

Table of Contents

Introduction

(Marion Weschka) 1

A. General research aspects 3

| | |
|---|----|
| I. Problems with terminology and definitions (Michael Bader) | 5 |
| II. Etymological background and further clarifying remarks concerning chimeras and hybrids (Josef Kure) | 7 |
| 1. Introduction | 7 |
| 2. Semantic analysis..... | 7 |
| a. Chimera as an archetype | 7 |
| b. Etymological background..... | 10 |
| c. Chimera as a metaphor and as a terminus technicus..... | 11 |
| d. Hybrid..... | 12 |
| e. Some further differentiations | 14 |
| f. Chimera as a strategy | 15 |
| 3. Anthropological clarifications | 16 |
| a. Chimera and the deeper understanding of humanity..... | 16 |
| b. Should we cross boundaries?..... | 18 |
| c. The art of slowness | 19 |
| III. Scientific background (Michael Bader, Regine Schreiner, Eckhard Wolf) | 21 |
| 1. Introduction | 21 |
| 2. Intra-species mixtures | 24 |
| a. Intra-species chimeras..... | 24 |
| b. Intra-species hybrids..... | 28 |
| 3. Inter-species mixtures..... | 28 |
| a. Inter-species chimeras..... | 28 |
| b. Inter-species hybrids..... | 32 |

VIII Table of Contents

| | |
|--|----|
| c. Examples of inter-species mixtures | |
| aa. Xenotransplantation (<i>Marion Weschka</i>)..... | 35 |
| bb. Transgenic animals carrying human genes (<i>Marion Weschka</i>)..... | 39 |
| cc. Nuclear transfer research (<i>Andras Dinnyes, Marion Weschka, Qi Zhou</i>) | 43 |
| dd. Transplantation of human embryonic stem cells into animal brain (<i>Marion Weschka</i>)..... | 51 |
| ee. Hamster test: Testing human sperm capacity with hamster ova (<i>Marion Weschka</i>) | 52 |
| ff. Mixing of embryos (<i>Marion Weschka</i>)..... | 53 |
| gg. Interspecies gestation (<i>Marion Weschka</i>)..... | 54 |
| hh. Other mixtures (Matrixes) | 55 |
| - Remarks to the matrix „Chimeras and Hybrids” (<i>Hans-Peter Bernhard</i>) | 55 |
| - Matrix Chimeras and Hybrids: Human-Animal mixtures (Chimbrids) | 57 |
| - Encompassing Matrix | 59 |
| IV. Ethics | |
| (Autumn Fieste, Marcus Düwell) | 61 |
| 1. Introduction..... | 61 |
| 2. The Fundamental Debates on Moral Status: What Makes Entities Morally Significant? | 62 |
| a. Preliminary Remarks | 62 |
| b. Moral Status Based on Sentience (i.e., on the ability to feel pain or suffer) | 63 |
| c. Moral Status Based on Agency, Self-Consciousness or Rationality | 64 |
| d. Moral Status Based on the Significance of the Human Species .. | 65 |
| e. Moral Status Based on the Intrinsic Value of Animals..... | 66 |
| aa. Applications of Moral Status: Potentiality, Precaution and Symbolic Extensions of Status | 67 |

| | |
|---|----|
| bb. Applications of Moral Status: Potentiality..... | 67 |
| cc. Applications of Moral Status: Precaution | 68 |
| dd. Applications of Moral Status: Symbolic Meanings | 68 |
| f. The Moral Status of Human Embryos..... | 70 |
| 3. Specific Moral Considerations in Evaluating Chimbrids: An Ethical Matrix | 70 |
| a. Preliminary Remarks | 71 |
| b. Moral Considerations in Research Ethics..... | 71 |
| c. Moral Considerations in Animal Ethics..... | 73 |
| V. Law | 79 |
| 1. Legal tools and strategies for the regulation of chimbrids <i>(Elisabeth Rynning)</i> | 79 |
| a. Introduction | 79 |
| b. Determining the aims of the regulatory project..... | 80 |
| c. Identifying the appropriate regulator | 81 |
| d. The choice of regulatory instruments | 81 |
| e. Decision-making in individual cases | 84 |
| f. Monitoring and sanctions | 84 |
| g. Some challenges in the regulation of chimbrids | 85 |
| 2. Which Beings Should Be Entitled to Human Rights? <i>(Erwin Bernat)</i> | 88 |
| a. The General Concept of Personhood | 88 |
| b. Human Rights – Their Meaning and Their Foundation..... | 89 |
| c. Human Rights and the Constitution..... | 91 |
| aa. The Paradigm: Born of a Human (the Natural Person) | 91 |
| bb. Does the Unborn Human Being Enjoy Constitutionally Protected Human Rights? | 92 |
| cc. Indicators of Personhood | 94 |
| d. The Status of Chimeras and Chimeric Embryos..... | 95 |
| 3. Chimbrids and International Law <i>(Marion Weschka)</i> | 98 |

X Table of Contents

| | |
|--|-----|
| 4. EU Law and Council of Europe Law applicable to chimera and hybrid research <i>(Rainer J. Schweizer, Hans-Peter Bernhard)</i> | 116 |
| a. Relevant facts..... | 116 |
| b. Research law..... | 116 |
| c. Protection of human-beings by the fundamental rights of the European Union..... | 119 |
| d. Protection of human rights and the dignity of the human being within the Council of Europe's Legal Framework..... | 119 |
| e. Protection of biotechnological inventions..... | 121 |
| f. Protection of personal data..... | 122 |
| g. Protection of Health..... | 123 |
| h. Protection of animals in the case of animal experiments..... | 129 |
| i. Genetics in the non-human domain | 131 |
| 5. National law | 132 |
| a. EU member states | 132 |
| aa. Austria <i>(Marion Weschka)</i> | 132 |
| bb. France <i>(Marion Weschka)</i> | 136 |
| cc. Germany <i>(Marion Weschka)</i> | 140 |
| dd. Sweden <i>(Marion Weschka)</i> | 145 |
| ee. Spain <i>(Marion Weschka)</i> | 150 |
| ff. United Kingdom <i>(Marion Weschka)</i> | 151 |
| b. Other Countries..... | 158 |
| aa. Switzerland <i>(Rainer J. Schweizer, Hans-Peter Bernhard)</i> | 158 |
| bb. Israel <i>(Marion Weschka)</i> | 165 |
| cc. United States <i>(Marion Weschka)</i> | 169 |

| | |
|--|------------|
| dd. Canada <i>(Marion Weschka)</i> | 173 |
| ee. China <i>(Marion Weschka)</i> | 178 |
| ff. Japan <i>(Marion Weschka)</i> | 180 |
| B. Key Cases in chimbrids research..... | 185 |
| I. Case 1 – Muotri: Transfer of human embryonic stem cell-derived neurons in mouse brain..... | 187 |
| 1. Scientific considerations <i>(Gisela Badura-Lotter)</i> | 187 |
| 2. Ethical considerations <i>(Autumn Fiester)</i> | 190 |
| 3. Legal regulation in different countries <i>(Deryck Beyleveld)</i> | 196 |
| II. Case 2 – Chen: Interspecies somatic cell nuclear transfer | 201 |
| 1. Scientific considerations <i>(Gisela Badura-Lotter)</i> | 201 |
| 2. Ethical considerations <i>(Gisela Badura-Lotter)</i> | 205 |
| 3. Legal regulation in different countries <i>(Marion Weschka)</i> | 209 |
| III. Case 3 – Bailey: Animal-Human Xenotransplantation..... | 231 |
| 1. Scientific considerations <i>(Hans-Peter Bernhard)</i> | 231 |
| 2. Ethical considerations <i>(Gisela Badura-Lotter)</i> | 235 |
| 3. Legal regulation in different countries <i>(Marion Weschka)</i> | 237 |
| IV. Case 4 – Fink: Porcine Xenografts in Parkinson’s Disease and Huntington’s Disease patients | 263 |
| 1. Scientific considerations <i>(Hans-Peter Bernhard)</i> | 263 |
| 2. Ethical considerations <i>(Gisela Badura-Lotter)</i> | 267 |

XII Table of Contents

| | |
|---|-----|
| 3. Legal regulation in different countries <i>(Jan C. Joerden)</i> | 271 |
| V. Case 5 – McCune: The SCID-hu Mouse | 287 |
| 1. Scientific considerations <i>(Hans-Peter Bernhard)</i> | 287 |
| 2. Ethical considerations <i>(Autumn Fiesteर)</i> | 290 |
| 3. Legal regulation in different countries <i>(Sonia Desmoulin)</i> | 293 |
| VI. Case 6 – EMEA: Transgenic goat producing human antithrombin | 317 |
| 1. Scientific considerations <i>(Michael Bader)</i> | 317 |
| 2. Ethical considerations <i>(Dominik Groß)</i> | 320 |
| 3. Legal regulation in different countries <i>(Sylvie Bordet)</i> | 324 |
| VII. Case 7 – O’Doherty: Mouse with human chromosome | 353 |
| 1. Scientific considerations <i>(Michael Bader)</i> | 353 |
| 2. Ethical considerations <i>(Dominik Groß)</i> | 356 |
| 3. Legal regulation in different countries <i>(Sylvie Bordet)</i> | 360 |
| VIII. Case 8 – Yanagimachi: Hamster egg penetration test..... | 361 |
| 1. Scientific considerations <i>(Hans-Peter Bernhard)</i> | 361 |
| 2. Ethical considerations <i>(Gisela Badura-Lotter)</i> | 364 |
| 3. Legal regulation in different countries <i>(Carlos María Romeo Casabona, Iñigo de Miguel Beriain)</i> | 367 |
| IX. Case 9 – Fehilly: Human-animal embryo mixing..... | 379 |
| 1. Scientific considerations <i>(Michael Bader)</i> | 379 |
| 2. Ethical considerations <i>(Dominik Groß)</i> | 381 |

| | |
|---|------------|
| 3. Legal regulation in different countries <i>(Marion Weschka)</i> | 385 |
| X. Case 10 – Nan et al.: Interspecies gestation..... | 405 |
| 1. Scientific considerations <i>(Michael Bader)</i> | 405 |
| 2. Ethical considerations <i>(Josef Kuře)</i> | 407 |
| 3. Legal regulation in different countries <i>(Carlos María Romeo Casabona, Iñigo de Miguel Beriain)</i> | 410 |
| XI. Short Remarks to the cases 1-10 in the light of European legal order <i>(Rainer J. Schweizer, Hans-Peter Bernhard)</i> | 427 |
| C. Summary, Conclusions and Recommendations..... | 433 |
| I. General remarks | 435 |
| II. Scientific overview of human-animal mixtures | 437 |
| III. Ethical Aspects | 441 |
| 1. Moral status | 441 |
| 2. Human research ethics | 443 |
| 3. Animal ethics | 444 |
| 4. Appearance and Symbolic Meaning | 445 |
| 5. Plurality of ethical theories and legal regulations | 446 |
| IV. Legal Aspects | 449 |
| 1. The regulatory needs and challenges | 449 |
| 2. Regulatory tools and strategies applied | 450 |
| 3. Concluding remarks..... | 452 |
| V. Recommendations | 455 |
| Annex..... | 459 |
| Annex A. Chimbrids – Scientific, Ethical and Legal reports..... | 461 |
| I. Science | 463 |
| 1. Transgenic animals carrying human genes: Methods and Ethical Aspects <i>(Michael Bader)</i> | 463 |

XIV Table of Contents

| | |
|--|-----|
| 2. Xenotransplantation – Aspects of Chimerism <i>(Regine Schreiner, Regina Klose, Eckhard Wolf)</i> | 475 |
| 3. Nuclear Transfer, Chimeras and Hybrids: Activities and legal Aspects of Research in Hungary <i>(Andras Dimnyes)</i> | 501 |
| 4. Interspecies Nuclear Transfer Research in China <i>(Qi Zhou)</i> | 524 |
| 5. Developing Human-Nonhuman Chimeras in Human Stem Cell Research: Ethical Issues and Boundaries <i>(Philip Karpowicz, Cynthia B. Cohen, Derek van der Kooy)</i> | 535 |
| 6. Chimeras in developmental biology: scientific objectives and ethical issues <i>(Béatrice de Montera, Isabelle Hue, Jean-Paul Renard)</i> | 556 |
| II. Ethics | 571 |
| 1. Man-made chimeras, hybrids and mosaics – ethical perspectives <i>(Gisela Badura-Lotter, Marcus Düwell)</i> | 571 |
| 2. Ethical Issues in Transgenesis: Biopharming, Xenotransplantation & Recreational Transgenesis <i>(Autumn Fieste)</i> | 592 |
| III. Law | 603 |
| 1. Theses concerning chimerisation and hybridisation from an ethical and legal perspective <i>(Jan C. Joerden, Cornelia Winter)</i> | 603 |
| 2. The Regulation of Hybrids and Chimeras in the UK <i>(Deryck Beyleveld, Tom Finnegan, Shaun D. Pattinson)</i> | 645 |
| 3. Providing a legal framework for chimeras - French Report <i>(Sonia Desmoulin)</i> | 667 |
| 4. Legal Aspects of Human-Animal Chimeras and Hybrids: Country Report Sweden <i>(Elisabeth Rynning)</i> | 689 |
| 5. Chimeras and Other Human-Animal Mixtures in Relation to the Swiss Constitution and Swiss Laws: A Case for Regulatory Action <i>(Rainer J. Schweizer, Hans-Peter Bernhard)</i> | 706 |
| 6. Die rechtliche Regelung von Chimären und Hybridwesen – ein österreichischer Landesbericht <i>(Erwin Bernat)</i> | 716 |
| 7. New types of chimeras and hybrids: a challenge for biolaw <i>(Carlos María Romeo Casabona, Iñigo de Miguel Beriain)</i> | 734 |

| | |
|---|------------|
| 8. The legislation on chimeras and hybrids in Spain <i>(Carlos María Romeo Casabona, Iñigo de Miguel Beriain)</i> | 741 |
| 9. Discussing the European Union Competences to Legislate on Chimbrids Research <i>(Filip Krepelka)</i> | 743 |
| 10. Legal Issues involving Hybrids and Chimeras: United States Country Report <i>(Timothy Stoltzfus Jost)</i> | 754 |
| 11. Legal Aspects of Human-Animal Combinations in Canada <i>(Sylvie Bordet)</i> | 778 |
| 12. Legal and Ethical Aspects of Chimera and Hybrid Research in Israel: Country Report with Comparative Observations <i>(Amos Shapira)</i> | 798 |
| 13. Bioethical Discussions on Specified Embryos in Japan <i>(Motomu Shimoda)</i> | 809 |
| 14. The Law Concerning Regulations Relating to Human Cloning Techniques, Handling of a Specified Embryo and Animal Experiment in Japan <i>(Fumio Tokotani)</i> | 817 |
| 15. Human embryonic stem cell research in China <i>(Dai Kuisheng)</i> | 819 |
| Annex B. Country Reports on the 10 Cases | 827 |
| I. Germany: Case 1-10 according to German Law <i>(Jan C. Joerden, Marion Weschka)</i> | 829 |
| 1. Case 1 – Muotri Case..... | 829 |
| 2. Case 2 – Chen Case (interspecies SCNT human into rabbit)..... | 833 |
| 3. Case 3 – Animal-Human Xenotransplantation | 835 |
| 4. Case 4 – Fink | 837 |
| 5. Case 5 – McCune..... | 838 |
| 6. Case 6 – EMEA | 841 |
| 7. Case 7 – O’Doherty | 842 |
| 8. Case 8 – Golden Hamster test..... | 843 |
| 9. Case 9 – Mixing of embryos | 844 |
| 10. Case 10 – Interspecies gestation | 844 |

XVI Table of Contents

| | |
|--|-----|
| II. UK: Case 1-10 according to UK law <i>(Deryck Beyleveld)</i> | 847 |
| 1. Muotri Case | 847 |
| 2. Chen Case | 848 |
| 3. Bailey Case. Baboon to Human Cardiac Xentotransplant in Neonates..... | 849 |
| 4. Fink Case Porcine Xenografts for Huntington's..... | 850 |
| 5. McCune Case: SCID..... | 850 |
| 6. Transgenic Goat Case | 851 |
| 7. Mice with Down's Syndrome Phenotypes..... | 851 |
| 8. Golden Hamster Test | 851 |
| 9. Mixing of Embryos..... | 852 |
| 10. Interspecies Gestation | 852 |
| III. France Legal Issues in French Law: the case studies <i>(Sonia Desmoulin)</i> | 855 |
| 1. Case 1 – Muotri | 855 |
| 2. Case 2 – Chen | 860 |
| 3. Case 3 – Chen (alternative)..... | 863 |
| 4. Case 4 – Fink | 867 |
| 5. Case 5 – McCune..... | 868 |
| 6. Case 6 – EMEA | 872 |
| 7. Case 7 – O'Doherty | 875 |
| 8. Case 8 – Golden Hamster test..... | 876 |
| 9. Case 9 – Mixing of Embryos | 878 |
| 10. Case 10 – Interspecies gestation | 880 |
| IV. Sweden – Case 1-10 according to Swedish law <i>(Elisabeth Rynning)</i> | 883 |
| 1. Case 1 – Muotri, A.R. et al. (2005)..... | 883 |
| 2. Case 2 – Chen, Y. et al. (2003)..... | 884 |
| 3. Case 3 – Bailey Leonard L. et al. (1985) | 886 |
| 4. Case 4 – Fink, J.S. et al. (2000) | 887 |
| 5. Case 5 – McCune et al. (1988)..... | 888 |

| | |
|---|-----|
| 6. Case 6 – EMEA | 890 |
| 7. Case 7 – O’Doherty, A. et al. (2005) | 890 |
| 8. Case 8 – Hoo Lee M. et al. (2007)..... | 891 |
| 9. Case 9 – Mixing of embryos..... | 892 |
| 10. Case 10 – Interspecies gestation | 894 |
| V. Spain – Case 1-10 according to Spanish law | |
| <i>(Carlos María Romeo Casabona, Iñigo de Miguel Beriain)</i> | 897 |
| 1. Case 1 | 897 |
| 2. Case 2 | 898 |
| 3. Case 3 | 901 |
| 4. Case 4 | 903 |
| 5. Case 5 | 905 |
| 6. Case 6 | 908 |
| 7. Case 7 | 909 |
| 8. Case 8 – Golden Hamster test..... | 912 |
| 9. Case 9 – Mixing of embryos..... | 912 |
| 10. Case 10 – Interspecies gestation | 914 |
| VI. Austria – Case 1-10 according to Austrian Law | |
| <i>Erwin Bernat)</i> | 917 |
| 1. Case 1 – Muotri case..... | 917 |
| 2. Case 2 – Chen case | 917 |
| 3. Case 3 – Bailey case | 918 |
| 4. Case 4 – Fink case | 918 |
| 5. Case 5 – McCune case | 919 |
| 6. Case 6 – Transgenic goat case | 919 |
| 7. Case 7 – O’Doherty case | 919 |
| 8. Case 8 – Hoo Lee case..... | 920 |
| 9. Case 9 – Fehilly case | 920 |
| 10. Case 10 – Nan case | 921 |
| VII. Switzerland Case 1 to 10 according to Swiss Law | |
| <i>(Rainer J. Schweizer, Hans-Peter Bernhard)</i> | 923 |
| 1. Case 1 - Muotri | 923 |

XVIII Table of Contents

| | |
|--|-----|
| 2. Case 2 - Chen..... | 931 |
| 3. Case 3 - Bailey..... | 933 |
| 4. Case 4 - Fink..... | 937 |
| 5. Case 5 - McCune..... | 939 |
| 6. Case 6 - EMEA..... | 940 |
| 7. Case 7 - O'Doherty..... | 945 |
| 8. Case 8 - Yanagimachi | 947 |
| 9. Case 9 - Fehilly | 947 |
| 10. Case 10 - Nan et al..... | 951 |
| 11. Alternative to Case 10 - Zavos and Illmensee | 951 |
| VIII. USA – Case comments | |
| <i>(Timothy Stoltzfus Jost)</i> | 955 |
| 1. Case 1: Human embryonic stem cells into brain of mouse embryo/ foetus at day 14 | 955 |
| 2. Case 2, Chen, Y. et al. (2003): Embryonic stem cells generated by nuclear transfer of human somatic nuclei into rabbit oocytes | 958 |
| 3. Case 3: Solid organ xenotransplantation of xenograft into human being | 959 |
| 4. Case 4: Porcine xenografts (porcine foetal neuronal cells) in Parkinson's Disease and Huntington's Disease Patients | 963 |
| 5. Case 5: Human foetal cells into adult mice..... | 966 |
| 6. Case 6: Transgenic goats that secrete human antithrombine into their milk; transfer of human DNA into goat zygotes | 968 |
| 7. Case 7: Aneuploid mouse strain carrying human chromosome 21 with Down's syndrome phenotypes; transfer of almost full human chromosome 21 into mouse embryonic stem cells; afterwards injection into mouse blastocysts | 970 |
| 8. Case 8: Golden Hamster Test | 971 |
| 9. Case 9: Mixing embryos of non-human species with embryos of human species..... | 972 |
| 10. Case 10: Interspecies Gestation | 975 |
| IX. Canada | |
| <i>(Sylvie Bordet)</i> | 977 |
| A. Introduction..... | 977 |

Table of Contents XIX

| | |
|--|-------------|
| 1. Case Study No. 1 | 983 |
| 2. Case Study No. 2 | 991 |
| 3. Case Study No. 3 | 994 |
| 4. Case Study No. 4 | 1002 |
| 5. Case Study No. 5 | 1003 |
| 6. Case Study No. 6 | 1006 |
| 7. Case Study No. 7 | 1008 |
| 8. Case Study No. 8 | 1010 |
| 9. Case Study No. 9 | 1013 |
| 10. Case Study No. 10 | 1016 |
| X. Israel – Case 1-10 according to Israeli law | |
| <i>(Amos Shapira)</i> | 1019 |
| 1. Case 1 – Muotri | 1019 |
| 2. Case 2 – Chen | 1019 |
| 3. Case 3 – Chen (alternative)..... | 1020 |
| 4. Case 4 – Fink | 1021 |
| 5. Case 5 – McCune..... | 1022 |
| 6. Case 6 – EMEA | 1023 |
| 7. Case 7 – O'Doherty..... | 1023 |
| 8. Case 8 – Golden Hamster Test | 1024 |
| 9. Case 9 – Mixing of Embryos | 1025 |
| 10. Case 10 – Interspecies Gestation: Transfer of an Animal Embryo into the Uterus of a Woman and Transfer of a Human Embryo into the Uterus of an Animal..... | 1026 |
| XI. Japan – Case 1-10 according to Japanese Law | |
| <i>(Fumio Tokotani)</i> | 1029 |
| Table of Authors..... | 1031 |
| Index..... | 1037 |