

Barbara Römer

2001/20/EC - A European Directive?

Major Regulatory Objectives
for a Real Harmonisation in Europe

Tectum Verlag

Barbara Römer

2001/20/EC - A European Directive?

Major Regulatory Objectives for a Real Harmonisation in Europe

ISBN: 978-3-8288-2056-2

Umschlagabbildung: © dem10 | istockphoto.de

© Tectum Verlag Marburg, 2009

Besuchen Sie uns im Internet

www.tectum-verlag.de

Bibliografische Informationen der Deutschen Nationalbibliothek

Die Deutsche Nationalbibliothek verzeichnet diese Publikation in der Deutschen Nationalbibliografie; detaillierte bibliografische Angaben sind im Internet über <http://dnb.ddb.de> abrufbar.

Table of Contents

List of Tables.....	13
List of Figures	15
List of Abbreviations.....	17
1 EXECUTIVE SUMMARY	21
2 Introduction	23
2.1 History of the legal framework of clinical trials.....	23
2.2 Current legal framework of clinical trials	24
2.3 The Clinical Trials Directive.....	26
2.3.1 Scope of the Clinical Trials Directive	28
2.3.2 Phases of clinical trials	28
2.3.2.1 Clinical trials during the development stage (Phase I - III)	29
2.3.2.2 Post authorisation safety studies	29
2.3.3 Implementation of Clinical Trials Directive.....	30
3 Country-specific Implementation of Clinical Trials Directive.....	33
3.1 Austria	33
3.1.1 Legal Basis.....	33
3.1.2 Clinical trial authorisation procedure.....	33
3.1.2.1 Competent authority procedure	33
3.1.2.2 Ethics committee procedure	36
3.1.2.3 Submission package to the competent authority	38
3.1.2.4 Submission package to the ethics committee.....	38

3.2	Belgium.....	39
3.2.1	Legal Basis.....	39
3.2.2	Clinical trial authorisation procedure.....	39
3.2.2.1	Competent authority procedure	39
3.2.2.2	Ethics committee procedure	40
3.2.2.3	Submission package to the competent authority	45
3.2.2.4	Submission package to the ethics committee.....	45
3.3	Czech Republic.....	45
3.3.1	Legal Basis.....	45
3.3.2	Clinical trial authorisation procedure.....	46
3.3.2.1	Competent authority procedure	46
3.3.2.2	Ethics committee procedure	47
3.3.2.3	Submission package to the competent authority	49
3.3.2.4	Submission package to the ethics committee.....	49
3.4	Germany.....	50
3.4.1	Legal Basis.....	50
3.4.2	Clinical trial authorisation procedure.....	50
3.4.2.1	Competent authority procedure	51
3.4.2.2	Ethics committee procedure	53
3.4.2.3	Submission package to the competent authority	55
3.4.2.4	Submission package to the ethics committee.....	55
3.5	Spain	56
3.5.1	Legal Basis.....	56
3.5.2	Clinical trial authorisation procedure.....	57
3.5.2.1	Competent authority procedure	57
3.5.2.2	Ethics committee procedure	60

3.5.2.3	Submission package to the competent authority	64
3.5.2.4	Submission package to the ethics committee.....	65
3.6	Italy	66
3.6.1	Legal Basis.....	66
3.6.2	Clinical trial authorisation procedure.....	66
3.6.2.1	Competent authority procedure	66
3.6.2.2	Ethics committee procedure	67
3.6.2.2.1	Single-centre trial	68
3.6.2.2.2	Multi-centre trial	70
3.6.2.3	Submission package to the competent authority	72
3.6.2.4	Submission package to the ethics committee.....	72
3.7	The Netherlands.....	72
3.7.1	Legal Basis.....	72
3.7.2	Clinical trial authorisation procedure.....	72
3.7.2.1	Competent authority procedure	76
3.7.2.2	Ethics committee procedure	76
3.7.2.3	Submission package to the competent authority	79
3.7.2.4	Submission package to the ethics committee.....	80
3.8	Poland.....	80
3.8.1	Legal Basis.....	80
3.8.2	Clinical trial authorisation procedure.....	81
3.8.2.1	Competent authority procedure	82
3.8.2.2	Ethics committee procedure	84
3.8.2.3	Submission package to the competent authority	85
3.8.2.4	Submission package to the ethics committee.....	86

3.9	Slovenia	86
3.9.1	Legal Basis.....	86
3.9.2	Clinical trial authorisation procedure.....	87
3.9.2.1	Competent authority procedure	87
3.9.2.2	Ethics committee procedure	88
3.9.2.3	Submission package to the competent authority	90
3.9.2.4	Submission package to the ethics committee.....	90
3.10	United Kingdom	91
3.10.1	Legal Basis.....	91
3.10.2	Clinical trial authorisation procedure.....	91
3.10.2.1	Competent authority procedure	91
3.10.2.2	Ethics committee procedure	94
3.10.2.3	Submission package to the competent authority	99
3.10.2.4	Submission package to the ethics committee.....	99
4	Situation appraisal.....	101
4.1	Topics of non-harmonisation	101
4.1.1	Time-frame for evaluation.....	101
4.1.1.1	Time-frame for evaluation – solution approaches.....	103
4.1.2	Cooperation competent authority/ethics committee.....	103
4.1.2.1	Cooperation competent authority/ethics committee – solution approaches	105
4.1.3	Role and definition of competent authority.....	105
4.1.3.1	Role of competent authorities – solution approaches.....	106
4.1.4	Different ethics committee systems	107

4.1.4.1	Different ethics committee systems – solution approaches	108
4.1.5	Submission packages.....	108
4.1.5.1	Submission packages – solution approaches	110
4.1.6	Different definition of applicant.....	111
4.1.6.1	Different definition of applicant – solution approach.....	111
4.1.7	Arbitration and consensus finding.....	111
4.1.7.1	Arbitration and consensus finding – solution approach.....	112
4.2	Consequences of non-harmonised procedures	112
4.3	Reasons for non-harmonised procedures.....	113
4.3.1	Insufficient instructions provided by Clinical Trials Directive and guidelines	113
4.3.2	Available instructions give too much room for interpretation.....	113
4.3.3	Disregarding of instructions	114
4.3.4	Different clinical practice.....	114
5	Further topics of non-Harmonisation	117
5.1	Issues in conjunction with EU clinical trials legislation and its implementation	117
5.1.1	Diversity of safety-reporting requirements and of safety definitions.....	117
5.1.2	Divergences concerning definition of investigational medicinal product.....	117
5.1.3	Divergences concerning GMP requirements	118
5.1.4	Inconsistencies regarding substantial and non-substantial amendments	118
5.2	Issues beyond the Clinical Trials Directive.....	119
5.2.1	Medicines for children	119

5.2.2	Summary of product characteristics requirements.....	120
5.2.3	Post authorisation safety studies (PASSs).....	120
6	Objectives for improvement.....	125
7	Conclusion.....	137
8	References.....	139
9	Appendices.....	147
9.1	Appendix 1: Tabular overview of competent authority procedure requirements according to Directive 2001/20/EC, guideline ENTR/CT1 and Directive 2005/28/EC.....	148
9.2	Appendix 2: Tabular overview of ethics committee procedure requirements according to Directive 2001/20/EC, guideline ENTR/CT2 and Directive 2005/28/EC.....	152
9.3	Appendix 3: Tabular overview of different procedural steps of competent authority and ethics committee procedures	157
9.4	Appendix 4: Tabular overview of time-frames regarding competent authority procedures	159
9.5	Appendix 5: Tabular overview of time-frames regarding ethics committee procedures.....	163
9.6	Appendix 6: Tabular overview of core documents (to be submitted to competent authorities of almost all Member States)	166
9.7	Appendix 7: Tabular overview of country-specific competent authority documents.....	168
9.8	Appendix 8: Checklist regarding documents to be submitted to the Austrian competent authority.....	175
9.9	Appendix 9: Comparison of documents to be submitted to the ethics committee according to Clinical Trials Directive versus guideline ENTR/CT2.....	177
9.10	Appendix 10: Competent authority average approval times (Phase I)	179

9.11 Appendix 11: Competent authority average approval times (Phase II).....	180
9.12 Appendix 12: Competent authority average approval times (Phase III)	181
9.13 Appendix 13: Tabular overview of UK Oxycodone SmPC wording compared to respective SmPC wording in AT, CZ, DE, ES, NL, SI	182
10 Acknowledgement	185