

Contents

<i>Preface</i>	(v)
1. Analytical Procedure Development	1
1.1. Introduction	1
1.2. Classical Methods of Analysis	2
1.3. Instrumental Methods of Analysis	3
1.4. Analytical Procedure Development	3
1.5. Approaches to Analytical Procedure Development	4
1.6. Minimal Approach	5
1.7. Enhanced Approach	6
2. Analytical Quality by Design (AQbD)	10
2.1. Introduction	10
2.2. Key Components of Quality by Design	11
2.3. Analytical Quality by Design (AQbD).....	11
2.4. Terminology of AQbD	13
2.5. AQbD Strategic Principles	14
2.6. Workflow of Analytical Quality by Design (AQbD).....	16
2.7. Regulatory Perspective on AQbD	17
3. Design of Experiments (DoE).....	22
3.1. Introduction	22
3.2. DoE Vital Principles	23
3.3. DoE Basic Terminology.....	24
3.4. DoE Basic Techniques	25
3.5. Screening Designs.....	25
3.6. Optimization Designs.....	28
3.7. Other Optimization Designs.....	32
3.8. Software Employed in Experimental Design	33
3.9. Selection of DOE Tools	35
3.10. Basic Approach to a Design of Experiments	36

viii | Contents

4. Implementation of QbD in Analytical Procedure Development	45
4.1. Introduction.....	45
4.2. Steps involved in AQbD lifecycle.....	47
4.3. Creation of Knowledge space	47
4.4. Establishment of Analytical Target Profile (ATP).....	48
4.5. Analytical Method Performance Characteristics (AMPCs)	50
4.6. Selection of Analytical Techniques	51
4.7. Identification of CAAs and CMPs	51
4.8. Risk Assessment	53
4.9. Design of Experiments (DoE)	59
4.10. Defining Design Space/MODR and Surface Plots.....	60
4.11. Control strategy.....	64
4.12. Continuous Method Monitoring/Lifecycle Management.....	65
5. AQbD for UV-Visible spectrophotometric method development.....	67
5.1. Introduction.....	67
5.2. Selecting the Optimum Parameters for UV-Vis Measurements.....	69
5.3. Classical approach for UV-Visible spectrophotometric method development	71
5.4. AQbD Elements for UV-Visible Spectrophotometric Method Development.....	73
5.5. Practical examples.....	76
Estimation of Trospium Chloride in Capsule Dosage Form	76
Determination of Chlorpheniramine maleate in bulk & Tablet Dosage Form	81
Estimation of Ambrisentan in Bulk and Pharmaceutical Dosage Forms	86
Estimation of Cefixime Trihydrate using Ninhydrin Reagent	90
6. AQbD for HPLC Method Development	98
6.1. Introduction.....	98
6.2. Principle of HPLC.....	98
6.3. Classical Approach for HPLC Method Development.....	100

6.4. AQbD Elements for HPLC Method Development	101
6.5. Practical Examples	105
Determination of Raloxifene HCl in Pure and Tablets	105
Estimation of Valsartan in Rat Plasma.....	112
Estimation of Gliclazide and its Impurity (gliclazide impurity A).....	120
Simultaneous estimation of Saxagliptin and Dapagliflozin	125
7. AQbD for GC Method Development.....	130
7.1. Introduction.....	130
7.2. Principle of GC	131
7.3. Classical Approach for GC Method Development	131
7.4. AQbD Elements for GC Method Development	133
7.5. Practical Examples	137
Identification & Estimation of Essential Oils in Herbal Formulation.....	137
Quantitation of Alkyl Camphor Sulfonates as Potential Genotoxic Impurities	145
Analysis of Essential Oils from Salvia Officinalis.....	153
Quantitation of 19 Alkyl Halides as Potential Genotoxic Impurities	157
8. AQbD for HPTLC Method Development.....	167
8.1. Introduction.....	167
8.2. Principle of HPTLC	167
8.3. Classical Approach for HPTLC Method Development	169
8.4. AQbD Elements for HPTLC Method Development	170
8.5. Practical Examples	174
Estimation of Mangiferin in Bio-Analytical Samples	174
Estimation of Anagliptin in Bulk and In-House Tablets.....	182
Determination of Apremilast based on Failure Mode Effect Analysis (FMCA).....	191
Simultaneous Estimation of Lornoxicam and Eperisone HCl	200

x | **Contents**

9. AQbD for Bio-analytical Method Development	207
9.1. Introduction.....	207
9.2. Bio-analytical Method.....	207
9.3. LC-MS	208
9.4. GC-MS	209
9.5. CE-MS	209
9.6. Preparation and Extraction of Sample.....	210
9.7. Classical Approach for LC-MS Method Development.....	212
9.8. AQbD Elements for Bio-analytical Method Development	215
9.9. Practical Examples	219
Quantitation of Fluoxetine in Human Plasma.....	219
Quantitation of Paracetamol and Diclofenac in Human Plasma	225
Quantitation of Enzalutamide in Plasma Sample	231
Quantitation of Sildenafil in Human Plasma.....	237
<i>References</i>	243
<i>Index</i>	247