THE ETHICS AND REGULATION OF RESEARCH WITH HUMAN SUBJECTS

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THE ETHICS AND REGULATION OF RESEARCH WITH HUMAN SUBJECTS

Second Edition

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Dedication

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

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

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.

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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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

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

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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