

 WILEY

# Cleanroom Technology

Fundamentals of Design, Testing and Operation

W. WHYTE



# **Cleanroom Technology**



# Cleanroom Technology

Fundamentals of Design,  
Testing and Operation

**W. Whyte**

*University of Glasgow, UK*

JOHN WILEY & SONS, LTD

Chichester • New York • Weinheim • Brisbane • Singapore • Toronto

Copyright © 2001 W. Whyte  
Published by John Wiley & Sons Ltd,  
Baffins Lane, Chichester,  
West Sussex PO19 1UD, England  
National 01243 779777  
International (+44) 1243 779777

e-mail (for order and customer service enquiries):  
cs-books@wiley.co.uk

Visit our Home Page on <http://www.wiley.co.uk> or  
<http://www.wiley.com>

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning or otherwise, except under the terms of the Copyright, Designs and Patents Act 1988 or under the terms of a licence issued by the Copyright Licensing Agency, 90 Tottenham Court Road, London, UK W1P 9HE, without the permission in writing of the author.

*Other Wiley Editorial Offices*

John Wiley & Sons, Inc., 605 Third Avenue,  
New York, NY 10158-0012, USA

WILEY-VCH Verlag GmbH, Pappelallee 3,  
D-69469 Weinheim, Germany

Jacaranda Wiley Ltd, 33 Park Road, Milton,  
Queensland 4064, Australia

John Wiley & Sons (Asia) Pte Ltd, 2 Clementi Loop #02-01,  
Jin Xing Distripark, Singapore 129809

John Wiley & Sons (Canada) Ltd, 22 Worcester Road,  
Rexdale, Ontario M9W 1L1, Canada

***British Library Cataloguing in Publication Data***

A catalogue record for this book is available from the British Library

ISBN 0 471 86842 6

Produced from computer files supplied by the author  
Printed and bound in Great Britain by Biddles Ltd, Guildford and King's Lynn  
This book is printed on acid-free paper responsibly manufactured from sustainable forestry,  
in which at least two trees are planted for each one used for paper production.

# Contents

<b>Preface</b> .....	<b>xiii</b>
Acknowledgements.....	xiv
<b>1 Introduction</b> .....	<b>1</b>
1.1 What is a Cleanroom?.....	1
1.2 The Need for Cleanrooms.....	2
1.3 Types of Cleanrooms.....	5
1.5 What is Cleanroom Technology?.....	7
<b>2 The History of Cleanrooms</b> .....	<b>9</b>
2.1 The Early Years.....	9
2.2 Ventilated Operating Rooms.....	12
2.3 Early Industrial Cleanrooms.....	15
2.4 Unidirectional Flow Cleanrooms.....	17
<b>3 Cleanroom Classification Standards</b> .....	<b>21</b>
3.1 The History.....	21
3.2 The Basis of Cleanroom Standards.....	22
3.3 Federal Standard 209.....	24
3.3.1 <i>The earlier Federal Standards 209 (A to D)</i> .....	24
3.3.2 <i>Federal Standard 209 E</i> .....	24
3.4 ISO Standard 14644-1.....	26
3.5 Pharmaceutical Cleanroom Classification.....	30
3.5.1 <i>European Union Guide to Good Manufacturing Practice</i> .....	30
3.5.2 <i>Guideline on Sterile Drug Products Produced by Aseptic Processing</i> .....	33
<b>4 Information Sources</b> .....	<b>37</b>
4.1 The International Confederation of Contamination Control Societies (ICCCS).....	37
4.2 International Cleanroom Standards.....	38
4.2.1 <i>ISO standards</i> .....	38
4.2.2 <i>Federal Standard 209E</i> .....	41
4.2.3 <i>Pharmaceutical standards</i> .....	41
4.3 Cleanroom Books.....	43

4.4	Recommended Practices and Guides of the Institute of Environmental Sciences and Technology (IEST).....	43
4.4.1	<i>IEST Recommended Practices (RPs)</i> .....	44
4.4.2	<i>IEST Guides</i> .....	47
4.5	Cleanroom Journals and Magazines .....	47
4.5.1	<i>Free distribution</i> .....	47
4.5.2	<i>Journals and magazines available on subscription</i> .....	49
4.6	Sources of Pharmaceutical Cleanroom Documents.....	50
4.7	International Cleanroom Forum.....	51
<b>5</b>	<b>The Design of Turbulently Ventilated and Ancillary Cleanrooms .....</b>	<b>53</b>
5.1	Turbulently Ventilated Cleanrooms.....	53
5.1.1	<i>Air supply</i> .....	55
5.1.2	<i>High efficiency air filters</i> .....	57
5.1.3	<i>Air movement within a turbulently ventilated cleanroom</i> .....	57
5.1.4	<i>Room pressurisation and air movement control between rooms</i> .....	59
5.1.5	<i>Construction materials and finishes</i> .....	62
5.2	Ancillary Cleanrooms .....	63
5.2.1	<i>Clothing change area</i> .....	63
5.2.2	<i>Materials transfer area</i> .....	66
5.3	Containment Rooms .....	67
<b>6</b>	<b>Design of Unidirectional Cleanrooms and Clean Air Devices .....</b>	<b>71</b>
6.1	Unidirectional Cleanrooms .....	71
6.1.1	<i>Vertical flow unidirectional cleanrooms</i> .....	73
6.1.2	<i>Horizontal flow unidirectional flow rooms</i> .....	74
6.1.3	<i>Unidirectional flow rooms used in semiconductor manufacturing</i> ...	76
6.2	Clean Air Devices.....	81
6.2.1	<i>Unidirectional air devices</i> .....	81
6.2.2	<i>Isolators and minienvironments</i> .....	83
<b>7</b>	<b>Construction Materials and Surface Finishes .....</b>	<b>91</b>
7.1	General Requirements.....	91
7.2	Conventional Building Techniques .....	93
7.3	Modular Construction.....	95
7.3.1	<i>Studless wall systems</i> .....	95
7.3.2	<i>Framed wall systems</i> .....	96

7.4	Doors and Windows.....	98
7.5	Floors .....	98
7.6	Ceilings .....	99
7.7	Outgassing and Electrostatic Properties .....	100
<b>8</b>	<b>High Efficiency Air Filtration.....</b>	<b>103</b>
8.1	Air Filters Used in Cleanrooms .....	103
8.2	The Construction of High Efficiency Filters .....	104
8.3	Particle Removal Mechanisms.....	106
8.4	Testing of High Efficiency Filters .....	109
8.4.1	<i>Military Standard 282</i> .....	109
8.4.2	<i>Sodium Flame Test (Eurovent 4/4)</i> .....	110
8.4.3	<i>Institute of Environmental Sciences (IEST) Recommended Practice 'Testing ULPA Filters'</i> .....	110
8.4.4	<i>European Standard (EN 1822)</i> .....	110
8.5	Probe (Scan) Testing of High Efficiency Filters .....	111
8.6	Filter Housings for High Efficiency Filters .....	112
<b>9</b>	<b>Cleanroom Testing and Monitoring.....</b>	<b>115</b>
9.1	Principles of Cleanroom Testing .....	116
9.2	Cleanroom Tests .....	116
9.2.1	<i>Air supply and extract quantities</i> .....	117
9.2.2	<i>Air movement control between areas</i> .....	117
9.2.3	<i>Filter installation leak test</i> .....	118
9.2.4	<i>Containment leak testing</i> .....	118
9.2.5	<i>Air movement control within the room</i> .....	118
9.2.6	<i>Airborne particles and microbial concentrations</i> .....	118
9.2.7	<i>Additional tests</i> .....	118
9.3	Testing in Relation to Room Type and Occupation State .....	119
9.4	Re-testing to Demonstrate Compliance .....	120
9.5	<i>Monitoring of Cleanrooms</i> .....	121
<b>10</b>	<b>Measurement of Air Quantities and Pressure Differences .....</b>	<b>123</b>
10.1	Air Quantities.....	123
10.1.1	<i>Measuring air quantities from within a cleanroom</i> .....	124
10.1.2	<i>Anemometers</i> .....	125
10.2	Differential Pressure Tests.....	127



10.2.1	<i>Apparatus for measuring pressure differences</i> .....	128
10.2.2	<i>Methods of checking pressure differences</i> .....	129
<b>11</b>	<b>Air Movement Control Between and Within Cleanrooms</b> .....	<b>131</b>
11.1	Cleanroom Containment Leak Testing.....	131
11.1.1	<i>Methods of checking infiltration</i> .....	132
11.2	Air Movement Control within a Cleanroom.....	133
11.2.1	<i>Air movement visualisation</i> .....	134
11.3	Recovery Test Method.....	139
<b>12</b>	<b>Filter Installation Leak Testing</b> .....	<b>141</b>
12.1	The Use of Aerosol Test Challenges.....	144
12.2	Artificial Smoke and Particle Test Challenges.....	145
12.2.1	<i>Cold-generated oils</i> .....	145
12.2.2	<i>Hot generated smokes</i> .....	146
12.2.3	<i>Polystyrene latex spheres</i> .....	147
12.3	Apparatus for Measuring Smoke Penetration.....	147
12.3.1	<i>Photometer</i> .....	147
12.3.2	<i>Single particle counters</i> .....	148
12.4	Methods of Testing Filters and Filter Housings.....	149
12.4.1	<i>Scanning methods</i> .....	149
12.4.2	<i>Testing filters in unidirectional flow rooms</i> .....	150
12.4.3	<i>Filter testing in conventionally ventilated room</i> .....	151
12.4.4	<i>Repair of leaks</i> .....	151
<b>13</b>	<b>Airborne Particle Counts</b> .....	<b>153</b>
13.1	Airborne Particle Counters.....	153
13.2	Continuous Monitoring Apparatus for Airborne Particles.....	156
13.3	Particle Counting in Different Occupancy States.....	158
13.4	Measurement of Particle Concentrations (ISO 14644-1).....	160
13.4.1	<i>Sample locations and number</i> .....	160
13.4.2	<i>Airborne sampling volume</i> .....	161
13.4.3	<i>Acceptance criteria</i> .....	162
13.5	Worked Example of ISO 14644-1 Test Method.....	162
13.5.1	<i>Number of locations</i> .....	162
13.5.2	<i>Minimum air sampling volume</i> .....	163
13.5.3	<i>Sampling results</i> .....	163

<b>14 Microbial Counts .....</b>	<b>167</b>
14.1 Microbial Sampling of the Air.....	167
14.1.1 Impaction onto agar.....	168
14.2 Microbial Deposition onto Surfaces .....	171
14.2.1 Settle plate sampling.....	171
14.2.2 Calculation of the likely airborne contamination.....	172
14.3 Microbial Surface Sampling .....	173
14.3.1 Contact surface sampling.....	173
14.3.2 Swabbing .....	174
14.4 Personnel sampling.....	175
<b>15 Operating a Cleanroom: Contamination Control .....</b>	<b>177</b>
15.1 Step 1: Identification of Sources and Routes of Contamination.....	178
15.1.1 Sources of contamination .....	178
15.1.2 Airborne and contact routes of transfer .....	179
15.1.3 Construction of a risk diagram.....	180
15.2 Step 2: Assessment of the Importance of Hazards .....	182
15.3 Step 3: Identification of Methods to Control Hazards.....	185
15.4 Step 4: Sampling Methods to Monitor Hazards and Control Methods..	186
15.5 Step 5: Establishing a Monitoring Schedule with Alert and Action Levels .....	189
15.6 Step 6: Verification and Reappraisal of the System .....	190
15.7 Step 7: Documentation.....	190
15.8 Step 8: Staff Training.....	191
<b>16 Cleanroom Disciplines .....</b>	<b>193</b>
16.1 People Allowed into Cleanrooms. ....	193
16.2 Personal Items Not Allowed into the Cleanroom. ....	196
16.3 Disciplines within the Cleanroom.....	196
16.3.1 Air transfer .....	196
16.3.2 Personnel behaviour.....	198
16.3.3 Handling materials.....	206
16.4 Maintenance and Service Personnel .....	206
<b>17 Entry and Exit of Personnel.....</b>	<b>209</b>
17.1 Prior to Arriving at the Cleanroom .....	210
17.2 Changing into Cleanroom Garments .....	210

17.2.1. <i>Approaching the pre-change zone</i> .....	211
17.2.2 <i>Pre-change zone</i> .....	213
17.2.3. <i>Changing zone</i> .....	215
17.2.4 <i>Cleanroom entrance zone</i> .....	217
17.3 Exit Changing Procedures. ....	220
<b>18 Materials, Equipment and Machinery</b> .....	<b>223</b>
18.1 Choice of Materials.....	223
18.2 Items Supplied from Outside Manufacturing Sources.....	225
18.3 Wrapping Materials .....	226
18.4 Transfer of Materials and Small Pieces of Equipment through an Airlock.....	228
18.4.1 <i>Transfer area with a bench</i> .....	229
18.4.2 <i>Transfer area without a bench</i> .....	232
18.5 Entry of Machinery .....	233
18.6 Transfer of Materials through Hatches and Sterilisers .....	235
<b>19 Cleanroom Clothing</b> .....	<b>237</b>
19.1 Sources and Routes of Inert Particle Dispersion .....	238
19.1.1 <i>Sources of particles and mechanisms of release</i> .....	239
19.1.2 <i>Routes of transfer of particles</i> .....	242
19.2 Routes and Sources of Microbial Dispersion .....	243
19.2.1 <i>Sources of micro-organisms</i> .....	241
19.2.2 <i>Routes of microbial dispersion</i> .....	244
19.3 Types of Cleanroom Clothing.....	245
19.3.1 <i>Clothing designs</i> .....	245
19.3.2 <i>Cleanroom fabrics</i> .....	246
19.3.3 <i>Garment construction</i> .....	249
19.3.4 <i>Choice of garments</i> .....	249
19.3.5 <i>Comfort</i> .....	251
19.4 Processing of Cleanroom Garments and Change Frequency.....	252
19.4.1 <i>Processing</i> .....	252
19.4.2 <i>Frequency of change</i> .....	255
19.5 The Effect of Laundering and Wear .....	256
19.6 Testing of Cleanroom Clothing .....	256
19.6.1 <i>Fabric tests</i> .....	257
19.6.2 <i>Dispersal of airborne bacteria and particles</i> .....	257

19.7	Static Dissipative Properties of Clothing.....	261
<b>20</b>	<b>Cleanroom Masks and Gloves .....</b>	<b>263</b>
20.1	Cleanroom Masks .....	263
20.1.1	<i>Dispersion from the mouth</i> .....	263
20.1.2	<i>Face masks</i> .....	266
20.1.3	<i>Powered exhaust headgear</i> .....	268
20.2	Cleanroom Gloves .....	269
20.2.1	<i>Hand contamination and gloves</i> .....	269
20.2.2	<i>Glove manufacturing process</i> .....	270
20.2.3	<i>Types of gloves</i> .....	270
20.2.4	<i>Testing of Gloves</i> .....	272
<b>21</b>	<b>Cleaning a Cleanroom .....</b>	<b>275</b>
21.1	Why a Cleanroom Must be Cleaned .....	275
21.2	Cleaning Methods and the Physics of Cleaning Surfaces.....	276
21.2.1	<i>Vacuuming</i> .....	277
21.2.2	<i>Wet wiping</i> .....	278
21.2.3	<i>Tacky rollers</i> .....	278
21.3	Implements Used to Clean Cleanrooms.....	279
21.3.1	<i>Dry and wet vacuum systems</i> .....	279
21.3.2	<i>Moping systems</i> .....	280
21.3.3	<i>Wipers</i> .....	283
21.3.4	<i>Tacky rollers</i> .....	285
21.3.5	<i>Floor scrubbing systems</i> .....	286
21.4	Liquids Used in Cleaning Cleanrooms .....	286
21.4.1	<i>Cleaning liquids</i> .....	286
21.4.2	<i>Disinfectants</i> .....	288
21.5	How Should a Cleanroom be Cleaned? .....	290
21.5.1	<i>General points</i> .....	290
21.5.2	<i>Cleaning methods with respect to area type</i> .....	291
21.5.3	<i>Cleaning methods</i> .....	293
21.6	Test Methods.....	295
	<b>Index.....</b>	<b>297</b>



# Preface

The dirt and bacterial-free conditions provided by cleanrooms are essential for much of modern manufacturing industry. Without clean conditions, products get contaminated and either malfunction or become hazardous to people. In recent years there has been a considerable increase in the number of cleanrooms. They are now used for the manufacture of items used in computers, cars, aeroplanes, spacecraft, televisions, disc players and many other electronic and mechanical devices, as well as the manufacture of medicines, medical devices and convenience foods. This rapid increase in the use of cleanrooms has created a demand for good quality information about cleanrooms that is free from the 'hype' of sales and marketing jargon. Information is also required to teach production personnel about their working environment, and how to conduct themselves within the cleanroom to minimise contamination.

Cleanroom technology can be divided into three parts: design, testing and operation. Cleanrooms have to be first designed and constructed; they then have to be tested to ensure they achieve their design specification and continue to do so; finally they have to be operated in such a way as to minimise contamination. This book covers, in a holistic way, these three main facets of cleanroom technology.

This book has been written using the principals generally accepted within cleanroom industries. However, I have found many areas where no sound advice exists and have had to develop guidance using my knowledge and experience. Because of this, I have tried wherever possible to give the scientific reasons for the contamination control measures suggested, so that the worth of my opinions may be judged. However, many of the principals are one man's opinion, and this should be borne in mind.

This book is intended for anyone involved with cleanrooms who wishes an overview of the fundamentals of cleanroom design, testing and operation. However, it is inevitable that with my teaching background I would wish to help those who instruct, or are about to instruct, the subject of 'Cleanroom Technology' either at college, or to their cleanroom personnel. I hope the information given in this book is helpful in achieving these requirements.

## Acknowledgements

During my many years of involvement with cleanrooms I have been fortunate to meet many of the people who pioneered and developed cleanroom technology. Many of them I now consider as friends. From these people I received information that assisted me during my career; it is from my career experience that this book has been written. It would be impossible to name all of these people, and they must forgive me if they see an idea that they know was theirs. I must confine myself to acknowledging the help of those people who directly contributed to this book. This contribution has been in the nature of: being a co-author of an article that I have used when writing this book; reading and commenting on a chapter; helping in producing photographs. These people are (in alphabetical order) Neil Bell, Chuck Bernt, Roger Diener, Gordon Farquharson, Gordon King, Lynn Morrison, Bob Peck, Martin Reeves, Hal Smith and Neil Stephenson. I should also like to acknowledge the support of the Scottish Society for Contamination Control.

The photographs on the cover of this book are reproduced by permission of Aberdeen City Council, Library and Information Service, Pentagon Technology, Analog Devices and Evanite Fiber Corporation. The permission to use other photographs, tables and drawings used within the book is acknowledged at the end of each chapter. Isabelle Lawson produced most of the drawings in this book, and Barbara McLeod read and commented on the script.

# 1

## Introduction

### 1.1 What is a Cleanroom?

It is clear that a cleanroom is a room that is clean. However, a cleanroom now has a special meaning and it is defined in the International Organization for Standardization (ISO) standard 14644-1 as:

*A room in which the concentration of airborne particles is controlled, and which is constructed and used in a manner to minimise the introduction, generation, and retention of particles inside the room and in which other relevant parameters, e.g. temperature, humidity, and pressure, are controlled as necessary.*

The first two thirds of the definition is, in essence, what a cleanroom is. It is a room that minimises the introduction, generation and retention of particles. This is achieved, firstly, by supplying it with exceptionally large quantities of air that has been filtered with high efficiency filters. This air is used to (1) dilute and remove the particles and bacteria dispersed from personnel and machinery within the room and, (2) pressurise the room and ensure that no dirty air flows into the cleanroom. Secondly, a cleanroom is built with materials that do not generate particles and can be easily cleaned. Finally, cleanroom personnel use clothing that envelops them and minimises their dispersion of particles and micro-organisms. These and other similar measures that minimise the introduction, generation and retention of contamination in a cleanroom are discussed in this book. Cleanrooms can also control the temperature, humidity, sound, lighting, and vibration. However, these parameters are not exclusive to cleanrooms, and are therefore not discussed in any detail in this book.





**Figure 1.1** A cleanroom with personnel wearing special cleanroom clothing.

## 1.2 The Need for Cleanrooms

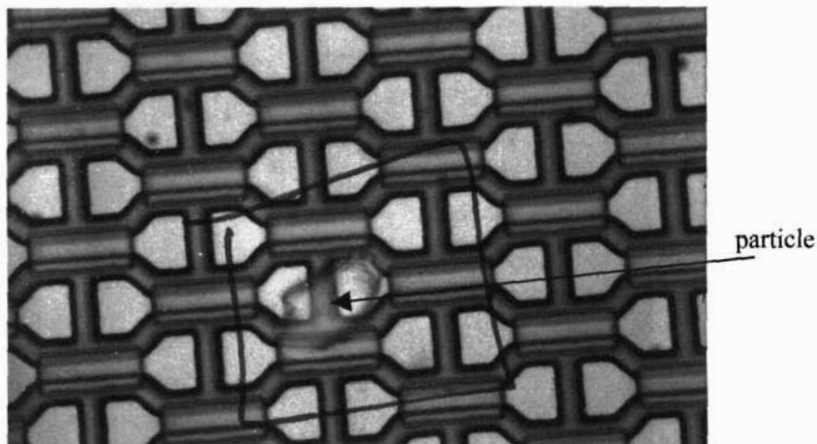
The cleanroom is a modern phenomenon. Although the roots of cleanroom design and management go back for more than 100 years and are rooted in the control of infection in hospitals, the need for a clean environment for industrial manufacturing is a requirement of modern society. Cleanrooms are needed because people, production machinery and the building structure generate contamination. As will be discussed later in this book, people and machinery produce millions of particles, and conventional building materials can easily break up. A cleanroom controls this dispersion and allows manufacturing to be carried out in a clean environment.

The uses of cleanrooms are diverse; shown in Table 1.1 is a selection of products that are now being made in cleanrooms.

**Table 1.1** Some cleanroom applications

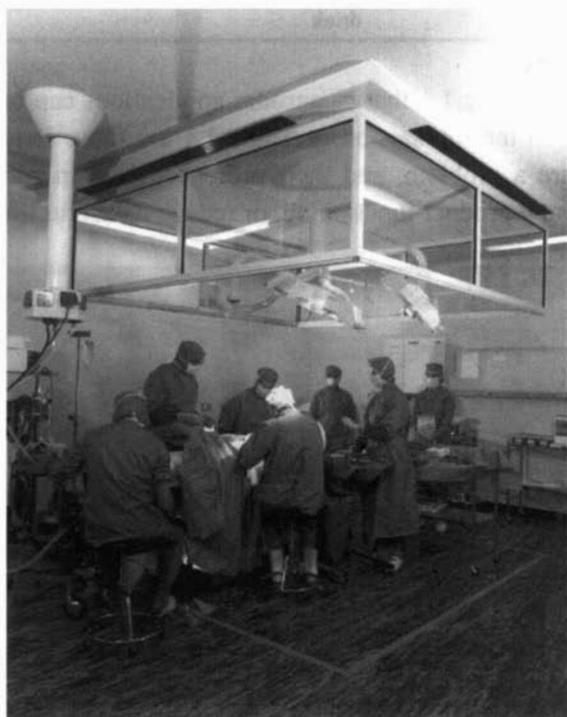
Industry	Product
Electronics	Computers, TV-tubes, flat screens
Semiconductor	Production of integrated circuits used in computer memory and control
Micromechanics	Gyroscopes, miniature bearings, compact-disc players
Optics	Lenses, photographic film, laser equipment
-----	
Biotechnology	Antibiotic production, genetic engineering
Pharmacy	Sterile pharmaceuticals, sterile disposables
Medical Devices	Heart valves, cardiac by-pass systems
Food and Drink	Brewery production, unsterilized food and drink

It may be seen in Table 1.1 that cleanroom applications can be broadly divided into two. In the top section of Table 1.1 are those industries where dust particles are a problem, and their presence, even in sub-micrometre size, may prevent a product functioning, or reduce its useful life.

**Figure 1.2** Contaminating particle on a semiconductor

A major user of cleanrooms is the semiconductor fabrication industry, where processors are produced for use in computers, cars and other machines. Figure 1.2 shows a photomicrograph of a semiconductor with a particle on it. Such particles can cause an electrical short and ruin the semiconductor. To minimise contamination problems, semiconductors are manufactured in cleanrooms with very high standards of cleanliness.

The bottom section of Table 1.1 shows manufacturers who require the absence of micro-organisms, as their growth in a product (or in a hospital patient) could lead to human infection. The healthcare industry is a major user of cleanrooms, as micro-organisms or dirt must not be injected or infused into patients through their products. Hospital operating rooms also use cleanroom technology to minimise wound infection (Figure 1.3).



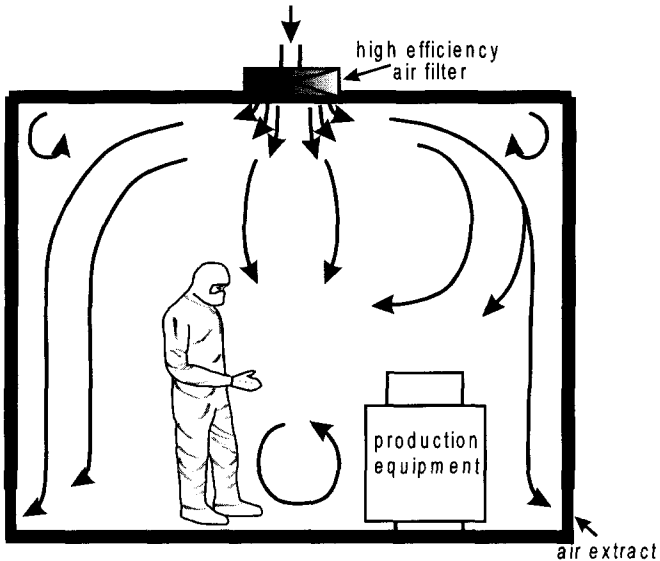
**Figure 1.3** Unidirectional flow system in an operating room

It may also be seen from Table 1.1 that many of the examples are recent innovations and this list will certainly be added to in the future, there being a considerable and expanding demand for these type of rooms.

### 1.3 Types of Cleanrooms

Cleanrooms have evolved into two major types and they are differentiated by their method of ventilation. These are *turbulently ventilated* and *unidirectional flow cleanrooms*. Turbulently ventilated cleanrooms are also known as ‘nonunidirectional’. Unidirectional flow cleanrooms were originally known as ‘laminar flow’ cleanrooms. The unidirectional type of cleanroom uses very much more air than the turbulently ventilated type, and gives superior cleanliness.

The two major types of cleanroom are shown diagrammatically in Figures 1.4 and 1.5. Figure 1.4 shows a turbulently ventilated room receiving clean filtered air through air diffusers in the ceiling. This air mixes with the room air and removes airborne contamination through air extracts at the bottom of the walls.



**Figure 1.4** Conventionally ventilated type of cleanroom