

# Table of Contents

<b>1</b>	<b>Introduction .....</b>	<b>7</b>
1.1	Overview .....	7
1.2	Objectives .....	7
1.3	Scope .....	7
1.4	Benefits .....	8
1.5	Key Concepts .....	9
1.6	Guidance Structure .....	10
<b>2</b>	<b>Drug Product .....</b>	<b>13</b>
2.1	Introduction .....	13
2.2	Development of Formulation and Process .....	14
2.3	Overall Conclusion .....	89
<b>3</b>	<b>Drug Substance .....</b>	<b>91</b>
3.1	Introduction .....	91
3.2	Development of Drug Substance Process .....	94
3.3	Conclusion .....	131
<b>4</b>	<b>Control Strategy .....</b>	<b>133</b>
4.1	Introduction .....	133
4.2	What Must Be Controlled – CQAs Impacted by the Manufacturing Process .....	134
4.3	Real-Time Release Testing Summary .....	160
4.4	Control Strategy Summary .....	161
4.5	Conclusion .....	164
<b>5</b>	<b>Implementation in Manufacturing .....</b>	<b>167</b>
5.1	Introduction .....	167
5.2	Technology Transfer .....	168
5.3	Knowledge Management (Information Transfer) .....	169
5.4	Identifying Gaps in the PQS Using Quality Risk Management .....	169
5.5	Readying Personnel for Implementation .....	170
5.6	Implementing Some Elements of the Control Strategy .....	170
5.7	Process Validation/Qualification and Continuous Process Verification .....	177
5.8	Batch Release .....	180
5.9	Conclusion .....	181
<b>6</b>	<b>Continual Improvement .....</b>	<b>183</b>
6.1	Introduction .....	183
6.2	Product Lifecycle and Opportunities for Continual Improvement .....	185
6.3	Continual Improvement Methodology Examples .....	186
6.4	Conclusion .....	196
<b>7</b>	<b>Conclusion .....</b>	<b>197</b>

<b>8</b>	<b>Appendix 1</b> .....	<b>199</b>
8.1	Risk Identification.....	200
8.2	Risk Analysis.....	200
8.3	Risk Evaluation .....	202
<b>9</b>	<b>Appendix 2 – Risk Assessment after Formulation Development and IVVC Studies Using FMEA</b> .....	<b>205</b>
<b>10</b>	<b>Appendix 3 – Risk Assessment of PaQLInol Tablet Process Using Failure Mode, Effects, and Criticality Analysis (FMECA)</b> .....	<b>209</b>
<b>11</b>	<b>Appendix 4</b> .....	<b>215</b>
<b>12</b>	<b>Appendix 5 – References</b> .....	<b>219</b>
12.1	References.....	220
12.2	Further Reading.....	222
<b>13</b>	<b>Appendix 6 – Glossary</b> .....	<b>223</b>
13.1	Acronyms.....	224
13.2	Definitions .....	225