Contents

Preface xiii Acknowledgements xvi

1 Origin of the ethical review of medical research 1

The Declaration of Helsinki 2
The evolution of ethics committees 4
General ethical principles 6
What is medical research? 7

2 Medical research ethics committees: protecting patients, researchers and institutions 12

Who decides what research can be done on patients? 12
Local research ethics committees and their role 12
Who should be responsible for setting up ethics committees? 14
Who should sit on an ethics committee? 15
Evaluation of a research proposal 22
Standard proposal form 23
Chairperson's action / expedited review 29
Charging for submissions to local research ethics committees 32
Potential weak points in the system of local research ethics
committees 36
Ethical review of multicentre research 41

3 Researchers and their facilities 50

The researcher 50
The facilities available 55

4 Importance of informed consent 57

Requirements for informed consent 57

Provision of information 58

Full opportunity and encouragement to ask questions 63

Consent must be freely given 64

Can active deception ever be ethical? 71

Allow adequate time to make a decision 73

A signed form as evidence of informed consent 76

Research on patients without informed consent 81

The right to withdraw consent 83

5 Evaluating risks and benefits 87

Do the potential benefits justify the risks? 87

Assessing risks 88

Minimising the risks 92

The well-being of the researcher and support staff 94

Determining benefits 96

Research on participants without direct medical benefit 98

6 Acceptable research procedures 104

Non-invasive procedures 104
Ionising radiation 105
Invasive procedures 106
What should be the time interval between studies? 112

7 Confidentiality 115

Accessing medical records and databases 116
Contacting patients 118
Computerised case registers and other databases 119
Medical audit 121
The UK data protection act 122
Disclosure of personal information derived from research 128
The use of video/audio recordings 131
Avoiding inadvertent breaches of confidentiality 131

8 Clinical trials 133

Development of a new drug or procedure 133 The International Conference on Harmonisation: Guideline for Good Clinical Practice 133 Mutual responsibilities of investigators and ethics committees 136 The process of developing a new therapeutic drug 139 Reporting of adverse events and serious adverse events 145

9 Research with healthy volunteers 149

Justification for research with volunteers 149 Recruitment of volunteers 150 Susceptible groups of healthy volunteers 151 Ensuring that healthy volunteers really are healthy 155

10 Are placebos ethical? 159

The placebo effect 159 Is a placebo control always necessary? 160 Is the use of a placebo ethical? 161 Guidelines for the use of placebos in clinical trials 167

Arrangements for compensation 169

Clinical trials sponsored by a pharmaceutical company 169 Studies not sponsored by a pharmaceutical company 172

12 Research with children, seriously ill patients, persons with learning disability and other vulnerable groups 174

Children 175 Seriously ill patients 187 Patients with learning disability, serious psychiatric problems and all forms of dementia 190

Research on surplus blood and other tissue 200 13

Must patients' permission be obtained? 200 Is the intended use of the tissue ethical? 201 The detection of unexpected illness 203 Genetic studies on archived tissues 203

x Contents

Uses less likely to raise serious ethical issues 204
Is the tissue really spare? 205
Proposed guidelines for consent for the use of spare blood and other tissue 206

14 Questionnaire and interview studies 208

Epidemiological questionnaires 208

Quality of life questionnaires 209

Audit questionnaires 210

Questionnaires that raise patients' expectations 210

Intrusive questions with significant ethical implications 211

Questionnaires for the seriously ill 212

Intrinsically distressing questionnaire studies 213

Questions suitable for some but not for others 214

Is informed consent required for questionnaire studies? 214

Avoid exhausting the participant with too many questionnaires 215

Arranging a home interview 215

Questionnaire studies on the Internet 216

If in doubt, seek the advice of the ethics committee 218

15 Epidemiological studies 219

Types of epidemiological study 219
Nutrition, an example of the ethical complexities of a typical national survey 220
When informed consent must be obtained 223
Epidemiological studies which may not require informed consent 225
Confidentiality of groups 226

16 Genetic research – special ethical considerations 228

Informed consent for genetic testing 230
Aims of genetic research 232
Identifying and approaching a patient with a known condition 233
Should relatives be sought? 235

The problem of explaining risks 238

Ensure that adequate counselling is available 240

Advantages and disadvantages of early detection 241

Confidentiality in genetic studies 244

Development of new methods of prenatal diagnosis 248

When the outcome of genetic research becomes normal clinical practice 251

Research involving genetic testing 254

17 Genetherapy 259

What is gene therapy? 259
Regulation of gene therapy 261
Gene therapy in practice 263
Germ-line gene therapy 266

18 Research on fetuses 267

Research on fetuses universally regarded as unethical 268
Separation of the source of tissue from the research 269
Potential uses to which tissue from a fetus may be put 270
Informed consent for research on aborted fetuses 271
Other considerations 275
Embryo research 276
Cloning 279

19 Animal to human transplantation 281

The practicalities 281
When will animal to human transplantation trials be justified? 285
A central advisory committee 286
Informed consent from transplant recipients 287
Follow-up of animal transplant recipients 288
Longer term implications for patients 289
Conclusion 291

20 Post-approval monitoring of research by ethics committees 292 Monitoring of research by the Tayside Committee on Medical Research Ethics 294

Appendixes 306

- 1 Declaration of Helsinki 306
- 2 A specimen local medical research ethics committee constitution 311
- 3 Specimen medical research ethics committee application form 319
- 4 Guide to constructing a patient/volunteer information sheet 339
- 5 A specimen consent form for patients 351
- 6 A specimen letter and confidential questionnaire for patients/healthy volunteers 353
- 7 A specimen review questionnaire for researchers 360

Further reading 365
Some useful websites 372
Some useful addresses 375
Bibliography 378
Index 391