

Section 6

1
BS EN ISO 14644-1:1999 Cleanrooms and associated controlled environments. Classification of air cleanliness.

2 The MHRA
Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007.

3
IEST-RP-CC003: Garment System Considerations for Cleanrooms and Other Controlled Environments.

4
ASTM F51-00 (2007) Standard Test Method for Sizing and Counting Particulate Contaminant In and On Clean Room Garments.

5
HSG (95)18: Hospital laundry arrangements for used and infected linen.

6
ISO 11137-2:2006 Sterilisation of healthcare products.

7
BS EN 1149-1:2006 Protective clothing. Electrostatic properties. Test method for measurement of surface resistivity.

Section 7

1
BS EN ISO 14644-5:2004 Cleanrooms and associated controlled environments. Operations.

2
Eaton T. Cleanroom Airborne Particulate Limits and 70% Isopropyl Alcohol (IPA)–a Lingering Problem for Pharmaceutical Manufacturing? PDA Journal, 2009.

3
BS EN 1276:2009 Chemical disinfectants and antiseptics. Quantitative suspension test for the evaluation of bactericidal activity of chemical disinfectants and antiseptics used in food, industrial, domestic, and institutional areas. Test method and requirements.

4
CEN EN 13697:2001 Chemical disinfectants and antiseptics. Quantitative non-porous surface test for the evaluation of bactericidal and/or fungicidal activity of chemical disinfectants used in food, industrial, domestic and institutional areas. Test method and requirements without mechanical action (phase 2/step 2).

5
BS EN 1650:2008 Chemical disinfectants and antiseptics. Quantitative suspension test for the evaluation of fungicidal or yeasticidal activity of chemical disinfectants and antiseptics used in food, industrial, domestic and institutional areas. Test method and requirements (phase 2, step 1).

6
BS EN 13704:2002 Chemical disinfectants. Quantitative suspension test for the evaluation of sporicidal activity of chemical disinfectants used in food, industrial, domestic and institutional areas. Test method and requirements (phase 2, step 1).

Useful Contacts and Sources of Information

British Standards Institution www.bsigroup.com
BSI Group provides a range of services; develops private, national and international standards, certifies management systems and products, provides testing and certification of products and services, provides training and information on standards and international trade and provides performance management and supply chain management software solutions.

ISO - International Organisation for Standardisation www.iso.org
ISO is a non-governmental organisation comprising a network of the national standards bodies of some 160 countries, one per country, from all regions of the world. Each ISO member is the principal standards organisation in its country. The members propose the new standards, participate in their development and provide support in collaboration with ISO Central Secretariat for nearly 3,280 technical groups that actually develop the standards. When their work is published as an ISO International Standard, it may be translated and adopted as a national standard by the ISO members.

ASTM www.astm.org
ASTM International (ASTM), originally known as the American Society for Testing and Materials, is an international standards organisation that develops and publishes voluntary consensus technical standards for a wide range of materials, products, systems, and services. The organisation's headquarters is in West Conshohocken, Pennsylvania, USA.

ASTM, founded in 1898, pre-dates other standards organisations but differs from these in that it is not a national standards body, (that role being taken in the United States by ANSI). However, ASTM has a dominant role among standards developers in the USA, and claims to be the world's largest developer of standards.

BTTG - The British Textile Technology Group www.bttg.co.uk
BTTG was founded 1989 by the merger of the Shirley Institute and Wool Industry Research Association, with histories stretching back 85 years.

The Group has two operating companies :
BTTG Testing & Certification specialises in the testing and Certification of Personal Protective Equipment, Geosynthetics, Floorcoverings and other construction products. It offers Certification to EU Directives.
Shirley Technologies provides a broad range of services to the traditional apparel sector. It specialises in chemical testing and provides certification to the Oeko-tex scheme.

IEST -The Institute of Environmental Sciences and Technology www.iest.org
IEST is an international, technical society of engineers, scientists, and educators that serves its members and the industries they represent (simulating, testing, controlling, and teaching the environments of earth and space) through education and the development of recommended practices and standards.

Pharmaceutical and Healthcare Sciences Society www.phss.co.uk
The Pharmaceutical and Healthcare Sciences Society exists as a science based forum for individuals active in the fields of Pharmaceutical and Healthcare Sciences. The society evolved from the former Parenteral Society, which was primarily focused on sterile injectable and implantable drugs and devices.

MHRA - The Medicines and Healthcare Products Regulatory Agency www.mhra.gov.uk
The MHRA was set up in April 2003 from a merger of the Medicines Control Agency and the Medical Devices Agency. The MHRA is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe. The MHRA is an executive agency of the Department of Health.