

Contents

- Preface and Acknowledgement 3**
- Chapter 1. Introduction 15**
 - 1.1. Scope and purpose of this guide 15
 - 1.2. European Committee of Experts on Organ Transplantation, the European Directorate for the Quality of Medicines and Healthcare, and the Council of Europe..... 17
 - 1.3. Recommendations and regulations from other stakeholders 18
 - 1.4. Benefits of transplantation 19
 - 1.5. Risks of transplantation..... 20
 - 1.6. Risk levels and risk assessment 22
 - 1.7. Information about the donor..... 24
 - 1.8. Ethical issues 26
 - 1.8.1. Protection against abuse 27
 - 1.9. References..... 28
- Chapter 2. Assessment of donors 31**
 - 2.1. General requirements..... 31
 - 2.2. Deceased donors..... 32
 - 2.2.1. Definitions 32
 - 2.2.2. The active detection system for deceased donors 33
 - 2.2.3. Evaluation of the deceased potential donor 37
 - 2.2.4. Donor documentation 60
 - 2.2.5. Deceased organ and tissue donor maintenance..... 61
 - 2.3. Living donors 62
 - 2.3.1. Living organ donor..... 62
 - 2.3.1.1. Pre-donation counselling of the potential living donor, informed consent and legal requirements..... 63

2.3.1.2. Evaluation of the potential donor	64
2.3.1.3. Living organ donor selection and follow-up	65
2.3.1.4. Haematopoietic progenitor cell donor selection	66
2.3.1.5. Domino transplantation.....	68
2.3.2. Living tissue donors.....	69
2.3.2.1. Re-testing of living donors of stored allogeneic material	70
2.4. References.....	70
Chapter 3. Organ procurement and preservation	73
3.1. Deceased donors	73
3.1.1. Facilities, personnel and equipment for organ procurements	74
3.1.2. Multi-organ procurement procedures.....	74
3.2. Living donation.....	76
3.2.1. Kidney donation	76
3.2.2. Liver donation	77
3.2.3. Facilities and equipment for organ recovery	77
3.3. Organ preservation, packaging, transportation and traceability	77
3.3.1. Preservation.....	77
3.3.1.1. New and modified preservation techniques	78
3.3.2. Packaging and transport containers for organs.....	79
3.3.3. Organ transportation	80
3.3.4. Traceability of organs.....	81
3.3.5. Feedback	81
3.4. References.....	82
Chapter 4. Risk of transmission of infectious diseases	83
4.1. Introduction	83
4.2. Existing medical data, information about social history or risk behaviour for infection.....	87
4.3. Viral infections	88
4.3.1. Basic screening for viral infections	88

4.3.2. Specific viral infections	90
4.3.2.1. Cytomegalovirus (CMV)	90
4.3.2.2. Epstein-Barr Virus (EBV)	91
4.3.2.3. Hepatitis A Virus (HAV)	92
4.3.2.4. Hepatitis B Virus (HBV)	92
4.3.2.5. Hepatitis C Virus (HCV)	95
4.3.2.6. Hepatitis D Virus (HDV)	97
4.3.2.7. Herpes viruses (EBV and CMV excluded)	97
4.3.2.8. Human Immunodeficiency Virus (HIV)	98
4.3.2.9. Human T-Lymphotropic Virus (HTLV)	99
4.3.2.10. Other viruses	100
4.4. Bacterial infections	101
4.4.1. Acute infections	101
4.4.2. Bacteraemia and bacterial meningitis	103
4.4.3. Pulmonary infections	104
4.4.4. Urinary tract infections (UTI)	104
4.4.5. Special cases	105
4.5. Fungal infections	106
4.6. Parasites	107
4.7. Prion-related diseases	108
4.8. Pitfalls of serologic screening	109
4.8.1. Unexpected results	109
4.8.2. Haemodilution	110
4.8.3. False-negative and false-positive results	110
4.8.4. Blood samples drawn after cardiac arrest	110
4.8.5. Procurement from Newborns	111
4.9. Vigilance methods and tracing of serious adverse reactions or events	111
4.10. Preventive strategies in graft recipients	111
4.11. Tables and figures	112
4.11.1. Geographically-restricted, rare or critical infectious diseases	112
4.11.2. Synonyms and abbreviations used in viral screening, haemodilution	123

4.11.3. Screening algorithm for organ donors	125
4.12. References	129
Chapter 5. Risk of transmission of neoplastic diseases	135
5.1. Introduction.....	135
5.2. General recommendations to follow in the donation process to prevent the transmission of tumours	136
5.2.1. Clinical history of the donor and physical examination	136
5.2.2. Laboratory determinations, tumour markers	137
5.2.3. Radiological tests.....	137
5.2.4. Donor and organ examination during procurement	138
5.2.5. Histopathological examination	138
5.3. Guidelines for the prevention of transmission of neoplasias	142
5.3.1. General considerations	142
5.3.2. Solid organ tumours	146
5.3.2.1. Renal cell carcinoma	147
5.3.2.2. Prostate carcinoma	149
5.3.2.3. Breast cancer.....	152
5.3.2.4. Lung cancer	152
5.3.2.5. Colorectal carcinoma	153
5.3.2.6. Oesophageal carcinoma, gastric carcinoma, pancreatic carcinoma, hepatocellular carcinoma	153
5.3.2.7. Thyroid carcinoma.....	154
5.3.2.8. Oropharyngeal cancer.....	154
5.3.2.9. Ovarian cancer.....	155
5.3.2.10. Cancer of the uterus / uterine cervix, cancer of the urinary bladder	155
5.3.2.11. Choriocarcinoma.....	156
5.3.2.12. Sarcoma and gastrointestinal stromal tumour	157
5.3.2.13. Malignant melanoma	158
5.3.2.14. Non-melanoma skin cancer (basal cell and squamous spindle cell carcinoma).....	159
5.3.2.15. Carcinoma <i>in situ</i>	159
5.3.3. Hematopoietic malignancies (lymphoma, leukemia).....	160
5.3.4. Primary tumours of the central nervous system.....	161

5.4. Review of tumours of the central nervous system	168
5.4.1. Neuroectodermic tumours.....	168
5.4.1.1. Medulloblastoma.....	168
5.4.1.2. Gliomas	169
5.4.1.3. Ependymomas.....	174
5.4.1.4. Plexus choroid tumours.....	175
5.4.1.5. Pineocytomas and pineoblastomas.....	176
5.4.2. Other intracranial primitive tumours	176
5.5. Final considerations	180
5.6. References.....	182
Chapter 6. Risk of transmission of other diseases.....	187
6.1. Poisoning.....	187
6.1.1. Pathway	189
6.1.2. Poisoning agents.....	190
6.2. Inherited diseases.....	195
6.2.1. Background information.....	196
6.2.2. Pathway.....	197
6.2.3. Examples of inherited disorders in cases of organ donation	198
6.3. References	199
Chapter 7. Tissue and cell procurement	201
7.1. Procurement from deceased donors.....	201
7.2. Procurement from living donors	202
7.3. Unique donor identifier	202
7.4. Labelling and packaging.....	203
7.5. Procurement documentation	204
7.6. Storage and transportation to processing facility.....	205
7.6.1. Temporary storage and transportation.....	205
7.6.2. Quality control of procurement and transportation	205
7.7. Haematopoietic progenitor cells (HPC): specific issues	205

7.7.1. Types of donation.....	205
7.7.2. General considerations for HPC collection.....	205
7.7.3. Dose requirements.....	206
7.7.4. Additional testing.....	207
Chapter 8. Tissue establishments.....	209
8.1. General organisational requirements of a tissue establishment (TE).....	209
8.1.1. Institutional identity.....	209
8.1.2. Organisation.....	210
8.2. Facilities and equipment.....	213
8.2.1. Facilities and equipment in a tissue establishment.....	213
8.2.2. Environmental safety of tissue establishment.....	214
8.3. Tissue and cell processing, preservation and storage.....	215
8.3.1. General.....	215
8.3.2. Reagents and preservation solutions.....	216
8.3.3. Pooling.....	216
8.3.4. Quality control.....	216
8.3.5. Processing and processing environment.....	216
8.3.6. Novel processes.....	217
8.3.7. Preservation and storage.....	218
8.3.8. Labelling.....	218
8.3.9. Package insert.....	221
8.3.10. Packaging.....	222
8.3.11. Quarantining and quarantine areas.....	223
8.4. Release of tissues or cells.....	223
8.5. Distribution.....	224
8.6. Traceability.....	224
8.7. Transportation.....	224
8.8. Return into inventory.....	224
8.9. Exceptional release.....	225
8.10. Adverse reactions and events, and non-conformances.....	225

8.10.1. Notification	225
8.10.2. Recall	226
8.11. Hospital tissue and cell storage and distribution	226
Chapter 9. Reporting of adverse events.....	229
9.1. Informed consent	229
9.2. Definition of serious adverse reactions and events	231
9.2.1. Forecast of serious adverse reactions and events	233
9.2.2. Severity of serious adverse reactions and events	233
9.2.3. Imputability of serious adverse reactions	234
9.3. Traceability	235
9.4. Reporting adverse events and reactions.....	236
9.5. References.....	238
Chapter 10. Quality management	239
10.1. General introduction to quality management	239
10.2. Applied quality management in donation and transplantation	241
10.2.1. Organisational issues.....	241
10.2.1.1. Governmental responsibilities.....	242
10.2.1.2. Education and training	242
10.2.1.3. Implementation of standards	242
10.2.1.4. Vigilance system	243
10.2.1.5. Organ allocation	243
10.2.1.6. Time frame in organ, tissue and cell transplantation	244
10.2.1.7. International and bi-lateral co-operation	245
10.2.2. Personnel and organisation	245
10.2.3. Premises, equipment and materials	246
10.2.4. Contractual arrangements	248
10.2.5. Documentation and record-keeping	248
10.2.6. The assessment and mitigation of risks	250
10.2.7. Selection, procurement, testing and processing/handling.....	250

10.2.8. Quality control and proficiency testing	251
10.2.9. Traceability.....	252
10.2.10. Review system.....	252
10.2.11. Complaints and recall.....	253
10.2.12. Investigation and reporting of non-conformance.....	253
10.2.13. Self-assessment, internal audit and external audit	254
10.3. References.....	254
Appendices	257
Appendix 1 – Members of the European Committee (Partial Agreement) on Organ Transplantation (CD-P-TO) (31/10/2010)	259
Appendix 2 – List of relevant standards/guidelines.....	277
Appendix 3 – Donor risk factors for transmissible diseases.....	285
Appendix 4 – Glossary.....	287
Appendix 5 – Examples of questionnaires and forms for documentation of the donation processes	299
REVISED TEXTS	
Chapter 7 (revised). Tissue and cell recovery.....	317
7.1. Recovery from deceased donors	317
7.2. Recovery from living donors.....	318
7.3. Unique donor/donation identifiers	318
7.4. Labelling and packaging	319
7.5. Recovery documentation.....	322
7.6. Storage and transportation to processing facility.....	323
7.6.1. Temporary storage.....	323
7.6.2. Quality control of recovery and transportation	323
7.7. Haematopoietic progenitor cells: specific issues.....	323
7.7.1. Types of donation.....	323
7.7.2. General considerations for HPC collection.....	323

7.7.3. Dose requirements.....	326
7.7.4. Additional testing.....	326
7.8. References.....	327
Chapter 8 (revised). Tissue establishments	329
8.1. General organisational requirements of a tissue establishment (tissue establishments).....	329
8.1.1. Institutional identity.....	329
8.1.2. Organisation	330
8.2. Facilities and equipment	337
8.2.1. Facilities and equipment in a tissue establishment.....	337
8.2.2. Safety of personnel in the tissue establishment	340
8.3. Tissue and cell processing, preservation and storage	342
8.3.1. General.....	342
8.3.2. Acceptance of tissues and cells.....	342
8.3.3. Reagents and preservation solutions	343
8.3.4. Pooling	343
8.3.5. Quality control.....	344
8.3.6. Processing.....	344
8.3.7. Tissue and cell process validation	344
8.3.8. Tissue and cell storage.....	346
8.3.9. Packaging.....	346
8.3.10. Release of tissues or cells.....	347
8.3.11. Labelling.....	348
8.3.12. Package insert.....	350
8.4. Distribution	352
8.5. Transportation	352
8.6. Return into inventory of release tissues or cells: exceptional rules.....	353
8.7. Exceptional release	353
8.8. Recall.....	354
8.9. Hospital tissue and cell storage and distribution	354
8.10. References.....	358