

Table of Contents

1	Principles of Pharma 4.0 and Focus of the Baseline Guide.....	9
1.1	Introduction	9
1.2	Purpose and Scope of this Baseline Guide	10
1.3	Triggers for Pharma 4.0	11
1.4	The Pharmaceutical Industry Benefits of Pharma 4.0.....	13
1.5	How to Use this Guide	15
2	Digital Transformation - Pathways to Success	17
2.1	General	17
2.2	Governance	17
2.3	Define the Vision, Goals, and Priorities	18
2.4	Positioning Your Organization/Stepwise Implementation.....	21
2.5	Different Approaches to Execute the Transformation	22
3	Holistic Control Strategy.....	25
3.1	Rationale for Implementation	25
3.2	The ICH-Based Control Strategy	26
3.3	The Pharma 4.0-Based Holistic Control Strategy Definition	26
4	Quality Management in the Digital Age	33
4.1	Need and Opportunity.....	33
4.2	Digitalization and General Principles of Quality Management.....	33
4.3	Validation 4.0	37
4.4	Real Time Release Testing	39
4.5	Quality and Performance	40
4.6	New Ways of Working in Digital Quality Management – Quality 4.0.....	42
4.7	Quality Culture in a Digitalized Environment.....	48
5	The Human Element: People, Organization, and Culture	49
5.1	Introduction	49
5.2	Leadership in the Pharma 4.0 Environment.....	49
5.3	Organizational/Operating Model Considerations	49
5.4	Roles, Skills, and Capabilities for Pharma 4.0.....	50
5.5	OCM and Cultural Considerations	51
6	Navigating Regulations in a Digital World.....	53
6.1	Selected GMP Requirements for Electronic Data and Records	54
6.2	Guidelines, Guidances, and Concept Papers	57
6.3	Technical Standards.....	59
6.4	Regulatory Initiatives Related to New Technologies	59
7	Process and Data Management.....	63
7.1	Introduction	63
7.2	Data Use	63
7.3	Data and Processes.....	64

8	Plug & Produce: Principles and Challenges.....	73
8.1	Introduction	73
8.2	Plug & Produce Objectives and Benefits	73
8.3	Plug & Produce Framework	76
8.4	Plug & Produce Best Practices and Recommendations	87
8.5	OT Cybersecurity Considerations for Pharma 4.0	91
8.6	Transformation from the Status Quo to the Desired Pharma 4.0 State	97
9	Engineering Design and Construction	99
9.1	General Introduction	99
9.2	Key Principles for Design and Construction for Pharma 4.0 Facilities	99
9.3	Information Technology/Operational Technology (IT/OT)	99
9.4	Infrastructure Considerations for A Facility's Design to Enable Pharma 4.0	100
9.5	Greenfield Versus Brownfield.....	100
9.6	Engineering Implementation Roadmap.....	103
9.7	Applications for Pharma 4.0 In Facilities.....	104
9.8	Digitalization for Critical Environments – Connecting the Building Envelope with IoT Solutions	106
9.9	Digitalization in Building Design and Construction.....	106
10	Technologies Enabling Digital Transformation.....	109
10.1	Benefits of Enabling Technologies	110
10.2	Level of Adoption of Enabling Technologies	111
10.3	Key Characteristics of a Digital Solution Composed by One or More Enabling Technologies.....	112
10.4	Opportunities and Challenges for Enabling Technologies in the Case Studies	114
11	Appendix 1 – Case Studies.....	139
11.1	Case Study Number 12: Selecting Vial Container Components Intelligently with a Modeling Platform.....	141
11.2	Case Study Number 22: Using MI and Trending to Detect Data Integrity Issues	143
11.3	Case Study Number 34: Predictive Production Yield, AI-Based	144
11.4	Case Study Number 109: Wearables-Enabled Operations for Maintenance Operators.....	147
11.5	Case Study Number 231a: AI-Assisted Rescheduling of Filling Line.....	149
11.6	Case Study Number 231b: AI-Assisted Predictive Calibration of Cleanroom Monitoring Sensors.....	151
11.7	Case Study Number 236: Pharmacovigilance Improvement with Robotic Process Automation.....	154
11.8	Case Study Number 237: Electronic Product Information to Eliminate the Folder Package, Blockchain-Based	155
11.9	Case Study Number 238: Optimization of a Biotech Chromatography Process – AI/ML-based.....	158
11.10	Case Study Number 243: Cleanroom Operator Training Based on Virtual Reality.....	159
11.11	Case Study Number 242: Maintenance Reporting through Speech Recognition	161
11.12	Case Study Number 246: Autonomous Mobile Robot in Grade A Lyophilization	162
11.13	Case Study Number 247: Safe, Secure and Timely Individualized Cell and Gene Therapies (ICGT).....	164
11.14	Case Study Number 248: 3D Digital Product Development and Manufacturing.....	167
11.15	Case Study Number 249: Manufacturing Deviations Analysis with NLP	170
11.16	Case Study Number 250: Operational Excellence – A Data-Driven Approach Based on Process Mining Techniques	172
11.17	Case Study Number 251: Implementation of First-Principle Driven, Analytical Design Space Modeling for Faster Time-To-Market.....	175
11.18	Case Study Number 252: Standard eData Exchange Platform	178
11.19	Case Study Number 253: Revolutionizing Visual Inspection through AI.....	181
11.20	Case Study Number 254: Integrated, Digital Engineering with Digital Twin	183
11.21	Case Study Number 257: Flexible Line and Lean Logistics for Packaging	186
11.22	Case Study Number 308: Modular Automation for R&D Laboratories.....	189
11.23	Case Study Number 306: Enhanced Batch Release with Big Data and IIoT.....	192
11.24	Case Study Number 305: eClinical.....	195

11.25	Case Study Number 310: Digitizing a Manufacturing Process to Capture Key Process Knowledge – Increasing People Capability and Reducing Human Error.....	197
11.26	Case Study Number 309: Real Time Release	199
11.27	Case Study Number 302: Predictive Maintenance of Isolators Using Edge Computing.....	201
11.28	Case Study Number 332: Building a Sustainable Asset Optimization Framework	202
11.29	Case Study Number 303: Enhanced Collaboration During Design Phase of Isolators (Design Review Thanks to VR).....	204
11.30	Case Study Number 258: Optimization of a Pharmaceutical Drying Process with AI.....	206
11.31	Case Study Number 256: Automated Line Clearance with Image Recognition/ML/AR.....	208
11.32	Case Study Number 307: Digital Paperless Validation	210
11.33	Case Study Number 312: Lean, Compliant, and Digital QC Laboratory.....	212
11.34	Case Study Number 331: COINs, <u>C</u> omplaints <u>I</u> ntake <u>S</u> upport Chat Bot	215
11.35	Case Study Number 333: Reality Capture for Virtual Collaboration Using 360 Degree Cameras.....	217
12	Appendix 2 – The Pharma 4.0 Operating Model – Principles.....	221
12.1	Pharma 4.0 Operating Model Elements.....	222
12.2	Pharma 4.0 Operating Model Enablers.....	224
13	Appendix 3 – Pharma 4.0 Maturity Assessment.....	225
13.1	Pharma 4.0 Maturity Assessment Overview	225
13.2	The Benefits of the Pharma 4.0 Maturity Assessment	227
13.3	Definition Pharma 4.0 Maturity and Positioning (Pharma 4.0 Versus Digital Maturity)	227
13.4	How to Use It (and Who Should Perform It).....	228
13.5	Interpreting the Resulting Maturity and Setting Goals	228
13.6	Pharma 4.0 Maturity Self-Assessment Tool	229
14	Appendix 4 – Reporting Schemes	237
14.1	Reporting Scheme for Product and Process Performance	237
14.2	Reporting Scheme for Pharmaceutical Quality System and Site Performance	238
14.3	Reporting Scheme for Supply Chain Performance and Risk Management.....	239
14.4	Reporting Scheme for Digital Transformation Readiness (Pharma 4.0 Operating Model)	240
15	Appendix 5 – Roles and Responsibilities	241
16	Appendix 6 – References	243
17	Appendix 7 – Glossary.....	253
17.1	Acronyms and Abbreviations	253
17.2	Definitions	258