

THE ETHICS AND  
REGULATION OF  
RESEARCH WITH HUMAN  
SUBJECTS

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# THE ETHICS AND REGULATION OF RESEARCH WITH HUMAN SUBJECTS

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## Second Edition

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## *Dedication*

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This book is dedicated to our esteemed colleague and dear friend Nancy Neveloff Dubler, Professor Emerita in the Department of Family and Social Medicine, Albert Einstein College of Medicine, for her critical contributions to the first edition of this book, as well as for the enormous influence she has had on the field of bioethics generally.





## *Preface to the Second Edition*

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Since the first edition of this book was published in 2005, those involved in designing, conducting, and overseeing research with human subjects have faced a growing range of challenges, including fundamental questions about the continued vitality of the centerpiece of the contemporary regulatory system, the federal Common Rule. As this book goes to press, federal officials are actively considering proposed revisions to the Common Rule first announced by the Department of Health and Human Services in 2012, but no final regulatory proposal has yet been released. Throughout this volume, we have highlighted key areas that would be affected if the changes proposed in 2012 are eventually adopted, but readers should be aware that the final regulatory changes — if, indeed, there are any — may end up being considerably different from the proposals previously announced. One of our goals in this second edition is to help lawyers, administrators, researchers, and other professionals involved in the oversight of human subject research to become conversant with the relevant ethical and regulatory issues so that they will have the knowledge and skills necessary to critically assess any future regulatory changes.

The genesis of this book was our desire to develop a set of teaching materials that could be used in an academic course on human subject research in a broad range of professional school settings. In developing these materials, we were mindful that our readers would include tomorrow's advisers, managers, and regulators of researchers and research institutions. If students are to be effective in these roles, they must not only understand the history of human subject protection and the relevant ethical and regulatory issues; they must begin to think critically about the existing regulatory system and to consider the desirability of policy reform.

We have, therefore, adopted as a model for this book a variation of the traditional law school "casebook," which has been used successfully by generations of law students. These books are designed to foster critical thinking about the subject matter involved at least as much as to familiarize students with a given body of law and regulations. That does not mean that we have designed this book primarily with law students in mind; on the contrary, we have gone to great lengths to make the material accessible to non-law students, including those at schools of medicine, nursing, public health, and health administration. All of us have taught in one or more of those settings, and we have found that the law school casebook format works remarkably well there. Nonetheless, recognizing that the book will be used by students in a variety of disciplines, we have modified the traditional casebook approach to make it equally accessible to those who have had no legal training whatsoever. As a result, some basic legal concepts that may seem obvious to law students or lawyers are accompanied by brief explanations. In like fashion, understanding that some readers will have little or no clinical background, we have provided similar basic explanations, where appropriate, of clinical concepts. Outside of degree-granting programs, we envision that the book will be useful in training programs for professionals whose work requires an appreciation of the ethical and regulatory issues surrounding human subject research, such as members and professional staff of institutional review boards.

The book is largely comprised of primary source documents, including governmental regulations, guidance statements, and court decisions, and excerpts from the voluminous commentary produced by scholars, advisory commissions, and others. These materials are

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## *Preface to the Second Edition*

accompanied by extensive notes and questions, which expand on some of the issues raised in the primary readings and ask the reader to think about the gaps, ambiguities, and conflicts those readings raise. In true law school style, many of the questions have no indisputably correct answer. Instead, they are offered to stimulate discussion, provoke independent thinking, or simply lead to quiet moments of thoughtful puzzlement by students as they review the readings outside of class.

Although we have tried our best to keep the book to a manageable size, we have added several chapters to this second edition that were not covered in the original volume, including new material on research in the armed forces, research with emerging technologies, and international research. The book retains its original focus on biomedical research, as opposed to research in the social sciences. Although most of this book's content should be equally applicable to both types of research, to the extent that there are special issues that arise in social science research, those issues are not discussed at any significant length here. In addition, because this is a book about the use of human subjects in research, it provides little coverage of research integrity issues that are not unique to research involving human subjects, such as falsification of data or authorship practices.

### Organization of the Book

This book is divided into three parts. Part I provides a general overview of the history of research with human subjects, the existing regulatory framework, and the major entities involved in overseeing research. Part II examines the key ethical and regulatory issues that arise in every research protocol. Part III looks at special situations that raise issues beyond the general considerations addressed in Part II. Finally, the Appendices contain a variety of primary source materials discussed throughout the book.

### Stylistic Conventions

Most of the excerpts that appear in this book have been edited. Excerpted pieces commonly omit text that appeared in the original before or after the excerpted portion, and no notations have been used to indicate such deletions. Where text has been deleted within the excerpted piece, however, ellipses have been inserted. Citations or footnotes appearing in the original text have in most cases been deleted without any notation.

Recognizing that URLs have limited lifespans, and that it is usually possible to retrieve documents online simply by inserting the title or relevant key words into any online search engine, we have omitted URLs for most online sources, except for those that are not readily accessible without a specific Internet address. If no URL or other citation information is provided, consult your favorite search engine. In addition, the full text of statutes or judicial opinions can usually be found at FindLaw or at Cornell University Law School's Legal Information Institute.

The journal whose full name is IRB: Ethics & Human Research (previously known as IRB: A Review of Human Subjects Research) is cited throughout this book, for simplicity purposes, with the shortened name IRB.

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*Preface to the Second Edition*

**For Readers without a Legal Background:  
A Brief Description of the U.S. Legal System**

The basic structure of the American legal system is established by the United States Constitution. It creates a *federal* system, a term that refers to a system of government in which a group of smaller political units join together and agree to give up some of their power to a centralized government. In the case of the United States, the smaller units are each of the separate states, and the centralized government is the national (sometimes called federal) government. On the one hand, the Constitution spells out the details of how power is shared between the national government and the states. Under the Constitution's "supremacy clause," federal laws will generally override any conflicting laws enacted by the states. On the other hand, the Constitution does not say much about how each of the state's own internal governments will operate: for that very reason, each state has its own constitution.

In most instances, law is created from one of three sources: legislatures, administrative agencies, and courts. (Contracts — legally binding agreements created by private parties — represent an additional source of law, although one that is binding only on parties who voluntarily agree to accept a contract's terms.) The legislature for the national government is, of course, the United States Congress, which is comprised of the Senate and the House of Representatives. It has the authority to enact statutes, which in most cases need to be signed by the President before they become effective. Each state's constitution determines the structure of that state's legislature, which has the power to enact state statutes.

Statutes, whether on the federal or state level, often will only provide a broad outline of what the law is supposed to be. The fleshing out of the details of the law, together with performing the day-to-day implementation of what a particular statute requires, is often left to administrative agencies. One of the most important functions of administrative agencies is to issue regulations and to interpret those regulations. As will be explained in this book, a great deal of the law relating to protecting research subjects is found in regulations issued and interpreted by two federal administrative agencies, the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA), both of which are part of the Department of Health and Human Services (DHHS).

Controversies often arise over the interpretation of state or federal laws, and in those instances the courts often are asked to resolve the dispute. There are separate court systems at the federal and state levels. In the federal court system, the initial trial of a case usually takes place in what are called "district courts." Any party who is not satisfied with the decision of a federal district court can appeal the decision to one of the circuit courts of appeals. Decisions of the court of appeals can be reviewed by the United States Supreme Court, but in contrast to the court of appeals, which is usually required to take appeals from the federal district courts, the U.S. Supreme Court has a great deal of discretion in deciding which cases it wishes to review. The U.S. Supreme Court has the final word in interpreting federal law, and in resolving conflicts between federal laws and state laws. Each state has its own system of trial and appellate courts, including one highest court similar to the U.S. Supreme Court, which has the authority to make a final determination of how that state's laws should be interpreted.

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*Preface to the Second Edition*

Courts also establish and enforce legal principles that do not derive from statutes or regulations. These principles, known as the “common law,” can be traced back to old English judicial decisions, although they have been revised substantially over the centuries. Common-law principles are particularly important in resolving disputes over personal injuries (a body of law known as “torts”) and contracts. Each state develops its own body of common-law principles. While there is a great deal of similarity in the common law of the various states, some important state-by-state variations exist.

## *About the Authors*

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Carl H. Coleman is Professor of Law and Academic Director of the Division of Online Learning at Seton Hall Law School. Before joining the Seton Hall faculty, he served as Executive Director of the New York State Task Force on Life and the Law, a nationally recognized interdisciplinary commission with a mandate to develop policy recommendations on issues raised by medical advances. He received a J.D., magna cum laude, from Harvard University, where he also received an A.M. in East Asian Studies. He holds a B.S.F.S., cum laude, from Georgetown University's School of Foreign Service. He has written and lectured extensively on legal and regulatory issues related to human subject research, public health ethics, assisted reproductive technologies, genetic testing and screening, and medical decision making at the end of life. He has served as Bioethics and Law Adviser at the World Health Organization in Geneva, Switzerland, and as a member of the Institutional Review Boards at Seton Hall University and the University of Medicine and Dentistry of New Jersey.

Jerry A. Menikoff is director of the Office for Human Research Protections, within the U.S. Department of Health and Human Services. He previously was Associate Professor of Law, Ethics, and Medicine and Director of the Institute for Bioethics, Law, and Public Policy, University of Kansas School of Medicine, and Associate Professor of Law, University of Kansas School of Law. He received A.B., J.D. (both magna cum laude) and M.P.P. degrees from Harvard University, and an M.D. from Washington University. He has been a fellow at the University of Chicago's McLean Center for Clinical Medical Ethics, and at Harvard's Center for Ethics and the Professions. He is the author of *LAW AND BIOETHICS: AN INTRODUCTION* (Georgetown University Press), and *WHAT THE DOCTOR DIDN'T SAY: THE HIDDEN TRUTH ABOUT MEDICAL RESEARCH* (Oxford University Press).

Jesse A. Goldner is the John D. Valentine Professor of Law at Saint Louis University, where he also has held secondary appointments as Professor of Law in Psychiatry and Professor of Pediatrics at the University's School of Medicine, Professor of Health Care Administration in the University's School of Public Health and Departmental Adjunct Professor in its Center for Health Care Ethics. He has taught at Saint Louis University since 1973. He co-founded and has served as the Director of the School of Law's Center for Health Law Studies. In addition, for 17 years he was a member of the University's Institutional Review Board, including six years as its chair. He was a member and the initial chair of the Accreditation Committee of the Association for the Accreditation of Human Research Protection Programs and has served on the Ethics Committee of Cardinal Glennon Children's Hospital in St. Louis since 1978. Professor Goldner was co-editor-in-chief of the *JOURNAL OF HEALTH LAW*, published by the American Health Lawyers Association. In 2004 he was awarded the Jay Healy Distinguished Health Law Teacher of the Year by the American Society of Law, Medicine & Ethics. He received his A.B. (in political science) and M.A. (in psychology) from Columbia University and his J.D. from Harvard Law School.

Efthimios Parasidis is Associate Professor of Law and Public Health at The Ohio State University, where he holds a joint appointment in the Moritz College of Law and the College of Public Health and is a member of the College of Medicine's Center for Bioethics and Medical Humanities. He also is a Faculty Scholar in Bioethics with The Greenwall

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*About the Authors*

Foundation. He writes and lectures extensively on the law and ethics of human subjects research, FDA law, health information technology, and military medical ethics, and has provided consultation to the American College of Physicians on financial conflicts of interest in the medical and pharmaceutical industries. As a Fulbright Scholar he researched medical ethics in Greece; he also was selected as a Health Law Scholar by the American Society of Law, Medicine & Ethics. Prior to joining the Ohio State faculty, he was a faculty member with the Center for Health Law Studies at Saint Louis University, worked as an attorney in private practice, and was an Assistant Attorney General for the State of New York. While in Missouri, he was a member of the Law and Policy workgroup of Missouri Health Connection, the entity creating and administering Missouri's health information exchange. He earned a B.A. in Philosophy (magna cum laude) from The College of New Jersey, and a J.D. and M. Bioethics from the University of Pennsylvania.

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# Table of Contents

<b>Part I</b>	<b>BACKGROUND AND REGULATORY CONTEXT</b>	<b>1</b>
<b>Chapter 1</b>	<b>HISTORICAL ANTECEDENTS</b>	<b>3</b>
§ 1.01	EARLY EXAMPLES OF HUMAN EXPERIMENTATION	4
[A]	Ancient Activity Through the Close of the 19th Century	4
	Notes and Questions	6
[B]	Approaches Through the Mid-Twentieth Century	6
[1]	European Medical Education and Practice	6
[2]	Statistics and Research	7
[3]	The Revolution in American Medical Education	8
[4]	Early Experiments on Sexually Transmitted Diseases	9
	THE MEMOIRS OF A PHYSICIAN	9
	Notes and Questions	10
[5]	Rabies and Yellow Fever	11
	STRANGERS AT THE BEDSIDE	12
	Notes and Questions	12
§ 1.02	AMERICAN JUDICIAL REACTION TO EXPERIMENTATION	13
	<i>An Overview of Legal Controls on Human Experimentation and the</i>	
	<i>Regulatory Implications of Taking Professor Katz Seriously</i>	13
	Notes and Questions	14
§ 1.03	NAZI GERMANY AND THE NUREMBERG CODE	15
[A]	Introduction	15
[B]	The Indictment	16
	1 TRIALS OF WAR CRIMINALS BEFORE THE NUERNBERG MILITARY	
	TRIBUNALS UNDER CONTROL COUNCIL LAW No. 10, 8–17	16
[C]	Opening Statement	18
	1 TRIALS OF WAR CRIMINALS BEFORE THE NUERNBERG MILITARY	
	TRIBUNALS UNDER CONTROL COUNCIL LAW No. 10, 27–28, 37–38,	
	68–71	18
[D]	The Trial	20
[1]	Testimonial Evidence (Excerpts)	20
	Excerpts from the Testimony of FATHER LEO MIECHALOWSKI	20
[2]	Documentary Evidence (Excerpts)	23
	1 TRIALS OF WAR CRIMINALS BEFORE THE NUERNBERG MILITARY	
	TRIBUNALS UNDER CONTROL COUNCIL LAW No. 10, 228	23
[E]	Defendants’ Final Statements	23
	2 TRIALS OF WAR CRIMINALS BEFORE THE NUERNBERG MILITARY	

---

*Table of Contents*

	TRIBUNALS UNDER CONTROL COUNCIL LAW NO. 10, 160–63 . . . . .	23
[F]	Excerpts from the Judgment of the Tribunal, Including The Nuremberg Code . . . . .	24
	2 TRIALS OF WAR CRIMINALS BEFORE THE NUERNBERG MILITARY TRIBUNALS UNDER CONTROL COUNCIL LAW NO. 10, 181–83 . . . . .	24
	Notes and Questions . . . . .	27
§ 1.04	MEDICAL RESEARCH CONDUCTED BY NORTH AMERICAN INVESTIGATORS FROM 1900 TO THE EARLY 1970s . . . . .	30
[A]	Post-World War I Research Activities . . . . .	30
[B]	Funding of U.S. Research through World War II . . . . .	31
[C]	United States Medical Research in Guatemala from 1946–1948 . . . . .	32
	“ETHICALLY IMPOSSIBLE”: STD RESEARCH IN GUATEMALA FROM 1946 TO 1948 . . . . .	33
	Notes and Questions . . . . .	36
[D]	Canadian Malnutrition Studies in Indigenous Children (1942–1952) . . . . .	36
[E]	The Developing Public Role in Research . . . . .	37
[F]	The Need to Conduct Appropriate Research: Thalidomide and DES . . . . .	38
	Notes and Questions . . . . .	39
[G]	The Beecher Article (1966) . . . . .	40
	Notes and Questions . . . . .	40
[H]	Jewish Chronic Disease Hospital (1963) and Willowbrook (1956–1971) . . . . .	41
	Notes and Questions . . . . .	43
[I]	Tuskegee (1932–1972) . . . . .	44
	REPORT OF THE TUSKEGEE SYPHILIS STUDY . . . . .	44
	REPORT OF THE TUSKEGEE SYPHILIS . . . . .	45
	Notes and Questions . . . . .	45
[J]	Radiation Experiments (1944–1974) . . . . .	47
	Notes and Questions . . . . .	48
[K]	Behavior and Social Science Research: The Milgram Experiments . . . . .	50
	Notes and Questions . . . . .	51
<b>Chapter 2</b>	<b>THE CHANGING FACE OF RESEARCH: NEW REGULATIONS, NEW PLAYERS, NEW PLACES, NEW AGENDAS . . . . .</b>	<b>53</b>
§ 2.01	GOVERNMENTAL OVERSIGHT OF RESEARCH . . . . .	53
[A]	Federal Oversight: 1960s to 1990s . . . . .	53
	<i>An Overview of Legal Controls on Human Experimentation and the         Regulatory Implications of Taking Professor Katz Seriously</i> . . . . .	53
	Notes and Questions . . . . .	56
[B]	Directions in Federal Regulation: 1996–2003: The Rise of Significant	



---

*Table of Contents*

	Government Oversight . . . . .	58
	Notes and Questions . . . . .	59
§ 2.02	BIOMEDICAL ADVANCES, NEW FUNDING, NEW PLACES, NEW PLAYERS . . . . .	62
[A]	Research Successes from the 1980s to 2012 . . . . .	62
	SELECTED RESEARCH ADVANCES OF NIH . . . . .	63
[B]	How Much Do We Spend on Research? . . . . .	65
	Notes and Questions . . . . .	66
[C]	The Changing Role of Academic Health Centers in Research . . . . .	68
[1]	The Bayh-Dole Act . . . . .	70
	PATENTS: PART II. PATENTABILITY OF INVENTIONS AND GRANT OF PATENTS . . . . .	70
	<i>Dealing with Conflicts of Interest in Biomedical Research: IRB Oversight as the Next Best Solution to the Abolitionist Approach</i> . . . . .	70
	Notes and Questions . . . . .	71
[2]	Clinical Research Funding Streams . . . . .	73
	<i>Curing Conflicts of Interest in Clinical Research: Impossible Dreams and Harsh Realities</i> . . . . .	73
	Notes and Questions . . . . .	76
[D]	Federal Sources of Research Funding . . . . .	77
[1]	National Institutes of Health . . . . .	77
[2]	Other DHHS Departments . . . . .	78
[3]	Other Federal Agencies . . . . .	78
[4]	New Federal Funding . . . . .	79
[a]	The Center for Quality Improvement and Patient Safety . . . . .	79
[b]	Patient-Centered Outcomes Research Institute . . . . .	80
	Notes and Questions . . . . .	82
[E]	Private Industry Funding of Research . . . . .	84
[1]	Pharmaceutical Companies . . . . .	84
[2]	Biotech Companies . . . . .	85
[3]	mHealth . . . . .	86
§ 2.03	THE MOVEMENT OF RESEARCH FROM ACADEMIC HEALTH CENTERS TO PRIVATE PHYSICIANS' OFFICES AND THE RISE OF CONTRACT RESEARCH ORGANIZATIONS . . . . .	86
	Notes and Questions . . . . .	88
	<i>The Private Practicing Physician-Investigator: Ethical Implications of Clinical Research in the Office Setting</i> . . . . .	88
	Notes and Questions . . . . .	90
	<i>Remaining Faithful to the Promises Given: Maintaining Standards in Changing Times</i> . . . . .	92

---

*Table of Contents*

	Notes and Questions . . . . .	93
§ 2.04	DEVELOPING NEW RESEARCH AGENDAS . . . . .	96
[A]	Setting NIH Priorities . . . . .	96
	SETTING RESEARCH PRIORITIES AT THE NATIONAL INSTITUTES OF HEALTH . . . . .	96
	Notes and Questions . . . . .	99
	<i>Medicine and Society: Priority Setting in Biomedical Research</i> . . . . .	100
	Notes and Questions . . . . .	102
[B]	The Role of Advocacy . . . . .	103
	WHEN SCIENCE OFFERS SALVATION . . . . .	103
[1]	Legislative Advocacy . . . . .	104
	WHEN SCIENCE OFFERS SALVATION . . . . .	105
[2]	Advocacy Regarding the Manner in Which Research Is Conducted . . . . .	106
	WHEN SCIENCE OFFERS SALVATION . . . . .	106
	Notes and Questions . . . . .	109
<b>Chapter 3</b>	<b>THE FEDERAL AND STATE REGULATORY STRUCTURE . . . . .</b>	<b>111</b>
§ 3.01	OVERVIEW OF THE LEGAL STRUCTURE . . . . .	111
§ 3.02	DEPARTMENT OF HEALTH AND HUMAN SERVICES REGULATIONS . . . . .	112
[A]	The Common Rule . . . . .	112
[1]	Scope of Coverage . . . . .	113
[2]	Definition of Research . . . . .	113
	Notes and Questions . . . . .	113
[a]	What Is a Research Protocol? . . . . .	114
[b]	Research Versus Clinical Innovation . . . . .	115
	THE BELMONT REPORT: ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS . . . . .	115
	<i>Ancheff v. Hartford Hospital</i> . . . . .	115
	Notes and Questions . . . . .	118
[c]	Research Versus Quality Improvement . . . . .	121
	<i>The Quality Improvement-Research Divide and the Need for     External Oversight</i> . . . . .	121
	Notes and Questions . . . . .	124
[d]	Research Versus Public Health Initiatives . . . . .	126
	DISTINGUISHING PUBLIC HEALTH RESEARCH AND PUBLIC HEALTH NONRESEARCH . . . . .	126
	Notes and Questions . . . . .	127
[3]	Definition of Human Subject . . . . .	129

---

*Table of Contents*

	Notes and Questions . . . . .	129
[4]	Exempt Studies . . . . .	130
	Notes and Questions . . . . .	130
[5]	Proposed Changes to the Common Rule . . . . .	133
	ADVANCE NOTICE OF PROPOSED RULEMAKING . . . . .	133
	Notes and Questions . . . . .	135
[B]	Additional DHHS Regulations Governing Vulnerable Populations . . . . .	136
	<i>The Invisible Vulnerable: The Economically and Educationally</i>	
	<i>Disadvantaged Subjects of Clinical Research</i> . . . . .	136
	<i>Regulating Research on the Terminally Ill: A Proposal for</i>	
	<i>Heightened Safeguards</i> . . . . .	138
	Notes and Questions . . . . .	139
	1 ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN	
	PARTICIPANTS . . . . .	140
	Notes and Questions . . . . .	146
[C]	The DHHS Office for Human Research Protections . . . . .	147
	<i>Who’s Watching the Watchdogs? Responding to the Erosion of</i>	
	<i>Research Ethics by Enforcing Promises</i> . . . . .	147
	Notes and Questions . . . . .	148
	COMPLIANCE OVERSIGHT PROCEDURES FOR EVALUATING	
	INSTITUTIONS . . . . .	149
	Notes and Questions . . . . .	150
§ 3.03	FOOD AND DRUG ADMINISTRATION REGULATIONS . . . . .	151
[A]	Human Subject Protections . . . . .	151
	Notes and Questions . . . . .	152
[B]	The Drug Approval Process . . . . .	153
	<i>United States v. Rutherford</i> . . . . .	153
	<i>Beyond Abigail Alliance: The Reality Behind the Right to Get</i>	
	<i>Experimental Drugs</i> . . . . .	156
	Notes and Questions . . . . .	159
	<i>The Architecture of Government Regulation of Medical Products</i> . . . . .	161
	<i>Eli Lilly &amp; Co. v. Commissioner</i> . . . . .	162
	Notes and Questions . . . . .	165
	INFORMATION SHEETS: GUIDANCE FOR INSTITUTIONAL REVIEW	
	BOARDS AND CLINICAL INVESTIGATORS, “OFF-LABEL” AND	
	INVESTIGATIONAL USE OF MARKETED DRUGS, BIOLOGICS	
	AND DEVICES . . . . .	167
	Notes and Questions . . . . .	168
[C]	The Device Approval and Clearance Process . . . . .	170
	<i>Medtronic, Inc. v. Lohr</i> . . . . .	170

---

*Table of Contents*

	INFORMATION SHEETS GUIDANCE FOR IRBs, CLINICAL INVESTIGATORS AND SPONSORS: FREQUENTLY ASKED QUESTIONS	
	ABOUT MEDICAL DEVICES . . . . .	172
	Notes and Questions . . . . .	174
[D]	The FDA Office for Good Clinical Practice . . . . .	175
	<i>FDA and the Quality and Integrity of Research</i> . . . . .	175
§ 3.04	RESEARCH NOT COVERED BY THE FEDERAL REGULATIONS . . . . .	175
	Notes and Questions . . . . .	176
§ 3.05	STATE LAWS . . . . .	177
	<i>Oversight of Human Subject Research: The Role of the States</i> . . . . .	177
	Notes and Questions . . . . .	180
	MARYLAND CODE ANNOTATED, HEALTH-GENERAL . . . . .	181
	Notes and Questions . . . . .	181
<b>Chapter 4</b>	<b>INSTITUTIONAL REVIEW BOARDS . . . . .</b>	<b>183</b>
§ 4.01	PURPOSE AND DUTIES . . . . .	183
	HUMAN SUBJECTS RESEARCH: UNDERCOVER TESTS SHOW THE INSTITUTIONAL REVIEW BOARD SYSTEM IS VULNERABLE TO UNETHICAL MANIPULATION . . . . .	183
	<i>Local Institutional Review Boards, in NATIONAL BIOETHICS ADVISORY COMMISSION, 2 ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS K-1</i> . . . . .	184
	Notes and Questions . . . . .	186
§ 4.02	COMPOSITION . . . . .	188
	Notes and Questions . . . . .	188
	<i>Local Institutional Review Boards, in NATIONAL BIOETHICS ADVISORY COMMISSION, 2 ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS</i> . . . . .	189
	Notes and Questions . . . . .	190
§ 4.03	PROCESS OF IRB REVIEW . . . . .	192
[A]	Full Review . . . . .	192
	GUIDANCE ON WRITTEN IRB PROCEDURES . . . . .	192
	Notes and Questions . . . . .	193
	<i>What Does It Mean to “Review” a Protocol? Johns Hopkins &amp; OHRP</i> . . . . .	195
	Notes and Questions . . . . .	198
	<i>Rationalizing Risk Assessment in Human Subject Research</i> . . . . .	199
	Notes and Questions . . . . .	200
	<i>The Role of Institutional Review Boards in Protecting Human Subjects: Are We Really Ready to Fix a Broken System?</i> . . . . .	201

---

*Table of Contents*

	Notes and Questions . . . . .	205
[B]	Expedited Review . . . . .	209
	Notes and Questions . . . . .	210
§ 4.04	PROPRIETARY AND INDEPENDENT IRBS . . . . .	211
	<i>Institutional Review Boards: The Emergence of Independent Boards</i> . . .	212
	Notes and Questions . . . . .	215
§ 4.05	ACCREDITATION . . . . .	216
	<i>Accrediting Programs to Protect Participants in Human Research: The IOM Report</i> . . . . .	217
	Notes and Questions . . . . .	218
§ 4.06	IMPACT OF IRB REVIEW . . . . .	219
	<i>How Do We Know That Research Ethics Committees Are Really Working?</i> . . . . .	219
	Notes and Questions . . . . .	222
<b>Chapter 5</b>	<b>CONFLICTS OF INTEREST . . . . .</b>	<b>223</b>
§ 5.01	INVESTIGATOR CONFLICTS . . . . .	224
	<i>The Death of Jesse Gelsinger: New Evidence of the Influence of Money and Prestige in Human Research</i> . . . . .	225
	Notes and Questions . . . . .	231
	CONFLICTS OF INTEREST IN CLINICAL TRIAL RECRUITMENT & ENROLLMENT: A CALL FOR INCREASED OVERSIGHT . . . . .	233
	Notes and Questions . . . . .	237
§ 5.02	INSTITUTIONAL CONFLICTS . . . . .	241
	<i>Financial Conflicts of Interest in Human Subjects Research: The Problem of Institutional Conflicts</i> . . . . .	241
	PROTECTING SUBJECTS, PRESERVING INTEGRITY, ADVANCING HEALTH: ACCELERATING THE IMPLEMENTATION OF COI POLICIES IN HUMAN SUBJECTS RESEARCH . . . . .	243
	Notes and Questions . . . . .	245
§ 5.03	IRB CONFLICTS . . . . .	246
	<i>Members of the Same Club: Challenges and Decisions Faced by US IRBs in Identifying and Managing Conflicts of Interest</i> . . . . .	246
	Notes and Questions . . . . .	248
	Letter from Bernard A. Schwetz . . . . .	249
	Notes and Questions . . . . .	252
§ 5.04	MITIGATING CONFLICTS OF INTEREST . . . . .	252
	CONFLICT OF INTERESTS IN MEDICAL RESEARCH, EDUCATION, AND PRACTICE . . . . .	252
	Notes and Questions . . . . .	255

---

*Table of Contents*

§ 5.05	SHARING THE PROFITS FROM RESEARCH . . . . .	259
	<i>Moore v. Regents of the University of California</i> . . . . .	259
	Notes and Questions . . . . .	264
	<i>Greenberg v. Miami Children’s Hospital Research Inst.</i> . . . . .	266
	Notes and Questions . . . . .	268
<hr/>		
<b>Part II</b>	<b>REVIEWING RESEARCH PROPOSAL: GENERAL CONSIDERATIONS . . . . .</b>	<b>273</b>
<b>Chapter 6</b>	<b>RISK-BENEFIT ASSESSMENT . . . . .</b>	<b>275</b>
<hr/>		
§ 6.01	THE ROLE OF RISK-BENEFIT ASSESSMENT IN RESEARCH OVERSIGHT . . . . .	275
	Notes and Questions . . . . .	276
§ 6.02	IDENTIFYING RISKS . . . . .	277
[A]	The Concept of Risk . . . . .	277
	<i>Trust, Emotion, Sex, Politics, and Science: Surveying the Risk Assessment Battlefield</i> . . . . .	277
	Notes and Questions . . . . .	279
[B]	Risks to Research Subjects . . . . .	280
[1]	Introduction: A Typology of Research Risks . . . . .	280
	<i>Institutional Review Board Assessment of Risks and Benefits Associated with Research</i> . . . . .	280
	Notes and Questions . . . . .	282
[2]	Distinguishing the Risks of Research from the Risks of Interventions That Would Otherwise Be Performed . . . . .	283
	IRB GUIDEBOOK CHAPTER 3A . . . . .	284
	Notes and Questions . . . . .	284
[3]	The Concept of Clinical Equipoise . . . . .	285
	<i>Equipoise and the Ethics of Clinical Research</i> . . . . .	286
	Notes and Questions . . . . .	289
[4]	Clinical Equipoise and the Use of Placebo Controls . . . . .	291
	<i>What Makes Placebo-Controlled Trials Unethical?</i> . . . . .	291
	<i>Avoiding a Jekyll-and-Hyde Approach to the Ethic of Clinical Research and Practice</i> . . . . .	295
	Notes and Questions . . . . .	297
[C]	Risks to Others . . . . .	300
	NATIONAL BIOETHICS ADVISORY COMMISSION, 1 ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS . . . . .	300
	Notes and Questions . . . . .	301
[D]	“Minimal Risk” Research Under the Federal Regulations . . . . .	301

---

*Table of Contents*

	1 ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS . . . . .	302
	Notes and Questions . . . . .	303
[E]	Transparency as a Strategy for Managing Research Risks . . . . .	303
	Notes and Questions . . . . .	304
	<i>The Imperative to Share Clinical Study Reports: Recommendations from the Tamiflu Experience</i> . . . . .	305
	Notes and Questions . . . . .	308
§ 6.03	IDENTIFYING BENEFITS . . . . .	309
[A]	Potential Benefits to Research Subjects . . . . .	310
	ETHICS AND REGULATION OF CLINICAL RESEARCH . . . . .	310
	<i>Defining and Describing Benefit Appropriately in Clinical Trials</i> . . . . .	312
	Notes and Questions . . . . .	313
[B]	The Production of Knowledge as a Benefit of Research . . . . .	314
	<i>Institutional Review Board Assessment of Risks and Benefits Associated with Research</i> . . . . .	314
	Notes and Questions . . . . .	315
§ 6.04	BALANCING RISKS AND BENEFITS . . . . .	316
	ETHICAL PRINCIPLES AND GUIDELINES FOR THE PROTECTION OF HUMAN SUBJECTS OF RESEARCH (THE BELMONT REPORT) . . . . .	316
	<i>The Incommensurability of Research Risks and Benefits: Practical Help for Research Ethics Committees</i> . . . . .	317
	NATIONAL BIOETHICS ADVISORY COMMISSION, 1 ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS . . . . .	319
	Notes and Questions . . . . .	321
§ 6.05	MINIMIZING RISKS . . . . .	322
	SAFEGUARDING HEALTHY RESEARCH SUBJECTS: PROTECTING VOLUNTEERS FROM HARM . . . . .	323
	Notes and Questions . . . . .	323
<b>Chapter 7</b>	<b>INFORMED CONSENT . . . . .</b>	<b>325</b>
§ 7.01	FROM CONSENT TO MEDICAL CARE TO CONSENT TO RESEARCH . . . . .	325
[A]	Informed Consent to Medical Care . . . . .	325
	<i>Canterbury v. Spence</i> . . . . .	327
	Notes and Questions . . . . .	329
[B]	Informed Consent to Innovative Treatment . . . . .	330
	<i>Waived Consent for Emergency Research</i> . . . . .	331
	Notes and Questions . . . . .	332
[C]	Informed Consent to Research . . . . .	333

---

*Table of Contents*

	<i>Human Experimentation and Human Rights</i> . . . . .	333
	Notes and Questions . . . . .	335
	Notes and Questions . . . . .	337
§ 7.02	FEDERAL REGULATIONS GOVERNING INFORMED CONSENT TO RESEARCH . . . . .	338
[A]	General Requirements . . . . .	338
	Notes and Questions . . . . .	338
[B]	Waivers and Alterations of the Usual Requirements . . . . .	340
	Veterans Administration, Office of Research Oversight, Bi-Monthly Teleconference . . . . .	340
	Notes and Questions . . . . .	340
	Notes and Questions . . . . .	342
§ 7.03	IMPLEMENTING THE FEDERAL REGULATIONS . . . . .	344
[A]	The Consent Form . . . . .	344
	PHASE 2 CONSENT FORM EXAMPLE NATIONAL CANCER INSTITUTE . . . . .	344
	Notes and Questions . . . . .	348
	<i>The Hidden Alternative: Getting Investigational Treatments Off-Study</i> . . . . .	351
	Notes and Questions . . . . .	353
	<i>Defining and Describing Benefit Appropriately in Clinical Trials</i> . . . .	355
	Notes and Questions . . . . .	357
	LETTER FROM OHRP TO UNIVERSITY OF ALABAMA REGARDING THE SUPPORT STUDY . . . . .	359
	Notes and Questions . . . . .	363
[B]	Informed Consent as a Process . . . . .	368
	RESPONSIBLE RESEARCH: A SYSTEMS APPROACH TO PROTECTING RESEARCH PARTICIPANTS . . . . .	368
	MORAL SCIENCE: PROTECTING PARTICIPANTS IN HUMAN SUBJECTS RESEARCH . . . . .	371
	Notes and Questions . . . . .	371
	<i>Remaining Faithful to the Promises Given: Maintaining Standards in Changing Times</i> . . . . .	372
	RESPONSIBLE RESEARCH: A SYSTEMS APPROACH TO PROTECTING RESEARCH PARTICIPANTS . . . . .	373
	Notes and Questions . . . . .	374
[C]	An Informed Consent Script . . . . .	375
	AN INFORMED CONSENT SCRIPT FOR ADOLESCENT TRIALS NETWORK (ATN) 105 . . . . .	375
	Notes and Questions . . . . .	378
§ 7.04	DEFICIENCIES IN THE INFORMED CONSENT PROCESS . . . . .	378



---

*Table of Contents*

[A]	The Therapeutic Misconception . . . . .	378
	<i>False Hopes and Best Data: Consent to Research and the Therapeutic Misconception</i> . . . . .	378
	Final Report Advisory Committee on Human Radiation Experiments (ACHRE) . . . . .	381
	<i>The Ubiquity and Utility of the Therapeutic Misconception</i> . . . . .	382
	Notes and Questions . . . . .	384
[B]	Failure to Convey Information . . . . .	386
	<i>Family's Debate Mirrored Scientists' on Gene Therapy Risk</i> . . . . .	386
	Notes and Questions . . . . .	387
[C]	Cultural and Gender-Based Barriers to Informed Consent . . . . .	389
	<i>Ethnicity and Attitudes Toward Patient Autonomy</i> . . . . .	389
	Notes and Questions . . . . .	389
	<i>Gender Matters: Implications for Clinical Research and Women's Health Care</i> . . . . .	390
	Notes and Questions . . . . .	391
<b>Chapter 8</b>	<b>RECRUITING AND PAYING SUBJECTS . . . . .</b>	<b>393</b>
§ 8.01	RECRUITING SUBJECTS . . . . .	393
[A]	Regulatory Views of the Issues . . . . .	393
[1]	The OIG . . . . .	393
	RECRUITING HUMAN SUBJECTS: PRESSURES IN INDUSTRY SPONSORED CLINICAL RESEARCH . . . . .	393
	Notes and Questions . . . . .	397
[2]	The FDA . . . . .	401
	INFORMATION SHEETS: GUIDANCE FOR INSTITUTIONAL REVIEW BOARDS AND CLINICAL INVESTIGATORS, RECRUITING STUDY SUBJECTS . . . . .	401
	Notes and Questions . . . . .	403
[3]	Office for Protection from Research Risks (OPRR) [a precursor to the Office for Human Research Protections] . . . . .	404
	INSTITUTIONAL REVIEW BOARD GUIDEBOOK, CHAPTER 3. BASIC IRB REVIEW — SECTION C. SELECTION OF SUBJECTS . . . . .	404
	Notes and Questions . . . . .	406
	Office for Human Research Protections (OHRP) Guidance on Institutional Review Board Review of Clinical Trial Websites . . . . .	407
	Notes and Questions . . . . .	410
[B]	Institutional Policies . . . . .	413
	ADVERTISEMENT POLICY . . . . .	413
	Notes and Questions . . . . .	414

---

*Table of Contents*

[C]	Recruiting Normal Healthy Subjects . . . . .	416
	SAFEGUARDING HEALTH RESEARCH SUBJECTS: PROTECTING	
	VOLUNTEERS FROM HARM . . . . .	416
	INSTITUTIONAL REVIEW BOARD GUIDEBOOK, <i>Chapter 6, Special</i>	
	<i>Classes of Subjects — Section J.</i> . . . . .	417
	Notes and Questions . . . . .	418
[D]	Soliciting Students or Employees of Researchers . . . . .	420
	INSTITUTIONAL REVIEW BOARD GUIDEBOOK, <i>Chapter 6, Special</i>	
	<i>Classes of Subjects — Section J. Students, Employees and</i>	
	<i>Normal Volunteers</i> . . . . .	420
	Notes and Questions . . . . .	422
§ 8.02	PAYING SUBJECTS . . . . .	424
[A]	Agency Guidance . . . . .	424
[1]	FDA . . . . .	425
	INFORMATION SHEETS: GUIDANCE FOR INSTITUTIONAL REVIEW	
	BOARDS AND CLINICAL INVESTIGATORS, <i>Payment to Research</i>	
	<i>Subjects</i> . . . . .	425
	Notes and Questions . . . . .	425
[2]	OHRP . . . . .	426
	INSTITUTIONAL REVIEW BOARD GUIDEBOOK, <i>Chapter 3, Basic IRB</i>	
	<i>Review — Section G. Incentives for Participation</i> . . . . .	426
	FREQUENTLY ASKED QUESTIONS ABOUT HUMAN RESEARCH	
	INFORMED CONSENT . . . . .	428
	Notes and Questions . . . . .	429
[B]	Determining an Appropriate Level of Payment . . . . .	433
	Notes and Questions . . . . .	435
[C]	Structuring Payments . . . . .	436
	GUIDELINES FOR COMPENSATION OF RESEARCH SUBJECTS . . . . .	437
	Notes and Questions . . . . .	438
<b>Chapter 9</b>	<b>RESEARCH AND JUSTICE: PROMOTING THE</b>	
	<b>INCLUSION OF WOMEN AND MINORITIES . . . . .</b>	<b>441</b>
§ 9.01	THE CONCEPT OF JUSTICE IN RESEARCH WITH HUMAN	
	SUBJECTS . . . . .	441
	THE BELMONT REPORT NATIONAL COMMISSION FOR THE PROTECTION	
	OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH . . .	441
	45 CFR § 46.111(a)(3):CRITERIA FOR IRB APPROVAL OF RESEARCH . . .	443
	INSTITUTIONAL REVIEW BOARD GUIDEBOOK, <i>Chapter 3, Basic IRB</i>	
	<i>Review — Section C. Selection of Subjects</i> . . . . .	444
	Notes and Questions . . . . .	446

---

*Table of Contents*

§ 9.02	JUSTICE AND WOMEN	447
[A]	FDA Policy Prior to 1993	447
	Notes and Questions	448
	<i>Wanted: Single, White Male for Medical Research</i>	448
	Notes and Questions	455
[B]	1993 Revisions to FDA Policies	456
	Notes and Questions	459
[C]	1998 FDA Rule on New Drug Applications (NDAs)	459
[D]	Current NIH Guidelines	461
	<i>NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research</i>	461
	Notes and Questions	465
[E]	Evaluation of Sex Differences in Medical Device Clinical Studies	468
[F]	Research with Pregnant Women	469
	<i>Justice in Health Research: Beyond Protection from Risks</i>	470
§ 9.03	JUSTICE AND RACIAL AND ETHNIC MINORITIES	471
[A]	Early OPRR Statement	472
	INSTITUTIONAL REVIEW BOARD GUIDEBOOK, <i>Chapter 6, Special Classes of Subjects — Section I. Minorities</i>	472
[B]	Early NIH Statement	474
	<i>NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research</i>	474
[C]	Current NIH Guidelines	475
	<i>NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research National Institutes of Health</i>	475
	Notes and Questions	476
<b>Chapter 10</b>	<b>CONFIDENTIALITY</b>	<b>487</b>
§ 10.01	OVERVIEW OF MEDICAL CONFIDENTIALITY	487
[A]	Confidentiality as an Ethical Principle	487
	PRINCIPLES OF BIOMEDICAL ETHICS	487
[B]	Legal Sources of Medical Confidentiality	489
[1]	State Laws	489
	INFORMATION PRIVACY LAW	489
	Notes and Questions	490
[2]	Federal Law	491
§ 10.02	CONFIDENTIALITY ISSUES IN RESEARCH	492
[A]	Maintaining the Confidentiality of Research Data	492
[1]	General Issues	492
	IRB GUIDEBOOK, <i>Chapter 3D</i>	492

---

*Table of Contents*

	Notes and Questions . . . . .	494
[2]	Certificates of Confidentiality . . . . .	496
	UNITED STATES CODE, TITLE 42, PUBLIC HEALTH AND WELFARE	
	SECTION 6A: THE PUBLIC HEALTH SERVICE, GENERAL POWERS	
	AND DUTIES 42 U.S.C. § 241(D): RESEARCH AND	
	INVESTIGATIONS GENERALLY . . . . .	496
	CERTIFICATES OF CONFIDENTIALITY: BACKGROUND	
	INFORMATION . . . . .	497
	Notes and Questions . . . . .	498
[B]	Overseeing the Use and Disclosure of Medical Records . . . . .	499
[1]	Human Subject Protection Regulations . . . . .	499
	IRB GUIDEBOOK <i>Chapter 3D</i> . . . . .	499
	Notes and Questions . . . . .	501
[2]	HIPAA Regulations . . . . .	502
	Notes and Questions . . . . .	504
<b>Chapter 11            MONITORING OF ONGOING RESEARCH . . . . .</b>		<b>509</b>
§ 11.01	CONTINUING REVIEW . . . . .	509
	GUIDANCE ON IRB CONTINUING REVIEW OF RESEARCH . . . . .	509
	Notes and Questions . . . . .	513
§ 11.02	ADVERSE EVENT REPORTING . . . . .	515
	GUIDANCE FOR INDUSTRY AND INVESTIGATORS SAFETY REPORTING	
	REQUIREMENTS FOR INDS AND BA/BE STUDIES . . . . .	516
	GUIDANCE FOR CLINICAL INVESTIGATORS, SPONSORS, AND IRBS:	
	ADVERSE EVENT REPORTING TO IRBS — IMPROVING HUMAN	
	SUBJECT PROTECTION . . . . .	519
	<i>IRB Review of Adverse Events in Investigational Drug Studies</i> . . . . .	522
	Notes and Questions . . . . .	523
§ 11.03	DATA AND SAFETY MONITORING BOARDS . . . . .	525
	GUIDELINES ON DATA SAFETY MONITORING FOR HUMAN	
	SUBJECTS RESEARCH . . . . .	525
	<i>Ethical Issues Arising When Interim Data in Clinical Trials Is</i>	
	<i>Restricted to Independent Data Monitoring Committees</i> . . . . .	529
	Notes and Questions . . . . .	531
	NBCC RAISES CONCERNS ABOUT HALTING OF LETROZOLE CLINICAL	
	TRIAL . . . . .	532
	Notes and Questions . . . . .	533
§ 11.04	A RISK-BASED APPROACH TO MONITORING . . . . .	535
	GUIDANCE FOR INDUSTRY OVERSIGHT OF CLINICAL INVESTIGATIONS —	
	A RISK-BASED APPROACH TO MONITORING . . . . .	535

---

*Table of Contents*

	Notes and Questions .....	538
<b>Chapter 12</b>	<b>COMPENSATION FOR RESEARCH INJURIES .....</b>	<b>539</b>
§ 12.01	ETHICAL CONSIDERATIONS .....	539
	COMPENSATION FOR RESEARCH INJURIES .....	539
	Notes and Questions .....	545
	MORAL SCIENCE: PROTECTING PARTICIPANTS IN HUMAN SUBJECTS	
	RESEARCH PRESIDENTIAL COMMISSION FOR THE STUDY OF	
	BIOETHICAL ISSUES .....	546
	Notes and Questions .....	553
§ 12.02	THE REGULATORY FRAMEWORK .....	554
	<i>Research-Related Injury Compensation Policies of U.S. Research</i>	
	<i>Institutions</i> .....	554
	Notes and Questions .....	556
§ 12.03	TORT LIABILITY .....	558
[A]	The Emerging Role of Tort Litigation in Human Subject Research .....	558
	<i>The Rise of Litigation in Human Subjects Research</i> .....	558
	Notes and Questions .....	559
[B]	Defining Researchers' Duties to Subjects .....	562
	<i>Duties to Subjects in Clinical Research</i> .....	562
	Notes and Questions .....	567
[C]	Additional Issues in Informed Consent Cases .....	570
	<i>Medical Research Litigation and Malpractice Tort Doctrines: Courts</i>	
	<i>on a Learning Curve</i> .....	570
	Notes and Questions .....	576
§ 12.04	NO-FAULT COMPENSATION .....	577
[A]	Voluntary No-Fault Compensation Schemes .....	579
	HUMAN SUBJECTS ASSISTANCE PROGRAM .....	579
	Notes and Questions .....	580
[B]	Proposals for Comprehensive No-Fault Compensation Systems .....	580
	RESPONSIBLE RESEARCH: A SYSTEMS APPROACH TO PROTECTING	
	RESEARCH PARTICIPANTS .....	580
	Notes and Questions .....	581
<b>Part III</b>	<b>REVIEWING RESEARCH PROPOSALS: SPECIAL SITUATIONS ..</b>	<b>585</b>
<b>Chapter 13</b>	<b>RESEARCH WITH CHILDREN .....</b>	<b>587</b>
§ 13.01	RESEARCH WITH CHILDREN: PAST AND PRESENT .....	587
	<i>Research with Children</i> .....	587
	<i>Speed, Safety, and Dignity: Pediatric Pharmaceutical Development</i>	

---

*Table of Contents*

	<i>in an Age of Optimism</i> . . . . .	589
	Notes and Questions . . . . .	589
§ 13.02	THE REGULATORY FRAMEWORK . . . . .	593
[A]	Decision-Making Authority of Parents and Children . . . . .	593
[1]	Parental Authority: Permission and Refusal . . . . .	593
	<i>Speed, Safety, and Dignity: Pediatric Pharmaceutical Development</i> <i>in an Age of Optimism</i> . . . . .	593
	Notes and Questions . . . . .	595
[2]	Soliciting a Minor’s Assent . . . . .	597
	<i>Informed Consent, Parental Permission, and Assent in Pediatric</i> <i>Practice</i> . . . . .	597
	Notes and Questions . . . . .	597
[3]	Allocating Decision-Making Authority in Research with Adolescents . . . . .	598
	<i>Guidelines for Adolescent Health Research: A Position Paper</i> <i>of the Society for Adolescent Medicine</i> . . . . .	598
	Notes and Questions . . . . .	599
[B]	Categories of Permissible Risks . . . . .	600
[1]	General Principles . . . . .	600
	<i>American Academy of Pediatrics Statement Before the Institute of</i> <i>Medicine Committee on Clinical Research Involving Children:</i> <i>Participation and Protection of Children in Clinical Research</i> . . . . .	601
	Notes and Questions . . . . .	601
	Notes and Questions . . . . .	603
	<i>American Academy of Pediatrics Statement Before the Institute of</i> <i>Medicine Committee on Clinical Research Involving Children:</i> <i>Participation and Protection of Children in Clinical Research</i> . . . . .	605
	Notes and Questions . . . . .	606
[2]	Applying the Standards: The Fenfluramine Studies . . . . .	607
	<i>Research with Children</i> . . . . .	607
	Notes and Questions . . . . .	609
[C]	DHHS Review of Research Not Otherwise Approvable . . . . .	610
[1]	Cystic Fibrosis in Neonates . . . . .	611
	APPLICATION FOR APPROVAL OF RESEARCH INVOLVING HUMAN SUBJECTS: CHARACTERIZATION OF MUCUS AND MUCINS IN BRONCHOALVEOLAR LAVAGE FLUIDS FROM INFANTS WITH CYSTIC FIBROSIS . . . . .	611
	Notes and Questions . . . . .	615
[2]	Smallpox Vaccination in Young Children . . . . .	616
	A MULTICENTER, RANDOMIZED DOSE RESPONSE STUDY OF THE	

---

*Table of Contents*

	SAFETY .....	616
	Notes and Questions .....	620
§ 13.03	PEDIATRIC RESEARCH IN THE COURTS: THE KENNEDY KRIEGER CASE .....	622
	<i>Grimes v. Kennedy Krieger Institute, Inc.</i> .....	622
	Notes and Questions .....	633
<b>Chapter 14</b>	<b>ADULTS WHO LACK DECISION-MAKING CAPACITY .....</b>	<b>639</b>
§ 14.01	THE APPROPRIATENESS OF CONDUCTING RESEARCH WITH ADULTS WHO LACK DECISION-MAKING CAPACITY .....	640
	REPORT AND RECOMMENDATIONS: RESEARCH INVOLVING THOSE INSTITUTIONALIZED AS MENTALLY INFIRM .....	640
	1 RESEARCH INVOLVING PERSONS WITH MENTAL DISORDERS THAT MAY AFFECT DECISIONMAKING CAPACITY: REPORT AND RECOMMENDATIONS .....	642
	REPORT AND RECOMMENDATIONS FOR RESEARCH WITH HUMAN SUBJECTS WHO LACK CONSENT CAPACITY .....	643
	Notes and Questions .....	644
§ 14.02	DETERMINING WHETHER SUBJECTS LACK DECISION-MAKING CAPACITY .....	646
[A]	Defining Decision-Making Capacity .....	646
	<i>Assessing Decision-Making Capacity</i> .....	646
	REPORT AND RECOMMENDATIONS FOR RESEARCH WITH HUMAN SUBJECTS WHO LACK CONSENT CAPACITY .....	646
	<i>Probing Informed Consent in Schizophrenia Research</i> .....	647
	Notes and Questions .....	648
[B]	Assessing Decision-Making Capacity .....	650
	1 RESEARCH INVOLVING PERSONS WITH MENTAL DISORDERS THAT MAY AFFECT DECISIONMAKING CAPACITY: REPORT AND RECOMMENDATIONS .....	650
	Notes and Questions .....	651
§ 14.03	INFORMED CONSENT .....	653
[A]	Surrogate Decision Making .....	653
	1 RESEARCH INVOLVING PERSONS WITH MENTAL DISORDERS THAT MAY AFFECT DECISIONMAKING CAPACITY .....	654
	Notes and Questions .....	657
	Notes and Questions .....	660
[B]	Research Living Wills .....	662
	<i>Mentally Disabled Research Subjects: The Enduring Policy Issues</i> ...	662
	1 RESEARCH INVOLVING PERSONS WITH MENTAL DISORDERS	

---

*Table of Contents*

	THAT MAY AFFECT DECISIONMAKING CAPACITY . . . . .	662
	Notes and Questions . . . . .	662
[C]	Subject Assent and Refusal . . . . .	663
	REPORT AND RECOMMENDATIONS: RESEARCH INVOLVING THOSE	
	INSTITUTIONALIZED AS MENTALLY INFIRM . . . . .	663
	Notes and Questions . . . . .	664
[D]	Waiver of Informed Consent in Emergency Research . . . . .	665
	<i>Critical Care Research and Informed Consent</i> . . . . .	665
	REPORT: INFORMED CONSENT REQUIREMENTS IN EMERGENCY	
	RESEARCH . . . . .	668
	Notes and Questions . . . . .	670
§ 14.04	LIMITATIONS ON PERMISSIBLE RISKS . . . . .	674
	1 RESEARCH INVOLVING PERSONS WITH MENTAL DISORDERS	
	THAT MAY AFFECT DECISIONMAKING CAPACITY . . . . .	675
	<i>Regulating Research with Decisionally Impaired Individuals: Are We</i>	
	<i>Making Progress?</i> . . . . .	678
	Notes and Questions . . . . .	679
§ 14.05	CONSTITUTIONAL CONSIDERATIONS . . . . .	682
	<i>T.D. v. New York State Office of Mental Health</i> . . . . .	682
	Notes and Questions . . . . .	687
<b>Chapter 15</b>	<b>PRISONERS . . . . .</b>	<b>691</b>
§ 15.01	GENERAL CONSIDERATIONS . . . . .	691
[A]	Health Status and Health Care in Prisons . . . . .	691
	<i>On Research on HIV Infection and AIDS in Correctional</i>	
	<i>Institutions</i> . . . . .	691
	<i>Prevention and Control of Infection with Hepatitis</i>	
	<i>Viruses in Correctional Settings</i> . . . . .	692
	<i>The Health and Health Care of U.S. Prisoners: Results of a</i>	
	<i>Nationwide Survey</i> . . . . .	692
	<i>Mental Health Problems of Prison and Jail Inmates Bureau of</i>	
	<i>Justice Statistics, Special Report</i> . . . . .	694
	Notes and Questions . . . . .	696
[B]	History of Medical Research in Prisons . . . . .	700
	<i>Beneficial and Unusual Punishment: An Argument in Support of</i>	
	<i>Prisoner Participation in Clinical Trials</i> . . . . .	700
	<i>Bailey v. Lally</i> . . . . .	702
	Notes and Questions . . . . .	706
§ 15.02	FEDERAL REGULATION OF PRISON RESEARCH . . . . .	707
[A]	Overview of Subpart C . . . . .	707



---

*Table of Contents*

	Notes and Questions . . . . .	707
[B]	SACHRP Subcommittee on Subpart C . . . . .	709
	LETTER FROM ERNEST D. PRENTICE, PH.D., CHAIR, SACHRP, TO THE HONORABLE MICHAEL O. LEVITT . . . . .	709
	Notes and Questions . . . . .	710
[C]	Institute of Medicine Report on Ethical Considerations for Research Involving Prisoners . . . . .	711
	ETHICAL CONSIDERATIONS FOR RESEARCH INVOLVING PRISONERS . . .	711
	Notes and Questions . . . . .	714
§ 15.03	THE SHIFT FROM PROTECTION TO ACCESS . . . . .	716
	<i>On Research on HIV Infection and AIDS in Correctional Institutions</i> . . .	716
	Notes and Questions . . . . .	717
§ 15.04	RESEARCH WITH INCARCERATED CHILDREN . . . . .	718
	<i>Prevention and Control of Infections with Hepatitis Viruses in Correctional Settings</i> . . . . .	718
	<i>Biomedical and Behavioral Research on Juvenile Inmates: Uninformed Choices and Coerced Participation</i> . . . . .	719
	Notes and Questions . . . . .	720
<b>Chapter 16 MEMBERS OF THE ARMED SERVICES . . . . .</b>		<b>723</b>
§ 16.01	HISTORY OF RESEARCH INVOLVING SERVICE MEMBERS . . . . .	723
	<i>Justice and Beneficence in Military Medicine and Research</i> . . . . .	723
	Notes and Questions . . . . .	727
§ 16.02	MEDICAL RESEARCH AND THE MODERN WARFIGHTER . . . . .	729
	<i>Informed Consent and Ethical Issues in Military Medical Research</i> . . . .	729
	<i>Neuroscience, Ethics, and National Security: The State of the Art</i> . . . . .	731
	<i>Enhanced Warfighters: Risk, Ethics, and Policy</i> . . . . .	732
	Notes and Questions . . . . .	737
§ 16.03	MILITARY LAW . . . . .	737
	<i>Perry v. Wesely</i> . . . . .	738
	<i>United States v. Washington</i> . . . . .	739
	<i>Doe v. Rumsfeld</i> . . . . .	740
	Notes and Questions . . . . .	742
§ 16.04	SOVEREIGN IMMUNITY AND MILITARY RESEARCH . . . . .	744
	<i>United States v. Stanley</i> . . . . .	744
	Notes and Questions . . . . .	750
<b>Chapter 17 FETUSES AND EMBRYOS . . . . .</b>		<b>751</b>
§ 17.01	FETAL RESEARCH . . . . .	751
[A]	Research on Fetuses in Utero . . . . .	751

---

*Table of Contents*

	Notes and Questions . . . . .	752
[B]	Research on Tissue from Aborted Fetuses . . . . .	753
[1]	Federal Law . . . . .	754
	Notes and Questions . . . . .	754
[2]	State Law . . . . .	754
	<i>Forbes v. Napolitano</i> . . . . .	755
	Notes and Questions . . . . .	757
§ 17.02	EMBRYO AND EMBRYONIC STEM CELL RESEARCH . . . . .	757
[A]	Perspectives on Embryo and Embryonic Stem Cell Research . . . . .	758
	<i>Testimony on Behalf of the Juvenile Diabetes Research Foundation</i> <i>International Regarding Federal Support of Juvenile Diabetes</i> <i>Research Before the Senate Permanent Subcommittee on</i> <i>Investigations</i> . . . . .	758
	<i>Instruction on Respect for Human Life in Its Origins and on the</i> <i>Dignity of Procreation</i> . . . . .	759
	REPORT OF THE HUMAN EMBRYO RESEARCH PANEL . . . . .	761
	Notes and Questions . . . . .	763
	<i>Respecting What We Destroy: Reflections on Human Embryo</i> <i>Research</i> . . . . .	764
	Notes and Questions . . . . .	767
[B]	Federal Law and Policy . . . . .	768
[1]	General Federal Policy on Embryo Research . . . . .	768
	ASSISTED REPRODUCTIVE TECHNOLOGIES: ANALYSIS AND RECOMMENDATIONS FOR PUBLIC POLICY NEW YORK STATE TASK FORCE ON LIFE AND THE LAW . . . . .	768
	Notes and Questions . . . . .	770
[2]	Application of Federal Embryo Research Policies to Research on Embryonic Stem Cells . . . . .	771
	<i>Sherley v. Sebelius</i> . . . . .	773
	Notes and Questions . . . . .	775
[C]	State Law and Policy . . . . .	776
	Notes and Questions . . . . .	776
[D]	Consent to Embryo and Embryonic Stem Cell Research . . . . .	777
	<i>Donating Embryos for Human Embryonic Stem-Cell (hESC)</i> <i>Research: A Committee Opinion</i> . . . . .	777
	NATIONAL INSTITUTES OF HEALTH GUIDELINES FOR RESEARCH USING HUMAN STEM CELLS . . . . .	779
	Notes and Questions . . . . .	781
§ 17.03	CLONING . . . . .	783
[A]	What Is Cloning? . . . . .	783

---

*Table of Contents*

	FREQUENTLY ASKED QUESTIONS ABOUT HUMAN CLONING AND THE COUNCIL’S REPORT, “HUMAN CLONING AND HUMAN DIGNITY: AN ETHICAL INQUIRY” . . . . .	783
	Notes and Questions . . . . .	784
[B]	Perspectives on Cloning . . . . .	784
	FREQUENTLY ASKED QUESTIONS ABOUT HUMAN CLONING AND THE COUNCIL’S REPORT, “HUMAN CLONING AND HUMAN DIGNITY: AN ETHICAL INQUIRY” . . . . .	784
	<i>Cloning, Ethics, and Religion</i> . . . . .	786
	Notes and Questions . . . . .	789
[C]	Federal Law . . . . .	789
	Notes and Questions . . . . .	790
[D]	State Law . . . . .	791
	Notes and Questions . . . . .	791
	STATEMENT OF THE EMPIRE STATE STEM CELL BOARD ON THE COMPENSATION OF OOCYTE DONORS . . . . .	792
	Notes and Questions . . . . .	793
<b>Chapter 18</b>	<b>RESEARCH INVOLVING EMERGING TECHNOLOGIES . . . . .</b>	<b>795</b>
§ 18.01	GENETICS RESEARCH . . . . .	795
[A]	The Regulatory Framework . . . . .	796
	GUIDANCE ON RESEARCH INVOLVING CODED PRIVATE INFORMATION OR BIOLOGICAL SPECIMENS . . . . .	796
	GUIDANCE ON THE GENETIC INFORMATION NONDISCRIMINATION ACT: IMPLICATIONS FOR INVESTIGATORS AND INSTITUTIONAL REVIEW BOARDS . . . . .	801
	Notes and Questions . . . . .	804
[B]	Ethical, Legal, and Societal Implications . . . . .	806
	GENETIC TESTING AND SCREENING IN THE AGE OF GENOMIC MEDICINE . . . . .	806
	<i>What Research Ethics Should Learn from Genomics and Society Research: Lessons from the ELSI Congress of 2011</i> . . . . .	808
	Notes and Questions . . . . .	814
[C]	Gene Transfer Research . . . . .	816
	<i>RAC Oversight of Gene Transfer Research: A Model Worth Extending?</i> . . . . .	817
	Notes and Questions . . . . .	819
[D]	Genetic Research in the Courts . . . . .	821
	<i>Havasupai Tribe v. Arizona Bd. of Regents</i> . . . . .	821

---

*Table of Contents*

	Notes and Questions . . . . .	822
	<i>Ande v. Rock</i> . . . . .	823
	Notes and Questions . . . . .	826
§ 18.02	NANOTECHNOLOGY RESEARCH . . . . .	826
[A]	Regulating “Known Unknowns” . . . . .	827
	<i>Nanotechnology: The Challenge of Regulating Known Unknowns</i> . . . . .	827
[B]	Policy Principles . . . . .	830
	<i>Policy Principles for the U.S. Decision-Making Concerning Regulation and Oversight of Applications of Nanotechnology and Nanomaterials</i> . . . . .	830
[C]	Regulatory Preparedness . . . . .	835
	<i>Expert Views on Regulatory Preparedness for Managing Risks of Nanotechnologies</i> . . . . .	835
	Notes and Questions . . . . .	837
§ 18.03	NEUROSCIENCE RESEARCH . . . . .	838
[A]	Ethical, Legal, and Societal Implications . . . . .	839
	<i>Neuroethics: The Ethical, Legal, and Societal Impact of Neuroscience</i> . . . . .	839
[B]	Innovation and Regulatory Safeguards . . . . .	840
	<i>Reducing Barriers to Ethics in Neuroscience</i> . . . . .	840
	Notes and Questions . . . . .	843
<b>Chapter 19</b>	<b>INTERNATIONAL RESEARCH . . . . .</b>	<b>845</b>
§ 19.01	THE GLOBALIZATION OF MEDICAL RESEARCH . . . . .	845
	<i>Ethical and Scientific Implications of the Globalization of Clinical Research</i> . . . . .	845
	Notes and Questions . . . . .	856
§ 19.02	KEY ETHICAL ISSUES IN INTERNATIONAL RESEARCH . . . . .	857
[A]	Choice of Control Groups and the Standard of Care . . . . .	858
	PLACEBOS: A RECENT ETHICAL CONTROVERSY IN INTERNATIONAL RESEARCH . . . . .	858
	INTERNATIONAL ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS . . . . .	860
	Notes and Questions . . . . .	862
[B]	Benefits to Research Participants and Communities . . . . .	864
	DECLARATION OF HELSINKI: ETHICAL PRINCIPLES FOR RESEARCH INVOLVING HUMAN SUBJECTS . . . . .	864
	INTERNATIONAL ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS . . . . .	864
	<i>Addressing Exploitation: Reasonable Availability Versus Fair</i>	

---

*Table of Contents*

	<i>Benefits</i> . . . . .	865
	Notes and Questions . . . . .	870
[C]	Informed Consent and Voluntariness . . . . .	872
	<i>Voluntary Informed Consent</i> . . . . .	872
	Notes and Questions . . . . .	881
[D]	Local Ethics Review . . . . .	883
	<i>The Structure and Function of Research Ethics Committees in Africa: A Case Study</i> . . . . .	883
	Notes and Questions . . . . .	887
§ 19.03	THE U.S. REGULATORY FRAMEWORK . . . . .	888
[A]	The Common Rule . . . . .	888
	REPORT OF THE EQUIVALENT PROTECTIONS WORKING GROUP . . . . .	889
	Notes and Questions . . . . .	890
[B]	Food and Drug Administration Regulations . . . . .	891
	Notes and Questions . . . . .	893
§ 19.04	SELECTED FOREIGN REGULATORY FRAMEWORKS . . . . .	894
[A]	The European Union . . . . .	895
	THE NEW EU CLINICAL TRIALS REGULATION: HOW NHS RESEARCH AND PATIENTS WILL BENEFIT . . . . .	896
	Notes and Questions . . . . .	899
[B]	India . . . . .	900
	ORDER DIRECTORATE GENERAL OF HEALTH SERVICES . . . . .	901
	Notes and Questions . . . . .	902
[C]	Africa . . . . .	903
	<i>Ethical and Legal Constraints to Children’s Participation in Research in Zimbabwe: Experiences from the Multicenter Pediatric HIV ARROW Trial</i> . . . . .	903
	Notes and Questions . . . . .	907
§ 19.05	INTERNATIONAL LAW . . . . .	908
	<i>Abdullahi et al. v. Pfizer, Inc.</i> . . . . .	908
	Notes and Questions . . . . .	919

**Appendix A            U.S. CODE OF FEDERAL REGULATIONS  
                                  TITLE 45 — PUBLIC WELFARE AND HUMAN  
                                  SERVICES PART 46 — PROTECTION OF  
                                  HUMAN SUBJECTS . . . . . 921**

---

Subpart A	— Basic HHS Policy for Protection of Human Research Subjects . . . . .	921
§ 46.101	TO WHAT DOES THIS POLICY APPLY? . . . . .	921
§ 46.102	DEFINITIONS. . . . .	923
§ 46.103	ASSURING COMPLIANCE WITH THIS POLICY — RESEARCH CONDUCTED OR SUPPORTED BY ANY FEDERAL DEPARTMENT	

---

*Table of Contents*

OR AGENCY. . . . .	924
§§ 46.104–46.106 [Reserved] . . . . .	926
§ 46.107 IRB MEMBERSHIP. . . . .	926
§ 46.108 IRB FUNCTIONS AND OPERATIONS. . . . .	927
§ 46.109 IRB REVIEW OF RESEARCH. . . . .	927
§ 46.110 EXPEDITED REVIEW PROCEDURES FOR CERTAIN KINDS OF RESEARCH INVOLVING NO MORE THAN MINIMAL RISK, AND FOR MINOR CHANGES IN APPROVED RESEARCH. . . . .	928
§ 46.111 CRITERIA FOR IRB APPROVAL OF RESEARCH. . . . .	929
§ 46.112 REVIEW BY INSTITUTION. . . . .	929
§ 46.113 SUSPENSION OR TERMINATION OF IRB APPROVAL OF RESEARCH. . . . .	930
§ 46.114 COOPERATIVE RESEARCH. . . . .	930
§ 46.115 IRB RECORDS. . . . .	930
§ 46.116 GENERAL REQUIREMENTS FOR INFORMED CONSENT. . . . .	931
§ 46.117 DOCUMENTATION OF INFORMED CONSENT. . . . .	933
§ 46.118 APPLICATIONS AND PROPOSALS LACKING DEFINITE PLANS FOR INVOLVEMENT OF HUMAN SUBJECTS . . . . .	933
§ 46.119 RESEARCH UNDERTAKEN WITHOUT THE INTENTION OF INVOLVING HUMAN SUBJECTS. . . . .	934
§ 46.120 EVALUATION AND DISPOSITION OF APPLICATIONS AND PROPOSALS FOR RESEARCH TO BE CONDUCTED OR SUPPORTED BY A FEDERAL DEPARTMENT OR AGENCY . . . . .	934
§ 46.121 [Reserved] . . . . .	934
§ 46.122 USE OF FEDERAL FUNDS. . . . .	934
§ 46.123 EARLY TERMINATION OF RESEARCH SUPPORT: EVALUATION OF APPLICATIONS AND PROPOSALS. . . . .	934
§ 46.124 CONDITIONS. . . . .	935
Subpart B — Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research . . . . .	935
§ 46.201 TO WHAT DO THESE REGULATIONS APPLY? . . . . .	935
§ 46.202 DEFINITIONS. . . . .	935
§ 46.203 DUTIES OF IRBS IN CONNECTION WITH RESEARCH INVOLVING PREGNANT WOMEN, FETUSES, AND NEONATES. . . . .	936
§ 46.204 RESEARCH INVOLVING PREGNANT WOMEN OR FETUSES. . . . .	936
§ 46.205 RESEARCH INVOLVING NEONATES. . . . .	937
§ 46.206 RESEARCH INVOLVING, AFTER DELIVERY, THE PLACENTA, THE DEAD FETUS OR FETAL MATERIAL. . . . .	938
§ 46.207 RESEARCH NOT OTHERWISE APPROVABLE WHICH PRESENTS AN OPPORTUNITY TO UNDERSTAND, PREVENT, OR ALLEVIATE A SERIOUS PROBLEM AFFECTING THE HEALTH OR WELFARE OF PREGNANT WOMEN, FETUSES, OR NEONATES. . . . .	938

---

*Table of Contents*

Subpart C — Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects . . . . .	939
§ 46.301 APPLICABILITY. . . . .	939
§ 46.302 PURPOSE. . . . .	939
§ 46.303 DEFINITIONS. . . . .	939
§ 46.304 COMPOSITION OF INSTITUTIONAL REVIEW BOARDS WHERE PRISONERS ARE INVOLVED. . . . .	940
§ 46.305 ADDITIONAL DUTIES OF THE INSTITUTIONAL REVIEW BOARDS WHERE PRISONERS ARE INVOLVED. . . . .	940
§ 46.306 PERMITTED RESEARCH INVOLVING PRISONERS. . . . .	941
Subpart D — Additional Protections for Children Involved as Subjects in Research . . .	942
§ 46.401 TO WHAT DO THESE REGULATIONS APPLY? . . . . .	942
§ 46.402 DEFINITIONS. . . . .	942
§ 46.403 IRB DUTIES. . . . .	942
§ 46.404 RESEARCH NOT INVOLVING GREATER THAN MINIMAL RISK. . . . .	943
§ 46.405 RESEARCH INVOLVING GREATER THAN MINIMAL RISK BUT PRESENTING THE PROSPECT OF DIRECT BENEFIT TO THE INDIVIDUAL SUBJECTS. . . . .	943
§ 46.406 RESEARCH INVOLVING GREATER THAN MINIMAL RISK AND NO PROSPECT OF DIRECT BENEFIT TO INDIVIDUAL SUBJECTS, BUT LIKELY TO YIELD GENERALIZABLE KNOWLEDGE ABOUT THE SUBJECT’S DISORDER OR CONDITION. . . . .	943
§ 46.407 RESEARCH NOT OTHERWISE APPROVABLE WHICH PRESENTS AN OPPORTUNITY TO UNDERSTAND, PREVENT, OR ALLEVIATE A SERIOUS PROBLEM AFFECTING THE HEALTH OR WELFARE OF CHILDREN. . . . .	943
§ 46.408 REQUIREMENTS FOR PERMISSION BY PARENTS OR GUARDIANS AND FOR ASSENT BY CHILDREN. . . . .	944
§ 46.409 WARDS. . . . .	945

---

*Table of Contents*

<b>Appendix B</b>	<b>DEPARTMENT OF HEALTH AND HUMAN SERVICES CATEGORIES OF RESEARCH THAT MAY BE REVIEWED BY THE INSTITUTIONAL REVIEW BOARD (IRB) THROUGH AN EXPEDITED REVIEW PROCEDURE .....</b>	<b>947</b>
<b>Appendix C</b>	<b>FOOD AND DRUG ADMINISTRATION SIGNIFICANT DIFFERENCES IN FDA AND HHS REGULATIONS FOR PROTECTION OF HUMAN SUBJECTS .....</b>	<b>951</b>
<b>Appendix D</b>	<b>NUREMBERG CODE .....</b>	<b>953</b>
<b>Appendix E</b>	<b>DECLARATION OF HELSINKI .....</b>	<b>955</b>
<b>Appendix F</b>	<b>THE BELMONT REPORT ETHICAL PRINCIPLES &amp; GUIDELINES FOR RESEARCH INVOLVING HUMAN SUBJECTS .....</b>	<b>961</b>
Part A:	Boundaries Between Practice & Research .....	961
Part B:	Basic Ethical Principles .....	962
Part C:	Applications .....	965
<b>Table of Cases</b>	<b>.....</b>	<b>TC-1</b>
<b>Index</b>	<b>.....</b>	<b>I-1</b>

---