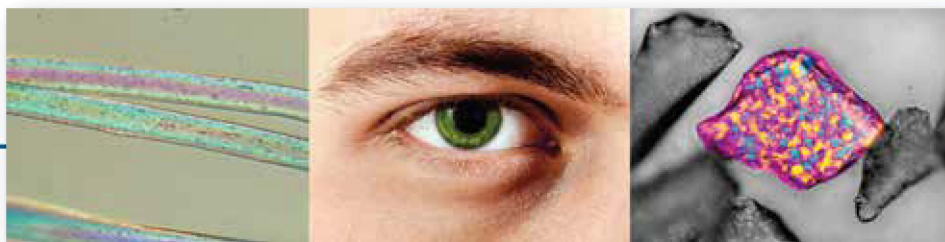


# VISUAL INSPECTION AND PARTICULATE CONTROL



D. Scott Aldrich, Roy T. Cherris  
and John G. Shabushnig

[www.pda.org/bookstore](http://www.pda.org/bookstore)

---

---

# CONTENTS

<b>Prologue</b>	<b>vii</b>
<b>About the Authors</b>	<b>xi</b>
<b>Introduction</b>	<b>xv</b>
<b>Goals</b>	<b>xvii</b>
<b>I BACKGROUND</b>	<b>I</b>
Introduction and Definitions	1
Patient Safety	5
Compendial Considerations	7
Regulatory Considerations	16
Particle Detection	25
Current GxP (Industry Standard Practice)	27
Conclusion	32
References	32

<b>2</b>	<b>DETECTION</b>	<b>41</b>
	Introduction	41
	The Dark Ages of Visual Inspection	44
	The Renaissance of the Contemporary Visual Inspection Process	47
	Test Sets	72
	Manual Visual Inspection	79
	Semi-Automated Visual Inspection	88
	Automated Visual Inspection	93
	Inspection for Batch Release	105
	Conclusion	113
	References	113
<b>3</b>	<b>ISOLATION, CHARACTERIZATION AND IDENTIFICATION</b>	<b>121</b>
	Isolation Methods	121
	Level 1 Verification and Isolation	122
	Level 2 Characterization by Forensic Microscopy	135
	Microscopy Fundamentals	141
	Other Microscopical Methods	154
	Identification	158
	Level 3 Further Identification Methods	178
	Common Particles	184
	Fibers	195
	Conclusion	204
	References	204
<b>4</b>	<b>REMEDIATION AND PREVENTION</b>	<b>211</b>
	Introduction	211
	Microbial Environmental Monitoring as a Model	212
	Particulate and Defect Tracking	216
	Reject Classification Programs	217
	DMAIC and CAPA Initiatives	227
	Conclusion	227
	References	228
<b>5</b>	<b>LIFE-CYCLE APPROACH</b>	<b>231</b>
	Introduction	231
	Holistic Model for Defect Prevention and Control	232
	Information Silos	237
	Development of Products	238

Component Supplier Auditing and Quality Agreements	253
Incoming Component or Material Acceptance	261
Component and Equipment Processing	264
Glass Breakage and Line Clearance	278
Filling Operations	278
API Bulk Characterization and Particulate Control	280
API Large Molecule Liquids	283
Inspection Life-Cycle for a Diverse Array of Parenteral Dosage Forms	285
Stability Sample Inspection Concepts	298
Retention Sample Inspection Concepts	299
Customer Complaints	301
CMO Considerations and Competitive Advantage to all Parenteral Producers	302
Medical Device Industry	304
Conclusion	307
References	307
<b>6 CASE HISTORIES — EXAMPLES OF PRODUCT FAILURE</b>	<b>319</b>
Introduction	319
Silicone — The Special Case of N-alkyl-silicones or Polydimethylsiloxanes	321
Extrinsic Particles	323
Intrinsic Additive Particles	324
Stability — Change Over Time	335
Vendor	341
Stability — Container/Closure Compatibility	342
Product Robustness	343
Difficult-to-Inspect Parenterals	347
Conclusion	360
References	360
<b>7 EPILOGUE</b>	<b>353</b>
Top 10 Lessons Learned	353
Where do we go from here?	354
<b>APPENDIX A</b>	
<b>STEREOMICROSCOPICAL ISOLATION STATION     ELEMENTS — WHAT’S NEEDED?</b>	<b>357</b>

<b>APPENDIX B</b>	
<b>LEVEL 1-2-3 FLOW CHART</b>	<b>359</b>
<b>APPENDIX C</b>	
<b>PARTICLE DESCRIPTORS</b>	<b>361</b>
<b>APPENDIX D</b>	
<b>MICROCHEMICAL TESTS</b>	<b>363</b>
<b>APPENDIX E</b>	
<b>AN EXAMPLE OF AN INTERNAL     MICROSCOPY-BASED DATABASE</b>	<b>369</b>
<b>APPENDIX F</b>	
<b>METHOD FOR DESTRUCTIVE TESTING     OF DIFFICULT-TO-INSPECT PRODUCTS</b>	<b>373</b>