History of Cleanrooms

BY PHILIP NAUGHTON, MEMBER ASHRAE

Cleanrooms are areas in which particle concentration and environmental conditions are controlled within specified limits. The limits of the particle concentrations are normally set by the requirements of the process occurring within the space so that contamination of people, processes and equipment can be mitigated. Today cleanroom applications have increased from its early days in hospitals and precision manufacturing to include:[1]

- Pharmaceuticals/Biotechnology. Preparations of pharmaceutical, biological and medical products require clean spaces to control viable (living) and nonviable particles that could impact product sterility.
- Microelectronics/Semiconductors. Feature sizes in semiconductors are smaller than many molecules, and controlling the concentration of particles pushes these cleanrooms to limits of cleanroom technology.
- Flat Panel Display: flat panel display (FPD) factories are some of the largest cleanrooms in the world, with some cleanroom spaces greater than 2,000,000 ft^2 (200,000 m^2). New FPD factories are controlling particles and chemical concentrations.
- Aerospace. Cleanrooms were first developed for aerospace applications to manufacture and assemble gyroscopes, precision ball bearings, satellites and aerospace electronics.
- Hospitals. Controlling infection during surgery was the driver for many early contamination control techniques.
- Miscellaneous Applications. Cleanrooms are also used in aseptic food processing and packaging, microelectronic and nanotech applications, medical device manufacturing, automotive paint booths, crystal, laser/optic industries, and advanced materials research.

Design of clean spaces covers much more than traditional control of particles concentrations. Controlling other environmental parameters may also be necessary to a process within the clean space. Additional factors may include air temperature and humidity; electrostatic discharge (ESD); molecular and gaseous contamination; airflow patterns; air pressurization; sound and vibration.

The objective of good cleanroom design is to maintain effective contamination control while ensuring required levels of reliability, productivity, installation and operating costs. Cleanrooms are a specially constructed enclosed space with environmental control of particulates, temperatures, humidity, air pressure, airflow patterns, air motion, vibration, noise, viable organisms and lighting (ASHRAE, 2018).[1] Cleanrooms are used in advanced manufacturing, controlling contamination to the manufacturing process and in medical operations where controlling the spread of infection is of utmost importance.

Philip Naughton is a senior engineer and energy manager for Applied Materials Inc. He is past chair of ASHRAE TC 9.11 Clean Spaces, and is current subcommittee chair for TC 9.11 Energy Efficiency for Cleanrooms and is ASHRAE liaison to U.S. TAG for ISO 14644 Cleanrooms and Associated Controlled Environments. He also participates in other committees and industry activities related to cleanrooms.

Contamination and Contamination Control

Contamination is an impurity, or some other undesirable element, that soils, infects, makes unfit, or makes inferior a material, a physical body, a natural environment, a workplace, a product, etc. The contamination may be viable, such as bacteria, microbes or viruses, or it may be in the form of nonviable particles such as metals, organic or inorganic compounds, pollution or dust. Airborne contamination may also be gaseous or molecular contamination. Contamination may be brought into a space by people, materials and equipment and/or airborne contaminants located outside the space. Controlling contamination in a space is accomplished in two major ways: prevention of contamination from entering the space and prevention of contamination generated within the space from contaminating a person, product or material. People, equipment and materials can be cleaned prior to their introduction into the space. Proper filtration and the use of positive pressure can mitigate airborne contamination.

Hospitals

Hospitals were the first spaces to attempt to control the air where patients were located. Controlling the ventilation of hospital spaces was seen in first-century Roman military hospitals. Over the centuries, hospitals were large, open halls that were well heated and ventilated. Florence Nightingale made dramatic improvements in the mortality rates of wounded soldiers by insisting on scrupulously clean, well-ventilated hospital rooms.[2]

Louis Pasteur is remembered for his breakthrough in the causes and prevention of diseases. His medical discoveries provided direct support for the germ theory of disease and its application in clinical medicine. Pasteur performed experiments that showed that without contamination, microorganisms could not develop. He demonstrated that in sterilized and sealed flasks, nothing ever developed, and in sterilized but open flasks, microorganisms could grow.[3]

The control of infection during surgery was a significant driver to controlling contamination. Early pioneers included British surgeon and advocate of antiseptic surgery Joseph Lister, who pioneered the use of disinfectants; American surgeon William Keen and his efforts at cleaning the surgical suite; and German Gustav Neuber, who in 1883 designed a "cleanable" surgical suite containing nonporous surfaces, glass and metal furnishings and in-room sterilization equipment. Neuber-style surgery suites were adopted in many locations.[4] These early innovations provided guidance to manufacturers also concerned with controlling contamination in their precision manufacturing operations.

Precision Manufacturing and Contamination Control

Many manufacturers understood the need to keep particles out of the products they were building. Increased cleaning was an obvious solution, but preventing the particles from entering the space proved more challenging. Contamination in the manufacturing process results in defects and unfit products. Precision manufacturing operations, such as watch making and ball bearing manufacturing, were early adopters of contamination control techniques and the need to clean materials and have clean workstations.

In the latter part of the 1800s, Aaron Dennison and Edward Howard relocated their watch factory from downtown Roxbury/Boston, where traffic on unpaved roads was disastrous to the precise watch parts, to the suburbs of Waltham to avoid the heavy dust. During World War II the need for more precise military parts increased the demand for clean manufacturing environments. Precision bearings were used in gyroscopes and bomb sites before and during World War II.[4]

After the war the U.S. military continued to develop advanced aircraft with advanced guidance systems and miniature parts. 1947 saw the invention of the first transistor, and by the mid 1950s *The New York Times* spoke about 'the business of making things smaller' as central to new aircraft performance. Two years later *Time* magazine hailed miniaturization as a key to business growth; acknowledging that military needs drove the trend, it forecast that 'miniaturization will in time spread through civilian U.S. life.' Already, pocket radios, tiny hearing aids and other electronic devices had grown smaller; in the future, so too would 'giant electronic brains.'[4]

Early Cleanrooms

Similar to surgery suites, manufacturers needed a special room where they could control contamination. Constant cleaning, while effective, was not very productive. Manufacturers of precision military products started to request designs for "ultra-clean" rooms and "white rooms" (or cleanrooms). Some claim that Western Electric's "dust-free" room built in 1955 was the

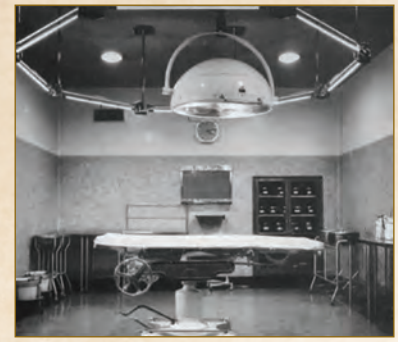
first production cleanroom.[5] The Western Electric room was designed using 99.95% filters (see sidebar, *History of HEPA Filters*, Page 42) and positive pressurization. Others have claimed the Olmsted Air Force Base in Pennsylvania or the U.S. Navy's North Island Naval Air Station in San Diego were the home of the first installations.[6]

Convergence of Ideas

While advances in contamination control were occurring in manufacturing operations during the 20th century, the medical profession was also experimenting with new contamination control methods.

Much research had been conducted in the first half of the 20th century on the benefits of mechanical ventilation. Another important step in the field of airborne infections was the use of ultraviolet lighting in combination with mechanical ventilation. Deryl Hart found that ultraviolet light would reduce the airborne bacteria in the operating room.[7] While the use of UV lighting was not directly part of the ventilation system, it was integrated with the ventilation system to ensure adequate mixing of the air. An operating room at the Hospital for Sick Children in Toronto combining air-conditioning ultraviolet lamps was constructed in 1936 (*Figure 1*). The design allowed testing the efficacy of air changes and UV lights in removing bacteria from the space. Air supply was slow enough to avoid a feeling of draft but was of sufficient volume to produce 480 air changes per hour. The results indicated significant reduction in airborne contamination.[7]

Figure 1 1936 Operating room showing UV lamps. Air inlet in the upper left.[7]



Other studies, guides and regulations covered ventilation and its effect on disease transmission, fever therapy, patient comfort and draft perception, CO_2 concentrations,

History of HEPA Filters

In addition to the pioneering work of Willis Whitfield and his laminar flow cleanroom, cleanrooms would not have been practical without the invention of "absolute," "super-interception," and "super-efficiency" air filters. The development of absolute filters dates back to pre-World War II Germany. Germany had developed filter paper for use in gas masks using finely ground asbestos dispersed in esparto grass. A captured German gas mask canister was sent to the U.S. Army Chemical Warfare laboratory where additional research was performed. The German paper was studied, and the mixture of asbestos and esparto grass had unusually high particle retention characteristics, acceptable resistance to airflow, good dust storage and resistance to plugging from oil-type screening smokes. Hollingsworth and Vose Company (H&V) of Massachusetts manufactured filter paper using conventional papermaking machinery.

In the 1950s the U.S. Atomic Energy Commission (AEC) wanted to create super-interceptor filter media using domestic materials rather than relying on imported asbestos and esparto grass. Johns Manville and Owens Corning developed sub-micron diameter glass fibers, and in 1951 an all-glass-fiber paper made partly from superfine glass fibers with diameters substantially less than 1.0 µm was produced. In 1953 Walter Smith, working with Arthur D. Little, developed the "absolute" filter for the AEC. By the end of the 1950s ,multiple companies were producing absolute filters, and in 1961 the generic acronym "HEPA filter" was coined by Humphrey Gilbert, a former Manhattan Project safety engineer. It came from the title of a 1961 AEC report called "High-Efficiency Particulate Air Filter Units, Inspection, Handling, Installation." A HEPA filter was defined as a throwaway, dry-type filter with a minimum particle removal efficiency of 99.95% (which was later raised to 99.97%) for a 0.3-µm monodisperse particle cloud. In later years, as advances in filter media continued, new filters with removal efficiencies greater than 99.99% were developed. These new filters were referred to as ultra low penetrating air filters, or ULPA filters.[27]

ASHRAE RESEARCH

ASHRAE has also funded several research projects related to cleanrooms over the years.

RP-202 Ventilation Requirements in Operating Rooms

Hospital operating rooms must meet one of the most complex set of control requirements of any indoor environment, if acceptable performance is to be achieved. The overall objective of this research project was to identify and demonstrate control strategies that could reduce energy requirements while not producing deleterious effects on the environmental quality within the operating room.

The objective was achieved through an extensive literature search in which more than 1,400 citations were referenced, through the development of mathematical and biophysical models, and through analysis of data obtained in two existing operating rooms with different system performance characteristics. Principal Investigator: Woods, J.E., Iowa State University; Publish Date: January 1984

RP-652 Optimum Airflow Velocity in Cleanrooms

Findings from the research show that nominal airflow velocities as low as 60 fpm (0.3 m/s) are possible without a loss of cleanliness for specific work sites in the cleanroom. Cross contamination between adjacent workspace on the cleanroom bench was found not to be a significant problem. However, the room airflow rate required depends on the room configuration as well as the location and strength of the source of contamination. Therefore, a nominal velocity of 60 fpm (0.3 m/s) may not be appropriate for all cleanrooms. Principal Investigator: Iowa State University; Publish Date: October 1994

RP-1344 Cleanroom Pressurization Strategy Update—Quantification and Validation of Minimum Pressure Differentials for Basic Configurations and Applications

The research illustrated that room air leakage rate is a critical variable in determining the room "flow offset" value. Particle migration from a less-clean room into a cleanroom is not only driven by pressure differential, but also by particle concentration differential in a form of mass diffusion. The recommendations included a "Minimum Pressure Differential (PD) Requirements Across Cleanroom Envelope" table grouped by cleanliness class difference. Principal Investigator: Wei Sun, P.E.; Keith B. Flyzik; John Mitchell; Aashish Watave; Publish Date: October 2011

RP-1431 Analysis of Transient Characteristics, Effectiveness, and Optimization of Cleanroom Airlocks

A cleanroom airlock is a transitional space that has two doors in series to separate cleanroom and corridor which often have different air cleanliness and pressures. An airlock performs as a particle, microbial or chemical fume contaminant barrier by minimizing contaminated air to flow into a protective area. To study the performance and transient nature of airlock, especially when a door is in motion-during opening and closing, a new terminology called Contamination Ratio (CR) was mathematically defined which can be used to quantify a relative contamination level from contaminated area into protective area across a barrier such as a single door or an airlock. The research has also analyzed the scenarios between the "walk-in" and "walk-out" by people, and between the "push-door-in" and "pull-door–out," in terms of particle transmissions. A recommendation table of airlock application has been also included in the report. Principal Investigator: Wei Sun, P.E.; Keith B. Flyzik; John Mitchell; Aashish Watave; Publish Date: October 2011

RP-1399 Survey of Particle Production Rates from Process Activities in Pharmaceutical and Biological Cleanrooms

The aim of this research project was to understand particle sizes and the rates of particle generation for representative processes in pharmaceutical and biotechnological cleanrooms. This was achieved via field measurements and data collection in several pharmaceutical and biotechnology cleanrooms. Field measurements were performed using certified and calibrated particle counters and airflow meters. The airflow data, particle data, and cleanroom air conditions were recorded for both 'operational' and 'at rest' conditions to deduce the particle generation rate. Principal Investigator: Li Song; Oluwaseyi T. Ogunsola; Junke Wang; Publish Date: June 2018

Ongoing Research

RP-1604, Demand-Based Control for Cleanrooms, is examining this concept and collecting qualitative data on the effectiveness of the use of demand controlled filtration.

humidity, etc. Anesthesia gas use in surgery was commonplace, such that air-conditioning engineers and medical professionals were concerned with controlling the atmosphere in operating suites due to the explosive nature of the anesthesia gases. One of the earliest publications of suggested air change rates in hospitals was published in the 1938 ASHVE Guidebook: "Copious ventilation, from 6 to 12 air changes per hour, is necessary to preclude accumulation of explosive mixtures and to reduce the concentration of anesthetics to below the physiologic threshold so that the surgeon and his personnel will not be affected.[8,9]

In 1946 Robert Bourdillon and Dr. Leonard Colebrook showed that sepsis of burns and wounds could be caused by bacterial contamination from the air and that well-designed ventilation equipment could play a large part in preventing this. Additional work on the design of surgical suites was conducted in the 1950s on plenum ventilation and the use of designed inlet and outlet room conditions.[10]

Disturbed by the large amount of septic cases and postoperative infections, hip-replacement surgeon John Charnley began investigating new methods of operating room ventilation. Building upon the work of Bourdillon

90 fpm & Laminar Flow

One of the most enduring questions concerning cleanroom standards is "why 90 fpm?" FED-STD-209A, B, which were in effect for over 20 years, had specified 90 fpm ±20 fpm (0.5 m/s ±0.1 m/s) in the facility design guidance. Numerous anecdotes and second- and third-hand stories speak about that the origins of the velocity used in Willis Whitfield's laminar flow system. Some had speculated this was the velocity theoretically calculated to remove a particle dropped in front of the supply filter in the first laminar flow room at Sandia Corporation. Another opinion was that the only air supply fan available to Willis Whitfield produced this air velocity. Another said that the 90 fpm (0.5 m/s) was the minimum velocity needed to overcome buoyancy effects of a hot surface in the workspace.[5]

90 fpm (0.5 m/s) is almost equal to 1 mph (0.4 m/s), and velocities greater than 100 fpm (0.5 m/s) can produce a sensation of draft for some people. Whitfield had said "The real value of filtered laminar airflow is the high degree of cleanliness that it maintains at very low velocities, well below personnel discomfort levels. The 100 lineal fpm (0.5 m/s) air velocity utilized in these rooms was well below the rate of 150 fpm to 200 fpm (0.8 m/s to 1.0 m/s), which is generally considered to be the threshold of personnel discomfort." [13] Others have quoted Whitfield, who said that the fans used in his cleanroom could produce between 50 fpm and 200 fpm (0.3 m/s to 1.0 m/s). 50 fpm (0.3 m/s) could not remove particles fast enough if more than one person was in the room, and above 100 fpm (0.5 m/s) the noise from the fans became annoying.[5] This seems more in alignment with Whitfield's explanation in 1963. The most logical answer is a combination of items, worker comfort (sound and draft) and recovery rate.

In addition to the origins of 90 fpm (0.5 m/s) and equally controversial was Whitfield's decision to use the term *laminar flow* when describing his unidirectional airflow in the ultra-cleanroom. It was known that from a purely scientific basis, airflow in this room was not laminar. During an interview in 2005, Willis responded to a question from Sandia Lab News: "Lab News then asked just what was 'laminar' about the so-called 'laminar flow cleanroom' — the usual term used to describe his group's invention. 'Nothing,' said Willis, who described the word as a preexisting marketing term and a catchy name. 'The air is just unidirectional.' " [28] Mr. Whitfield has also said he very carefully puts 'laminar flow' in quotation marks when outlining the innovation and refers instead to 'unidirectional air flow.' Whitfield traces the application of the name to his innovation to the meetings of the group that devised Standard 209. [21]

and Colebrook in 1946, and Blowers and Crew in the 1950s, Dr. Charnley and air-conditioning engineer James Howarth built one of the first unidirectional airflow rooms using sterile air supply and displacement ventilation.[11,4]

Beginnings of Modern Cleanrooms

The watershed event in the history of the cleanroom was the invention of the first "laminar flow" or true unidirectional concept of ventilation in 1960 – 1961 by physicist Willis Whitfield, Ph.D., at the Sandia Laboratories in Albuquerque, N.M., while working with the U.S. Atomic Energy Commission (AEC).[5] In 1959 Whitfield and his team were investigating why cleanrooms could not stay clean. The problem was that while previous cleanrooms could achieve a desired level of cleanliness, they did not remain clean without continuous cleaning by personnel. The problem was still that some of the best cleanrooms and clean hoods would average no better than approximately 100,000 particles of 0.5 micron and larger per cubic foot. The focus was on keeping contaminants out, not on removing any generated by the work or personnel inside the room.[12]

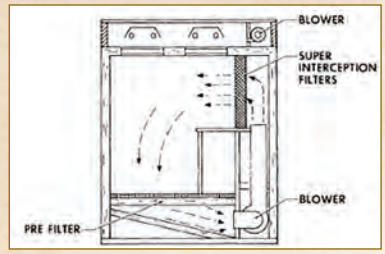
New products being manufactured required continuous cleaning, and the generation of particles was exceeding the ability of the those cleaning the space. The problem was particles generated within the space stayed in the space unless they were removed by the cleaning staff. Previous work was focused on cleaning people, isolating the contamination from people with improved clothing, continuous cleaning of work surfaces, disinfecting surfaces and materials and providing clean filtered air to the space. Whitfield's team needed a method to keep providing clean air and to remove the particles generated within the space. Whitfield and team's approach to the problem was to create a "radical design"—by comparison with a conventional cleanroom. Conventional cleanroom problems were grouped

into three general categories:[13,14]

- Conventional cleanrooms did not have a *self-cleaning* capability to offset contamination brought into the room by personnel and equipment or not captured by the air filtration system.
- Airflow patterns in conventional cleanrooms are generally not uniform, nor are they directed in a manner that carries particulate matter away from critical work areas. In addition, they will not remove airborne contamination from the room as quickly as it is brought in.
- Since all personnel in a conventional cleanroom contribute heavily to room contamination, rigid personnel controls were required.

Whitfield's team focused on the need for self-cleaning, examining the airflow volume and air patterns within the space. It appeared that greater airflow would be a partial solution. However, it was known that when airflow was increased in a previous cleanroom design, the contamination level rose. This is partly due to agitation of settled particles, and partly to the fact that particles blown off personnel and equipment was dispersed into the air. The use of air blasts was also evaluated, but the same problem of just moving the particles around the room persisted. Therefore, they wanted to avoid an air blast from supply diffusers.[15] Trying to avoid the air blast problem, the team initially considered a design using single-pass unidirectional airflow using the ceiling as a large diffuser. This solution would slow the air down and mitigate the perceived air blast and particle dispersion, avoid the perception of draft by the workers and provide a quieter environment. This solved the supply side—but how to remove the air from the space?

Figure 2 Willis Whitfield's "laminar flow" cleanroom design.[13]



At first Whitfield's team was going to use a large number of return grilles located near the floor at the walls. The problem with this was larger particles would still settle to the floor. The concept of using a perforated floor was proposed and a pilot test conducted. Having the air leave at the floor would allow for air movement to assist in the natural settling of particles by gravity. A prefilter was installed just below the floor to capture the particles and avoid their being reintroduced into the space (*Figure 2*). Early concerns that the constantly moving air would irritate workers in the space were allayed by the actual rate of movement. The air moved at about 1 mph (1.6 km/h), resulting in about 10 changes of air per minute.

By the end of 1961 the team had constructed a "laminar flow" cleanroom. The room was relatively small, only 6 ft × 10 ft (1.8 m × 3.0 m) with a 7 ft (2.1 m) high ceiling (*Figure 3*). After testing the first version, a "portable" version was also built (*Figure 4*), and later a knock-down version was built, allowing for disassembly of the room where all components could fit through a 3 ft (0.9 m) wide door.

This cleanroom was 1,000 times cleaner than the contemporary cleanrooms of the time and 100 times cleaner than clean work hoods. Circulating large amounts of air provided a "sweeping" function over the working area. Whitfield said "the room almost 'cleans' itself."[16] Whitfield gave his initial paper on what was then called the "ultra-clean room" at the Institute of Environmental Sciences meeting in Chicago in 1962.[13,17] (*Figure 5*).

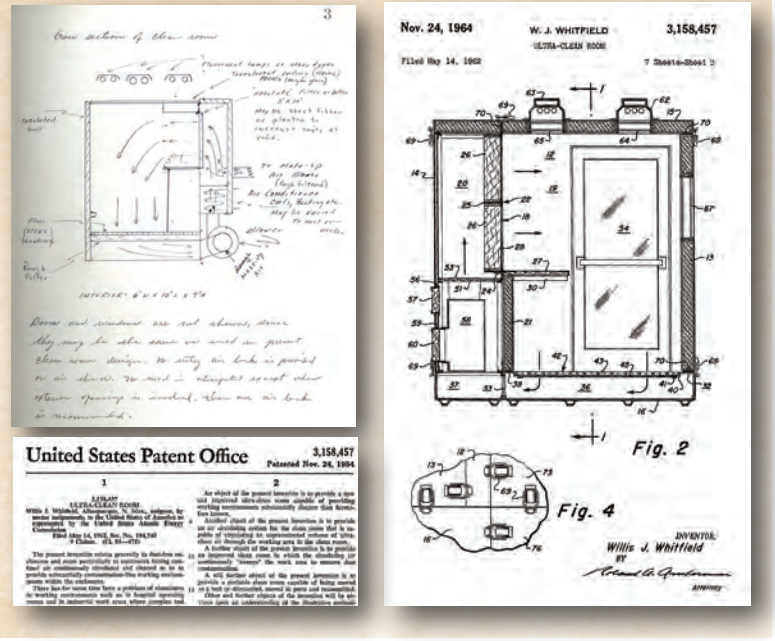
Figure 3 Willis Whitfield in prototype "laminar flow" cleanroom.[13]

Figure 4 Willis Whitfield's "knock-down" portable cleanroom.[13]

The success of the laminar flow cleanroom and clean bench quickly spread to other agencies and contractors supporting military products and space products. Even the popular press jumped into anointing Whitfield "Mr. Clean."[18] Sandia was inundated with requests to see the ultra-clean room.[19] The ability of laminar flow to reduce

microbiological contamination was also investigated, with Dr. Randy Lovelace, M.D., seeking to use a cleanroom during operating procedures, and NASA was seeking proposals to have cleanrooms used in the space program. RCA and General Motors Co. were early adopters of the cleanroom, and the invention revolutionized the pharmaceuticals and microelectronics industries.[17] By the end of 1962 more than 20 companies had been licensed to construct and build clean benches and cleanrooms for various projects.

Figure 5 Excerpt from Willis Whitfield Lab Notebook (left) and Patent Application.[12,16]



Specifications and Standards for Cleanrooms

Even before the ink was dry on Whitfield's laminar flow cleanroom patent application (*Figure 5*), the demand on air-conditioning engineers and equipment manufacturers for supplying cleanrooms and clean systems had been increasing. Procurement managers were struggling to understand what a cleanroom was in their procurement specifications. Various agencies and companies were seeking a uniform specification, but how

TABLE 1 Cleanroom standards timeline.

1960s	1970s	1980s	1990s	2000s	2010s
U.S. Air Force TO 00-25-203	Federal Standard 209B	Federal Standard 209C	Federal Standard 209E	ISO 14644-3	ISO 14644-1 (2015)
US-MIL-STD-1246	Australian AS 1386	Federal Standard 209D	ISO 14644-1 (1999)	ISO 14644-4	ISO 14644-2 (2015)
Federal Standard 209	British BS 5295		ISO 14644-2 (1999)	ISO 14644-5	ISO 14644-10
Federal Standard 209A	Japan JIS B 9920			ISO 14644-6	ISO 14644-12
	France AFNOR 44101			ISO 14644-7	ISO 14644-13
	Germany VDI 2083:3			ISO 14644-8	ISO 14644-14
	Holland VCCN 1			ISO 14644-9	ISO 14644-15
					ISO 14644-16
					ISO 14644-17

did you define "uniform"? There was a need to have repeatability and cost control when procuring cleanrooms from various suppliers.

To help with procurement of its cleanrooms, in 1961 the U.S. Air Force issued Air Force Technical Order 00-25-203, *Standard Functional Criteria for The Design and Operation of Clean Rooms*. This is considered the first widely accepted cleanroom standard. TO 00-25-203 specified 4 cleanroom levels from 1 to 4.[5] The Air Force was in the process of updating U.S. Air Force Technical Order 00-25-203 when the announcement of Whitfield's "laminar flow" cleanroom indicated cleaner cleanrooms could be achieved using Whitfield's design. There was much excitement from government agencies and industries seeking to publish their own cleanroom standards.[20] By 1963, the lack of a set of cleanroom standards was evident, and in April 1963 a major cleanroom conference was announced, to be hosted by Sandia Laboratories in Albuquerque, New Mexico.

A working group chaired by Mr. J. Gordon King was formed, and together they created the first federal standard, titled *Cleanroom and Work Station Requirements, Controlled Environments*. It was issued by the U.S. General Services Administration (GSA) and assigned the code FED-STD-209.[19] During 1964, use of "laminar flow" devices spread quickly with variants in both vertical and horizontal cross flow cleanrooms. The design was quickly being applied into industry, medicine, NASA centers, the military, and some use was noted in Europe. The AEC was the owner of the Whitfield's "Ultra-Clean Room" and freely allowed others to use the design. The Western Electric Co. in Allentown, Pa., reported that it had installed 900 "laminar flow clean benches" by the end of 1964, and RCA completed a 20,000 ft^2 (1859 m^2) facility for color CRT picture tubes.[21,22]

The increased reliance upon cleanroom standards for various applications warranted continued amending and updating of cleanroom standards. Many countries completely adopted FED-STD-209, while others made their own national version, similar to FED-STD-209. Some made minor changes to the classes to comply with the metric system. Federal Standard 209, being used around the world, was amended multiple times (*Table 1*). The 209, 209A, 209B (1973 and 1976 amended version) identified only 4 cleanliness classes similar to TO 00-25-203. Particle sizes specified down to 0.5 µm were included in the 209A,B documents. A major revision was undertaken with 209C (1987), with the addition of two more cleanliness classes, Class 1 and Class 10. 209C allowed interpretations of intermediate class (e.g., Class 50), but not the extrapolation of particle concentrations outside a set range for each cleanliness classification. The inclusion of particle sizes down to 0.1 µm was also added along with more defined testing, sampling requirements and statistical analysis. The term "laminar flow" was officially replaced with unidirectional airflow and non-laminar flow replaced by nonunidirectional.

A minor revision of FED-STD-209C was issued in version 209D (1988), while the next major revision was the last and final version 209E (1992). FED-STD-209E introduced a metric equivalent for cleanroom classes, changes in sampling for determination of class, the addition of new cleanroom classifications (M Classes) and conversion to SI units of measure.

While the final versions of FED-STD-209E were being published, a group of international contamination control stakeholders had already begun work on an international standard to replace all national standards. In 1992

the International Standards Organization (ISO) established Technical Committee ISO/TC 209 with a goal of producing a harmonization of international standards. ISO 14644 Parts 1 and 2 were issued in 1999, and several other sections have been issued since. 14644 introduced two cleaner classes and one less clean class (*Table 2*). ISO/TC 209 continues to meet and guide updates and issuing of 14644 documents (*Table 3*).

TABLE 2 Cleanroom classifications.

ISO STANDARD	U.S.A. 209A,B	U.S.A. 209C	U.S.A. 209D	U.S.A. 209E	BRITAIN BS 5295	AUSTRALIA AS 1386	FRANCE AFNOR X44101	GERMANY VDI.2083	JAPAN JACA	EU GGMP	ISO STANDARD
ISO Class 1											ISO Class 1
ISO Class 2							–	0			ISO Class 2
ISO Class 3		1	1	M1.5	C	0.035	–	1	3	–	ISO Class 3
ISO Class 4		10	10	M2.5	D	0.35	–	2	4	–	ISO Class 4
ISO Class 5	100	100	100	M3.5	E or F	3.5	4,000	3	5	A/B	ISO Class 5
ISO Class 6		1,000	1,000	M4.5	G or H	35	–	4	6	–	ISO Class 6
ISO Class 7	10,000	10,000	10,000	M5.5	J	350	400,000	5	7	C	ISO Class 7
ISO Class 8	100,000	100,000	100,000	M6.5	K	3,500	4,000,000	6		D	ISO Class 8
ISO Class 9											ISO Class 9

TABLE 3 ISO 14644 cleanroom standards.

PART 1	Classification of air cleanliness by particle concentration
PART 2	Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration
PART 3	Test methods
PART 4	Design, construction and start-up
PART 5	Operations
PART 7	Separative devices (clean air hoods, gloveboxes, isolators and minienvironments)
PART 8	Classification of air cleanliness by chemical concentration (ACC)
PART 9	Classification of surface cleanliness by particle concentration
PART 10	Classification of surface cleanliness by chemical concentration
PART 12	Classification of air cleanliness by nanoscale particle concentration
PART 13	Cleaning of surfaces to achieve defined levels of cleanliness in terms of particle and chemical classifications
PART 14	Assessment of suitability for use of equipment by airborne particle concentration
PART 15	Assessment of suitability for use of equipment and materials by airborne chemical concentration
PART 16	Energy Efficiency in Cleanrooms and Clean Air Devices
PART 17	Particle deposition rate applications

Applications and Cleanroom Technology

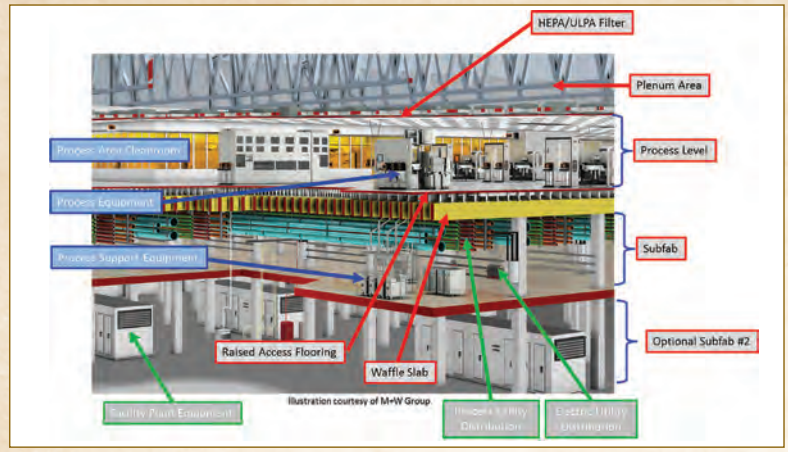
Cleanroom applications spread quickly to other industries in the 1960s and 1970s, including NASA's space program, transistor and integrated circuit manufacturing, pharmaceutical manufacturing and hospitals. Dr. Randy Lovelace and The Bataan Hospital in Albuquerque put the first "laminar flow" surgical suite into operation during 1966. Dr. E. O. Goodrich, M.D. (St. Vincent's Hospital in Santa Fe, N.M.) began studies in using a "laminar flow" operating table module, also in 1966. 1967 saw M.D. Anderson's chemotherapy treatment center begin experimenting with cleanrooms. Over 300 "laminar flow" systems were being used in hospitals by 1972. Burn centers, joint replacement surgery and other operations needing strict aseptic control were all starting to deploy laminar flow technology. A study of airflow patterns and levels of airborne contamination at various critical sites in a simulated operating room equipped with a horizontal unidirectional airflow system was published in 1969.[23] Medical device manufacturers and even food packaging facilities were also adapting cleanroom to their needs.[21]

Whitfield's development coincided with the introduction of integrated circuits into electronics design and manufacturing. Based on breakthroughs by Jack Kilby at Texas Instruments (1958), Robert Noyce and Jean Hoerni at Fairchild Semiconductor, and Kurt Lehovec of Sprague Electric Company, the first functional semiconductor integrated circuit was introduced in 1960. Initially, feature sizes of these integrated devices were 200 µm, but by 1971 they were 10 µm and less than 1 µm by the early '80s. The rapid development of new and more complex integrated circuits required the semiconductor industry to pioneer many new advances in cleanroom designs, including the multilevel vertical unidirectional cleanroom capable of achieving Class 1 cleanroom conditions (*Table 2*).

The 1970s also saw the publication of key good manufacturing practices (GMP) documents. GMPs for drugs

(21 CFR Parts 210 and 211) and medical devices (21 CFR 820) were made final in 1978. They were intended to help ensure the safety and efficacy of all products and referenced cleanrooms and cleanroom standard FED-STD-209A and later amendments. GMP requirements for devices were intended to govern the methods used in and the facilities and controls used for the design, manufacture, packaging, labeling, storage, installation, and servicing of all finished medical devices intended for human use.[24,25]

Figure 6 Semiconductor Multilevel Cleanroom.[26] Courtesy M+W Group



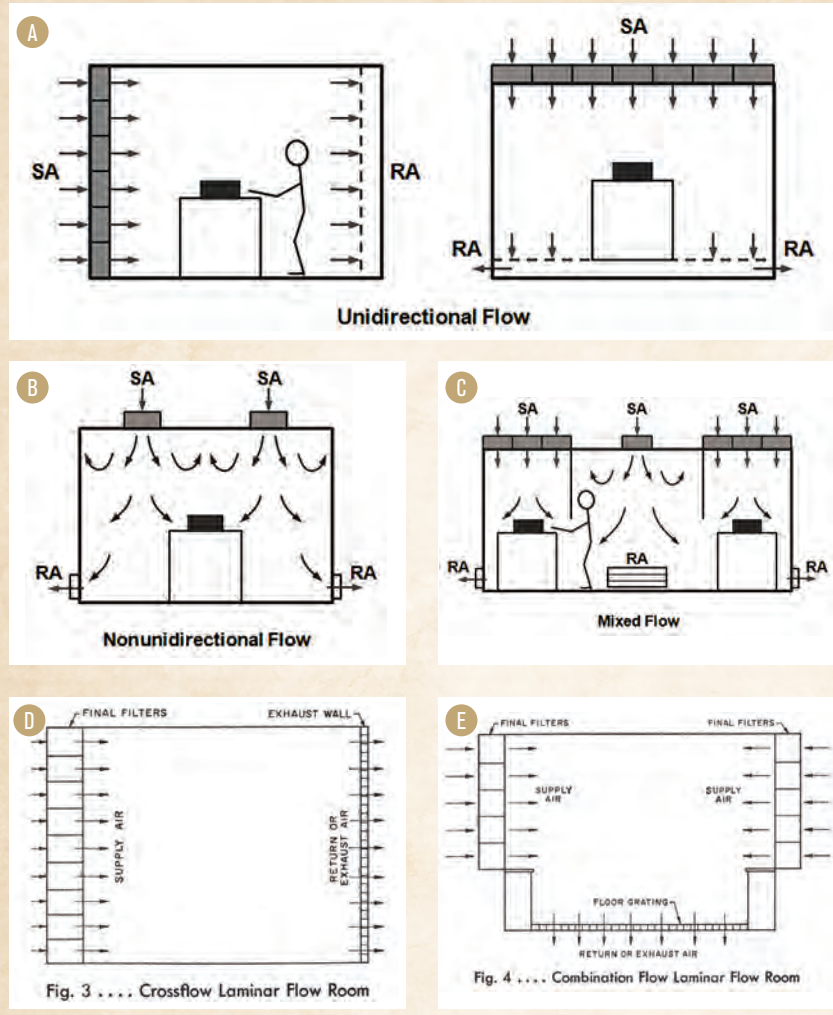
Cleanroom Technology

Cleanroom HVAC designs have seen changes since Whitfield's first "laminar flow" cleanroom, but his principal idea of self-cleaning cleanrooms has remained the same. Unidirectional cleanrooms are still based upon vertical or horizontal air movement. Industries like semiconductors and microelectronics created multi-level vertical unidirectional cleanrooms (*Figure 6*) to allow for their complex process requirements. The spread of cleanroom applications spurred the creation of industries focused on the design and manufacture of cleanrooms and cleanroom

components. Specialty firms focused on development of cleanroom walls, floors, doors and windows that met the needs of the application owner. Designs were binned into those using unidirectional airflow and those needing less clean spaces where nonunidirectional airflow would suffice. A variant of nonunidirectional airflow was also coined using the term mixed airflow (*Figure 7*).[26] As the new cleanroom industry matured, new products, including fan filter units that combined small power fans with advanced HEPA and ULPA filters integrated into a single product, were being marketed, and "turnkey" cleanroom companies were offering complete services to all of the major application users.

Some of the more innovative changes in cleanrooms were the development of isolation technology using barriers (restrictive access barrier system, RABS) and minienvironments.* Cleanroom operators understood that cleanroom space was expensive, and minimizing the spaces that need a control particle concentration could reduce the overall capital cost of their operations. Pharmaceutical facilities started to isolate spaces by sterility requirements with nonsterile and sterile designs. Barrier technology systems must be designed to fit the specific application and can be highly customized to allow the tasks required to accomplish the process needs. Applications vary widely based on product, process equipment and throughput volume. Barrier technology systems may also be designed for applications requiring operator protection from high-potency and cytotoxic compounds while maintaining a sterile internal environment. (ASHRAE, 2018)[1]

Figure 7 (a) Unidirectional Flow; (b) Nonunidirectional Flow; (c) Mixed Flow;[26] (d) Crossflow Laminar Flow; (e) Combination Flow Laminar Flow; (d–e) from *ASHRAE 1967 Handbook*



The use of minienvironments is now commonplace in semiconductors, flat panel display, disk drives and other microelectronics applications.

ASHRAE and Cleanrooms

ASHRAE first introduced the application of cleanrooms in its *1964 Guide and Data Book* (later to become the *ASHRAE Handbook*) in a chapter covering laboratories, engine test facilities, computer rooms and cleanrooms. This first instance provided some general guidance under the oversight of the Industrial Air Conditioning Technical Committee. Since the initial introduction in 1964, ASHRAE has continued to publish guidance

*This excludes isolation technology such as glove boxes or flexible film isolators (e.g. Trexler Isolators) which are not considered a cleanroom in the context of this article.

for engineers on the application of clean spaces.† The 1966 and 1971 Handbooks combined "clean spaces" with computer rooms, while 1974 saw the first solitary chapter covering "clean spaces." A terminology section was added in 1966. Clean space applications continued to warrant special attention as Task Group in TC 9.2 Industrial Air Conditioning until its elevation to a Technical Committee TC 9.11 in 1996.

ASHRAE guidebooks and handbooks have followed advances in cleanroom standards referencing FED-STD-209 in the 1966 handbook and the ISO Standards soon after their publication in the early 2000s. The *Handbook* added a section on the use of computational fluid dynamics (CFD) in 1995, providing updates on CFD application and benefits ever since. Energy savings in cleanrooms were also added in the 1990s.

Under the auspices of TC 9.11, Clean Spaces, and seeking input from experts around the world, the *ASHRAE Design Guide for Cleanrooms: Fundamentals, Systems, and Performance* was published in 2018. The design guide covers the latest information on fundamentals of contamination control, cleanroom air management, particle theory, application of CFD and select industry applications.[26]

†ASHRAE Guide Books and Handbooks combined clean spaces and computer rooms until 1974 when Clean Spaces became a standalone chapter in the *ASHRAE Handbook—HVAC Applications*.

Conclusion

The application of cleanrooms has become a common method of controlling contamination and improving the environment for people, equipment and materials. ASHRAE has been providing air-conditioning engineers guidance on cleanrooms for over 50 years and will continue into the future.

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