

# Contents

<b>About the Author</b>	<b>xii</b>
<b>Preface</b>	<b>xiii</b>
<b>Acknowledgements</b>	<b>xiv</b>
<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	6
1.4 What is Cleanroom Technology?	8
<b>2 The History of Cleanrooms</b>	<b>11</b>
2.1 The Earliest Years	11
2.2 Ventilated Operating Rooms	16
2.3 Early Industrial Cleanrooms	19
2.4 Unidirectional Airflow Cleanrooms	21
<b>3 Cleanroom Classification Standards</b>	<b>25</b>
3.1 The History of Standards	25
3.2 The Basis of Cleanroom Standards	26
3.3 Federal Standard 209	28
3.4 ISO Standard 14644-1:1999	29
3.5 Pharmaceutical Cleanroom Classification	33
3.6 Classification of Cleanrooms with Airborne Chemical Contamination	39
3.7 Classification of Cleanrooms with Surface Contamination	40
<b>4 Information Sources</b>	<b>41</b>
4.1 The International Confederation of Contamination Control Societies (ICCCS)	41
4.2 The ICEB	42
4.3 International Cleanroom Standards	43
4.4 Cleanroom Books	46
4.5 Recommended Practices and Guides of the Institute of Environmental Sciences and Technology (IEST)	48

---

4.6	Cleanroom Journals and Magazines	52
4.7	Sources of Pharmaceutical Cleanroom Documents	54
4.8	Training Videos/DVDs	55
<b>5</b>	<b>Non-unidirectional Airflow and Ancillary Cleanrooms</b>	<b>57</b>
5.1	Non-unidirectional Airflow Cleanrooms	57
5.2	Ancillary Cleanrooms	71
<b>6</b>	<b>Unidirectional Airflow Cleanrooms</b>	<b>75</b>
6.1	Types of Unidirectional Cleanrooms	75
6.2	Vertical Unidirectional Airflow Cleanrooms	77
6.3	Horizontal Unidirectional Airflow Rooms	78
6.4	The Application of Unidirectional Airflow	81
<b>7</b>	<b>Separative Clean Air Devices and Containment Zones</b>	<b>87</b>
7.1	Unidirectional Airflow Devices	87
7.2	Mini-environments, Isolators and RABS	89
7.3	Containment Zones	99
<b>8</b>	<b>Construction and Clean-build</b>	<b>103</b>
8.1	Constructional Materials and Methods	103
8.2	Outgassing and Electrostatic Properties	111
8.3	Clean-build	112
<b>9</b>	<b>High Efficiency Air Filtration</b>	<b>117</b>
9.1	Air Filters Used in Cleanrooms	117
9.2	The Construction of High Efficiency Filters	118
9.3	Particle Removal Mechanisms	120
9.4	Testing of High Efficiency Filters	123
9.5	Scan Testing of High Efficiency Filters	125
9.6	Filter Housings for High Efficiency Filters	126
9.7	Removal of Airborne Chemical Contamination	128
<b>10</b>	<b>Cleanroom Testing and Monitoring</b>	<b>129</b>
10.1	Principles of Cleanroom Testing	130
10.2	Cleanroom Tests	131
10.3	Testing in Relation to Room Type and Occupation State	134

---

10.4	Re-testing to Demonstrate Compliance	134
10.5	Monitoring of Cleanrooms	136
<b>11</b>	<b>Measurement of Air Quantities and Pressure Differences</b>	<b>139</b>
11.1	Air Quantities	140
11.2	Differential Pressure Tests	145
<b>12</b>	<b>Air Movement Control: Containment, Visualization and Recovery</b>	<b>151</b>
12.1	Cleanroom Containment Leak Testing	152
12.2	Air Movement Control within a Cleanroom	153
12.3	Recovery Test Methods	162
12.4	Recovery Rate Requirement in the EU GGMP	164
<b>13</b>	<b>Filter Installation Leak Testing</b>	<b>167</b>
13.1	The Use of Aerosol Test Challenges	169
13.2	Artificial Aerosol Test Challenges	170
13.3	Apparatus for Measuring Aerosol Penetration	173
13.4	Methods of Testing Filters and Filter Housings	175
13.5	Repair of Leaks	177
<b>14</b>	<b>Airborne Particle Counts</b>	<b>179</b>
14.1	Airborne Particle Counters	179
14.2	Continuous Monitoring Apparatus for Airborne Particles	181
14.3	Particle Counting in Different Occupancy States	184
14.4	Measurement of Particle Concentrations	185
14.5	Worked Example of ISO 14644-1 Test Method	188
<b>15</b>	<b>Microbial Sampling</b>	<b>193</b>
15.1	Microbial Sampling of the Air	193
15.2	Microbial Deposition onto Surfaces	197
15.3	Microbial Surface Sampling	199
15.4	Personnel Sampling	202
<b>16</b>	<b>Operating a Cleanroom: Managing the Risk from Contamination</b>	<b>203</b>
16.1	Step 1: Identification of Sources and Routes of Contamination	204

---

16.2	Step 2: Risk Assessment and the Control of Sources of Contamination	208
16.3	Step 3: Establish an Effective Monitoring Programme	225
16.4	Step 4: Verification and Reappraisal of the System	230
16.5	Step 5: Documentation	231
16.6	Step 6: Staff Training	231
<b>17</b>	<b>Cleanroom Disciplines</b>	<b>233</b>
17.1	People Allowed into Cleanrooms	233
17.2	Personal Items Not Allowed into the Cleanroom	236
17.3	Disciplines within the Cleanroom	237
17.4	Maintenance and Service Personnel	248
<b>18</b>	<b>Entry and Exit of Personnel</b>	<b>251</b>
18.1	Prior to Arriving at the Cleanroom	252
18.2	Changing into Cleanroom Garments	253
18.3	Exit Changing Procedures.	262
<b>19</b>	<b>Materials, Equipment and Machinery</b>	<b>265</b>
19.1	Choice of Materials for use in a Cleanroom	266
19.2	Items Supplied from Outside Manufacturing Sources	270
19.3	Wrapping and Transportation of Materials	271
19.4	Transfer of Items and Small Pieces of Equipment through a Materials Transfer Airlock	273
19.5	Entry of Heavy Machinery and Bulky Items	279
19.6	Transfer of Materials through Hatches and Sterilisers	283
<b>20</b>	<b>Cleanroom Clothing</b>	<b>287</b>
20.1	Sources and Routes of Inert Airborne Particle Dispersion	288
20.2	Sources and Routes of Airborne Microbial Dispersion	293
20.3	Types of Cleanroom Clothing	295
20.4	Processing of Cleanroom Garments and Change Frequency	302
20.5	The Effect of Laundering and Wear	306
20.6	Testing of Cleanroom Clothing	306
20.7	Static Dissipative Properties of Clothing	310

---

<b>21 Cleanroom Masks and Gloves</b>	<b>315</b>
21.1 Cleanroom Masks	315
21.2 Cleanroom Gloves	321
<b>22 Cleaning a Cleanroom</b>	<b>327</b>
22.1 Why a Cleanroom must be Cleaned	327
22.2 Cleaning Methods and the Physics of Cleaning Surfaces	328
22.3 Implements Used to Clean Cleanrooms	331
22.4 Liquids Used in Cleaning Cleanrooms	339
22.5 How Should a Cleanroom be Cleaned?	343
22.6 Cleaning Programme	350
22.7 Test Methods	354
<b>Index</b>	<b>357</b>