CHAPTER 2

INFORMED CONSENT: LEGAL PROTECTION OF PATIENTS AND HUMAN SUBJECTS

Introduction. In Chapter 1, we learned about the importance of consent to American tort and constitutional law. In *Cruzan*, Chief Justice Rehnquist described the history of consent law in the following words:

> At common law, even the touching of one person by another without consent and without legal justification was a battery. Before the turn of the century, this Court observed that "[n]o right is held more sacred, or is more carefully guarded, by the common law, than the right of every individual to the possession and control of his own person, free from all restraint or interference of others, unless by clear and unquestionable authority of law." This notion of bodily integrity has been embodied in the requirement that informed consent is generally required for medical treatment. Justice Cardozo, while on the Court of Appeals of New York, aptly described this doctrine: "Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault, for which he is liable in damages." *Schloendorff v. Society of New York Hospital,* 211 N.Y. 125, 129–130, 105 N.E. 92, 93 (1914). The informed consent doctrine has become firmly entrenched in American tort law.

Cruzan v. Dir., Mo. Dep't of Health, 497 U.S. 261, 267 (1990). We also learned that consent protects the bioethical principle of autonomy, the patient's right to make her own choices about medical care and treatment. *Quinlan* and *Cruzan* were landmark cases precisely because they involved incompetent patients who could not consent to treatment for themselves.

In this chapter, we learn more details about consent and the different contexts in which *informed consent* is necessary. Informed consent is a process by which patients give their permission for medical interventions, both in the treatment and research contexts. The law requires not only that patients give their consent, but also that such consent be *informed:* patients must be provided with all relevant information (such as risks and benefits) before being asked to agree. We build on our knowledge of patients and informed consent to focus on the subject of research on human subjects. Our area of legal practice shifts as well. At the beginning of the chapter, in Section A, we consider old tort

and constitutional law cases that are relevant to the subject of consent. From there we move to regulatory subjects as we consider which administrative systems and regulations best protect informed consent. Much of our focus will be on the meaning of consent in the context of research on human subjects.

Unfortunately, the history of human medicine and research includes many terrible episodes where lack of consent was linked to the victimization of vulnerable individuals. Most notorious is the history of Nazi experimentation, which we consider in Section B below. The Nazi experiments were part of a broader eugenics movement that aimed to improve or eliminate those deemed inferior, including the mentally retarded, criminals, gays and lesbians, Jews, and other vulnerable minorities. The eugenics movement was also influential in the United States, where beginning in the early twentieth century, thirty-five states passed laws allowing sterilization of prisoners and persons deemed mentally deficient. The laws reflected elite and popular opinion that criminality and mental illness were inherited traits.

The first case in this chapter, *Canterbury v. Spence*, establishes the standard for informed consent pertaining to treating patients. It is followed by *Buck v. Bell*, a case that demonstrates what occurs when there is no informed consent standard. *Buck* is a 1927 Supreme Court opinion that upheld the involuntary sterilization of Carrie Buck, a "feeble-minded" young woman. In *Buck*, Justice Oliver Wendell Holmes, one of the most respected Justices in Supreme Court history, upheld the sterilization in a brief opinion that included the offhand remark "[t]hree generations of imbeciles are enough." The "three generations" remark reflected the belief that sterilization would prevent the hereditary passage of negative physical and character traits to subsequent generations. See Paul A. Lombardo, Three Generations, No Imbeciles: Eugenics, the Supreme Court, and *Buck v. Bell* (2008). After considering *Canterbury*, *Buck*, and its legacy, Section A1 concludes with a report on recent sterilizations of women prisoners in California.

American history also includes terrible examples of exploitation of research subjects. Section A2 considers the exploitation of African American men with syphilis in Tuskegee, Alabama. It was the discovery of the Tuskegee experiments, where informed consent was never given, that led to the development of Institutional Review Boards (IRBs), which are considered in Section B. The current status of IRBs can help you decide if informed consent is better protected today than it was in 1927.

A. THE HISTORICAL RECORD

1. THE STANDARD FOR INFORMED CONSENT

Canterbury v. Spence

United States Court of Appeals, District of Colombia, 1972.
150 U.S. App. D.C. 263, 464 F.2d 772.

■ SPOTTSWOOD W. ROBINSON, III, CIRCUIT JUDGE.

I.

. . . The record we review tells a depressing tale. A youth troubled only by back pain submitted to an operation without being informed of a risk of paralysis incidental thereto. A day after the operation he fell from his hospital bed after having been left without assistance while voiding. A few hours after the fall, the lower half of his body was paralyzed, and he had to be operated on again. Despite extensive medical care, he has never been what he was before. Instead of the back pain, even years later, he hobbled about on crutches, a victim of paralysis of the bowels and urinary incontinence. In a very real sense this lawsuit is an understandable search for reasons.

At the time of the events which gave rise to this litigation, appellant was nineteen years of age, a clerk-typist employed by the Federal Bureau of Investigation. In December, 1958, he began to experience severe pain between his shoulder blades.

Dr. Spence examined appellant in his office at some length but found nothing amiss. On Dr. Spence's advice appellant was x-rayed, but the films did not identify any abnormality. Dr. Spence then recommended that appellant undergo a myelogram—a procedure in which dye is injected into the spinal column and traced to find evidence of disease or other disorder—at the Washington Hospital Center.

Appellant entered the hospital on February 4, 1959. The myelogram revealed a "filling defect" in the region of the fourth thoracic vertebra. Since a myelogram often does no more than pinpoint the location of an aberration, surgery may be necessary to discover the cause. Dr. Spence told appellant that he would have to undergo a laminectomy—the excision of the posterior arch of the vertebra—to correct what he suspected was a ruptured disc. Appellant did not raise any objection to the proposed operation nor did he probe into its exact nature.

Appellant explained to Dr. Spence that his mother was a widow of slender financial means living in Cyclone, West Virginia, and that she could be reached through a neighbor's telephone. Appellant called his mother the day after the myelogram was performed and, failing to contact her, left Dr. Spence's telephone number with the neighbor. When Mrs. Canterbury returned the call, Dr. Spence told her that the surgery was occasioned by a suspected ruptured disc. Mrs. Canterbury then

asked if the recommended operation was serious and Dr. Spence replied "not anymore than any other operation." . . .

Dr. Spence performed the laminectomy on February 11 at the Washington Hospital Center. Mrs. Canterbury traveled to Washington, arriving on that date but after the operation was over, and signed a consent form at the hospital. The laminectomy revealed several anomalies: a spinal cord that was swollen and unable to pulsate, an accumulation of large tortuous and dilated veins, and a complete absence of epidural fat which normally surrounds the spine. A thin hypodermic needle was inserted into the spinal cord to aspirate any cysts which might have been present, but no fluid emerged. In suturing the wound, Dr. Spence attempted to relieve the pressure on the spinal cord by enlarging the dura—the outer protective wall of the spinal cord—at the area of swelling.

For approximately the first day after the operation appellant recuperated normally, but then suffered a fall and an almost immediate setback. . . .

Several hours later, appellant began to complain that he could not move his legs and that he was having trouble breathing; paralysis seems to have been virtually total from the waist down. Dr. Spence was notified on the night of February 12, and he rushed to the hospital. Mrs. Canterbury signed another consent form and appellant was again taken into the operating room. The surgical wound was reopened and Dr. Spense [sic] created a gusset to allow the spinal cord greater room in which to pulsate.

Appellant's control over his muscles improved somewhat after the second operation but he was unable to void properly. As a result of this condition, he came under the care of a urologist while still in the hospital. In April, following a cystoscopic examination, appellant was operated on for removal of bladder stones, and in May was released from the hospital. He reentered the hospital the following August for a 10-day period, apparently because of his urologic problems. For several years after his discharge he was under the care of several specialists, and at all times was under the care of a urologist. At the time of the trial in April, 1968, appellant required crutches to walk, still suffered from urinal incontinence and paralysis of the bowels, and wore a penile clamp. . . .

II.

Appellant filed suit in the District Court on March 7, 1963, four years after the laminectomy and approximately two years after he attained his majority. The complaint stated several causes of action against each defendant. Against Dr. Spence it alleged, among other things, negligence in the performance of the laminectomy and failure to inform him beforehand of the risk involved. Against the hospital the complaint charged negligent post-operative care in permitting appellant to remain unattended after the laminectomy, in failing to provide a nurse or orderly

to assist him at the time of his fall, and in failing to maintain a side rail on his bed. The answers denied the allegations of negligence and defended on the ground that the suit was barred by the statute of limitations. . . .

At the close of appellant's case in chief, each defendant moved for a directed verdict and the trial judge granted both motions. . . .

The judge did not allude specifically to the alleged breach of duty by Dr. Spence to divulge the possible consequences of the laminectomy.

We reverse. The testimony of appellant and his mother that Dr. Spence did not reveal the risk of paralysis from the laminectomy made out a prima facie case of violation of the physician's duty to disclose which Dr. Spence's explanation did not negate as a matter of law. . . .

III.

Suits charging failure by a physician adequately to disclose the risks and alternatives of proposed treatment are not innovations in American law. They date back a good half-century, and in the last decade they have multiplied rapidly. There is, nonetheless, disagreement among the courts and the commentators on many major questions, and there is no precedent of our own directly in point. . . .

The root premise is the concept, fundamental in American jurisprudence, that "every human being of adult years and sound mind has a right to determine what shall be done with his own body. . . ." True consent to what happens to one's self is the informed exercise of a choice, and that entails an opportunity to evaluate knowledgeably the options available and the risks attendant upon each. The average patient has little or no understanding of the medical arts, and ordinarily has only his physician to whom he can look for enlightenment with which to reach an intelligent decision. From these almost axiomatic considerations springs the need, and in turn the requirement, of a reasonable divulgence by physician to patient to make such a decision possible. . . .

The context in which the duty of risk-disclosure arises is invariably the occasion for decision as to whether a particular treatment procedure is to be undertaken. To the physician, whose training enables a self-satisfying evaluation, the answer may seem clear, but it is the prerogative of the patient, not the physician, to determine for himself the direction in which his interests seem to lie. To enable the patient to chart his course understandably, some familiarity with the therapeutic alternatives and their hazards becomes essential. . . .

[W]e ourselves have found "in the fiducial qualities of [the physician-patient] relationship the physician's duty to reveal to the patient that which in his best interests it is important that he should know." We now find, as a part of the physician's overall obligation to the patient, a similar duty of reasonable disclosure of the choices with respect to proposed therapy and the dangers inherently and potentially involved. . . .

It is well established that the physician must seek and secure his patient's consent before commencing an operation or other course of treatment. . . . And it is evident that it is normally impossible to obtain a consent worthy of the name unless the physician first elucidates the options and the perils for the patient's edification. . . .

IV.

The majority of courts dealing with the problem have made the duty depend on whether it was the custom of physicians practicing in the community to make the particular disclosure to the patient. If so, the physician may be held liable for an unreasonable and injurious failure to divulge, but there can be no recovery unless the omission forsakes a practice prevalent in the profession. . . .

There are, in our view, formidable obstacles to acceptance of the notion that the physician's obligation to disclose is either germinated or limited by medical practice. To begin with, the reality of any discernible custom reflecting a professional consensus on communication of option and risk information to patients is open to serious doubt. . . .

Nor can we ignore the fact that to bind the disclosure obligation to medical usage is to arrogate the decision on revelation to the physician alone. Respect for the patient's right of self-determination on particular therapy demands a standard set by law for physicians rather than one which physicians may or may not impose upon themselves. . . .

We hold that the standard measuring performance of that duty by physicians, as by others, is conduct which is reasonable under the circumstances.

V.

Once the circumstances give rise to a duty on the physician's part to inform his patient, the next inquiry is the scope of the disclosure the physician is legally obliged to make. . . .

In our view, the patient's right of self-decision shapes the boundaries of the duty to reveal. That right can be effectively exercised only if the patient possesses enough information to enable an intelligent choice. The scope of the physician's communications to the patient, then, must be measured by the patient's need, and that need is the information material to the decision. Thus the test for determining whether a particular peril must be divulged is its materiality to the patient's decision: all risks potentially affecting the decision must be unmasked. . . .

[T]he physician's liability for nondisclosure is to be determined on the basis of foresight, not hindsight; no less than any other aspect of negligence, the issue on nondisclosure must be approached from the viewpoint of the reasonableness of the physician's divulgence in terms of what he knows or should know to be the patient's informational needs. If, but only if, the fact-finder can say that the physician's communication

was unreasonably inadequate is an imposition of liability legally or morally justified. . . .

The scope of the standard is not subjective as to either the physician or the patient; it remains objective with due regard for the patient's informational needs and with suitable leeway for the physician's situation. In broad outline, we agree that "[a] risk is thus material when a reasonable person, in what the physician knows or should know to be the patient's position, would be likely to attach significance to the risk or cluster of risks in deciding whether or not to forego the proposed therapy."

The topics importantly demanding a communication of information are the inherent and potential hazards of the proposed treatment, the alternatives to that treatment, if any, and the results likely if the patient remains untreated. The factors contributing significance to the dangerousness of a medical technique are, of course, the incidence of injury and the degree of the harm threatened. . . .

VII.

An unrevealed risk that should have been made known must materialize, for otherwise the omission, however unpardonable, is legally without consequence. Occurrence of the risk must be harmful to the patient, for negligence unrelated to injury is nonactionable. And, as in malpractice actions generally, there must be a causal relationship between the physician's failure to adequately divulge and damage to the patient.

A causal connection exists when, but only when, disclosure of significant risks incidental to treatment would have resulted in a decision against it. . . . The more difficult question is whether the factual issue on causality calls for an objective or a subjective determination. . . .

Better it is, we believe, to resolve the causality issue on an objective basis: in terms of what a prudent person in the patient's position would have decided if suitably informed of all perils bearing significance. If adequate disclosure could reasonably be expected to have caused that person to decline the treatment because of the revelation of the kind of risk or danger that resulted in harm, causation is shown, but otherwise not. The patient's testimony is relevant on that score of course but it would not threaten to dominate the findings. . . .

X.

This brings us to the remaining question, . . . whether appellant's evidence was of such caliber as to require a submission to the jury. . . . [T]he evidence was clearly sufficient to raise an issue as to whether Dr. Spence's obligation to disclose information on risks was reassonably [sic] met or was excused by the surrounding circumstances. Appellant testified that Dr. Spence revealed to him nothing suggesting a hazard associated with the laminectomy. His mother testified that, in response to her specific inquiry, Dr. Spence informed her that the laminectomy

was no more serious than any other operation. When, at trial, it developed from Dr. Spence's testimony that paralysis can be expected in one percent of laminectomies, it became the jury's responsibility to decide whether that peril was of sufficient magnitude to bring the disclosure duty into play. . . .

Reversed and remanded for a new trial.

NOTES AND QUESTIONS

1. *Patient Standard.* Why is it the "prerogative of the patient, not the physician, to determine for himself the direction in which his interests seem to be"? For many years tort law informed consent lawsuits were governed by the standard of how a reasonable physician would behave, and what the "custom" of physicians was. The professional standard is still the standard in about half of jurisdictions. See, e.g., Studdert et al., Geographic Variation in Informed Consent Law: Two Standards for Disclosure of Treatment Risks, 4 J. Empirical Leg. Stud. 103 (2007) (finding that twenty-five states use the physician standard, twenty-three use the patient standard, and Colorado and Georgia are not classified as either.). Why is the patient's decision about treatment favored over the knowledge of the physician in this case? What should Dr. Spence have told Canterbury in order to satisfy the demands of informed consent? Criticism of the doctrine as overly focused on physician information disclosure rather than on patient understanding has led some to advocate for a "shared decisionmaking" standard as a way to enhance informed consent. James F. Childress & Marcia Day Childress, What Does the Evolution From Informed Consent to Shared Decision Making Teach Us About Authority in Health Care?, 22 AMA J. Ethics E423 (2020).

2. *Foresight, Not Hindsight*. What does the court mean when it says that the physician's judgment must be assessed according to foresight, not hindsight? What information is available from foresight in this case? What is obvious in hindsight?

3. *Subjective or Objective.* What does the court mean when it says that the "scope of the standard is not subjective as to either the physician or the patient; it remains objective with due regard for the patient's informational needs and with suitable leeway for the physician's situation"? What is the difference between a subjective and an objective standard on these facts? Does the objective standard focus on Canterbury or on a reasonable patient? Whose interests are likely to be protected or excluded by each standard?

4. *Causal Relationship.* What does the court mean when it says "there must be a causal relationship between the physician's failure to adequately divulge an[y] damage to the patient"? How could Canterbury prove causation in this case?

5. *COVID Consent.* In the early days of the COVID-19 pandemic, many hospitals abandoned elective procedures to avoid the spread of the virus and to preserve hospital resources for an anticipated influx of COVID patients. Others continued to do some non-elective procedures, in addition to necessary emergency procedures. While the normal informed consent process requires a doctor to detail the many different outcomes, the possible

dangers associated with the procedure, and other necessary information, during the pandemic informed consent may also require disclosure of information relating to the possibility of contracting COVID-19 while in the hospital. This practice has been criticized, as there is always an inherent risk of contracting illness from surgery or other procedures while hospitalized—a risk already noted in many informed consent forms. Should the risks of pandemic diseases be addressed separately, or subsumed under current warnings regarding hospital-acquired infections? For a sample COVID informed consent form relating to plastic surgery, see https://www.plasticsurgery.org/documents/medical-professionals/COVID19-Informed-Consent.pdf.

6. *Elements of Informed Consent*. According to Professor Meisel, *Canterbury* identifies the "mainstay of informed consent: the source of a doctor's duty to provide information to a patient; the standard by which the adequacy of disclosure is to be measured; the requisite causal nexus between inadequate disclosure and the patient's injury; the type of injury that will support recovery; the physician's privilege to withhold information; the role of expert testimony in establishing the inadequacy of disclosure and causation; and the nature of the cause of action for inadequate disclosure, necessary to establish the appropriate statute of limitations and evidentiary rules. . . ." Alan Meisel, Canterbury v. Spence: The Inadvertent Landmark Case in Health Law & Bioethics: Cases in Context (S.H. Johnson et al. eds. 2009). Do you understand what all these elements entail? Consider how much you understand of how the case worked in practice before you read the following excerpt from Professor Meisel.

Canterbury v. Spence: The Inadvertent Landmark Case

Alan Meisel, 2009.
Health Law & Bioethics: Cases in Context, 9, 17–18, 21–22.

Theory of the Case

Canterbury's case was fraught with problems from the outset. The fundamental problem was the issue of what caused Canterbury's paralysis. Was it the very condition for which he sought treatment from Dr. Spence—the pain between his shoulder blades? Was it something that happened during the first surgery, the laminectomy, which was intended to treat this pain? Was it the fall from bed, and if so, was that because the doctors' orders were unclear, inadequate, or conflicting, or because the nurses (who were employees of the hospital, not of the doctors) did not carry them out correctly? Was it instead the second surgery immediately after the fall? Or was it some combination of these?

Closely related to the causation problem was the issue of negligence. Even if the cause of the paralysis was something one of the defendants did, the law said that neither Dr. Spence nor the hospital could be held liable unless what they did was negligent. To establish this, Davis (Canterbury's lawyer) had to show that their conduct failed to meet the

standard of care—what a reasonable physician of similar training, education, and experience would have done under the circumstances. To complicate matters even more, in most American jurisdictions at that time (D.C. among them), the locality rule required the plaintiff to establish what a reasonable physician in that locality would do, and that required the testimony of an expert witness—another physician from that locality. Unlike today, when it is a relatively simple matter to hire a professional expert witness, in the 1960s and 1970s the "conspiracy of silence" still reigned in many jurisdictions. Getting a doctor to testify against a peer—especially a doctor from the same locality, and perhaps the same hospital staff, same neighborhood, same church, or same country club—was nigh unto impossible.

Because of these difficulties, Davis also advanced legal theories focusing on Canterbury's lack of consent to treatment. One theory was fairly straightforward: Canterbury was, by the law of that time, a minor because he was under the age of 21. Consequently, his consent was not legally valid, and parental consent was necessary. It is clear Dr. Spence did not obtain consent from Canterbury's mother before the surgery. But even if legally valid consent to the laminectomy had not been obtained, the one-year statute of limitations on a battery cause of action—the theory that would have had to be pursued for lack of consent—had run by the time the complaint was filed.

However, because the statute of limitations had not yet run on a negligence cause of action, in addition to filing claims for garden variety negligence Davis gambled that he could also bring an action for lack of informed consent, couched in the language of negligence—which, while well-accepted today, was somewhat unusual at that time. . . .

What Was He Told and When Was He Told It?

Informed consent is a classic "he said, she said" issue. After the fact the patient invariably will say, "the doctor didn't tell me what could go wrong, and if he had, I never would have agreed to that." In contrast, the doctor invariably will say, "I told him that could go wrong, and he said he'd take his chances." As time has gone by and doctors and their lawyers have realized the legal risks of inadequate disclosure, they have devised written forms (the so-called "informed consent forms" widely used today) ostensibly to document that the patient was told exactly what those risks would entail. Some doctors have been surprised to learn that a signed consent form only establishes that the patient signed the form, but not that he really was provided with material information (or that he understood it—which is yet another complexity of the law and practice of informed consent). . . .

The Opinion

There must have been something in the air in 1972, for that was the year that informed consent came into its own—not just in the *Canterbury* decision, but in major opinions from the California and Rhode Island

Supreme Courts as well. For whatever reason, Judge Robinson seized on the issue and devoted all but five paragraphs of his 21-page opinion to the discussion of informed consent. In the end, the Court of Appeals recognized a cause of action for inadequate disclosure and held that it sounded in negligence, not battery, and therefore was not barred by the statute of limitations.

The core holding of *Canterbury* is that the fiduciary nature of the doctor-patient relationship imposes an affirmative obligation on physicians to disclose information about proposed treatment to patients. The scope of the information that must be disclosed is that which a reasonable person—not the patient in question—would find material to making a decision whether to undergo or forgo the proposed treatment, including information about the risks of treatment, the benefits of treatment, and alternative treatments. The scope of disclosure is most definitely not governed by the professional custom of physicians, for to do so would be completely inconsistent with the ethical underpinnings of informed consent—the patient's right to determine for himself his own medical interests (and, it might be added, because evidence of such a professional custom is completely lacking). The failure to fulfill this obligation constitutes professional negligence and—if it would lead a reasonable person in the patient's situation to undergo treatment and if that treatment causes physical harm to the patient—is the basis for an award of damages to the patient to compensate for his injuries. . . .

Now that you know the standard for informed consent, consider how that standard would have made a difference in the following case.

2. STERILIZATION

Buck v. Bell

Supreme Court of Appeals of Virginia, 1925.
143 Va. 310, 130 S.E. 516.

■ WEST, J., delivered the opinion of the Court.

Carrie Buck, by R. G. Shelton, her guardian and next friend, complains of a judgment of the Circuit Court of Amherst county by which Dr. J. H. Bell, Superintendent of the State Colony for Epileptics and Feeble-Minded, was ordered to perform on her the operation of salpingectomy, for the purpose of rendering her sexually sterile. See part of the Virginia sterilization act copied in the margin.[1]

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[1] The Virginia sterilization act (Acts 1924, chap. 394, p. 569) reads, in part, as follows:

'Whereas, both the health of the individual patient and the welfare of society may be promoted in certain cases by the sterilization of mental defectives under careful safeguard and by competent and conscientious authority; and

After requiring the service of a copy of the petition and notice of the time and place when the special board of directors will hear and act on the petition upon the inmate and her guardian, and, if the inmate be an infant, upon the living parents, and giving the inmate the right to be represented by counsel, the act further provides:

> 'The said special board may deny the prayer of the said petition, or if the said special board shall find that the said inmate is insane, idiotic, imbecile, feeble-minded, or epileptic, and by the laws of heredity is the probable potential parent of socially inadequate offspring likewise afflicted, that the said inmate may be sexually sterilized without detriment to his or her general health, and that the welfare of the inmate and of society will be promoted by such sterilization, the said special board may order the said superintendent to perform or to have performed by some competent physician to be named in such order upon the said inmate, after not less than thirty days from the date of such order, the operation of vasectomy if a male or of salpingectomy if a female; provided that nothing in this act shall be construed to authorize the operation of castration nor the removal of sound organs from the body.'

The statute then provides that the special board, the superintendent, the inmate or his committee, guardian or next friend, may appeal from the order of the board to the circuit court, and that any

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'Whereas, such sterilization may be effected in males by the operation of vasectomy and in females by the operation of salpingectomy, both of which said operations may be performed without serious pain or substantial danger to the life of the patient; and

'Whereas, the Commonwealth has in custodial care and in supporting in various State institutions many defective persons who if now discharged or paroled would likely become by the propagation of their kind a menace to society, but who if incapable of procreating might properly and safely be discharged or paroled and become self-supporting with benefit both to themselves and to society; and

'Whereas, human experience has demonstrated that heredity plays an important part in the transmission of insanity, idiocy, imbecility, epilepsy and crime; now, therefore,

'1. Be it enacted by the General Assembly of Virginia, That whenever the Superintendent of the Western State Hospital, or of the Eastern State Hospital, or of the Southwestern State Hospital, or of the Central State Hospital, or of the State Colony for Epileptics and Feeble-Minded, shall be of opinion that it is for the best interests of the patients and of society that any inmate of the institution under his care should be sexually sterilized, such superintendent is hereby authorized to perform, or cause to be performed by some capable physician or surgeon, the operation of sterilization on any such patient confined in such institution afflicted with hereditary forms of insanity that are recurrent, idiocy, imbecility, feeble-mindedness or epilepsy; provided that such superintendent shall have first complied with the requirements of this act.

'2. Such superintendent shall first present to the special board of directors of his hospital or colony a petition stating the facts of the case and the grounds of his opinion, verified by his affidavit to the best of his knowledge and belief, and praying that an order may be entered by said board requiring him to perform or have performed by some competent physician to be designated by him in his said petition or by said board in its order, upon the inmate of his institution named in such petition, the operation of vasectomy if upon a male and of salpingectomy if upon a female.'

party to such appeal in the circuit court may apply to the Supreme Court of Appeals for an appeal from the final order therein.

On the 23rd day of January, 1924, Carrie Buck was adjudged to be feeble-minded within the meaning of the Virginia statute, and committed to the State Colony for Epileptics and Feeble-Minded. On September 10, 1924, A. S. Priddy, then Superintendent of the Colony, presented to the special board of directors his petition praying for an order that Carrie Buck be sexually sterilized by the surgical operation known as salpingectomy. The hearing was conducted strictly in accordance with the provisions of the statute, and, upon the evidence introduced before them, the board entered the order prayed for. From this order an appeal was taken by Carrie Buck and R. G. Shelton, her guardian and next friend, to the Circuit Court of Amherst county. Upon the record and evidence introduced at the trial in the circuit court, the judgment complained of was entered, from which this appeal was allowed.

These facts, among others, appear from the evidence:

The operation of salpingectomy is the cutting of the fallopian tubes between the ovaries and the womb, and the tying of the ends next to the womb. The ovaries are left intact and continue to function. The operation of vasectomy consists of the cutting down of a small tube which runs from the testicle, without interference with the testicle. These operations do not impair the general health, or affect the mental or moral status of the patient, or interfere with his, or her, sexual desires or enjoyment. They simply prevent reproduction. In the hands of a skilled surgeon, they are 100 per cent successful in results.

At the time Carrie Buck was committed to the State Colony for Epileptics and Feeble-Minded, she was seventeen years old and the mother of an illegitimate child of defective mentality. She had the mind of a child nine years old, and her mother had theretofore been committed to the same Colony as a feeble-minded person. Carrie Buck, by the laws of heredity, is the probable potential parent of socially inadequate offspring, likewise affected as she is. Unless sterilized by surgical operation, she must be kept in the custodial care of the Colony for thirty years, until she is sterilized by nature, during which time she will be a charge upon the State. If sterilized under the law, she could be given her liberty and secure a good home, under supervision, without injury to society. Her welfare and that of society would be promoted by such sterilization.

The appellant contends that the judgment is void because the Virginia sterilization act is repugnant to the provisions of the State and Federal Constitution (Const. Va., Art. 1, secs. 9, 11; Const. U.S. Amends. 8, 14) in that—

(a) It does not provide due process of law;

(b) It imposes a cruel and unusual punishment; and

(c) It denies the appellant and other inmates of the State Colony the equal protection of the law.

1. An adjudication by an impartial tribunal vested with lawful jurisdiction to hear and determine the questions involved, after reasonable notice to the parties interested and an opportunity for them to be heard, fulfills all the requirements of due process of law. . . .

There is no controversy as to the legality or regularity of the proceedings by which appellant was adjudged to be feeble-minded and committed to the State Colony.

The statute under review clearly vests the special board of directors of the State Colony for Epileptics and Feeble-Minded, after notice according to law, with jurisdiction to hear and determine the prayer of any petition filed by the Superintendent of the Colony for the sexual sterilization of an inmate thereof.

In the instant case, the proceeding was strictly in conformity with the statute. The Superintendent of the Colony, having first served a copy of the petition and a notice of the time and place it would be presented on the inmate, her guardian and her mother, her father being dead, presented to the special board of directors of the Colony his petition, stating the facts of the case and the grounds of his opinion, verified by his affidavit and praying that an order be entered by the board requiring him, or some other competent physician, to perform upon Carrie Buck the operation of salpingectomy. Upon a later day, fixed by the board, the board proceeded in the presence of the inmate, her guardian and her attorney, to hear and consider the petition and evidence offered in support of and against the petition, and entered its final order, from which the inmate appealed to the circuit court and subsequently to this court.

The act complies with the requirements of due process of law.

2. The contention that the statute imposes cruel and unusual punishment cannot be sustained.

The act is not a penal statute. The purpose of the legislature was not to punish but to protect the class of socially inadequate citizens named therein from themselves, and to promote the welfare of society by mitigating race degeneracy and raising the average standard of intelligence of the people of the State.

The evidence shows that the operation, practically speaking, is harmless and 100 per cent safe, and in most cases relieves the patient from further confinement in the Colony. . . .

3. Does the statute deny to appellant and other inmates of the State Colony the equal protection of the law? This question must be answered in the negative.

It is not controverted that the State may, in proper cases, by due process of law, take into custody and deprive the insane, the feeble-

minded and other defective citizens of the liberty which is otherwise guaranteed them by the Constitution.

The right to enact such laws rests in the police power, which the States did not surrender when they entered the Federal Union, and the exercise of that power the Virginia Constitution provides shall never be abridged.

Where the police power conflicts with the Constitution, the latter is supreme, but the courts will not restrain the exercise of such power, except where the conflict is clear and plain.

. . . Disregarding other classes of mental defectives, upon whom the statute operates, the purpose of the act is to promote the welfare and prevent procreation by those who have been, or may hereafter be, judicially ascertained to be feeble-minded and are inmates of the State Colony for Epileptics and Feeble-Minded. The status of a feeble-minded person, who comes under the operation of the sterilization act, is not fixed until such patient, after judicial commitment to the Colony, shall have undergone expert observation for at least two months and been subjected to the Binet Simon measuring scale of intelligence, or some other approved test of mentality, and found to be feeble-minded. Code 1919, sec. 1083.

Code, section 1078, designates those who have not been adjudged to be feeble-minded as persons 'supposed to be feeble-minded.' The sterilization act has no reference to the latter class except in so far as they may be legally ascertained to belong to the former and are committed to the Colony. It cannot be said, as contended, that the act divides a natural class of persons into two and arbitrarily provides different rules for the government of each. The two classes existed before the passage of the sterilization act. The female inmate, unlike the woman on the outside, was already deprived of the power of procreation by segregation, and must remain so confined until sterilized by nature, unless it is ascertained that her welfare and the welfare of society will be promoted by her sterilization under the act. There can be no discrimination against the inmates of the Colony, since the woman on the outside, if in fact feeble-minded, can, by the process of commitment and afterwards a sterilization hearing, be sterilized under the act.

Appellants rely upon *Smith v. Board of Examiners of Feeble-Minded, Epileptics, etc.*, 85 N.J. Law, 46, 88 Atl. 963. The New Jersey act provided for the sterilization of epileptics who were 'inmates confined in the several charitable institutions in the counties and State.' The court held the act unconstitutional because the statute arbitrarily created two classes and applied the statutory remedy to that one of the classes to which it had the least application, and therefore denied Smith, who was an inmate of a charitable institution, the equal protection of the laws. The right to sterilize did not, as in Virginia, depend upon whether the welfare of the patient would be promoted by the operation. For the

reasons given in discussing the Virginia act, we decline to follow the New Jersey case.

The Indiana act was held invalid in *Williams v. Smith*, 190 Ind. 526, 131 N.E. 2, because it denied the appellee due process of law.

We have found no case involving similar statutes where the court has held that the State is without power to enact such laws, provided it be exercised through a statute which affords due process of law and equal protection of the laws to those affected by it.

For the foregoing reasons, we are of the opinion that the Virginia sterilization act is based upon a reasonable classification and is a valid enactment under the State and Federal Constitutions.

Affirmed.

NOTES AND QUESTIONS

1. *State Sterilization Laws*. Indiana was the first state to pass a eugenic sterilization law in 1907. Washington and California followed in 1909. Sterilization laws were perceived to correct two problems. First, they were seen as a cure for irregular sexual activities such as masturbation or prostitution. Second, because of the belief that criminality and immorality were hereditary, sterilization was thought to put an end to the birth of "defective" human beings. See Alexandra Minna Stern, From Legislation to Lived Experience: Eugenic Sterilization in California and Indiana, 1907–1979," 95–116, A Century of Eugenics in America: From the Indiana Experiment to the Human Genome Era (Paul A. Lombardo ed., 2011); Lombardo, Three Generations, No Imbeciles, *supra*.

The Indiana law authorized a committee composed of a physician, two board members, and two surgeons to decide whether any "criminals, idiots, rapists and imbeciles" held in state institutions should be sterilized because "procreation is inadvisable and there is no probability of improvement of the mental condition of the inmate." In Williams v. Smith, 131 N.E. 2 (Ind. 1921), which is cited in the Virginia case, the Indiana Supreme Court ruled that the statute denied Warren Wallace Smith due process of law; "the prisoner has no opportunity to cross-examine the experts who decide that this operation should be performed upon him. He has no chance to bring experts to show that it should not be performed; nor has he a chance to controvert the scientific question that he is of a class designated in the statute." Id.

Did Virginia learn a lesson from Indiana and, therefore, draft a law that satisfied due process by including hearings and appeals? Is there anything in the Virginia statute that makes you think it violated due process? Can you make the argument that the statute violated substantive due process but not procedural due process? What is the difference between substantive and procedural due process?

2. *State Arguments*. State authorities argued that, in contrast to New Jersey, Virginia's law protected liberty because it allowed Buck and others, once sterilized, to return to the community instead of remaining in colonies

for the feebleminded. Do you agree? Is there any way in which the sterilization laws protected or promoted Buck's well-being?

3. *Test Case*. Pro-eugenics reformers carefully drafted the Virginia law to ensure the law's survival and then engineered a test case to assure the law's constitutionality. Once they realized that Carrie Buck, an unmarried seventeen-year-old, had given birth to Vivian Buck immediately before being institutionalized at the Virginia Colony for Epileptics and Feeble-minded, where her mother, Emma, was already in residence, they had found their ideal plaintiff. The three generations could be used to illustrate the heredity of imbecility, feeblemindedness or other disorders. Lombardo, Three Generations, No Imbeciles, *supra*.

The pro-eugenics advocates chose attorney Irving Whitehead to represent Buck. Whitehead was an advocate of sterilization who had served on the Colony's board and was a childhood friend of Dr. Priddy, the head of the colony. Id. at 106. At trial, Whitehead did little to cross-examine the state's witnesses and rested his case without calling any witnesses on Buck's behalf. The state's expert witnesses testified that all three generations of Bucks—including six-month-old Vivian—demonstrated abnormal and feebleminded development. Later school records indicated that Vivian, who died at age nine, was an honor student. How does this information affect your assessment of the Virginia Supreme Court's opinion?

4. *Due Process*. Is there any way to protect due process in the context of sterilization? Do you agree with how the United States Supreme Court decided the case, as reprinted below?

Buck v. Bell

Supreme Court of the United States, 1927.
274 U.S. 200, 47 S.Ct. 584.

■ MR. JUSTICE HOLMES delivered the opinion of the Court. MR. JUSTICE BUTLER dissenting.

This is a writ of error to review a judgment of the Supreme Court of Appeals of the State of Virginia, affirming a judgment of the Circuit Court of Amherst County, by which the defendant in error, the superintendent of the State Colony for Epileptics and Feeble Minded, was ordered to perform the operation of salpingectomy upon Carrie Buck, the plaintiff in error, for the purpose of making her sterile. The case comes here upon the contention that the statute authorizing the judgment is void under the Fourteenth Amendment as denying to the plaintiff in error due process of law and the equal protection of the laws.

Carrie Buck is a feeble-minded white woman who was committed to the State Colony above mentioned in due form. She is the daughter of a feeble-minded mother in the same institution, and the mother of an illegitimate feeble-minded child. She was eighteen years old at the time of the trial of her case in the Circuit Court in the latter part of 1924. An Act of Virginia approved March 20, 1924 (Laws 1924, c. 394) recites that the health of the patient and the welfare of society may be promoted in

certain cases by the sterilization of mental defectives, under careful safeguard, etc.; that the sterilization may be effected in males by vasectomy and in females by salpingectomy, without serious pain or substantial danger to life; that the Commonwealth is supporting in various institutions many defective persons who if now discharged would become a menace but if incapable of procreating might be discharged with safety and become self-supporting with benefit to themselves and to society; and that experience has shown that heredity plays an important part in the transmission of insanity, imbecility, etc. The statute then enacts that whenever the superintendent of certain institutions including the above named State Colony shall be of opinion that it is for the best interest of the patients and of society that an inmate under his care should be sexually sterilized, he may have the operation performed upon any patient afflicted with hereditary forms of insanity, imbecility, etc., on complying with the very careful provisions by which the act protects the patients from possible abuse.

The superintendent first presents a petition to the special board of directors of his hospital or colony, stating the facts and the grounds for his opinion, verified by affidavit. Notice of the petition and of the time and place of the hearing in the institution is to be served upon the inmate, and also upon his guardian, and if there is no guardian the superintendent is to apply to the Circuit Court of the County to appoint one. If the inmate is a minor notice also is to be given to his parents, if any, with a copy of the petition. The board is to see to it that the inmate may attend the hearings if desired by him or his guardian. The evidence is all to be reduced to writing, and after the board has made its order for or against the operation, the superintendent, or the inmate, or his guardian, may appeal to the Circuit Court of the County. The Circuit Court may consider the record of the board and the evidence before it and such other admissible evidence as may be offered, and may affirm, revise, or reverse the order of the board and enter such order as it deems just. Finally any party may apply to the Supreme Court of Appeals, which, if it grants the appeal, is to hear the case upon the record of the trial in the Circuit Court and may enter such order as it thinks the Circuit Court should have entered. There can be no doubt that so far as procedure is concerned the rights of the patient are most carefully considered, and as every step in this case was taken in scrupulous compliance with the statute and after months of observation, there is no doubt that in that respect the plaintiff in error has had due process at law.

The attack is not upon the procedure but upon the substantive law. It seems to be contended that in no circumstances could such an order be justified. It certainly is contended that the order cannot be justified upon the existing grounds. The judgment finds the facts that have been recited and that Carrie Buck 'is the probable potential parent of socially inadequate offspring, likewise afflicted, that she may be sexually sterilized without detriment to her general health and that her welfare

and that of society will be promoted by her sterilization,' and thereupon makes the order. In view of the general declarations of the Legislature and the specific findings of the Court obviously we cannot say as matter of law that the grounds do not exist, and if they exist they justify the result. We have seen more than once that the public welfare may call upon the best citizens for their lives. It would be strange if it could not call upon those who already sap the strength of the State for these lesser sacrifices, often not felt to be such by those concerned, in order to prevent our being swamped with incompetence. It is better for all the world, if instead of waiting to execute degenerate offspring for crime, or to let them starve for their imbecility, society can prevent those who are manifestly unfit from continuing their kind. The principle that sustains compulsory vaccination is broad enough to cover cutting the Fallopian tubes. Jacobson v. Massachusetts, 197 U.S. 11. Three generations of imbeciles are enough.

But, it is said, however it might be if this reasoning were applied generally, it fails when it is confined to the small number who are in the institutions named and is not applied to the multitudes outside. It is the usual last resort of constitutional arguments to point out shortcomings of this sort. But the answer is that the law does all that is needed when it does all that it can, indicates a policy, applies it to all within the lines, and seeks to bring within the lines all similarly situated so far and so fast as its means allow. Of course so far as the operations enable those who otherwise must be kept confined to be returned to the world, and thus open the asylum to others, the equality aimed at will be more nearly reached.

Judgment affirmed.

■ MR. JUSTICE BUTLER dissents.

NOTES AND QUESTIONS

1. *Holmes' Opinion*. Do you agree with Justice Holmes? If so, why? If not, what do you find objectionable about his argument?

2. *Jacobson*. Justice Holmes cited another Court case, *Jacobson v. Massachusetts*, which upheld mandatory smallpox vaccination. Do you agree that the "principle that sustains compulsory vaccination is broad enough to cover cutting the Fallopian tubes?" Does *Buck* follow from *Jacobson*? In a COVID case ruling in favor of a religious groups' challenge to COVID-related restrictions on their worship, Justice Gorsuch asked how the Court had "mistaken this Court's modest decision in *Jacobson* for a towering authority that overshadows the Constitution during a pandemic." Roman Catholic Diocese of Brooklyn v. Cuomo, ___ U.S. ___, 141 S.Ct. 63, 71 (2020). What does that

Practice Exercise: Go back through the excerpted opinion and highlight any sentences or phrases that you find objectionable. Then, explain why you disagree with them.

statement tell you about the connection between the state's public health powers and religious freedom?

3. *Recusal*. Chief Justice William Howard Taft was a supporter of the eugenics movement. He offered his name to eugenics organizations and provided an introduction and endorsement to a prominent pro-eugenics book. See Lombardo, Three Generations, No Imbeciles, *supra*. Justice Holmes had also been an advocate of eugenics. Should the Justices have been recused from this case? Did they let their pro-eugenics views blind them to the situation of Carrie Buck?

Go to the website and watch the YouTube video as an example of how eugenics impacted legislation. (*Buck v. Bell* is mentioned at 4:30–6:04.)

Why do you think Justice Butler dissented from the opinion? Is it possible that the Roman Catholic Justice opposed sterilization because his church taught it was always immoral? If so, would that mean that the Justice was improperly influenced by his religious beliefs? See id. at 172 (evidence is inconclusive whether Butler dissented for religious reasons).

4. *Bioethics*. How does the study of bioethics relate to eugenics? Do you think issues raised by eugenics may have led to bioethics?

5. *Rape*. Buck reported that she became pregnant with Vivian after Clarence Garland, a nephew of her foster parents, raped her. How does this fact affect your assessment of the case? Id. Given the Supreme Court's reasoning, would the case have come out differently if Buck's rape had been submitted into the evidence at trial?

6. *Reproductive Freedom Exercise*. Draft an alternative opinion that acknowledges that reproductive freedom is a fundamental right. Would the case have turned out differently with such a right in place, or would the state have been able to prove that it had compelling reasons to sterilize Carrie Buck?

7. *Skinner*. In Skinner v. Oklahoma, 316 U.S. 535 (1942), the Court ruled that Oklahoma's Habitual Criminal Sterilization Act, which allowed criminals convicted two or more times for felonies involving moral turpitude to be sterilized, violated the Equal Protection Clause. The Court based its ruling upon the fact that the law allowed sterilization for felonies involving larceny, but not embezzlement. Because those two offenses were basically of the "same quality," it violated equal protection for the state to sterilize for one crime but not the other.

Buck v. Bell was not overruled even though the Court ruled that strict scrutiny applied in cases involving a fundamental right of procreation. Did the government have a compelling interest in sterilizing Carrie Buck? Can you distinguish *Skinner* from *Buck*? Justice Douglas' opinion for the Court, as well as concurrences by Chief Justice Stone and Justice Jackson, all distinguished *Buck v. Bell* from *Skinner* and found it unnecessary to overrule the sterilization precedent.

Acknowledging Justice Holmes' comment that it "is the usual last resort of constitutional arguments to point out shortcomings of this [equal protection] sort," Justice Douglas wrote that in *Skinner*, the "embezzlers are forever free," while the larcenists were imprisoned. In contrast, in *Buck* "the operations enable those who otherwise must be kept confined to be returned to the world, and thus open the asylum to others, the equality aimed at will be more nearly reached." Therefore, there was an equal protection violation in *Skinner* but not *Buck*. Does that argument make sense to you?

Chief Justice Stone distinguished the two cases on the grounds that while Skinner "was given a hearing to ascertain whether sterilization would be detrimental to his health, he was given none to discover whether his criminal tendencies are of an inheritable type. Undoubtedly a state may, after appropriate inquiry, constitutionally interfere with the personal liberty of the individual to prevent the transmission by inheritance of his socially injurious tendencies. Buck v. Bell, 274 U.S. 200." Are you surprised that, even by 1942, Supreme Court Justices accepted that courts could hold hearings about inheritable criminal tendencies? Skinner v. State of Okl. ex rel. Williamson, 316 U.S. 535, 544 (1942).

Justice Robert Jackson, who on May 2, 1945, became chief prosecutor for the United States at the Nuremberg trials of Nazi war criminals, wrote the following comparison of the two cases:

> I also think the present plan to sterilize the individual in pursuit of a eugenic plan to eliminate from the race characteristics that are only vaguely identified and which in our present state of knowledge are uncertain as to transmissibility presents other constitutional questions of gravity. This Court has sustained such an experiment with respect to an imbecile, a person with definite and observable characteristics where the condition had persisted through three generations and afforded grounds for the belief that it was transmissible and would continue to manifest itself in generations to come. *Buck v. Bell*, 274 U.S. 200.

Skinner v. State of Okl. ex rel. Williamson, 316 U.S. 535, 546 (1942) What do you think of Justice Jackson's analysis?

8. *Modern Medicine*. Do you think advances in modern medicine could lead to a new eugenics movement? If so, what would that movement look like? How do you think bioethics and the law could deal with it? Some commentators see a link between discussions of population control, eugenics, and reproductive justice. Caitlin Fendley, Eugenics is Trending. That's a Problem, Wash. Post, Feb. 17, 2020, www.washingtonpost.com/outlook/2020/02/17/eugenics-is-trending-thats-problem/. Scotland has already considered this issue. See Calum Mackellar, Eugenic Policies of the Past Teach Sobering Lessons, Scotsman Aug. 24, 2014, at http://www.scotsman.com/news/eugenic-policies-of-the-past-teach-sobering-lessons–1–3486562 (suggesting that developments in genetics will lead to new eugenics concerns). What do you think of Justice Clarence Thomas's argument that the "use of abortion to achieve eugenic goals is not merely hypothetical." Box v. Planned

Parenthood of Indiana & Kentucky, Inc., ___ U.S. ___, ___, 139 S.Ct. 1780, 1783 (2019). How can abortion be used eugenically?

9. *California's Sterilization Laws*. In 1909, California became the third state to pass a sterilization law. California's law applied broadly to the feebleminded, inmates, patients, and eventually to those "afflicted with mental disease which may have been inherited and is likely to be transmitted to descendants, the various degrees of feeblemindedness, those suffering from perversion or marked departures from normal mentality or from disease of a syphilitic nature." How was California's law different from the Virginia law?

According to Professor Stern, California's sterilization law was unique in 1) not providing any legal mechanisms or hearings to protect patients, 2) requiring no notification to a guardian and 3) never facing *any* serious legal challenge such as occurred in Indiana and Virginia. Therefore, for seventy years, California led the country in sterilizations—"more than 20,000 surgeries, or one-third of all those nationwide." (Virginia was second with 8,000.) See Alexandra Minna Stern, "From Legislation to Lived Experience: Eugenic Sterilization in California and Indiana, 1907–1979," 99–101, A Century of Eugenics in America: From the Indiana Experiment to the Human Genome Era (Paul A. Lombardo ed., 2011).

Stern also noted "the disproportionate number of operations carried out on those with Spanish surnames." Id. at 109. Does this history explain the recent experience of California prisoners described below?

10. *Sterilization Rates*. Rates of sterilization declined across the states during the 1950s. Why do you think that happened? See Stern, *supra* (new attitudes toward mental health and mental retardation and the growth of mental health agencies reversed the sterilization trend). Yet Indiana's law was not officially repealed until 1974 and California's until 1979.

11. *Compensation*. Should individuals who were sterilized by the states receive compensation for their injuries? See Katherine A. West, Following in North Carolina's Footsteps: California's Challenge in Compensating Its Victims of Compulsory Sterilization, 53 Santa Clara L. Rev. 301, 302 (2013) (recommending that California follow North Carolina's suggestion of offering $50,000 per person and estimating there are from 225 to 497 living survivors of the state's policy).

Does the next reading suggest that California officials still do not understand the dangers of eugenics and sterilization?

Sterilization of Female Inmates

California State Auditor, 2014.
Report 2013–120.

Summary

Results in Brief

The California Department of Corrections and Rehabilitation (Corrections) oversees the inmate population of the State's 33 adult

prisons. During our eight-year audit period—which we defined as fiscal years 2005–06 through 2012–13—four of these prisons housed substantially all of the female inmates: California Institution for Women, Central California Women's Facility, Folsom Women's Facility, and Valley State Prison for Women (Valley). Valley no longer houses women since its conversion to a men's prison in January 2013. For much of our audit period, Corrections' role in providing inmates with medical care was not significant; the more substantial role was played by California Correctional Health Care Services (Receiver's Office) under the direction of a federal court-appointed receiver. A receiver took control of prison medical care in 2006 and will retain control until the court finds that Corrections can maintain a constitutionally adequate prison medical care system.

From fiscal years 2005–06 through 2012–13, 144 female inmates were sterilized by a procedure known as a bilateral tubal ligation. The last of these female inmate sterilizations occurred in 2011. Although various surgical procedures may result in a female's sterilization, bilateral tubal ligations are generally surgical procedures that are performed for the sole purpose of sterilization, and state regulations impose certain requirements that must be met before such a procedure is performed. However, the state entities responsible for providing medical care to these inmates—Corrections[1] and the Receiver's Office—sometimes failed to ensure that inmates' consent for sterilization was lawfully obtained. Overall, we noted that 39 inmates[2] were sterilized following deficiencies in the informed consent process. We found two types of deficiencies. First, we found no evidence that the inmate's physician—the individual who would perform the procedure in a hospital or an alternate physician—signed the consent form as required by state regulations. Second, we noted potential violations of the required waiting period between when the inmate consented to the procedure and when the sterilization surgery actually took place. Some inmates were sterilized following violations of both of these requirements. Although neither Corrections nor employees of the Receiver's Office actually performed the sterilization procedures, we concluded that they had a responsibility to ensure that the informed consent requirements were followed in those instances when their employees obtained inmates' consent, which was the case for at least 19 of the 39 inmates. Either the

[1] Corrections was responsible for inmate health care between July 1, 2005, and the appointment of the first federal receiver, effective April 2006. During this time period, 15 inmates had tubal ligation procedures, and based on available and potentially incomplete medical records, documentation for at least four of these inmates demonstrated potential violations of informed consent requirements.

[2] The true number of inmates for whom Corrections or the Receiver's Office did not ensure that lawful consent was obtained before sterilization may be higher. For example, one hospital destroyed seven inmate medical records in accordance with its records retention policy. Five of these seven inmates consented to the sterilization procedure while in prison, and it is unclear—based on available records—whether physicians signed the sterilization consent forms just prior to surgery.

remaining 20 inmates signed their consent to be sterilized at a physical location other than a prison or the Receiver's Office had difficulty determining whether the individual who obtained consent was an employee.

Lawful consent is represented by key steps as defined by the California Code of Regulations, Title 22 (Title 22). For example, the physician or an alternate physician must sign the consent form just before performing the surgery, and a waiting period is required after the patient signs the consent form. The missing physicians' signatures on some of the inmates' consent forms are especially concerning because of what the physician signature certifies: that the required waiting period has been satisfied and that the patient appears mentally competent and understands the lasting effects of sterilization. The physician is the last check in the informed consent process and provides the patient with the final opportunity to change her mind.

All the bilateral tubal ligations we reviewed were performed at general acute care hospitals rather than in prison medical facilities. A lawyer for the Receiver's Office stated that the specific provisions of Title 22 do not apply to prison employees, because Title 22 applies only to general acute care hospitals. Nevertheless, because employees of the Receiver's Office played a significant role in these 19 inmates' care and in obtaining their consent to be sterilized, our legal counsel advised us that a court would likely find that the Receiver's Office had a responsibility to ensure that consent was lawfully obtained from these inmates in accordance with Title 22.

Although the consent forms we were able to review demonstrated that each female inmate signed a consent form, we have concerns about whether the female inmates undergoing bilateral tubal ligations received adequate counseling about their decision to be sterilized. Despite a Receiver's Office policy that prison medical staff must use progress notes—a term for documenting information made in an inmate's medical record—to summarize discussions with inmates, in no instance did we find a female inmate whose progress notes adequately reflected that she had been counseled about her decision to be sterilized. The lack of notes in the inmates' medical records regarding informed consent and sterilization made it impossible for us to reach a conclusion as to the quality and content of the consultations between prison medical staff and inmates. We were also unable to conclude whether inmates received educational materials, whether prison medical staff answered inmates' questions, or whether these staff provided the inmates with all of the necessary information to make such a sensitive and life-changing decision as sterilization.

The Receiver's Office also failed to ensure that the prison medical staff under its direction followed state regulations requiring specific approvals for bilateral tubal ligation procedures, including approvals by two committees made up of high-ranking prison medical staff and

medical executives from the Receiver's Office. The failure to obtain the necessary approvals was systemic; all but one of the 144 bilateral tubal ligation procedures lacked the necessary approvals. Overall, our file review demonstrated that prison medical staff infrequently requested approval to sterilize inmates, and when they did, it was not always clear that these requests were approved. In many cases, prison medical staff simply requested approval for other medical procedures—such as cesarean sections at hospitals—and did not indicate that the inmate was also to be sterilized.

Since January 2010, when the Receiver's Office asserts it became aware of the sterilization procedures—following allegations by a legal advocacy group—its medical claims data show that the number of female inmates who have undergone bilateral tubal ligations and other medical procedures that result in sterilization has greatly decreased. In addition, since that time we found that the Receiver's Office has better adhered to its processes for reviewing medical services for necessity and for obtaining required approvals for medical services. Nevertheless, because the function of approving a medical procedure has been and remains separate from the process for scheduling the procedure at a general acute care hospital or other community medical facility, the opportunity still exists for inmates to receive medical services that are not authorized. Until the Receiver's Office ensures that medical scheduling is driven by authorized requests for service, it risks subjecting inmates to potentially unnecessary medical procedures and cannot demonstrate that it is in full control of the medical care inmates receive.

Recommendations

To ensure that the necessary education and disciplinary action can be taken, the Receiver's Office should report to the California Department of Public Health, which licenses general acute care hospitals, and the Medical Board of California, which licenses physicians, the names of all hospitals and physicians associated with inmates' bilateral tubal ligations during fiscal years 2005–06 through 2012–13 for which consent was unlawfully obtained. The Receiver's Office should make these referrals as soon as is practicable.

To ensure that it can better monitor how its medical staff and contractors adhere to the informed consent requirements of Title 22, sections 70707.1 through 70707.7, the Receiver's Office should develop a plan by August 2014 to implement a process by December 2014 that would include the following:

- Providing additional training to prison medical staff regarding Title 22 requirements for obtaining informed consent for sterilization procedures, including the applicable forms and mandatory waiting period requirements, to ensure that consent is lawfully obtained.

- Developing checklists or other tools that prison medical staff can use to ensure that medical procedures are not scheduled until after the applicable waiting periods for sterilization have been satisfied.
- Periodically reviewing, on a consistent basis, a sample of cases in which inmates received treatment resulting in sterilization at general acute care hospitals, to ensure that all informed consent requirements were satisfied.
- Until such time as the Receiver's Office implements a process for obtaining inmate consent for sterilization under Title 22 that complies with all aspects of the regulations, it should discontinue its practice of facilitating an inmate's consent for sterilization in the prison and allow the general acute care hospital to obtain an inmate's consent.

To improve the quality of the information prison medical staff document in inmate medical records, the Receiver's Office should do the following:

- Train its entire prison medical staff on its policy in the inmate medical procedures related to appropriate documentation in inmates' medical records. This training should be completed by December 31, 2014.
- Either develop or incorporate into an existing process a means by which it evaluates prison medical staffs' documentation in inmate medical records and retrains prison medical staff as necessary. The Receiver's Office should develop and implement this process by June 30, 2015.

To ensure that inmates receive only medical services that are authorized through its utilization management process, the Receiver's Office should do the following:

- Develop processes by August 31, 2014, such that a procedure that may result in sterilization is not scheduled unless the procedure is approved at the necessary level of the utilization management process.
- By October 31, 2014, train its scheduling staff to verify that the appropriate utilization management approvals are documented before they schedule a procedure that may result in sterilization.

Agency Comments

In its response to the audit, the Receiver's Office generally agreed with the report's factual findings, but noted that it reached conclusions about its duty to ensure compliance with the sterilization and consent procedures set forth in Title 22 that differ from the report. Nevertheless, the Receiver's Office pledged to implement all of the recommendations.

NOTES AND QUESTIONS

1. *Recommendations*. How do you assess the recommendations provided in this report? How would you administer them to make sure the standards were enforced?

2. *Prison Officials' Role in Sterilization*. Is it appropriate for prison officials to recommend sterilization to prisoners? According to one prisoner, Christina Cordero, 34, who spent two years in prison for auto theft, "As soon as [the prison doctor] found out that I had five kids, he suggested that I look into getting it done. The closer I got to my due date, the more he talked about it, ... He made me feel like a bad mother if I didn't do it." Corey G. Johnson, Female Inmates Sterilized in California Prisons Without Approval, Reveal, Jul. 7, 2013, at https://revealnews.org/article/female-inmates-sterilized-in-california-prisons-without-approval/; Corey G. Johnson, California Female Inmates Sterilized Illegally, Desert Sun, Jun. 21, 2014, at http://www.desertsun.com/story/news/nation/2014/06/20/california-female-inmates-sterilized/11034317/.

Practice Exercise: Write out the full policy that you think the California prison system should adopt for sterilizations. How would informed consent be protected? What administrative procedures need to be in place to protect against abuse? Should sterilization of prisoners be legal under some circumstances or should it be completely banned? How do sterilizations relate to transgendered prisoners?

A Tennessee judge offered to remove 30 days from prisoners' sentences if they were sterilized. Male inmates would get permanent vasectomies, while women would get temporary birth control implants. 38 males and 32 females agreed to the procedure. The judge said, "I hope to encourage them to take personal responsibility and give them a chance, when they do get out, to not to be burdened with children. This gives them a chance to get on their feet and make something of themselves." Nick Thieme, A Tennessee Jail Is Offering Vasectomies for Reduced Prison Time: That's Wildly Unethical, Slate, Jul. 21, 2017, https://slate.com/technology/2017/07/tennessee-jails-vasectomy-plan-is-wildly-unethical.html. Do you agree with the judge?

3. *Equal Opportunities*. Do you agree with the prison official who said sterilization is "an empowerment issue for female inmates, providing them the same options as women on the outside?" Id.

4. *Informed Consent*. Can a woman in labor give informed consent to a sterilization? See id. (Professor Dorothy Roberts explains "courts have concluded that soliciting approval for sterilization during labor is coercive because pain and discomfort can impair a woman's ability to weigh the decision. . . . No woman should give consent on the operating table.").

5. *Reading Proficiency for Consent*. Investigators found that most of the women tested at less than a high school level of reading proficiency, and a third of them below the sixth-grade level. What level of reading proficiency does it take to give informed consent to a sterilization? Corey G. Johnson,

Female Prison Inmates Sterilized Illegally, California Audit Confirms, Reveal, Jun. 19, 2014, at https://revealnews.org/article/female-prison-inmates-sterilized-illegally-california-audit-confirms/.

6. *Potential Claims*. What lawsuits would you file on behalf of the California prisoners? What remedies would you seek? How can courts provide a remedy for sterilization?

7. *State Interests*. The prison doctor who performed the sterilizations told reporters "he provided an important service to poor women who faced health risks in future pregnancies because of past cesarean sections." When he learned that the state had paid $147,460 in fees to sterilization doctors, he commented, "Over a 10-year period, that isn't a huge amount of money . . . compared to what you save in welfare paying for these unwanted children—as they procreated more." Johnson, Female Inmates Sterilized in California Prisons Without Approval, *supra*. What interest does the state have in the number of children that a woman bears? That a woman prisoner bears?

8. *Eugenics*. Does the prison episode demonstrate that eugenics is still part of California culture despite the repeal of the twentieth-century eugenics laws? Should eugenics and sterilization always be prohibited?

Practice Exercise: Draft the model legislation that you think California should adopt. Then go to the website and compare your legislation with the bill that California adopted.

9. *Sterilization Legislation*. In response to the discovery of prison sterilizations, state legislators introduced a bill, SB 1135, to provide a proper policy on sterilization in state prisons. Governor Jerry Brown signed legislation banning sterilization as a means of birth control for the state's prisoners. Corey G. Johnson, California Bans Coerced Sterilization of Female Inmates, Reveal, Sept. 26, 2014, https://revealnews.org/article-legacy/california-bans-coerced-sterilization-of-female-inmates/. Is that the best approach to sterilization?

In California, the investigation showed that Mexican American women were sterilized disproportionately to their numbers in the population. See Roque Planas, Mexican Americans Sterilized Disproportionately In California Institutions, Study Says, Jun. 9, 2013, at http://www.huffingtonpost.com/2013/06/05/mexican-americans-sterilized_n_3390305.html. Are you surprised that discrimination occurred in the prison setting? Would you expect minorities to be treatment poorly in other places where informed consent is important, e.g., when they are patients or research subjects?

Native American women were also victims of sterilization. At least 25% of Native American women were sterilized after family planning legislation passed in 1970. In 1977, chief tribal judge Marie Sanchez told the United Nations that those women "were targets of the 'modern form' of genocide—sterilization." Brianna Theobald, A 1970 Law Led to the Mass Sterilization of Native American Women: That History Still Matters, Time, Nov. 28, 2019, https://time.com/5737080/native-american-sterilization-history/.

In the next section, we examine the long and troubling legacy of such racism in medical research.

3. RACISM AND RESEARCH

Racism and Research: The Case of the Tuskegee Syphilis Study

Allan M. Brandt, 1978.
8 Hastings Center Report 21–29.

In 1932 the U.S. Public Health Service (USPHS) initiated an experiment in Macon County, Alabama, to determine the natural course of untreated, latent syphilis in black males. The test comprised 400 syphilitic men, as well as 200 uninfected men who served as controls. The first published report of the study appeared in 1936 with subsequent papers issued every four to six years, through the 1960s. When penicillin became widely available by the early 1950s as the preferred treatment for syphilis, the men did not receive therapy. In fact on several occasions, the USPHS actually sought to prevent treatment. Moreover, a committee at the federally operated Center for Disease Control decided in 1969 that the study should be continued. Only in 1972, when accounts of the study first appeared in the national press, did the Department of Health, Education and Welfare halt the experiment. At that time seventy-four of the test subjects were still alive; at least twenty-eight, but perhaps more than 100, had died directly from advanced syphilitic lesions. In August 1972, HEW appointed an investigatory panel which issued a report the following year. The panel found the study to have been "ethically unjustified," and argued that penicillin should have been provided to the men. . . .

Racism and Medical Opinion

A brief review of the prevailing scientific thought regarding race and heredity in the early twentieth century is fundamental for an understanding of the Tuskegee Study. By the turn of the century, Darwinism had provided a new rationale for American racism. Essentially primitive peoples, it was argued, could not be assimilated into a complex, white civilization. Scientists speculated that in the struggle for survival the Negro in America was doomed. Particularly prone to disease, vice, and crime, black Americans could not be helped by education or philanthropy. Social Darwinists analyzed census data to predict the virtual extinction of the Negro in the twentieth century, for they believed the Negro race in America was in the throes of a degenerative evolutionary process.

The medical profession supported these findings of late nineteenth- and early twentieth-century anthropologists, ethnologists, and biologists. Physicians studying the effects of emancipation on health concluded almost universally that freedom had caused the "mental, moral, and

physical deterioration of the black population." They substantiated this argument by citing examples in the comparative anatomy of the black and white races. As Dr. W. T. English wrote: "A careful inspection reveals the body of the negro a mass of minor defects and imperfections from the crown of the head to the soles of the feet." Cranial structures, wide nasal apertures, receding chins, projecting jaws, all typed the Negro as the lowest species in the Darwinian hierarchy. . . .

According to these physicians, lust and immorality, unstable families, and reversion to barbaric tendencies made blacks especially prone to venereal diseases. One doctor estimated that over 50 percent of all Negroes over the age of twenty-five were syphilitic. Virtually free of disease as slaves, they were now overwhelmed by it, according to informed medical opinion. Moreover, doctors believed that treatment for venereal disease among blacks was impossible, particularly because in its latent stage the symptoms of syphilis become quiescent . . .

The Origins of the Experiment

In 1929, under a grant from the Julius Rosenwald Fund, the USPHS conducted studies in the rural South to determine the prevalence of syphilis among blacks and explore the possibilities for mass treatment. The USPHS found Macon County, Alabama, in which the town of Tuskegee is located, to have the highest syphilis rate of the six counties surveyed. The Rosenwald Study concluded that mass treatment could be successfully implemented among rural blacks. Although it is doubtful that the necessary funds would have been allocated even in the best economic conditions, after the economy collapsed in 1929, the findings were ignored. It is, however, ironic that the Tuskegee Study came to be based on findings of the Rosenwald Study that demonstrated the possibilities of mass treatment.

Three years later, in 1932, Dr. Taliaferro Clark, Chief of the USPHS Venereal Disease Division and author of the Rosenwald Study report, decided that conditions in Macon County merited renewed attention. Clark believed the high prevalence of syphilis offered an "unusual opportunity" for observation. From its inception, the USPHS regarded the Tuskegee Study as a classic "study in nature," rather than an experiment. As long as syphilis was so prevalent in Macon and most of the blacks went untreated throughout life, it seemed only natural to Clark that it would be valuable to observe the consequences. He described it as a "ready-made situation." Surgeon General H. S. Cumming wrote to R.R. Moton, Director of the Tuskegee Institute:

> The recent syphilis control demonstration carried out in Macon County, with the financial assistance of the Julius Rosenwald Fund, revealed the presence of an unusually high rate in this county and, what is more remarkable, the fact that 99 per cent of this group was entirely without previous treatment. This combination, together with the expected cooperation of your hospital, offers an unparalleled opportunity for carrying on this

> piece of scientific research which probably cannot be duplicated anywhere else in the world.

Although no formal protocol appears to have been written, several letters of Clark and Cumming suggest what the USPHS hoped to find. Clark indicated that it would be important to see how disease affected the daily lives of the men:

> The results of these studies of case records suggest the desirability of making a further study of the effect of untreated syphilis on the human economy among people now living and engaged in their daily pursuits.

It also seems that the USPHS believed the experiment might demonstrate that antisyphilitic treatment was unnecessary. As Cumming noted: "It is expected the results of this study may have a marked bearing on the treatment, or conversely the non-necessity of treatment, of cases of latent syphilis."

The immediate source of Cumming's hypothesis appears to have been the famous Oslo Study of untreated syphilis. Between 1890 and 1910, Professor C. Boeck, the chief of the Oslo Venereal Clinic, withheld treatment from almost two thousand patients infected with syphilis. He was convinced that therapies then available, primarily mercurial ointment, were of no value. When arsenic therapy became widely available by 1910, after Paul Ehrlich's historic discovery of "606," the study was abandoned. E. Bruusgaard, Boeck's successor, conducted a follow-up study of 473 of the untreated patients from 1925 to 1927. He found that 27.9 percent of these patients had undergone a "spontaneous cure," and now manifested no symptoms of the disease. Moreover, he estimated that as many as 70 percent of all syphilitics went through life without inconvenience from the disease. His study, however, clearly acknowledged the dangers of untreated syphilis for the remaining 30 percent.

Thus every major textbook of syphilis at the time of the Tuskegee Study's inception strongly advocated treating syphilis even in its latent stages, which follow the initial inflammatory reaction. In discussing the Oslo Study, Dr. J.E. Moore, one of the nation's leading venereologists wrote, "This summary of Bruusgaard's study is by no means intended to suggest that syphilis be allowed to pass untreated." If a complete cure could not be effected, at least the most devastating effects of the disease could be avoided. Although the standard therapies of the time, arsenical compounds and bismuth injection, involved certain dangers because of their toxicity, the alternatives were much worse. As the Oslo Study had shown, untreated syphilis could lead to cardiovascular disease, insanity, and premature death. . . . "Another compelling reason for treatment," noted Moore, "exists in the fact that every patient with latent syphilis may be, and perhaps is, infectious for others." In 1932, the year in which the Tuskegee Study began, the USPHS sponsored and published a paper

by Moore and six other syphilis experts that strongly argued for treating latent syphilis.

The Oslo Study, therefore, could not have provided justification for the USPHS to undertake a study that did not entail treatment. Rather, the suppositions that conditions in Tuskegee existed "naturally" and that the men would not be treated anyway provided the experiment's rationale. In turn, these two assumptions rested on the prevailing medical attitudes concerning blacks, sex, and disease. For example, Clark explained the prevalence of venereal disease in Macon County by emphasizing promiscuity among blacks:

> This state of affairs is due to the paucity of doctors, rather low intelligence of the Negro population in this section, depressed economic conditions, and the very common promiscuous sex relations of this population group which not only contribute to the spread of syphilis but also contribute to the prevailing indifference with regard to treatment.

In fact, Moore, who had written so persuasively in favor of treating latent syphilis, suggested that existing knowledge did not apply to Negroes. Although he had called the Oslo Study "a never-to-be-repeated human experiment," he served as an expert consultant to the Tuskegee Study:

> I think that such a study as you have contemplated would be of immense value. It will be necessary of course in the consideration of the results to evaluate the special factors introduced by a selection of the material from negro males. Syphilis in the negro is in many respects almost a different disease from syphilis in the white.

Dr. O. C. Wenger, chief of the federally operated venereal disease clinic at Hot Springs, Arkansas, praised Moore's judgment, adding, "This study will emphasize those differences." On another occasion he advised Clark, "We must remember we are dealing with a group of people who are illiterate, have no conception of time, and whose personal history is always indefinite."

The doctors who devised and directed the Tuskegee Study accepted the mainstream assumptions regarding blacks and venereal disease. The premise that blacks, promiscuous and lustful, would not seek or continue treatment, shaped the study. A test of untreated syphilis seemed "natural" because the USPHS presumed the men would never be treated; the Tuskegee Study made that a self-fulfilling prophecy. . . .

The HEW Final Report

HEW finally formed the Tuskegee Syphilis Study Ad Hoc Advisory Panel on August 28, 1972, in response to criticism that the press descriptions of the experiment had triggered. The panel, composed of nine members, five of them black, concentrated on two issues. First, was the study justified in 1932 and had the men given their informed consent?

Second, should penicillin have been provided when it became available in the early 1950s? The panel was also charged with determining if the study should be terminated and assessing current policies regarding experimentation with human subjects. The group issued their report in June 1973.

By focusing on the issues of penicillin therapy and informed consent, the *Final Report* and the investigation betrayed a basic misunderstanding of the experiment's purposes and design. The HEW report implied that the failure to provide penicillin constituted the study's major ethical misjudgment; implicit was the assumption that no adequate therapy existed prior to penicillin. Nonetheless medical authorities firmly believed in the efficacy of arsenotherapy for treating syphilis at the time of the experiment's inception in 1932. The panel further failed to recognize that the entire study had been predicated on nontreatment. Provision of effective medication would have violated the rationale of the experiment-to study the natural course of the disease until death. On several occasions, in fact, the USPHS had prevented the men from receiving proper treatment. Indeed, there is no evidence that the USPHS ever considered providing penicillin.

The other focus of the *Final Report*—informed consent—also served to obscure the historical facts of the experiment. In light of the deceptions and exploitations which the experiment perpetrated, it is an understatement to declare, as the *Report* did, that the experiment was "ethically unjustified," because it failed to obtain informed consent from the subjects. The *Final Report's* statement, "Submitting voluntarily is not informed consent," indicated that the panel believed that the men had volunteered *for the experiment*. The records in the National Archives make clear that the men did not submit voluntarily to an experiment; they were told and they believed that they were getting free treatment from expert government doctors for a serious disease. The failure of the HEW *Final Report* to expose this critical fact—that the USPHS lied to the subjects—calls into question the thoroughness and credibility of their investigation.

Failure to place the study in a historical context also made it impossible for the investigation to deal with the essentially racist nature of the experiment. The panel treated the study as an aberration, well-intentioned but misguided. Moreover, concern that the *Final Report* might be viewed as a critique of human experimentation in general seems to have severely limited the scope of the inquiry. The *Final Report* is quick to remind the reader on two occasions: "The position of the Panel must not be construed to be a general repudiation of scientific research with human subjects." The *Report* assures us that a better-designed experiment could have been justified:

> It is possible that a scientific study in 1932 of untreated syphilis, properly conceived with a clear protocol and conducted with suitable subjects who fully understood the implications of their

> involvement, might have been justified in the pre-penicillin era. This is especially true when one considers the uncertain nature of the results of treatment of late latent syphilis and the highly toxic nature of therapeutic agents then available.

This statement is questionable in view of the proven dangers of untreated syphilis known in 1932.

Since the publication of the HEW *Final Report,* a defense of the Tuskegee Study has emerged. These arguments, most clearly articulated by Dr. R.H. Kampmeier in the *Southern Medical Journal,* center on the limited knowledge of effective therapy for latent syphilis when the experiment began. Kampmeier argues that by 1950, penicillin would have been of no value for these men. Others have suggested that the men were fortunate to have been spared the highly toxic treatments of the earlier period. Moreover, even these contemporary defenses assume that the men never would have been treated anyway. As Dr. Charles Barnett of Stanford University wrote in 1974, "The lack of treatment was not contrived by the USPHS but was an established fact of which they proposed to take advantage." Several doctors who participated in the study continued to justify the experiment. Dr. J. R. Heller, who on one occasion had referred to the test subjects as the "Ethiopian population," told reporters in 1972:

> I don't see why they should be shocked or horrified. There was no racial side to this. It just happened to be in a black community. I feel this was a perfectly straightforward study, perfectly ethics, with controls. Part of our mission as physicians is to find out what happens to individuals with disease and without disease.

These apologies, as well as the HEW *Final Report,* ignore many of the essential ethical issues which the study poses. The Tuskegee Study reveals the persistence of beliefs within the medical profession about the nature of blacks, sex, and disease—beliefs that had tragic repercussions long after their alleged "scientific" bases were known to be incorrect. Most strikingly, the entire health of a community was jeopardized by leaving a communicable disease untreated. There can be little doubt that the Tuskegee researchers regarded their subjects as less than human. As a result, the ethical canons of experimenting on human subjects were completely disregarded.

The study also raises significant questions about professional self-regulation and scientific bureaucracy. Once the USPHS decided to extend the experiment in the summer of 1933, it was unlikely that the test would be halted short of the men's deaths. The experiment was widely reported for forty years without evoking any significant protest within the medical community. Nor did any bureaucratic mechanism exist within the government for the periodic reassessment of the Tuskegee experiment's ethics and scientific value. The USPHS sent physicians to Tuskegee every several years to check on the study's progress, but never subjected

the morality or usefulness of the experiment to serious scrutiny. Only the press accounts of 1972 finally punctured the continued rationalizations of the USPHS and brought the study to an end. Even the HEW investigation was compromised by fear that it would be considered a threat to future human experimentation.

In retrospect the Tuskegee Study revealed more about the pathology of racism than it did about the pathology of syphilis; more about the nature of scientific inquiry than the nature of the disease process. The injustice committed by the experiment went well beyond the facts outlined in the press and the HEW *Final Report.* The degree of deception and damages have been seriously underestimated. As this history of the study suggests, the notion that science is a value-free discipline must be rejected. The need for greater vigilance in assessing the specific ways in which social values and attitudes affect professional behavior is clearly indicated.

NOTES AND QUESTIONS

1. *Tuskegee*. Was there any positive justification for the Tuskegee study, as its defenders suggest? Write a list of the positive aspects of the study.

2. *Ethical Violations*. After writing your list, consider the following ethical problems with Tuskegee identified in Carol A. Heintzelman, The Tuskegee Syphilis Study and Its Implications for the 21st Century, 10(4) The New Social Worker (Fall 2003):

Practice Exercise: Write a list of the ethical violations or problems you can identify with the study and compare it to your list from Question 1.

a. *Deception in Recruiting*: "It was never explained to the subjects that the survey was designed to detect syphilis. The term 'bad blood,' which was a local colloquialism for everything from anemia to leukemia, was used by the doctors and never defined for the subjects. Subjects were never told they had syphilis, the course of the disease, or treatment. The treatment presented consisted of spinal taps, which were described as 'spinal shots.' "

b. *Withholding of Treatment for Research Purposes*: "researchers judged that the benefits of nontreatment outweighed the benefits of treatment." The researchers thought there might be toxic reaction to penicillin (such as fever, angina, or ruptured blood vessels), and were not sure if penicillin could do anything for patients in an advanced stage of syphilis. What do you think of the researchers' concerns that it might be ineffective to give penicillin to the Tuskegee men?

c. *Failure to Report.* Alabama had a state law dating from 1927 that required that state agencies be notified about venereal

diseases. Would such notification have protected the men's *wives* from infection?

d. *No Accurate Records* were kept.

e. *Stereotypes about African Americans* underlay the whole study.

f. *Medical Blindness.* Publications about the Tuskegee study existed for forty years without the ethics of the study being challenged by any medical researchers.

g. *Legacy of Distrust in the African American Community* persists today.

3. *Compensation*. Each survivor received a settlement of $40,000. Was that adequate to compensate for his damages? How would you compare the damages in the Tuskegee case with damages for sterilized individuals like Carrie Buck?

4. *Researchers' Contributions*. How important is it to you whether the Tuskegee men were infected with syphilis by the researchers? Is a study of men already afflicted with syphilis less troubling than one in which researchers infect the research subjects?

While researching Tuskegee, Professor Susan M. Reverby discovered the files of United States Public Health Service Dr. John C. Cutler at the University of Pittsburgh Archives. The papers showed that Cutler, with the support of U.S. health agencies, had conducted a study in Guatemala from 1946–1948. Susan M. Reverby, "Normal Exposure" and Inoculation Syphilis: A PHS "Tuskegee" Doctor in Guatemala, 1946–1948, 23 (1) J. of Pol. Hist. 6 (2011). According to Reverby, Guatemala differed from Tuskegee "in two majors [sic] ways: government doctors *did infect* people with syphilis (and gonorrhea and chancroid and then *did treat* them with penicillin." Id. at 9. In contrast to Tuskegee, where researchers wanted to watch the development of syphilis in already-infected individuals, in Guatemala the doctors wanted to test individual response to exposure and then determine if immediate treatment could stop the course of the disease. The researchers sent already-infected prostitutes into prisons to infect prisoners. They also infected prostitutes so they could infect the prisoners, and then, when the prisoners were slow to contract the disease, expanded the research population to non-prisoners and sought new, direct means of infection. No consent was ever requested or given to the study.

Reverby's research about Guatemala was confirmed by a U.S. government report, *Ethically Impossible.* According to the government's report, there was "no documentation of informed consent for study enrollment, any indication that subjects understood they were participating in research, or enumeration of incentives received by specific subjects for participation." In 2010 President Barack Obama apologized to the government and people of Guatemala for the experiments. How do you assess the ethics of Guatemala compared to the ethics of Tuskegee?

Go to the website and learn about the apology.

5. *Social Benefit*. According to Professor Reverby, "Cutler and his colleagues thought they might be making a great contribution to understanding this dreadful disease. Caught at the beginning of a paradigm shift in the disease's impact on humans—for penicillin was just then making its scourge seem less frightening—they believed they were doing the right thing even while acknowledging the risks and discussing the ethical edge they crossed. This should never be forgotten." Susan M. Reverby, Still "Ethically Impossible?" The Presidential Commission's Report on the STD Inoculation Studies in Guatemala, Bioethics Forum, Hastings Center, Sept. 22, 2011. Does Reverby's comment make you more or less sympathetic to Dr. Cutler and his fellow researchers? What lessons do you draw from Tuskegee?

6. *HeLa*. Does the following story of Henrietta Lacks confirm that American medical research is infected by racism?

Book Review Essay: The Immortal Life of Henrietta Lacks, Rebecca Skloot

Kate Scannell.
31 Journal of Legal Medicine 493 (2010).

ENCOUNTERING HENRIETTA LACKS

. . . I first "encountered" Henrietta Lacks in the early 1980s—more than three decades after she had died from cervical cancer in 1951. I had been asked to assist a fellow researcher with his experiment, by concocting various broths and "prepping" the cells he would require. Eager to avoid the tedium of my own research project, I dutifully assembled the requisite ingredients and glassware. And, as he had recommended, I met with "The Guy" who oversaw our cell cultures so I could learn how to handle them properly.

"These are HeLa cells," he informed me as he gently handed over a culture bottle on which was scrawled various numbers and initials. He explained that the cells were from an "eternal" human lineage—faithfully and perpetually reproducing for decades, generously providing researchers around the world with a standardized and plentiful supply of cells for experimental purposes.

His astounding description left me awestruck. I had been taught that all human cells were programmed to die—it was part of the natural order. What unique biophysical property did these undying cells possess? What separated these immortal cells from claims of the divine?

"The Guy" couldn't answer these questions. But he did offer that the cells had been so-named with the initials of the woman from whom they'd been taken: "Henrietta Lacks."

The following hour or so that I spent under a sterile hood prepping those HeLa cells affected me deeply. And though mesmerized by the cells' disembodied immortality, I was more powerfully preoccupied with their personification. I became intensely curious about Henrietta Lacks—the person whom those cells survived. Regrettably, however, I could find no

illuminating information about her in the medical texts available to me back then.

" . . . ON THE BANKS OF THE RIVER OF DEATH"

It is now 2010 and, sorting through the new arrivals at my local bookstore, I stumble upon *The Immortal Life of Henrietta Lacks* by Rebecca Skloot. On its dust jacket is an arresting photograph of a beautiful and clear-eyed woman who seems to be looking straight through time, to the precise moment in which I look at her. The cover text underneath the book's title reads: "Doctors took her cells without asking. Those cells never died. They launched a medical revolution and a multi-million dollar industry. More than twenty years later, her children found out. Their lives would never be the same."

I purchase the book and read it in one day. And, although made newly aware of many vital details that characterize Henrietta's life, still, I keenly feel her abiding absence. Indeed, having left no words or first-person narrative of her own, her story is wholly reconstructed through the second-hand accounts of family members and doctors. In the end, she remains—immortally—without a voice that we hear, without an identity of her own making.

Tellingly, even Henrietta's name was often misrepresented or confused within various medical and lay publications about HeLa cells. She died without an obituary and was buried in an unmarked grave.

In 1999, the book's author visits Henrietta's birthplace in Virginia—located off Route 360, "just past Difficult Creek on the banks of the River of Death." There Skloot hopes to find and interview any family members still living in the mile-long subsection of the area known as "Lacks Town." She drives past an unpainted shack that marks its entry and soon encounters Cootie, Henrietta's first cousin. He tells Skloot: "Everybody in Lacks Town kin to Henrietta, but she been gone so long, even her memory pretty much dead now. . . . Everything about Henrietta dead except them cells." Ten years later, when Skloot revisits the town where Henrietta grew up tending gardens and "planting tobacco behind mule-drawn plows," it is virtually gone and "it felt like everything related to Henrietta's history was vanishing."

The historical invisibility of women, blacks, and impoverished Americans is a figurative "river of death" that courses throughout this book. It is not only Henrietta's life which is submerged, but also the lives of her community and family members. A profoundly heartbreaking example of this involves Elsie, one of Henrietta's two daughters, who was committed with the problematic diagnosis of "idiocy" to the Crownsville State Hospital—known formerly as the Hospital for the Negro Insane. In 1955, four years after Henrietta's death and at the age of fifteen, Elsie died in that gruesome asylum all alone and unbeknownst to her sister, Deborah, through whom much of Henrietta's story is told.

In 2001, the author accompanies Deborah to Crownsville to fulfill her promise to help "figure[e] out what happened to Elsie." They meet a hospital director who informs them that most of the medical records from that time period had been contaminated by asbestos and "carted away in bags and buried." Still, because of some personal "habit of collecting potentially historic documents" he is able to locate an autopsy report and photograph of Elsie that he stored in a closet near his desk. In that photograph, Elsie "stares somewhere just below the camera, crying, her face misshapen and barely recognizable" and she "appears to be screaming" while her "head is twisted unnaturally to the left, chin raised and held in place by a large pair of white hands." In the end, the "picture" of Elsie we are left holding is one of terrible deafening silence, literalized by hands around her small throat.

RESEARCH QUESTIONS LEFT UNANSWERED

The medical research establishment figures prominently in this book, primarily in the ways it regarded Henrietta Lacks and HeLa cells. With a mostly even hand, Skloot holds up a lens through which she views the doctors and researchers who populated not only the hospitals and research labs where Henrietta and her cells resided but also the urgent medical questions that were left unanswered for the Lacks family.

Yet, for this reader, it is the brief side-trip to Crownsville that provides the most vividly distilled impression about the research establishment. Skloot, while trying to learn what happened to Elsie, uncovers troubling information about ostensibly covert research activities at Crownsville. The hospital director shares his private trove of documents and newspaper clippings with Skloot, allowing her to determine that, while Elsie was at Crownsville, "scientists often conducted research on patients there without consent." Research sometimes included the insertion of "metal probes into patients' brains" or pneumoencephalography—a painful (and now archaic) procedure in which holes are drilled through a person's skull, and spinal fluid is replaced with air in order to obtain clearer X-ray images of the brain. The hospital director evaluates the data at his disposal and makes a calculated guess that Elsie had been studied.

As affecting as they are, still, these haunting images and alarming reports concerning Elsie and Crownsville do not take center stage under the hot lights cast upon the research establishment. For that, we are transported to Baltimore; it is 1951, and Henrietta Lacks is seeking medical care for cervical cancer at John Hopkins Hospital—a charity hospital with a segregated ward for black patients. Before she receives caustic radium treatment, two "dime-sized" samples of her cervical tissue are removed, allegedly without her permission. The samples are given to George Gey, a tissue-culture scientist who for years has struggled to develop a continuously reproducing human cell line that could facilitate and advance cancer research.

As it turns out, Henrietta would die several months later, at 31 years of age. Her cancerous cells, however, would survive her and proliferate wildly in Gey's lab, "with mythological intensity." He would freely distribute them to scientists throughout the world, who, in turn, would often make amazing medical discoveries. Over time, for-profit cell banks and biotech companies would enter the picture and launch a "multimillion-dollar" industry from a "dime"-sized sample of Henrietta's cervix.

Meanwhile, Henrietta's children would struggle financially—some of them unable to afford basic health care—and they would not even learn about their mother's scientific legacy for decades to come. When first contacted by John Hopkins officials in 1973, they come to understand that the doctors want to test them for cancer, so they willingly comply with blood sampling. As Henrietta's husband later recounts: "They said they got my wife and she part alive. . . . They been doin' experiments on her and they wanted to test my children see if they got that cancer killed their mother." But, as the family grimly discovers, there's been an abysmal misunderstanding—in fact, the doctors only wanted the family's samples in order to conduct further HeLa cell experimentation. This painful revelation arrives as a shock for Deborah, who for days had been phoning Hopkins for her "cancer results," anxiously dreading that she may have inherited her mother's fatal disease.

The family's formidable distrust of researchers and doctors only expands when in 1976, reading an article in *Rolling Stone* magazine, they also learn about massive commercial profiteering from HeLa cells. As Deborah remarks, "if our mother cells done so much for medicine, how come her family can't afford to see no doctors? Don't make no sense. People got rich off my mother without us even knowin' about them takin' her cells, now we don't get a dime."

A SPECIMEN'S RED TOENAILS

And yet, above all else, it is the doctors' casual disregard and thudding incuriosity about the family's interest in their mother as a person and human being that destroys any last vestige of their trust. When Skloot makes her initial phone contact with Deborah and proposes writing a book about her mother, Deborah eagerly responds that such a book would be "great." Only one year old when Henrietta died, Deborah has tired of everyone's focus on her mother as though she were just some dehumanized assortment of cells. "Everything always about just the cells and don't even worry about her name and was HeLa even a person." She asks, "You know what I really want? I want to know, what did my mother smell like? For all my life I just don't know anything, not even the little common things, like what color she like? Did she like to dance?"

For decades, no researchers inform or consult with the Lacks family about the nature and scope of their experimentation with Henrietta's cells. Instead, popular media bombard the Lacks siblings with disturbing and weirdly evocative depictions of their mother, whose early death left

them with few memories of her. Deborah sees "a *Newsweek* article called PEOPLE-PLANTS that said that scientists had crossed Henrietta Lacks's cells with tobacco cells" which leads her to fear "they'd created a human plant-monster that was half her mother, half tobacco." Hearing that scientists had used HeLa cells to study viruses like AIDS and Ebola, Deborah imagines "her mother eternally suffering the symptoms of each disease: bone-crushing pain, bleeding eyes, suffocation." She is horrified to read that some people have even tried to kill HeLa cells.

Even while Henrietta lay dying a painful and agonizing death in the hospital, doctors write in the medical record: "Henrietta is still a miserable specimen." Later, during Henrietta's autopsy, one of Gey's assistants charged with collecting additional pathology samples gasps when she suddenly notes that "Henrietta's toenails were covered in chipped bright red polish." Recounting that episode years later, the assistant explains: "I nearly fainted. I thought, *Oh jeez, she's a real person*. I started imagining her sitting in the bathroom painting those toenails, and it hit me for the first time that those cells we'd been working with all this time and sending all over the world, they came from a live woman. I'd never thought of it that way."

A STORY MANY-STORIED

This story is many-storied—not only about "HeLa cells and Henrietta Lacks, but of Henrietta's family—particularly Deborah—and their life-long struggle to make peace with the existence of those cells, and the science that made them possible." Their colossal struggle intimately involves issues of race, gender, poverty, class, and health care inequality. It raises substantial questions about medical practice and research ethics, about societal care of the mentally ill, about the moral conduct of journalistic inquiry into other peoples' lives. It ignites legal and ethical debates about tissue ownership and the commercialization of human biological materials.

When the struggle is fueled by depersonalization and dehumanization of Henrietta Lacks and her family, we also wrestle with great philosophical disturbances; at this level, the book sounds a cautionary note about the valorization of medical and scientific "objectivity." We see how claims to such objectivity can actually derive from the denial of someone's subjectivity. How the "progress" of scientific research can depend upon dehumanizing the body and its parts which hauntingly reside as "specimens" within the freezers of commercial biobanks and unregulated storage facilities scattered throughout the country.

But underneath all of this—stripped bare of scientific mind, of political and ideological counsel, of celestial advisement and legal consideration, of professional belonging and identity—I would have to say that the book tells a remarkably simple story infused with a very old theme. In essence, the story is a fiercely human tale about the importance of seeing one another in the clarifying light of each other's unique and

radiant mortal being. We are reminded that this sometimes requires faith and forgiveness, the acute notice of a corpse's painted toenails, or a road trip to Crownsville. But, always, it requires a basic respect for persons that calls on us to seek each other out with curiosity and compassion, rejecting utilitarian yardsticks to measure our humanity or the value of others' lives. There is a moral to the story, and it is fully captured by Elie Wiesel in the book's epigraph:

> We must not see *any* person as an abstraction. Instead, we must see in every person a universe with its own secrets,
> With its own treasures, with its own sources of anguish,
> And with some measure of triumph.

NOTES AND QUESTIONS

1. *Public Access*. After European scientists published the genome of the HeLa cells and made it available for download (thus making public genetic information about Henrietta's relatives) the National Institutes of Health entered into an agreement with Lacks' family. The family receives no financial compensation, but the genome data are stored in NIH databases, where researchers can apply for access. Two members of the Lacks family will be members of the NIH committee that decides who gets access. See Carl Zimmer, A Family Consents to a Medical Gift, 62 Years Later, N.Y. Times, Aug. 7, 2013, at A1. Is this a satisfactory resolution of Henrietta's case? We examine the rules and standards governing tissue donation below in Section B.

HeLa cells are being used in research into vaccines against COVID-19. One writer has argued, "Now, the extraordinary events of 2020—the #BlackLivesMatter movement for racial justice, and the unequal toll of COVID-19 on communities of colour—are compelling scientists to reckon with past injustices." Editorial, Henrietta Lacks: Science Must Right A Historical Wrong, Nature, Sept. 1, 2020, https://www.nature.com/articles/d41586-020-02494-z. How could bioethics contribute to that goal to close the gap? Some people have called for a ban on the use of HeLa cells. Others, including Lacks's family members, have wanted attention paid to the memory of the real woman, Henrietta Lacks. Nature magazine argued that a "step must be to acknowledge and undo the disparities that are baked into basic research—because the systemic racism that existed when Lacks's cells were taken still exists today." Id. Some scientists donate money to the Lacks Foundation whenever they use the cells. "To give back now, researchers should not only study why the disease is more prevalent and severe among Black people, but also help to implement solutions to close the gap." Do you agree that "From the very start of the pandemic, elderly, disabled, and chronically ill people heard the

Develop a distribution policy for the COVID vaccine. Who should get it first? Who should get it last? What factors enter into your reasoning? What would be inappropriate factors to consider?

unusually clear message that we are less worthy of saving, that our lives are worth less"? Andrew Pulrang, What I've Learned As a Disabled Person From the COVID-19 Pandemic, Forbes, Dec. 28, 2020, https://www.forbes.com/sites/andrewpulrang/2021/12/28/what-ive-learned-as-a-disabled-person-from-the-covid-19-pandemic/?

2. *Societal Benefit*. Do you think it matters how much benefit HeLa cells provided for society? Did the ethical violations outweigh the positive results?

3. *Compensation*. Was Henrietta's family justly compensated? What do you consider when deciding this? How does this compensation compare to the compensation offered for Tuskegee survivors or victims of sterilization?

4. *Prevention*. What institutions and procedures could prevent the abuses involved in Tuskegee, Guatemala, and HeLa? In the next section we study in detail the standards and mechanisms that developed to protect research with human subjects. For research in the United States, the most important standard has been the Common Rule, and the most important mechanism has been the Institutional Review Board (IRB), both of which emerged in response to Tuskegee.

B. SETTING STANDARDS FOR RESEARCH WITH HUMAN SUBJECTS

1. *Historical Background*. The protection of human subjects has gone through numerous stages since World War II. Dr. Fischer describes the following seven stages of development. See Bernard A. Fischer IV, A Summary of Important Documents in the Field of Research Ethics, 32 (1) Schizophrenia Bull. 69 (2005).

a. *The Nuremberg Code*. Nazi scientists and doctors who had experimented with human beings were prosecuted for war crimes during the Nuremberg Trials. In 1947, the Nuremberg Military Tribunal issued a 10-point code focused on the idea that human participation in research must be *voluntary*.

b. *The Declarations of Geneva and Helsinki*. Again in response to the abuses of the Second World War, the World Medical Association issued a code of medical ethics in 1949 (the *Declaration of Geneva*) and then a more detailed code in 1953 (the *Declaration of Helsinki*). Both declarations emphasize that the health of the patient must be the doctor's first consideration. The declarations also expanded protections for voluntary participation in research and informed consent.

c. *The Beecher Paper*. Harvard Professor Henry K. Beecher was concerned about American research that violated the rights of human subjects and in 1966 published "Ethics and Clinical Research" in the *New England Journal of Medicine*. Beecher demonstrated that some studies pursued scientific knowledge at the expense of human health. Mentally retarded

children were infected with hepatitis, for example, even though there was *no* possible benefit to them from the inoculation.

d. *The Vancouver Group* was a group of medical journal editors who agreed that authors must disclose conflicts of interest and certify that their research complied with the *Declaration of Helsinki*.

e. *The Belmont Report*. The U.S. Department of Health, Education and Welfare established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1974. In 1979 the commission released the Belmont Report, which identified the fundamental ethical principles that must guide all research with human subjects. "The commission concluded that the primary principles underlying ethical research with human beings are respect for persons, beneficence, and justice. The methods used to recognize these principles are informed consent, risk/benefit analysis, and appropriate selection of patients." Id. at 72.

f. *The Common Rule*. The National Research Act of 1974 established a specific set of guidelines to protect informed consent. The Common Rule establishes the standards that must be met in research with human subjects; it governs sixteen federal agencies and researchers who receive federal funding. Most research involves federal funding and so the Common Rule is widely applied. Clinical trials that involve treatments other than drugs and devices, such as surgery or bone marrow transplants, are not regulated by the Food and Drug Administration (FDA) and are subject to Department of Health and Human Services (DHHS) regulation only if they are "conducted, supported or otherwise subject to regulation by any federal department or agency." 45 C.F.R. § 46.101.

2. *Clinical Trials.* According to the National Institutes of Health, most research involving human subjects takes place in clinical trials. "Clinical research is medical research that involves people like you. When you volunteer to take part in clinical research, you help doctors and researchers learn more about disease and improve health care for people in the future. Clinical research includes all research that involves people." See NIH Clinical Trials and You, at https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics. Clinical research usually begins in the scientist's laboratory, where he or she searches for promising treatments for diseases. Potential treatments are first tested in animals for safety and effectiveness. If a drug succeeds in animals, the researcher sends a request for permission to study the drug in humans (called an Investigational New Drug (IND) application) to the Food and Drug Administration (FDA). See Christine Grady, Clinical Trials, Hastings Center Bioethics Briefings, Sept. 21, 2015, https://www.the

hastingscenter.org/briefingbook/clinical-trials/. The research on human subjects proceeds in the following stages:

- **Phase I trials**: Researchers test a drug or treatment in a small group of people (20–80) for the first time. The purpose is to study the drug or treatment to learn about safety and identify side effects.
- **Phase II trials**: The new drug or treatment is given to a larger group of people (100–300) to determine its effectiveness and to further study its safety.
- **Phase III trials**: The new drug or treatment is given to large groups of people (1,000–3,000) to confirm its effectiveness, monitor side effects, compare it with standard or similar treatments, and collect information that will allow the new drug or treatment to be used safely.
- **Phase IV trials**: After a drug is approved by the FDA and made available to the public, researchers track its safety in the general population, seeking more information about a drug or treatment's benefits, and optimal use.

Go to the website and review one of the Phase I consent forms (Phase I(A) or Phase I(B)). Would you participate in this study? Why or why not? Do you prefer the sample language of form Phase I(C)? Consider the definition of Phase I above. Phase I is the first time that a drug has been tested in human beings. Why do you think Phase I studies are usually conducted on healthy volunteers? Are patients who suffer from the disease to be targeted by the drug or healthy volunteers better candidates for Phase I? Does anyone who participates in a Phase I study receive benefit from her participation?

NIH Clinical Trials and You, at https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics.

The "gold standard" for research with human subjects is the randomized control trial (RCT), which seeks to determine whether one treatment is equivalent to or superior to another. Participants are randomized—assigned by chance, usually by a computer program—to either the experimental treatment or the control treatment. The control group receives either a placebo and/or the standard treatment for the illness. In a single-blind study, the participants don't know which group they're in.

Practice Exercise: Think of a disease that is important to you, and then use the website to see if there are clinical trials about that disease in which you might be willing to participate.

In a double-blind study, neither the researchers nor the participants know which group the subjects are in. Grady, *supra*.

The researchers write a protocol explaining their proposed study, which goes to an institution's Institutional Review Board (IRB) for review. We study the details of IRBs in the following sections.

1. INTRODUCTION TO THE IRB

Regulating Clinical Research: Informed Consent, Privacy, and IRBs

Sharona Hoffman.
31 Capital University Law Review 71 (2003).

II. A Historical Overview of Research Abuses and the Development of Research Regulations

During World War II, the Nazis conducted large-scale, experiments on concentration camp prisoners that were designed not only to gather medical data, but also to torture and kill the subjects. In some camps, German doctors infected numerous healthy inmates with yellow fever, smallpox, typhus, cholera, and diphtheria germs that caused hundreds of them to die. In other camps Nazi physicians conducted experiments relating to high altitude, malaria, freezing, mustard gas, bone transplantation, sea water, sterilization, and incendiary bombs. The full scope and ghastliness of the Nazi medical experimentation was revealed and documented during the Nuremberg Trials after World War II.

In the United States, medical research was conducted for many decades without any regulatory oversight. Perhaps not surprisingly, in an environment devoid of regulation and monitoring, an alarming number of research abuses occurred in this country as well. In the early 1950s, nearly one hundred percent of participants in Phase I clinical trials, the first and riskiest phase of human research studies, were prisoners. In Ohio, for example, live cancer cells were introduced into both forearms of many prisoners. Two weeks after the injection, the affected area of one arm would be surgically removed for study, while the malignant cells were left in the other forearm for further observation. At the Ionia State Hospital in Michigan, at least 142 inmates were recruited for secret CIA psychological experiments. As late as 1969, eighty-five percent of new medications were still tested on prisoners.

Research abuses in the decades following WWII were not limited to the prison environment but also involved other vulnerable populations. For example, patients at the Jewish Chronic Disease Hospital in Brooklyn had live cancer cells injected under their skin, and retarded children in the Willowbrook State School on Staten Island were infected with a mild strain of hepatitis. The experiments were done without the subjects' knowledge or consent.

In 1972, news of the notorious Tuskegee syphilis study highlighted the problem of mistreatment of medical research subjects in the United States. The Tuskegee study, whose participants were all African-American men, was conducted from 1932 until the beginning of the 1970s and sought to analyze the natural progression of untreated syphilis. The researchers, therefore, did not provide patients with penicillin, an antibiotic that is a fully effective cure for syphilis and was widely available as early as 1953. The subjects, who believed they were receiving adequate care, continued to suffer unnecessarily from the debilitating effects of the disease.

The federal government finally responded to publicity concerning research abuses by promulgating oversight regulations. The FDA and the National Institutes of Health (NIH) developed internal policy guidelines in 1966 and 1971, respectively, and these became federal regulations in 1974. The National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research was established through the National Research Act of 1974 and operated for four years, until 1978. Pursuant to the Commission's recommendations, the federal regulations underwent revision in 1981, and they have remained in effect since then.

III. The Federal Regulations that Govern IRBs and Informed Consent

A. What Is Regulated?

Research studies, generally termed "clinical trials," for the development of new drugs and devices are regulated by the FDA. Medications that are the focus of study in clinical trials are called investigational new drugs (INDs). Clinical trials that involve treatments other than drugs and devices, such as surgery or bone marrow transplants, are not regulated by the FDA and are subject to DHHS regulation only if they are "conducted, supported or otherwise subject to regulation by any federal department or agency."

B. IRBs

Research that is conducted, supported, or regulated by DHHS, the FDA, or another federal agency must be reviewed by an IRB. An IRB is a committee designated by an institution to provide initial approval and periodic monitoring for biomedical research studies. The IRB's primary purpose is to protect the rights and welfare of human subjects. The IRB reviews a document known as the "protocol" for each proposed clinical trial, which describes the objectives of the research, its procedures, eligibility requirements for participants, the number of subjects to be tested, and other details. The material submitted to the IRB also includes a document known as the "informed consent" form, which is given to all potential enrollees in order to provide them with a detailed explanation of the clinical trial and an opportunity to agree to participation in the study. After the IRB approves the informed consent form, all those who

wish to become human subjects must sign a copy of the document, affirming the voluntariness of their choice.

The structure and duties of IRBs are governed by the DHHS and FDA regulations. Each IRB must be composed of at least five members with diverse cultural and ethnic backgrounds, and both men and women should be included. At least one member of the IRB should be a person whose principal concerns are in the scientific realm, and one individual's expertise should be nonscientific (e.g. a lawyer or minister). Furthermore, to enhance its objectivity, each IRB must include at least one member who is not otherwise affiliated with the research facility and who has no immediate family members affiliated with the entity. According to DHHS's Office for Protection from Research Risks (OPRR), now renamed the Office for Human Research Protection (OHRP), eighty-six percent of IRB members in 1995 were affiliated with academic research institutions as full-time faculty (56%), clinical and research staff (18%), and administrators (6%). Academic institutions do not compensate IRB members for their work, and thus these individuals must volunteer their time without receiving payment or relief from other job duties.

Unless an expedited review is conducted, research protocols must be reviewed at IRB meetings at which a majority of members are present, including a member whose expertise is nonscientific. Decisions concerning approval of each study are made by majority vote.

The IRB may approve, disapprove, or require modifications to the proposed research activities. Investigators must be given written notification of the IRB's decisions, and IRBs are required to monitor the clinical trials they approve at intervals of at least once a year, or more frequently, depending on the severity of the risks entailed. This periodic monitoring is known as "continuing review."

Before approving a clinical trial, the IRB must ensure that specific criteria are met. These include: (1) risks to participants are minimized; (2) risks to subjects are reasonable in light of anticipated benefits; and (3) selection of participants is equitable, and the protocol is sensitive to the particularized problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled individuals, or economically or educationally deprived persons.

C. Informed Consent

The contents of informed consent forms are also governed by the federal regulations. The informed consent document must be written in language that is accessible to subjects. Informed consent may not include language that waives any of the subject's rights or releases the institution or research personnel from liability for negligence. The regulations further require that informed consent be obtained in writing from each enrollee, though they allow for certain exceptions.

The regulations specify certain data that must be featured on the informed consent document. This information includes a description of

the research, an explanation of risks, benefits, and alternatives, a discussion of confidentiality, a list of contact people, and a statement that participation is voluntary and may be discontinued at any time.

D. Research Involving Only Existing Medical Records Or Tissue Samples

In some cases investigators conduct research that does not involve treatment of any human subject. Instead, the research entails the study of existing medical records or tissue samples. For example, researchers might want to determine whether patients who have a particular type of cancer suffered certain symptoms before their diagnosis and might attempt to make that determination through an examination of their recorded medical histories. Investigators are not required to obtain informed consent from subjects for such research if the information is publicly available or if the researcher will record the data in a way that will make it impossible for subjects to be identified.

Practice Exercise: Create your own IRB and see if it complies with federal regulations. Describe how you will create your IRB, who will serve on it, and what procedures you will follow. The regulations are on the website.

Go to the website after your IRB is formed and review two different research protocols: (1) SUPPORT Trial; and (2) Yale Tissue. After reviewing these protocols, would you vote to approve them? Why or why not?

In addition, the regulations provide that an IRB may waive informed consent requirements if it finds "[t]hat the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context." Accordingly, in limited circumstances in which subject welfare will not be compromised, this provision could allow for the use of identifiable medical records without subject consent.

Practice Experience

You have been asked to start an IRB at your hospital and, once the IRB is started, to review a research protocol to see if it complies with federal regulations. Professor Hoffman's article summarized some of the regulations and procedures governing IRBs, which are usually referred to as the "Common Rule." Parts of the Common Rule are reprinted below so you can practice working in a regulatory context.

To ensure that patients understand the consent form, it is essential—according to Professor Hoffman's article—to make the medical and legal terms intellectually accessible to laypersons.

After many years, the Common Rule was amended to include the following language, which became applicable in 2019.

The Common Rule for the Protection of Human Subjects

45 CFR Part 690.

45 C.F.R. § 690.101 To what does this policy apply?

(a) Except as detailed in § 690.104, this policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any Federal department or agency that takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by Federal civilian employees or military personnel, except that each department or agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint. It also includes research conducted, supported, or otherwise subject to regulation by the Federal Government outside the United States. Institutions that are engaged in research described in this paragraph and institutional review boards (IRBs) reviewing research that is subject to this policy must comply with this policy.

45 C.F.R. § 690.104 Exempt research.

(a) Unless otherwise required by law or by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the categories in paragraph (d) of this section are exempt from the requirements of this policy, except that such activities must comply with the requirements of this section and as specified in each category.

(d) Except as described in paragraph (a) of this section, the following categories of human subjects research are exempt from this policy:

(1) Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot

readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by § 690.111(a)(7).

(3) (i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(B) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by § 690.111(a)(7).

(ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

(4) Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

(5) Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including

procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

(i) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

45 C.F.R. § 690.107 IRB membership.

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members (professional competence), and the diversity of its members, including race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a category of subjects that is vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these categories of subjects.

(b) Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.

(c) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(d) No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

(e) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

45 C.F.R. § 690.111 Criteria for IRB approval of research.

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized:

(i) By using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and

(ii) Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted. The IRB should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by, § 690.116.

(5) Informed consent will be appropriately documented or appropriately waived in accordance with § 690.117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

45 C.F.R. § 690.116 General requirements for informed consent.

(b) Basic elements of informed consent. Except as provided in paragraph (d), (e), or (f) of this section, in seeking informed consent the following information shall be provided to each subject or the legally authorized representative:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others that may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and

(9) One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

(i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without

additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

(ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

(c) Additional elements of informed consent. Except as provided in paragraph (d), (e), or (f) of this section, one or more of the following elements of information, when appropriate, shall also be provided to each subject or the legally authorized representative:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the legally authorized representative's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject;

(6) The approximate number of subjects involved in the study;

(7) A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

(8) A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and

(9) For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

(d) Elements of broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens. Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or nonresearch purposes) is permitted as an alternative to the informed consent requirements in paragraphs (b) and (c) of this section. If the subject or the legally authorized representative

is asked to provide broad consent, the following shall be provided to each subject or the subject's legally authorized representative:

(1) The information required in paragraphs (b)(2), (b)(3), (b)(5), and (b)(8) and, when appropriate, (c)(7) and (9) of this section;

(2) A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted;

(3) A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens;

(4) A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite);

(5) Unless the subject or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies;

(6) Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject; and

(7) An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.

45 C.F.R. § 690.117 Documentation of informed consent.

(a) Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written informed consent form approved by the IRB and signed (including in an electronic format) by the subject or the subject's legally authorized representative. A written copy shall be given to the person signing the informed consent form.

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The IRB system is designed to protect human subjects from exploitation and to assure they give informed consent. However, the system is not designed to prevent all the flawed incentives that may influence researchers and keep them from fully protecting research subjects. We identify the flawed incentives that mar research in the next section.

2. FLAWED INCENTIVES IN RESEARCH

Given what you just learned about informed consent, was there a failure of informed consent in the following case? Is it relevant to the case whether you think of plaintiff John Moore as a patient or as a research subject? Should the same standards that applied to patients like Jerry Canterbury in Section A apply to John Moore in this case?

Moore v. Regents of the University of California

Supreme Court of California, 1990.
51 Cal.3d 120, 793 P.2d 479.

I. INTRODUCTION

■ PANELLI, JUSTICE.

We granted review in this case to determine whether plaintiff has stated a cause of action against his physician and other defendants for using his cells in potentially lucrative medical research without his permission. Plaintiff alleges that his physician failed to disclose preexisting research and economic interests in the cells before obtaining consent to the medical procedures by which they were extracted. The superior court sustained all defendants' demurrers to the third amended complaint, and the Court of Appeal reversed. We hold that the complaint states a cause of action for breach of the physician's disclosure obligations, but not for conversion.

II. FACTS

. . . The plaintiff is John Moore (Moore), who underwent treatment for hairy-cell leukemia at the Medical Center of the University of California at Los Angeles (UCLA Medical Center). The five defendants are: (1) Dr. David W. Golde (Golde), a physician who attended Moore at UCLA Medical Center; (2) the Regents of the University of California (Regents), who own and operate the university; (3) Shirley G. Quan, a researcher employed by the Regents; (4) Genetics Institute, Inc. (Genetics Institute); and (5) Sandoz Pharmaceuticals Corporation and related entities (collectively Sandoz).

Moore first visited UCLA Medical Center on October 5, 1976, shortly after he learned that he had hairy-cell leukemia. After hospitalizing Moore and "withdr[awing] extensive amounts of blood, bone marrow aspirate, and other bodily substances," Golde confirmed that diagnosis. At this time all defendants, including Golde, were aware that "certain

blood products and blood components were of great value in a number of commercial and scientific efforts" and that access to a patient whose blood contained these substances would provide "competitive, commercial, and scientific advantages."

On October 8, 1976, Golde recommended that Moore's spleen be removed. Golde informed Moore "that he had reason to fear for his life, and that the proposed splenectomy operation . . . was necessary to slow down the progress of his disease." Based upon Golde's representations, Moore signed a written consent form authorizing the splenectomy.

Before the operation, Golde and Quan "formed the intent and made arrangements to obtain portions of [Moore's] spleen following its removal" and to take them to a separate research unit. Golde gave written instructions to this effect on October 18 and 19, 1976. These research activities "were not intended to have . . . any relation to [Moore's] medical . . . care." However, neither Golde nor Quan informed Moore of their plans to conduct this research or requested his permission. Surgeons at UCLA Medical Center, whom the complaint does not name as defendants, removed Moore's spleen on October 20, 1976.

Moore returned to the UCLA Medical Center several times between November 1976 and September 1983. He did so at Golde's direction and based upon representations "that such visits were necessary and required for his health and well-being, and based upon the trust inherent in and by virtue of the physician-patient relationship. . . ." On each of these visits Golde withdrew additional samples of "blood, blood serum, skin, bone marrow aspirate, and sperm." On each occasion Moore travelled to the UCLA Medical Center from his home in Seattle because he had been told that the procedures were to be performed only there and only under Golde's direction.

"In fact, [however,] throughout the period of time that [Moore] was under [Golde's] care and treatment, . . . the defendants were actively involved in a number of activities which they concealed from [Moore]. . . ." Specifically, defendants were conducting research on Moore's cells and planned to "benefit financially and competitively . . . [by exploiting the cells] and [their] exclusive access to [the cells] by virtue of [Golde's] on-going physician-patient relationship. . . ."

Sometime before August 1979, Golde established a cell line from Moore's T-lymphocytes. On January 30, 1981, the Regents applied for a patent on the cell line, listing Golde and Quan as inventors. "[B]y virtue of an established policy . . . , [the] Regents, Golde, and Quan would share in any royalties or profits . . . arising out of [the] patent." The patent issued on March 20, 1984, naming Golde and Quan as the inventors of the cell line and the Regents as the assignee of the patent.

The Regents' patent also covers various methods for using the cell line to produce lymphokines. Moore admits in his complaint that "the true clinical potential of each of the lymphokines . . . [is] difficult to

predict, [but] . . . competing commercial firms in these relevant fields have published reports in biotechnology industry periodicals predicting a potential market of approximately $3.01 Billion Dollars by the year 1990 for a whole range of [such lymphokines]. . . ."

With the Regents' assistance, Golde negotiated agreements for commercial development of the cell line and products to be derived from it. Under an agreement with Genetics Institute, Golde "became a paid consultant" and "acquired the rights to 75,000 shares of common stock." Genetics Institute also agreed to pay Golde and the Regents "at least $330,000 over three years, including a pro-rata share of [Golde's] salary and fringe benefits, in exchange for . . . exclusive access to the materials and research performed" on the cell line and products derived from it. On June 4, 1982, Sandoz "was added to the agreement," and compensation payable to Golde and the Regents was increased by $110,000. "[T]hroughout this period, . . . Quan spent as much as 70 [percent] of her time working for [the] Regents on research" related to the cell line.

Based upon these allegations, Moore attempted to state 13 causes of action.[4]

III. DISCUSSION

A. Breach of Fiduciary Duty and Lack of Informed Consent

Moore repeatedly alleges that Golde failed to disclose the extent of his research and economic interests in Moore's cells before obtaining consent to the medical procedures by which the cells were extracted. These allegations, in our view, state a cause of action against Golde for invading a legally protected interest of his patient. This cause of action can properly be characterized either as the breach of a fiduciary duty to disclose facts material to the patient's consent or, alternatively, as the performance of medical procedures without first having obtained the patient's informed consent. . . .

[We reach] the following conclusions: (1) a physician must disclose personal interests unrelated to the patient's health, whether research or economic, that may affect the physician's professional judgment; and (2) a physician's failure to disclose such interests may give rise to a cause of action for performing medical procedures without informed consent or breach of fiduciary duty.

To be sure, questions about the validity of a patient's consent to a procedure typically arise when the patient alleges that the physician failed to disclose medical risks, as in malpractice cases, and not when the patient alleges that the physician had a personal interest, as in this case.

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[4] 1) "Conversion"; (2) "lack of informed consent"; (3) "breach of fiduciary duty"; (4) "fraud and deceit"; (5) "unjust enrichment"; (6) "quasi-contract"; (7) "bad faith breach of the implied covenant of good faith and fair dealing"; (8) "intentional infliction of emotional distress"; (9) "negligent misrepresentation"; (10) "intentional interference with prospective advantageous economic relationships"; (11) "slander of title"; (12) "accounting"; and (13) "declaratory relief."

The concept of informed consent, however, is broad enough to encompass the latter. "The scope of the physician's communication to the patient . . . must be measured by the patient's need, and that need is whatever information is material to the decision." . . .

It is important to note that no law prohibits a physician from conducting research in the same area in which he practices. Progress in medicine often depends upon physicians, such as those practicing at the university hospital where Moore received treatment, who conduct research while caring for their patients.

Yet a physician who treats a patient in whom he also has a research interest has potentially conflicting loyalties. This is because medical treatment decisions are made on the basis of proportionality—weighing the benefits *to the patient* against the risks *to the patient*. As another court has said, "the determination as to whether the burdens of treatment are worth enduring for any individual patient depends upon the facts unique in each case," and "the patient's interests and desires are the key ingredients of the decision-making process." A physician who adds his own research interests to this balance may be tempted to order a scientifically useful procedure or test that offers marginal, or no, benefits to the patient. The possibility that an interest extraneous to the patient's health has affected the physician's judgment is something that a reasonable patient would want to know in deciding whether to consent to a proposed course of treatment. It is material to the patient's decision and, thus, a prerequisite to informed consent.

Golde argues that the scientific use of cells that have already been removed cannot possibly affect the patient's medical interests. The argument is correct in one instance but not in another. If a physician has no plans to conduct research on a patient's cells at the time he recommends the medical procedure by which they are taken, then the patient's medical interests have not been impaired. In that instance the argument is correct. On the other hand, a physician who does have a preexisting research interest might, consciously or unconsciously, take that into consideration in recommending the procedure. In that instance the argument is incorrect: the physician's extraneous motivation may affect his judgment and is, thus, material to the patient's consent.

We acknowledge that there is a competing consideration. To require disclosure of research and economic interests may corrupt the patient's own judgment by distracting him from the requirements of his health. But California law does not grant physicians unlimited discretion to decide what to disclose. Instead, "it is the prerogative of the patient, not the physician, to determine for himself the direction in which he believes his interests lie." "Unlimited discretion in the physician is irreconcilable with the basic right of the patient to make the ultimate informed decision. . . ."

Accordingly, we hold that a physician who is seeking a patient's consent for a medical procedure must, in order to satisfy his fiduciary

duty and to obtain the patient's informed consent, disclose personal interests unrelated to the patient's health, whether research or economic, that may affect his medical judgment.

1. Dr. Golde

We turn now to the allegations of Moore's third amended complaint to determine whether he has stated such a cause of action. We first discuss the adequacy of Moore's allegations against Golde, based upon the physician's disclosures prior to the splenectomy.

Moore alleges that, prior to the surgical removal of his spleen, Golde "formed the intent and made arrangements to obtain portions of his spleen following its removal from [Moore] in connection with [his] desire to have regular and continuous access to, and possession of, [Moore's] unique and rare Blood and Bodily Substances." Moore was never informed prior to the splenectomy of Golde's "prior formed intent" to obtain a portion of his spleen. In our view, these allegations adequately show that Golde had an undisclosed research interest in Moore's cells at the time he sought Moore's consent to the splenectomy. Accordingly, Moore has stated a cause of action for breach of fiduciary duty, or lack of informed consent, based upon the disclosures accompanying that medical procedure.

We next discuss the adequacy of Golde's alleged disclosures regarding the postoperative takings of blood and other samples. In this context, Moore alleges that Golde "expressly, affirmatively and impliedly represented . . . that these withdrawals of his Blood and Bodily Substances were necessary and required for his health and well-being." However, Moore also alleges that Golde actively concealed his economic interest in Moore's cells during this time period. "[D]uring each of these visits . . ., and even when [Moore] inquired as to whether there was any possible or potential commercial or financial value or significance of his Blood and Bodily Substances, or whether the defendants had discovered anything . . . which was or might be . . . related to any scientific activity resulting in commercial or financial benefits . . ., the defendants repeatedly and affirmatively represented to [Moore] that there was no commercial or financial value to his Blood and Bodily Substances . . . and in fact actively discouraged such inquiries."

Moore admits in his complaint that defendants disclosed they "were engaged in strictly academic and purely scientific medical research. . . ." However, Golde's representation that he had no financial interest in this research became false, based upon the allegations, at least by May 1979, when he "began to investigate and initiate the procedures . . . for [obtaining] a patent" on the cell line developed from Moore's cells.

In these allegations, Moore plainly asserts that Golde concealed an economic interest in the postoperative procedures. Therefore, applying the principles already discussed, the allegations state a cause of action for breach of fiduciary duty or lack of informed consent. . . .

2. The Remaining Defendants

The Regents, Quan, Genetics Institute, and Sandoz are not physicians. In contrast to Golde, none of these defendants stood in a fiduciary relationship with Moore or had the duty to obtain Moore's informed consent to medical procedures. If any of these defendants is to be liable for breach of fiduciary duty or performing medical procedures without informed consent, it can only be on account of Golde's acts and on the basis of a recognized theory of secondary liability, such as respondeat superior. The procedural posture of this case, however, makes it unnecessary for us to address the sufficiency of Moore's secondary-liability allegations. . . .

NOTES AND QUESTIONS

1. *Informed Consent Law.* In Section A, we learned that in jurisdictions that follow *Canterbury*, tort law assesses informed consent from the perspective of the patient, not the doctor; with foresight, not hindsight; from an objective, not a subjective point of view; and requires causation as well as injury to the patient. Did the California Supreme Court apply the same standards of informed consent in *Moore*? What would an objective person in Moore's circumstances want to know about Golde's *research interests* in Moore? Could anyone predict with foresight that Moore's spleen would be valuable, or is that determination purely a matter of hindsight? Do you think Moore would have behaved any differently if Golde had informed him of his research interests in Moore's spleen? Does Moore really have any injuries for tort law to compensate? Does *Moore* give you additional reasons to prefer a patient-based standard of informed consent over one that relies on the physician's professional judgment of what should be disclosed?

2. How do you assess the argument that Dr. Golde owed Moore only the duty to inform him about his medical condition, and not about the benefits that would accrue to Golde through Golde's research on Moore's body parts?

3. Do you think the court was mistaken in allowing liability against Dr. Golde but not against the Regents, Quan, Genetics Institute and Sandoz? Do you think those individuals and institutions should be held accountable in some way, or did they act appropriately?

4. Professor Javitt argues that the court's reasoning was "flawed" because it "failed to distinguish between Moore as a patient and Moore as a research subject." According to Javitt:

> In failing to inform Moore that he planned to use the cells in research, Golde therefore committed a wrong to Moore the-research-subject independently of whatever duties he owed Moore as a patient. The court failed to acknowledge Moore's transition from patient to research subject, and therefore failed to consider the duties owed to Moore in that capacity. Had Golde not been his treating physician, or if he had had no inkling of the cells' potential research value at the time of the surgery, he would have been under

> no obligation, by the court's reasoning, to inform Moore of the value of his cells. Nor, by the court's reasoning, did Quan or UCLA have any duty to obtain Moore's consent to use his cells. The court's limited holding therefore does little to protect the interests of the vast majority of contributors of tissue samples.

Gail H. Javitt, Take Another Little Piece of My Heart: Regulating the Research Use of Human Biospecimens, 41 J.L. Med. & Ethics 424, 426 (2013). What standard can protect both patients and research subjects? Should researchers owe a fiduciary duty and a duty of informed consent to tissue donors?

5. The court observed that to "require disclosure of research and economic interests may corrupt the patient's own judgment by distracting him from the requirements of his health." Do you agree? If you were in John Moore's position and were informed by Dr. Golde about his research, would you have lost focus on your health?

6. *Conflicts of Interest.* When is a conflict of interest present between a doctor and a patient? Between a doctor and a research subject? Between an individual's interest as a patient and as a research subject? Between a researcher and a research subject? The court wrote that a

> physician who treats a patient in whom he also has a research interest has potentially conflicting loyalties. This is because medical treatment decisions are made on the basis of proportionality—weighing the benefits *to the patient* against the risks *to the patient.* As another court has said, "the determination as to whether the burdens of treatment are worth enduring for any individual patient depends upon the facts unique in each case," and "the patient's interests and desires are the key ingredients of the decision-making process." A physician who adds his own research interests to this balance may be tempted to order a scientifically useful procedure or test that offers marginal, or no, benefits to the patient. The possibility that an interest extraneous to the patient's health has affected the physician's judgment is something that a reasonable patient would want to know in deciding whether to consent to a proposed course of treatment. It is material to the patient's decision and, thus, a prerequisite to informed consent.

Would you describe a researcher's position differently?

Do you think that the types of disclosure and informed consent that we identified in Section B1 in the IRB context can solve all conflicts of interest? What do you think about the recommendations made by the Institute of Medicine (IOM) about conflicts of interest in the following report?

Conflict of Interest in Medical Research, Education, and Practice

Institute of Medicine (IOM) Report Brief, April 2009.

Collaborations between physicians or medical researchers and pharmaceutical, medical device, and biotechnology companies can

benefit society—most notably by promoting the discovery and development of new medications and medical devices that improve individual and public health. However, financial ties between medicine and industry may create conflicts of interest. Such conflicts present the risk of undue influence on professional judgments and thereby may jeopardize the integrity of scientific investigations, the objectivity of medical education, the quality of patient care, and the public's trust in medicine.

Recent news stories have documented troubling interactions between industry and physicians, researchers, and medical institutions. These situations, which could undermine public confidence in medicine, may include

- companies and academic investigators not publishing negative results from industry-sponsored clinical trials or delaying publication after trial completion;
- physicians and researchers failing to disclose substantial payments from pharmaceutical companies as required by universities, research sponsors, or medical journals; and
- settlements between federal prosecutors and medical device and pharmaceutical companies related to alleged illegal payments or gifts to physicians.

In an effort to prevent these types of situations, many academic medical centers, professional societies, medical journals, and other institutions have adopted stronger policies on conflict of interest.

In 2007, the Institute of Medicine (IOM) appointed the Committee on Conflict of Interest in Medical Research, Education, and Practice to examine conflicts of interest in medicine and to recommend steps to identify, limit, and manage conflicts of interest without negatively affecting constructive collaborations. The committee's report stresses the importance of preventing bias and mistrust rather than trying to remedy damage after it is discovered. This report specifically focuses on financial conflicts of interest involving pharmaceutical, medical device, and biotechnology companies.

DISCLOSING AND ASSESSING FINANCIAL RELATIONSHIPS

The committee recommends that medical institutions—including academic medical centers, professional societies, patient advocacy groups, and medical journals—establish conflict of interest policies that require disclosure and management of both individual and institutional financial ties to industry. Institutions should create conflict of interest committees to evaluate these ties. If necessary, a board-level committee should deal with conflicts of interest at the institutional level, which typically arise when research conducted within an institution could affect the value of an institution's investments or patents.

Disclosure of financial relationships with industry is an essential, though limited, first step in identifying and responding to conflicts of interest. Because current policies are highly variable and sometimes confusing, the committee recommends standardizing the content, format, and procedures for disclosing financial relationships physicians and researchers have with industry. Such standardization will provide institutions with specific information they need to assess the severity of conflicts and to determine whether the relationship needs to be eliminated or actively managed. It will also simplify requirements for physicians and researchers who must disclose information to multiple institutions. Physicians, researchers, academic medical centers, professional societies, consumer and patient advocacy groups, medical journals, accreditation and certification organizations, licensing boards, other government agencies, and organizations with experience in database development and management should be involved in developing uniform disclosure standards.

In addition to steps taken by the medical community, Congress should create a national reporting program that requires pharmaceutical, medical device, and biotechnology companies to make public all payments to physicians, researchers, health care institutions, professional societies, patient advocacy and disease groups, and providers of continuing medical education. Public reporting will enhance accountability by allowing academic medical centers, medical journals, and others to verify disclosures made to them by faculty members, article authors, and others.

IMPROVING CONFLICT OF INTEREST POLICIES IN MEDICAL RESEARCH, EDUCATION, AND PRACTICE

Although the committee recognizes that collaborations with industry can be beneficial, the committee recommends, as a general rule, that researchers should not conduct research involving human participants if they have a financial interest in the outcome of the research, for example, if they hold a patent on an intervention being tested in a clinical trial. The only exceptions should be if an individual's participation is judged to be essential for the safe and appropriate conduct of the research.

Financial relationships with industry are extensive in medical education. To reduce the risk for bias within the learning environment, academic medical centers and teaching hospitals should prohibit faculty from accepting gifts, making presentations that are controlled by industry, claiming authorship for ghost-written publications, and entering into consulting arrangements that are not governed by written contracts for expert services to be paid for at fair market value. Medical centers also should restrict visits by industry sales people and limit use of drug samples to patients who lack financial access to medications.

Many providers of accredited continuing medical education—a usual requirement for relicensure of physicians—receive the majority of their funding from industry. The report recommends a broad-based consensus

process to develop a new system for funding high-quality accredited continuing medical education that is free of industry influence. The committee recognizes that such a system may involve higher costs for physicians and require cost-cutting steps by education providers.

Acceptance of meals and gifts and other relationships with industry are also common among physicians who practice outside medical centers. Data suggest that these relationships may influence physicians to prescribe a company's medicines even when evidence indicates another drug would be more beneficial. Therefore, the committee recommends eliminating these problematic relationships between physicians and industry.

In addition, the committee recommends that community physicians should also follow the restrictions described previously regarding gifts, including meals, from companies; presentations or articles whose content is controlled by industry; meetings with sales representatives; and use of drug samples. Professional societies and health care facilities should adopt policies that reinforce this recommendation.

Clinical practice guidelines influence physician practice, quality measures, and insurance coverage decisions. Given this influence, clinical practice guidelines need to be developed with greater transparency and accountability. The committee recommends that professional societies and other groups that develop practice guidelines not accept direct industry funding for guideline development and generally exclude individuals with conflicts of interest from the panels that draft the guidelines. In addition, these groups should make public their conflict of interest policies, their funding sources, and any financial relationships panel members have with industry.

In order to promote the adoption of conflict of interest policies by institutions engaged in medical research, education, clinical care, or the development of practice guidelines, the report urges other organizations such as health insurers, accrediting bodies, and government agencies to develop incentives for policy change consistent with the recommendations in the committee's report. For example, health insurers and other organizations that use clinical practice guidelines should avoid using guidelines that were developed without strong conflict of interest protections.

The committee also recommends that the Department of Health and Human Services develop a research agenda to create a stronger evidence base for future conflict of interest policies. Such research should evaluate the impact of conflict of interest policies, including both desired outcomes and possible unwanted consequences.

CONCLUSION

Society traditionally has placed great trust in physicians and researchers, granting them the considerable leeway to regulate themselves. However, there is growing concern among lawmakers,

government agencies, and the public that extensive conflicts of interest in medicine require stronger measures. Responsible and reasonable conflict of interest policies and procedures will reduce the risk of bias and the loss of trust while avoiding undue burdens or harms and without damaging constructive collaborations with industry. Decisions about biomedical research, medical education, and patient care directly affect the public's health. The public needs to be able to trust that physicians' decisions are not inappropriately influenced by their financial relationships with industry.

NOTES AND QUESTIONS

1. *Disclosure.* What do you think of the report's recommendation that physicians and researchers disclose their financial relationships with industry? The report recommends "standardizing the content, format, and procedures for disclosing financial relationships physicians and researchers have with industry." How would you recommend that disclosure be standardized? Is there a certain format for disclosure you would recommend? What would the form say?

Can disclosure cure all conflicts of interest? Despite its emphasis on disclosure, the report recommends "as a general rule, that researchers should not conduct research involving human participants if they have a financial interest in the outcome of the research, for example, if they hold a patent on an intervention being tested in a clinical trial. The only exceptions should be if an individual's participation is judged to be essential for the safe and appropriate conduct of the research." Is this rule too strict? Would it wrongly keep all patent holders from research? How would such a standard have worked in *Moore* and the case of Henrietta Lacks? Why shouldn't these patent-holders conduct the research after full disclosure to the research subject?

2. *National Reporting Program: Sunshine.* The report recommends that Congress authorize a national reporting program "that requires pharmaceutical, medical device, and biotechnology companies to make public all payments to physicians, researchers, health care institutions, professional societies, patient advocacy and disease groups, and providers of continuing medical education." Do you agree that such a reporting program is necessary?

A section of the Affordable Care Act (ACA) called the Physician Payment Sunshine Act (PPSA) requires pharmaceutical, medical device and biologics manufacturers reimbursed by Medicaid or Medicare to disclose payments to teaching hospitals and physicians on a public website. That website is the Open Payments website, which is now operational and accessible to the public. Does this website promote transparency and disclosure? Do you think websites would provide any insight to patients? How would you design such a website? What format and information would be most helpful to patients? See Alison R. Hwong et al., A Systematic Review of State and Manufacturer Physician Payment Disclosure Websites: Implications for Implementation of the Sunshine Act, 42 J. L. Med. & Ethics 208 (2014).

Pharmaceutical companies and medical device makers paid $10.03 billion to doctors and teaching hospitals during 2019. The sum includes payments for consulting and speaking fees, travel, meals, entertainment, research grants, and ownership and investment interests. See The Facts About Open Payments Data (2019), https://openpaymentsdata.cms.gov/summary. How do you think consumers react to this information? While some may not like their doctors accepting money for consulting and trips, will others see it as a sign of their doctors' expertise?

Practice Exercise: Visit the website and see if you can find your doctor or a local doctor in the Open Payments system. Could you find any information about your own doctor? Can you imagine any circumstances in which you, or your friends and family, would consult this website? Could you glean any information regarding the quality of doctors from the site?

Professor Saver explains that the Sunshine Act's record has been "uneven," due in part to its "bumpy rollout" and the difficulty of presenting the financial information in the most accessible manner. He questions whether patients will really use the website. Nonetheless, "policymakers can more closely examine correlations between industry spending directed at individual physicians and their prescribing and referral decisions. Moreover, savvy counsel are recognizing that Sunshine Act information provides explosive evidence in private civil litigation and this Article explores the first wave of cases." Richard S. Saver, Deciphering the Sunshine Act: Transparency Regulation and Financial Conflicts in Health Care, 43:4 American Journal of Law and Medicine 303 (2017). If you were a savvy litigator, how would you use this information?

3. *Other Recommendations.* The IOM report also recommends, "[t]o reduce the risk for bias within the learning environment, academic medical centers and teaching hospitals should prohibit faculty from accepting gifts, making presentations that are controlled by industry, claiming authorship for ghost-written publications, and entering into consulting arrangements that are not governed by written contracts for expert services to be paid for at fair market value." Furthermore, the report advocates that meals and gifts and other relationships with industry not be allowed. Are these recommendations too strict?

4. *Researchers.* In another section of the report, IOM recommended that institutions use four criteria when assessing conflict of interest policies:

- Proportionality: Is the policy effective, efficient, and directed at the most important and most common conflicts?
- Transparency: Is the policy comprehensible and accessible to the individuals and institutions that may be affected by it?
- Accountability: Does the conflict of interest policy indicate who is responsible for monitoring, enforcing, and revising it?
- Fairness: Does the policy apply equally to all relevant groups within an institution and in different institutions?

Are these principles clear enough that they would provide enough guidance to you to draft a COI policy?

Professor Spece recommends direct disclosure of researcher conflicts of interest to participants in clinical trials. By "direct" disclosure, he means that researchers should reveal the source, amount and mechanism of their funding directly to the research subject, instead of indirectly (e.g., by the websites identified in Note 2). The mechanism of funding includes per capita payments to researchers. Would it influence your consent to participate in a clinical trial if you learned that your researcher earned a sum of money per capita, i.e., a payment for every individual enrolled? Do you agree that such detailed direct disclosure is a necessary part of informed consent? Roy G. Spece, Jr., Direct and Enhanced Disclosure of Researcher Financial Conflicts of Interest: The Role of Trust, 23 Health Matrix 409, 410–11 (2013).

Spece addressed the possibility that "strong empirical proof demonstrating the high likelihood of significant harm and little good resulting from direct disclosure might overcome a presumption in favor of subjects' individual rights to bodily integrity and autonomy in decision making." Id. at 411. Would you agree that this is possible, or argue instead that full and direct disclosure of financial conflicts of interest is an absolute requirement of informed consent? See id. at 412 ("currently there is no strong empirical proof of direct disclosure's effects on subjects' trust in their researchers that would overcome the presumption in favor of individual rights.")

What do you think of using "enhanced direct disclosure," which Spece illustrates in the following example:

> An example of an enhanced direct disclosure that might affect researcher-subject trust would be a requirement that subjects in studies funded on a per capita basis be told:
>
> This study is funded by Company X, which has paid Researcher Y $10,000 for each subject enrolled.
>
> [If true, add: "X and Y claim that these payments are not in excess of fair market value." If not true, add: "X and Y are not willing to state there are no excess payments."]
>
> This form of per capita funding (a set amount for each subject enrolled) risks payment to Y that exceeds the fair market value of resources, goods, and services supplied by Y to X. [If applicable, add: "especially when X and Y or those in similar positions refuse to state that there are no excess payments."].
>
> Excess payments present the risk of biasing, in favor of X, Y's decisions concerning the design of the research study, whether and when to enroll or keep each subject, and how to determine whether

> the data from the study demonstrate [the studied intervention] is safe and effective.

Practice Exercise: Draft a conflict of interest policy for a physician who conducts research on her patients at a teaching hospital. Did your policy include any non-financial interests, as Professor Saver argues in following reading?

Id. at 413–14. Should such a description be added to every informed consent study you analyzed above? Does this discussion about financial conflicts lead you to conclude that the subjects of human research should be reimbursed for their participation in clinical trials?

Is It Really All About the Money? Reconsidering Non-Financial Interests in Medical Research

Richard S. Saver.
40 J.L. Med. & Ethics 467 (2012).

Introduction

Conflicts of interest have been reduced to *financial* conflicts. The National Institutes of Health's (NIH) new rules for managing conflicts of interest in medical research, the first major change to the regulations in over 15 years, address only financial ties. Although several commentators urged that the regulations also cover non-financial interests, the Department of Health and Human Services declined to do so. Similarly, the Institute of Medicine's (IOM) influential 2009 Conflict of Interest Report focuses almost exclusively on financial conflicts. Institutional policies at academic medical centers and guidance from professional bodies and medical journals also primarily emphasize financial ties. Even broadly worded rules are applied more readily to financial ties than non-financial interests, such as the regulations that restrict institutional review board (IRB) members with conflicting interests from participating in protocol reviews.

Concern about financial ties crowds out consideration of other influences that may bias research conduct. But why? This article argues that we under-prioritize non-financial interests at our peril. It questions whether the distinctions between financial and nonfinancial interests call for widely different responses and critically assesses the commonly offered justifications for disparate regulatory focus. . . .

I. Non-Financial Interests in Medical Research

Definitional Issues

Certain interests arise in medical research that are not directly associated with the investigator's professional judgment and conduct. These secondary interests, including financial gain and enhanced reputation, may conflict with or negatively impact the primary research goals of promoting unbiased investigations, advancing knowledge, and protecting subjects from unnecessary risk. Secondary interests can

compromise the design, conduct, and reporting of research, while also threatening subject safety and undermining public trust. Non-financial, secondary interests have sometimes been labeled "intrinsic conflicts of interest" or "intellectual conflicts of interest," among other terms. This article uses the simpler term "nonfinancial interest" in the broadest sense to cover any non-financial source of bias that can unduly influence primary research goals. The phrasing "conflict of interest" is intentionally avoided. Often the non-financial interests do not pose a stark conflict with primary research goals, but they can still present misaligned incentives problems.

Non-financial interests include considerations other than direct economic gain that investigators still highly value, such as career advancement. Recruiting subjects and completing published studies are essential to an academic researcher's retention, tenure, and promotion. Apart from simple career advancement, investigators may be swayed by the prospects of enhanced reputation, professional honors and prestige, access to power, and general "glory-seeking." Social relationships formed in the research process, ranging from collegial to competitive to hierarchical, also create pressures and can compromise the actions of investigators, journal editors, peer reviewers, and other key stakeholders. In addition, intellectual or political predispositions can bias research conduct. Even the investigator's sincere interest in helping subjects presents complicating effects, as this can lead to overly optimistic estimations about a study's benefits and make it difficult to concede that a clinical trial should be halted or changed. Also, ambition to advance medical knowledge, investigative zeal, and intellectual passion can undermine investigator objectivity and subject protection. Non-financial interests can likewise arise at the institutional level. For example, reputational concerns and the reluctance to antagonize powerful faculty investigators complicate academic medical centers' institutional oversight.

Prevalence and Degree of Influence

While not attracting the same degree of current scrutiny as financial ties, non-financial interests have long been identified as important determinants of research conduct. Norman Levinsky authored a widely cited "Sounding Board" column in the *New England Journal of Medicine* in 2002 warning that "[t]he potential nonfinancial conflict between the personal interests of investigators and those of subjects is inherent in all research involving human subjects, including that in which there is also a financial conflict." It is also worth remembering that financial interests did not figure prominently, if at all, in many of the notorious research scandals, such as the Tuskegee Syphilis Study and the injection of live cancer cells into elderly patients at the Jewish Chronic Disease Hospital, that led to enactment of the National Research Act of 1974 and the current regulatory scheme for protecting research subjects.

Even in the current era of big-dollar, industry-funded research, concerns continue to recur about non-financial interests compromising research conduct. For example, the Institute of Medicine has warned that researchers' desire to add publications to their curriculum vitas may result in limited value studies. Such investigations provide publication opportunities but do little to advance the state of general medical knowledge, needlessly exposing subjects to harm and requiring them to expend human capital for limited benefit to themselves or the larger research enterprise. Investigative zeal concerns arose following a recent *New England Journal of Medicine* study examining treatment for mild gestational diabetes during pregnancy, even though no financial conflicts were present. Critics alleged that the researchers put the interests of the protocol ahead of subject safety, resulting in a trial design that exposed control subjects to considerable risk of harm. Investigative zeal also played a central role in the controversies surrounding Dr. Thomas Starzl, a pioneer in transplantation research at the University of Pittsburgh. Starzl came under fire for aggressively switching research subjects to a new immunosuppressant drug, even though he had forsaken any financial interest in the study medication. Non-financial interests have also been associated with publication bias. A 2007 World Health Organization (WHO) review of breastfeeding studies found that, in some instances, positive results were more likely to be published than other data. Because there was no industry funding involved, any publication bias was likely due to non-financial considerations, such as the researchers' uncritical, and perhaps ideological, belief in the value of breastfeeding.

Unfortunately, the evidence base is underdeveloped concerning the prevalence and influence of nonfinancial interests. Some studies purport to show that financial ties exert more powerful bias effects than non-financial interests. However, these studies are limited in scope and number. Meanwhile, other investigations suggest that financial conflicts and certain non-financial interests, such as allegiance to a particular treatment approach, raise comparable concerns. Both are associated with quite similar bias effects, including failure to publish negative results and selection of less effective interventions to compare against the favored approach. More importantly, even with financial conflicts, no conclusive evidence causally links financial ties to negative effects as few systematic studies exist and the data remains subject to differing interpretation. As such, it may be premature to conclude that non-financial interests pose considerably less risk than financial conflicts. At the very least, dismissing non-financial interests as too weak to merit serious regulatory attention seems ill-advised.

Indeed, the indirect and circumstantial evidence suggest that non-financial interests raise misaligned incentives problems on a regularly recurring basis. A review of scientific misconduct incidents reported on HHS' Office of Research Integrity's website concluded that many of the

reported incidents of faked data and other troubling actions to alter study results rarely appeared to involve researchers with conflicting financial interests. Instead, the misconduct likely related to "the more mundane but omnipotent pressures on researchers to produce good results so they can get more grants, keep their jobs, and move upward on the ladder of academic success." Apart from empirical studies, many researchers also anecdotally report that non-financial interests are widespread and, at times, pose more risk than financial interests. For example, the editors of PLoS Medicine note that "professional affinities and rivalries . . . scientific or technological competition, religious beliefs, and political or ideological views are often the fuels for [academic] passions and for [research] careers . . . [and these] interests are perhaps even more potent than financial ones." David Korn, writing in the *Journal of the American Medical Association*, observes that nonfinancial interests "may more powerfully influence faculty behavior than any prospect of financial enrichment." Other commentators make similar claims.

II. Why Regulate Differently? . . .

Boundary Confusion

[One] explanation for the heightened emphasis on financial ties is the contention that financial interests can be separated from the larger problem of secondary interests generally in medical research. This carve-out potential supposedly allows for narrowly tailored, efficient regulation. HHS justified the revised NIH conflict of interest rules addressing only financial interests in part because "[w]hile we acknowledge that non-financial conflicts of interest can influence the scientific process, we chose to retain the focus of these regulations on [financial conflict of interests] because we believe this is a discrete area in which there is heightened need to strengthen management and oversight."

But, such line-drawing seems inaccurate and incomplete because of considerable boundary confusion. It may not be possible or effective to treat financial interests as a discrete area of regulation because it is not always clear where financial ties end and non-financial interests begin. Non-financial rewards can also result in financial gain. An investigator's enhanced academic reputation may be monetizeable as it translates into increased ability to attract research grants or improvements in salary. At the institutional level, the prestige and acclaim associated with productive research can be critical to an academic medical center's financial success in terms of securing new grants, donations, and industry funding.

The boundary problems run in the other direction as well. Financial ties can introduce relationships that ultimately bring primarily social, not economic, pressures into the mix, further blurring the distinction between financial and non-financial interests. For example, commentators urge, and many institutions have increasingly adopted, restrictions on even de minimis financial ties, such as small gifts from

pharmaceutical firms. Proponents of these restrictions point to social science and psychological studies that suggest a gift of any amount imposes on its recipient a sense of indebtedness and an inclination to want to reciprocate. Reciprocity and social obligation, in turn, can bias key stakeholders in the research endeavor in subtle yet powerful ways. According to this view, it is the largely social relationship created between recipient and industry donor, not the minimal economic interest implicated, that ultimately poses the most risk and therefore warrants regulatory concern. . . .

Boundary Confusion and the Gelsinger Case

The notorious research scandal involving the death of Jesse Gelsinger demonstrates how boundary confusion complicates regulatory response to secondary interests in medical research. The Gelsinger episode has been typically portrayed as a cautionary tale of financial interests run amok. But it may have been the underlying non-financial interests that actually presented the most serious problems. Gelsinger died while enrolled in a gene therapy study at the University of Pennsylvania (Penn). The clinical trial evaluated a risky procedure for infusing genetically altered viruses as treatment for a rare genetic disorder that compromises liver function. Disturbing improprieties were alleged, including failure to follow the protocol's eligibility criteria and non-disclosure of adverse events in prior animal studies. One of the co-investigators, James Wilson, had patents on some aspects of the procedure and Wilson and Penn had equity interests in the company, Genovo, Inc., that partially funded Penn's Institute for Human Gene Therapy. Genovo had rights to market, and therefore stood to profit, from development of treatments that might result from the research.

Critics questioned whether the lure of financial gain led to lax oversight and a rush to proceed with dangerous experimentation. At first, Wilson steadfastly maintained that monetary gain played little part in the questionable research decisions. Instead, he acknowledged investigative zeal, academic passion, and related non-financial pressures: "I don't think about how my doing this work is going to make me rich. It's about leadership and notoriety and accomplishment. Publishing in first-rate journals. That's what turns us on. You've got to be on the cutting edge and take risks if you're going to stay on top."

Wilson later published an article in 2009, a condition of the settlement for the resulting litigation, in which he explored "lessons learned" from the Gelsinger affair. In this article, Wilson acknowledged the possibility of bias due to the financial ties. Yet he also observed the great difficulty in carving out financial ties from non-financial interests:

> [A]cademic medicine is a competitive profession with the primary measure of success being recognition by your colleague of your research accomplishments . . . The quest for this recognition influences work plans, priorities and decisions, and is a requisite means to the ultimate goal of furthering science.

> Incorporating the incentive for personal financial gain into this complex dynamic is problematic specifically as it relates to the conduct of clinical trials. I learned it is very hard to convincingly uncouple drivers for academic success from the incentives derived from potential financial gain.

In fact, it is plausible that the Gelsinger scandal still would have occurred even if Wilson and Penn had disavowed any financial interests in the outcome of the study. Wilson had ceded large degrees of control over patient care decisions to his co-investigators, who did not have the same financial conflicts, and it has not been clearly established that Wilson made the decision allegedly to violate the protocol's eligibility criteria in enrolling Gelsinger. Meanwhile, co-investigator Dr. Mark Batshaw, who did not have Wilson's financial conflict, spent a great deal of his clinical career dealing with victims of the liver disease. His heavy investment in finding a cure may have compromised judgment and encouraged imprudent risk-taking for the sake of helping future patients. Even Jesse Gelsinger's father, Paul Gelsinger, who initiated the lawsuit against Wilson and Penn, "faults not only Wilson's financial stake but the blind spots that [co-investigator] Batshaw's passion to cure children born with OTCD [the rare liver disease] may have caused."

It is also not clear that Penn's limited ownership interest in Genovo fully explains the University's conduct. Penn's institutional review board and conflict of interest committee allegedly were lax in approving the protocol and not insisting upon stricter conditions for management of Wilson's financial conflicts. But Penn's investment in Genovo, when viewed relative to its overall financial portfolio, was not significant. Also, if members of the IRB or conflict of interest committee felt pressure to "go easy" on Wilson in their review, it may have been less about the financial implications for Penn and more about the inclination to give a wide berth to a powerful "star" investigator and professional colleague whose cutting-edge research brought prestige to the institution as a whole.

Despite all the attention the financial conflicts generated, "[t]here is no evidence that the financial interests of [Penn] and Wilson in the success of the research had any relation to Gelsinger's death." Yet the fallout from the Gelsinger episode has, as a regulatory matter, mostly increased oversight of financial interests. Following the Gelsinger episode, the Food and Drug Administration and NIH did tighten regulation of gene transfer studies generally, including increasing inspections and developing better systems for adverse event reporting. But as for managing secondary interests, the regulatory response largely concerned financial ties. HHS issued new guidance on financial interests and various professional associations revised their conflict of interest policies, largely concentrating on financial conflicts.

The disproportionate focus on financial conflicts is hard to reconcile with the actual facts of the Gelsinger affair. The Gelsinger episode

demonstrates how predominant attention to financial ties leads to oversimplification of very difficult regulatory challenges. If we really want to avoid another Gelsinger episode, additional regulatory effort needs to be directed more systematically and thoughtfully to the non-financial side of the equation. We should not take false comfort from vigor in regulating financial interests, as this may simply not be sufficient.

NOTES AND QUESTIONS

1. *Non-Financial Interests*. What are the non-financial interests identified by the article? Write a list of those interests. Then rank them in order of which ones would be most likely to influence a researcher. How many of those non-financial interests would influence researchers more than financial ones?

2. *History*. Professor Saver explains that Tuskegee, the Jewish Chronic Disease Hospital, and the Gelsinger episode were all influenced by non-financial interests. Think back to what you learned about the experiments at Tuskegee. What role did financial and non-financial interests play in setting the structure of the research study at Tuskegee? The study in Guatemala?

Practice Exercise: How would you revise your conflict of interest policy in light of Professor Saver's article?

3. *Regulating Non-Financial Interests*. According to the article, NIH has focused on financial interests "because we believe this is a discrete area in which there is heightened need to strengthen management and oversight." Financial interests can be regulated through disclosure of the money paid to researchers and by the more detailed informed consent forms recommended by Professor Spece. Recall that Professor Spece proposed informed consent forms that state: "This study is funded by Company X, which has paid Researcher Y $10,000 for each subject enrolled."

How would non-financial interests be disclosed on an informed consent form? Should researchers explain to research subjects that their promotions depend upon the success of their research?

Practice Exercise: Go to the website and read summaries of the five most recent cases of scientific misconduct investigated by the Office of Research Integrity. Can you tell if the researchers were influenced by financial or non-financial interests? Do you think ORI is a good mechanism to limit research misconduct?

4. *How Valuable are IRBs?* Do you think members of the Penn IRB who reviewed the gene therapy study would have been willing to disapprove protocols offered by well-known doctors who worked at Penn? From your experience designing an IRB and reading about the regulations governing them, do you think the IRB system can adequately address both financial and non-financial interests of researchers?

In an op-ed in *The New York Times*, University of Minnesota Medical Ethics Professor Carl Elliott criticized his school's "string of slow, festering research scandals," which included a psychiatrist's felony conviction and research disqualification for fraud, another psychiatrist's suspension for enrolling illiterate Hmong refugees in a study without their consent, and the suicide of a young man enrolled in a department of psychiatry research protocol. Elliott blamed the "antiquated bureaucratic apparatus" of IRBs for some of the problems. He argued that the current regulatory system is "essentially an honor code," not a "formal regulatory system," because IRB members never meet the research subjects but instead rely on the honesty and truthfulness of the researchers in reporting their results. Carl Elliott, The University of Minnesota's Medical Research Mess, N.Y. Times, May 26, 2015, at A19. Do you agree with Elliott's criticisms of IRBs?

Practice Exercise: Professor Hoffman identified deficiencies in the IRB system. Can you add others based on your experience of reviewing protocols?

In the next section, we consider proposed reforms to the IRB system.

3. REFORMS OF THE SYSTEM

Regulating Clinical Research: Informed Consent, Privacy, and IRBs

Sharona Hoffman.
31 Capital University Law Review 71 (2003).

IV. Deficiencies In The Regulatory System

A. IRB Workloads

A 1998 statement issued by the Office of Inspector General of the U.S. Department of Health and Human Services (OIG) was highly critical of contemporary research oversight. The OIG stated that the enormous workloads of many IRBs currently prevent them from adequately performing their review functions. A follow-up report issued by the Office of Inspector General in April of 2000 concluded that in the intervening two years, only minimal progress had been made to diminish the workload pressures of IRBs. The number of initial reviews conducted by IRBs increased by an average of forty-two percent from 1993 to 1998, and some IRBs review up to 2,000 protocols per year. Some IRBs also receive 200 or more reports of adverse events each month concerning the clinical trials they oversee. An external review conducted at Johns Hopkins University after the death of a healthy human subject revealed that until June of 2001 a single IRB, meeting every two weeks, was responsible for the approval of 800 new protocols and the annual reviews they generated. The reviewers emphatically stated: "[w]e view this as grossly inadequate." As noted above, most IRB members have full time jobs on the faculties or staffs of research institutions, and are not paid for

their IRB services or relieved of other work duties. Consequently, the time members can spend on IRB work is limited, and IRBs generally meet only once or twice a month for a few hours.

OPRR expressed concern that the IRBs' work is also hampered by deficient expertise and resources. Some IRB members lack in-depth understanding of the federal regulations governing biomedical research, and IRBs do not have the space, privacy, and level of staff support necessary to perform their duties adequately. Small IRBs may have only one salaried staff member to coordinate all IRB activities and perform administrative tasks.

If IRBs become frequent defendants in lawsuits, the IRB system may be fundamentally threatened. Since IRBs rely heavily on the work of volunteers, they may find it difficult to recruit members in the future. Physicians who are concerned about potential liability may be very reluctant to offer their services to IRBs.

B. Flaws In The Informed Consent Process

An increasing volume of evidence indicates that the informed consent process is severely flawed in many cases. Often, human subjects either are given insufficient information or do not comprehend the data they receive.

The 1998 OIG statement was very critical of informed consent procedures. It noted, for example, that a 1995 Advisory Commission on Human Radiation Experiments found, after interviewing actual subjects that few realized they were involved in research, and many had little understanding of the informed consent forms they had signed.

Commonly, the problem is confusion about the differences between research and clinical treatment. While some research subjects are healthy volunteers who would not otherwise seek medical treatment, many are patients with particular illnesses who are recruited for clinical research by their treating physicians. These patients are vulnerable to a phenomenon known as the "therapeutic misconception." Because they are sick and are recruited for enrollment by their doctors, they become convinced that their research participation will be of definite medical benefit to them. These patients are therefore resistant to explanations that treatments involved in clinical trials are unproven and experimental, no matter how clearly and explicitly these explanations are given.

Numerous studies have focused on the issue of informed consent and have revealed very troubling evidence concerning the ability of research subjects to provide valid consent. In a labor-induction study with fifty-two participants, thirty-nine percent of the women were found to be unaware that they were participating in a research study although all had signed informed consent forms. Even those who realized they were research subjects often misunderstood essential aspects of the study and their role in it.

Several investigators asked fifty cancer patients to review a hypothetical consent form for participation in a placebo-controlled clinical trial. Subjects were asked to interpret four different statements in the consent form. Depending on the statement, the subjects provided incorrect answers twenty-six to fifty-four percent of the time.

In another survey, forty-seven percent of responding researchers indicated that they thought few of their subjects, enrolled in multinational studies in the 1980s, knew they were participating in controlled experiments, even though they had given written consent. In two additional studies, over three quarters of physicians who were questioned believed that subjects rarely understood all the data given to them.

The difficulty of obtaining informed consent is exacerbated by the fact that informed consent documents are generally written in language that is technical and sophisticated and consequently inappropriate for the intended audience. While many informed consent documents require a college level reading comprehension ability, the average American has only an eighth grade reading comprehension level. Rather than providing useful explanations for patients, the forms often serve to educate only the medically trained IRB members who review them.

The challenge of obtaining genuine consent from subjects has had grave consequences for some institutions. During 1998 and 1999, OPRR suspended federal research funding at Chicago's Rush-Presbyterian-St. Luke's Medical Center, the West Los Angeles VA Medical Center, Duke University Medical Center, the University of Illinois at Chicago, and six University of Colorado institutions, all of which are well-regarded research facilities. In January of 2000, research activities were suspended at the University of Pennsylvania and the University of Alabama at Birmingham. Prominent among the violations for which these entities were cited was the failure to obtain adequate informed consent from subjects.

[C]. Informed Consent Is Particularly Difficult To Obtain From Gravely Ill Patients

Genuine informed consent is particularly difficult to obtain when the patients at issue suffer from life-threatening diseases. The decision-making capacity of gravely ill patients is often compromised by the emotional trauma of their illnesses or by various social and familial pressures. Consequently, those who have the most to gain or lose from receiving experimental treatment are also those who are least able to provide meaningful informed consent.

Illness can be viewed as an "ontological assault" that undermines the patient's identity by "attacking the fundamental unity of mind and body." A patient suffering from multiple sclerosis described the experience of disease in these words:

> The most deeply held assumption of daily life is the assumption that I, personally, will continue to be alive and it is in light of this assumption that one engages in daily activities. The onset of illness, however, brings one concretely face-to-face with personal vulnerability. Thus, the person who is ill is unable readily to fit illness into the typified schema used to organize and interpret experience. One finds oneself preoccupied with the demands of the here and now, confined to the present moment, unable effectively to project into the future.

Commentators have noted that serious sickness creates in patients a strong desire to be cared for and to be free of the responsibility and stress of decision-making, as though they were once again children. Many scholars have noted that the thought processes of those suffering from prolonged or serious illnesses are often impaired and have urged that research protocols involving such patients be subject to heightened IRB scrutiny. One informed consent study found that as the seriousness of the illness increases, the ability of potential subjects to remember information relevant to their research participation decreases. Seriously ill patients may experience depression, extreme anxiety, rage, denial, or desperation to find a cure, all of which may cloud their judgment and hamper their ability to evaluate the benefits and risks of a clinical trial.

V. Recommendations

A. IRBs

It is clear that many IRBs inadequately perform their oversight functions. Their deficient performance, however, does not stem from deliberate misconduct or indifference towards the welfare of human subjects, but rather, from inadequate resources, unmanageable workloads, and, in some cases, insufficient expertise. Alleviating these problems is essential to enhancing protection for clinical trial participants.

An effective means of improving the functioning of IRBs would be the addition of more full-time, paid, professionals to their staffs. The size of the professional staff would vary in accordance with the workloads of the IRBs. The professional staff members should be charged with the review of all protocols that are submitted for initial approval, amendment, and continuing review to the IRB. One or two members of the IRB with relevant medical expertise should also read each protocol and provide comments to the staff. The professional staff should then provide written reports to the full IRB membership, summarizing the protocol and their recommendations. The IRB volunteers would be responsible for reading the reports, asking follow-up questions, and voting on whether to approve the protocol.

Under this system, each IRB member will not be required to read every page of every protocol, many of which are quite voluminous, and therefore IRB duties will become less burdensome. The system will also

expedite the review process so that investigators will not have to wait several months for approval of their submitted proposals. Finally, professional staffs would assure that each protocol actually receives a thorough and systematic initial review and continued monitoring, which many commentators have suggested does not always occur when these tasks are left exclusively in the hands of well-meaning, but overworked volunteers.

Additional funding would obviously be needed to support the hiring of adequate professional staffs. To obtain the necessary economic support, IRBs could charge commercial research sponsors for review of their protocols. Similarly, if the research is sponsored by a governmental entity, the sponsor could be required to add a fixed sum or a small percentage to its grant in order to support IRB activities. Nothing in the federal regulations prohibits the imposition of such charges.

NOTES AND QUESTIONS

1. *Overloaded IRBs*. Professor Hoffman's article discussed the fact that some IRBs are responsible for reviewing up to 2,000 protocols per year. When coupled with the statement that many IRBs meet twice per month, these IRBs would be responsible for reviewing over eighty new protocols each meeting. Even if each protocol took an average of fifteen minutes to approve or deny, the IRB would need to spend over twenty hours each meeting to review the new protocols. Given that many IRB members have full-time careers and serve as volunteers, do you think researchers should depend on this system and expect individuals to contribute this much time as a volunteer? Also, given that Professor Hoffman stated that most new protocols are quite voluminous, how long do you think it would take, on average, to adequately review each new protocol?

2. *Volunteers*. How extensive is the training you think necessary to become an IRB member? Did you know average citizens may apply to become IRB members? See Human Subjects Office, University of Iowa, Become an IRB Member, https://hso.research.uiowa.edu/become-irb-member. Who is likely to volunteer? Does the presence of volunteers affect the reliability of IRB decisions? The Iowa website mentions a "diverse membership." What would it mean for an IRB to have a diverse membership?

3. *Full-Time IRBs*. Do you agree with Professor Hoffman that IRBs should include full-time staff, which would alleviate the workload for the rest of the IRB? How would you recommend paying the full-time staff members (e.g., raising IRB fees for researchers, from the institution, etc.)?

4. *Rethink the Clinical Trial?* A more fundamental challenge comes from *The New York Times*: "do clinical trials even work? Or are the diseases of individuals so particular that testing experimental medicines in broad groups is doomed to create more frustration than knowledge?" Clifton Leaf, Op-Ed, Do Clinical Trials Work?, N.Y. Times, Jul. 14, 2013, at SR1. The author points out that 95% of drugs in initial clinical trials are not approved, that the subject populations of research do not match the characteristics of patients with the disease being studied, and that as the test population

increases in number from Phase I to Phase III, the percentage of drug effectiveness decreases. Id.; see also J.A. DiMasi et al., Trends in Risk Associated With New Drug Development: Success Rates for Investigational Drugs, 87:3 Nature 272 (March 2010) ("The clinical approval success rate in the United States was 16% for self-originated drugs (originating from the pharmaceutical company itself) during both the 1993–1998 and the 1999–2004 subperiods. For all compounds (including licensed-in and licensed-out drugs in addition to self-originated drugs), the clinical approval success rate for the entire study period was 19%."); J.A. DiMasi et al., Clinical Approval Success Rates for Investigational Cancer Drugs, 94:3 Nature 329 (September 2013) ("the estimated clinical approval success rate for cancer compounds was 13.4%").

Is there any replacement for the traditional clinical trial? What do you think of these suggestions?

> [D]esign small clinical trials and enroll only those who have the appropriate genetic or molecular signature; test[ ] up to a dozen drugs from multiple companies, phasing out those that don't appear to be working and subbing in others, without stopping the study. Part of the novelty lies in a statistical technique called Bayesian analysis that lets doctors quickly glean information about which therapies are working best.

Id. "It is important to maintain a philosophy of continual improvement with respect to clinical trials broadly and specifically with an aim towards optimizing every aspect of the research and development process." David B. Fogel, Factors Associated With Clinical Trials that Fail and Opportunities of Improving the Likelihood of Success: A Review, doi: 10.1016/j.conctc. 2018.08.001. How would you recommend repeatedly improving clinical trials?

5. *COVID Changes.* In Spring 2020, the Office for Human Research Protections (OHRP) released guidance on conducting research in light of the COVID-19 pandemic. OHRP Guidance on COVID-19, Apr. 8, 2020, https://www.hhs.gov/ohrp/regulations-and-policy/guidance/ohrp-guidance-on-covid-19/index.html. For studies not involving COVID treatments, tests, or vaccines, the OHRP has highlighted the ability to make changes to approved research prior to IRB review and approval if the changes are necessary to eliminate apparent immediate hazards to the research subject—for example, eliminating unnecessary in-person visits or converting those visits to telephone or video calls. The changes must be reported to the IRB, but may be made without IRB approval. Similar guidance has been issued by the FDA for research governed by that agency. FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic: Guidance for Industry, Investigators, and Institutional Review Boards, Mar., 2020 (updated Apr. 2, 2020), https://www.hhs.gov/ohrp/sites/default/files/fda-covid-guidance-2apr2020.pdf.

6. *Not Doing Enough for Patients?* Abigail Burroughs was battling cancer at age 21 when she ran out of conventional treatment options. She then worked hard to lobby people who could help "create wider access to

developmental cancer drugs and other drugs for serious life-threatening illnesses." Abigail died on June 9, 2001; however, Abigail Alliance, the organization founded by her father, remained to carry on her fight. The organization is dedicated to helping inform people about clinical trials and to work on getting drugs into the market more quickly.

Has the research system failed because it does not help those patients most in need, as Abigail Alliance suggested in the following case? This opinion should help you to review the entire IRB process that we have studied in this section as well as the constitutional law arguments that we learned in Chapter 1. Start to identify the key strengths and weaknesses of the system as you read the opinion.

Abigail Alliance for Better Access to Developmental Drugs v. von Eschenbach

United States Court of Appeals, District of Columbia Circuit, 2007.
495 F.3d 695.

■ GRIFFITH, CIRCUIT JUDGE:

This case presents the question whether the Constitution provides terminally ill patients a right of access to experimental drugs that have passed limited safety trials but have not been proven safe and effective. The district court held there is no such right. A divided panel of this Court held there is. Because we conclude that there is no fundamental right "deeply rooted in this Nation's history and tradition" of access to experimental drugs for the terminally ill, *see Washington v. Glucksberg*, we affirm the judgment of the district court.

I.

A.

The Abigail Alliance for Better Access to Developmental Drugs (the "Alliance") is an organization of terminally ill patients and their supporters that seeks expanded access to experimental drugs for the terminally ill. The Food, Drug, and Cosmetic Act ("FDCA" or "Act"), however, generally prohibits access to new drugs unless and until they have been approved by the Food and Drug Administration ("FDA"). *See* 21 U.S.C. § 355(a). Gaining FDA approval can be a long process. First, an experimental drug's sponsor (*e.g.,* a drug company) must submit an application for approval. Because no drug may be approved without a finding of "substantial evidence that the drug will have the effect it purports or is represented to have," an application must contain "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use." Such reports rely in large measure on clinical trials with human subjects.

But before a sponsor can even begin human testing, it must submit for the FDA's approval an investigational new drug application ("IND"). Once the application for human testing has been approved, several phases of clinical testing begin. The Alliance's amended complaint

alleges that this testing process is an extremely lengthy one, requiring nearly seven years for the average experimental drug.

Clinical testing for safety and effectiveness requires three or sometimes four phases. Phase I involves the initial introduction of a new drug into human subjects. A Phase I study usually consists of twenty to eighty subjects and is "designed to determine the metabolism and pharmacologic actions of the [new] drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness." Although gathering data on effectiveness may be part of Phase I, its primary focus is to determine whether the drug is safe enough for continued human testing. Phase II studies are "well controlled" and "closely monitored" clinical trials of no more than several hundred subjects, used to evaluate both the "effectiveness of the drug for a particular indication" and its "common short-term side effects and risks."

Phase III studies are expanded clinical trials of several hundred to several thousand subjects designed to "gather . . . additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling." [In some circumstances, a Phase IV review is conducted, which "delineate[s] additional information about the drug's risks, benefits, and optimal use."] At any time during the clinical trials, a drug sponsor is required to notify the FDA of "[a]ny adverse experience associated with the use of the drug that is both serious and unexpected," and the FDA may order a "clinical hold" halting the trials if it determines that safety concerns so warrant. To guide the clinical testing process, Congress has directed the FDA to establish "[s]cientific advisory panels" to "provid[e] expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug." These panels must include scientists from a variety of disciplines.

Terminally ill patients need not, however, always await the results of the clinical testing process. The FDA and Congress have created several programs designed to provide early access to promising experimental drugs when warranted. For example, under the "treatment IND" program, the FDA may approve use of an investigational drug by patients not part of the clinical trials for the treatment of "serious or immediately life-threatening disease[s]" if there exists "no comparable or satisfactory alternative drug or other therapy," if "[t]he drug is under investigation in a controlled clinical trial," and if the drug's sponsor "is actively pursuing marketing approval of the investigational drug with due diligence." The FDA reserves the right, however, to deny any treatment IND request if (1) the agency believes there is no "reasonable basis" to conclude that the drug is effective; or (2) granting the request "[w]ould . . . expose the patient [ ] . . . to an unreasonable and significant additional risk of illness or injury." Sponsors may not profit from any

approved treatment IND program and may only "recover costs of manufacture, research, development, and handling of the investigational drug."[4]

B.

Concluding that the FDA's current process for early access to new drugs was inadequate to meet the needs of its terminally ill members, the Alliance submitted its own proposals to the FDA. Those proposals culminated in a "citizen petition" to the FDA, *see* 21 C.F.R. § 10.25, arguing that there is a "different risk-benefit tradeoff facing patients who are terminally ill and who have no other treatment options." Although the Alliance agreed that "[e]xtensive marshalling of evidence regarding drug interactions, dose optimization, and the like" is "appropriate for new drugs to treat patients with other alternatives . . . these steps may well entail a delay that is fatal" for terminally ill patients. The Alliance contended that these patients "should have the ability to opt for a new treatment that has met a lower evidentiary hurdle with respect to safety and efficacy." The Alliance's proposal suggested that the FDA allow early access based upon "the risk of illness, injury, or death from the disease in the absence of the drug." Accordingly, the Alliance requested that the FDA promulgate new regulations that would allow sponsors to market experimental drugs, under some circumstances, after the completion of Phase I trials.

The FDA never responded to the Alliance's citizen petition, but did respond to the Alliance's earlier submissions. After noting that a number of senior FDA officials had reviewed those submissions, the agency concluded that the Alliance "raised several important questions about expanded access that we believe deserve further consideration," but questioned whether the specific proposal put forward by the Alliance "would have the intended desirable effects for patients." The officials concluded that the early access proposed by the Alliance "points to an area of significant range of opinion within the patient and provider communities about the standards that should be met before a drug is marketed." Although "some members of the cancer community have suggested that [the] FDA needs to maintain a strong clinical trial system as the basis of the approval of cancer drugs, . . . others, like [the Alliance],

[4] The FDA has several other regulatory programs designed to hasten research of the safety and effectiveness of drugs for terminally or severely ill patients and allow early access where scientifically and medically warranted. For example, under its "Fast Track" program, the agency has "established procedures designed to expedite the development, evaluation, and marketing of new therapies intended to treat persons with life-threatening and severely-debilitating illnesses, especially where no satisfactory alternative therapy exists." 21 C.F.R. § 312.80. Fast Track allows the FDA to waive its IND application requirement if it is "unnecessary or cannot be achieved," *id.* § 312.10, and even allows a waiver request to be made "[i]n an emergency . . . by telephone or other rapid communication," *id.* The "Accelerated Approval" program provides a truncated approval process for "certain new drug products that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments." *Id.* § 314.500. The FDA categorizes some new drugs, including nearly all cancer drugs, as "priority drugs" and seeks to accelerate their availability.

have criticized [the FDA] for relying too heavily on completing certain trials before approval." The FDA noted that "[i]n the realm of reviewing medical products to treat serious and life-threatening diseases, there is inevitable tension between early availability of products to patients, especially patients with refractory disease, and the need to obtain sufficient data to provide a reasonable expectation of benefit and lack of excessive harm."

Relying upon its experience exercising its scientific and medical judgment in creating its regulations for experimental drugs and, in certain circumstances, exceptions to those regulations for the terminally ill, the FDA noted that "a reasonably precise estimate of response rate" and "enough experience to detect serious adverse effects" are "critical" in determining when experimental drugs should be made available. For example, most experimental cancer drugs "have potentially lethal toxicity, with potentially large effects on a patient's remaining quality of life." Accordingly, "it does not serve patients well to make drugs too widely available before there is a reasonable assessment of such risks to guide patient decisions, and experience in managing them." The FDA concluded that accepting the Alliance's proposal "would upset the appropriate balance that [it is] seeking to maintain, by giving almost total weight to the goal of early availability and giving little recognition to the importance of marketing drugs with reasonable knowledge for patients and physicians of their likely clinical benefit and their toxicity."

Having thus been rejected by the FDA, the Alliance turned to the courts, arguing that the United States Constitution provides a right of access to experimental drugs for its members. In a complaint that mirrored much of its earlier submissions to the FDA, the Alliance argued that the FDA's lengthy clinical trials, combined with the "FDA's restrictions on pre-approval availability[,] amount to a death sentence for these [terminally ill] patients." Nor, the Alliance argues, are the FDA's exceptions to the clinical testing process sufficient to provide the terminally ill the access they need because they "are small, when they exist at all," and the ban on profits prevents many drug sponsors from participating.

"Terminally ill patients," in the Alliance's view, "are typically willing to assume risks. . . ." Before the district court, the Alliance argued that the Constitution guarantees them the right to do so. The district court rejected that argument, holding that "there is no constitutional right of access to unapproved drugs." A divided panel of this Court reversed, concluding that "where there are no alternative government-approved treatment options, a terminally ill, mentally competent adult patient's informed access to potentially life-saving investigational new drugs determined by the FDA after Phase I trials to be sufficiently safe for expanded human trials warrants protection under the Due Process Clause." We vacated that decision and granted rehearing *en banc*.

As framed by the Alliance, we now consider:

> Whether the liberty protected by the Due Process Clause embraces the right of a terminally ill patient with no remaining approved treatment options to decide, in consultation with his or her own doctor, whether to seek access to investigational medications that the [FDA] concedes are safe and promising enough for substantial human testing.

That is, we must determine whether terminally ill patients have a fundamental right to experimental drugs that have passed Phase I clinical testing. If such a right exists, the Alliance argues that both 21 C.F.R. § 312.34(b)(3) (preventing access to experimental drugs for terminally ill patients where there is insufficient evidence of effectiveness or where there is an unreasonable risk of injury) and 21 C.F.R. § 312.7 (prohibiting drug manufacturers from profiting on the sale of experimental drugs) must be subjected to strict scrutiny because they interfere with a fundamental constitutional right. We do not address the broader question of whether access to medicine might ever implicate fundamental rights.

II.

The Due Process Clause of the Fifth Amendment provides that "[n]o person shall be . . . deprived of life, liberty, or property, without due process of law." In *Glucksberg,* the Supreme Court described its "established method of substantive-due-process analysis" as having "two primary features."

> First, we have regularly observed that the Due Process Clause specially protects those fundamental rights and liberties which are, objectively, deeply rooted in this Nation's history and tradition and implicit in the concept of ordered liberty, such that neither liberty nor justice would exist if they were sacrificed. Second, we have required in substantive-due-process cases a careful description of the asserted fundamental liberty interest.

We will assume *arguendo* that the Alliance's description of its asserted right would satisfy *Glucksberg*'s "careful description" requirement. Looking to whether the Alliance has demonstrated that its right is deeply rooted in this Nation's history, tradition, and practices, the Alliance's claim for constitutional protection rests on two arguments: (1) that "common law and historical American practices have traditionally trusted individual doctors and their patients with almost complete autonomy to evaluate the efficacy of medical treatments"; and (2) that FDA policy is "inconsistent with the way that our legal tradition treats persons in all other life-threatening situations." More specifically, the Alliance argues that the concepts of self-defense, necessity, and interference with rescue are broad enough to demonstrate the existence of the fundamental right they seek-a right for "persons in mortal peril" to "try to save their own lives, even if the chosen means would otherwise be illegal or involve enormous risks."

A.

"We begin, as we do in all due process cases, by examining our Nation's history, legal traditions, and practices." The Alliance argues that its right can be found in our history and legal traditions because "the government never interfered with the judgment of individual doctors about the medical *efficacy* of particular drugs until 1962," *i.e.,* when major amendments were made to the Food, Drug, and Cosmetic Act. . . .

The Alliance has little to say, however, about our Nation's history of regulating the *safety* of drugs. The Alliance's effort to focus on efficacy regulation ignores one simple fact: it is unlawful for the Alliance to procure experimental drugs not only because they have not been proven effective, but because they have not been proven safe. Although the Alliance contends that it only wants drugs that "are safe and promising enough for substantial human testing," *i.e.,* drugs that have passed Phase I testing, current law bans access to an experimental drug on safety grounds until it has successfully completed all phases of testing. *See* 21 C.F.R. § 312.21(b) (requiring that Phase II studies examine "*common short-term side effects and risks*" of new drugs) (emphasis added); *id.* § 312.21(c) (requiring Phase III studies to "gather . . . additional information about effectiveness and *safety* that is needed to evaluate the overall benefit-risk relationship of the drug") (emphasis added). Thus, to succeed on its claim of a fundamental right of access for the terminally ill to experimental drugs, the Alliance must show not only that there is a tradition of access to drugs that have not yet been proven effective, but also a tradition of access to drugs that have not yet been proven safe.

. . . we conclude that our Nation has long expressed interest in drug regulation, calibrating its response in terms of the capabilities to determine the risks associated with both drug safety and efficacy.

Drug regulation in the United States began with the Colonies and States when the Colony of Virginia's legislature passed an act in 1736 that addressed the dispensing of more drugs than was "necessary or useful" because that practice had become "dangerous and intolerable." . . . By 1870, at least twenty-five states or territories had statutes regulating adulteration (impure drugs), and a few others had laws addressing poisons. In the early history of our Nation, we observe not a tradition of protecting a right of access to drugs, but rather governments responding to the risks of new compounds as they become aware of and able to address those risks. . . . In 1848, the Import Drug Act, ch. 70, 9 Stat. 237 (1848), banned "imported adulterated drugs" after a Congressional committee concluded that "this country had become the grand mart and receptacle of all the refuse [drug] merchandise . . ., not only from the European warehouses, but from the whole Eastern world." . . . Congress acted again when it passed the Biologics Controls Act of 1902, ch. 1378, 32 Stat. 728 (1902), in response to a series of deadly reactions to a tainted diphtheria vaccine that killed children in New

Jersey and Missouri. . . . Congress followed with the Pure Food and Drugs Act of 1906, which prohibited the manufacture of any drug that was "adulterated or misbranded."

The current regime of federal drug regulation began to take shape with the Food, Drug, and Cosmetic Act of 1938. The Act required that drug manufacturers provide proof that their products were safe before they could be marketed. The new Act also prohibited false therapeutic claims. . . .

We end our historical analysis where the Alliance would prefer it begin-with the 1962 Amendments to the FDCA. Undoubtedly, as the Alliance argues at length, Congress amended the FDCA in 1962 to explicitly require that the FDA only approve drugs deemed effective for public use. Thus, the Alliance argues that, prior to 1962, patients were free to make their own decisions whether a drug might be effective. But even assuming *arguendo* that efficacy regulation began in 1962, the Alliance's argument ignores our Nation's history of drug safety regulation described above. . . .

B.

The Alliance next turns to several common law doctrines, arguing that barring access to experimental drugs for terminally ill patients is "inconsistent with the way that our legal tradition treats persons in all other life-threatening situations." Specifically, the Alliance argues that three doctrines—(1) the doctrine of necessity; (2) the tort of intentional interference with rescue; and (3) the right to self-defense—each support the recognition of a right to self-preservation. Such a right to self-preservation, the Alliance believes, would permit "persons in mortal peril . . . to try to save their own lives, even if the chosen means would otherwise be illegal or involve enormous risks." Specifically, in this case, the Alliance believes that a right to self-preservation would give the terminally ill a constitutionally protected right of access to experimental drugs.

Looking first to the Alliance's necessity argument, the Alliance invokes the common law doctrine, which " 'traditionally covered the situation where physical forces beyond the actor's control rendered illegal conduct the lesser of two evils.' " . . . Nonetheless, the Supreme Court's analysis of the common law doctrine of necessity in *Oakland* leaves little room for the Alliance's argument that common law necessity could justify overriding the Food, Drug, and Cosmetic Act.

In *Oakland,* a group of patients seeking access to marijuana for medicinal purposes argued that "because necessity was a defense at common law, medical necessity should be read into the Controlled Substances Act." The Supreme Court rejected that argument because "[u]nder any conception of legal necessity, one principle is clear: The defense cannot succeed when the legislature itself has made a determination of values." Although the Court limited its analysis to the

statutory issue and did not address the defendant's constitutional arguments, the learning of *Oakland* is clear. Congress may limit or even eliminate a necessity defense that might otherwise be available. That is precisely what the FDCA has done. Congress has prohibited general access to experimental drugs, *see* 21 U.S.C. § 355(a), and has prescribed in detail how experimental drugs may be studied and used by the scientific and medical communities, *see id.* § 355(i). Given the Supreme Court's conclusion that the common law defense of necessity remains controversial and cannot override a value judgment already determined by the legislature, the common law doctrine of necessity provides little support to the Alliance's proposed right.

The Alliance next invokes the tort of intentional interference with lifesaving efforts, which the Restatement of Torts defines as "intentionally prevent[ing] a third person from giving to another aid *necessary* to his bodily security." But that is not this case. The Alliance seeks access to drugs that are experimental and have not been shown to be safe, let alone effective at (or "necessary" for) prolonging life. Indeed, the Alliance concedes that taking experimental drugs can "involve enormous risks." In essence, the Alliance insists on a constitutional right to assume any level of risk. It is difficult to see how a tort addressing interference with providing "necessary" aid would guarantee a constitutional right to override the collective judgment of the scientific and medical communities expressed through the FDA's clinical testing process. Thus, we cannot agree that the tort of intentional interference with rescue evidences a right of access to experimental drugs.

Finally, the Alliance looks to traditional self-defense principles to support its proposed constitutional right. The common law doctrine of self-defense provides that "[o]ne who is not the aggressor . . . is justified in using a reasonable amount of force against his adversary when he reasonably believes (a) that he is in immediate danger of unlawful bodily harm from his adversary and (b) that the use of such force is necessary to avoid this danger." Self-defense typically arises when a victim is being attacked by an aggressor and uses reasonable force to overcome immediate danger. The Alliance argues that self-defense permits victims to assume two types of risk: (1) the risk that the victim will kill the attacker; and (2) the risk that "[f]ighting back may dramatically increase the . . . harm" to the victim. So, the argument goes, if victims of crimes are allowed to assume these risks in defending their lives, terminally ill patients should also be allowed to assume the risk that an experimental drug may hasten their deaths.

That self-defense principles should be applied in the medical context is evidenced, the Alliance argues, by the Supreme Court's abortion jurisprudence. . . . *Roe* "recognized another, entirely separate right to abortion: a woman's right to abort a fetus *at any stage of a pregnancy* if doing so is necessary to preserve her life or health." "That right," the Alliance argues, "is grounded in traditional self-defense principles rather

than privacy. . . ." Applying that concept here, the Alliance argues that because its terminally ill members are in immediate danger of harm from cancer, they can use whatever medical means are necessary to defend themselves. Thus, they argue, even if a medical treatment might otherwise be prohibited by law, the doctrine of self-defense justifies access to that treatment, just as self-defense justifies an assault victim using physical force otherwise prohibited by law.

This analogy also fails because this case is not about using reasonable force to defend oneself (as in most cases involving self-defense), nor is it about access to life-saving medical treatment. This case is about whether there is a constitutional right to assume, in the Alliance's own words, "enormous risks," in pursuit of *potentially* life-saving drugs. Unlike the cases in which the doctrine of self-defense might properly be invoked, this case involves risk from drugs with no proven therapeutic effect, which at a minimum separates this example from the abortion "life of the mother" exception. Because terminally ill patients cannot fairly be characterized as using reasonable force to defend themselves when they take unproven and possibly unsafe drugs, the Alliance's desire that the terminally ill be free to assume the risk of experimental drugs cannot draw support from the doctrine of self-defense.

III.

Although it has not addressed the precise constitutional argument urged by the Alliance, we find it highly significant that the Supreme Court has rejected several similar challenges to the FDCA and related laws brought on statutory grounds. And other courts have rejected arguments that the Constitution provides an affirmative right of access to particular medical treatments reasonably prohibited by the Government.

In keeping with those decisions, we conclude that the Alliance has not provided evidence of a right to procure and use experimental drugs that is deeply rooted in our Nation's history and traditions. To the contrary, our Nation's history evidences increasing regulation of drugs as both the ability of government to address these risks has increased and the risks associated with drugs have become apparent. Similarly, our legal traditions of allowing a necessity defense, prohibiting intentional interference with rescue, and recognizing a right of self-defense cannot justify creating a constitutional right to assume any level of risk without regard to the scientific and medical judgment expressed through the clinical testing process.

IV.

Because the Alliance's claimed right is not fundamental, the Alliance's claim of a right of access to experimental drugs is subject only to rational basis scrutiny. . . . Applying the rational basis standard to the Alliance's complaint, we cannot say that the government's interest does

not bear a rational relation to a legitimate state interest. That conclusion is compelled by the Supreme Court's decision in *United States v. Rutherford,* 442 U.S. 544, 99 S.Ct. 2470, 61 L.Ed.2d 68 (1979). In that case, terminally ill patients sought to prevent the FDA from prohibiting access to the drug laetrile, even though the drug had not been approved for public use. In rejecting a challenge by terminally ill patients claiming that the FDCA's safety requirement did not apply to them, the Supreme Court held that "[f]or the terminally ill, as for anyone else, a drug is unsafe if its potential for inflicting death or physical injury is not offset by the possibility of therapeutic benefit." . . .

Although terminally ill patients desperately need curative treatments, as *Rutherford* holds, their deaths can certainly be hastened by the use of a potentially toxic drug with no proven therapeutic benefit. Thus, we must conclude that, prior to distribution of a drug outside of controlled studies, the Government has a rational basis for ensuring that there is a scientifically and medically acceptable level of knowledge about the risks and benefits of such a drug. We therefore hold that the FDA's policy of limiting access to investigational drugs is rationally related to the legitimate state interest of protecting patients, including the terminally ill, from potentially unsafe drugs with unknown therapeutic effects.

V.

For the foregoing reasons, the judgment of the district court is affirmed.

So ordered.

■ ROGERS, CIRCUIT JUDGE, with whom CHIEF JUDGE GINSBURG joins, dissenting:

Today, the court rejects the claim that terminally ill patients who have exhausted all government-approved treatment options have a fundamental right to access investigational new drugs. The court's opinion reflects a flawed conception of the right claimed by the Abigail Alliance for Better Access to Developmental Drugs and a stunning misunderstanding of the stakes. The court shifts the inquiry required by *Glucksberg,* by changing the nature of the right, by conflating the right with the deprivation, and by prematurely advancing countervailing government interests. The court fails to come to grips with the Nation's history and traditions, which reflect deep respect and protection for the right to preserve life, a corollary to the right to life enshrined in the Constitution. The court confuses this liberty interest with the manner in which the Alliance alleges that the liberty has been deprived, namely by denying terminally ill patients access to investigational medications under the narrow conditions described by the Alliance. The court conflates the inquiry as to whether a fundamental right exists at all with whether the government has demonstrated a compelling interest, when strictly scrutinized, rendering its restrictive policy constitutional.

These missteps lead the court to rely upon how rights and liberties have been limited and restricted—addressing regulations to prevent fraud in the sale of misbranded and adulterated medications or safety restrictions applicable to all medicines for any palliative purpose—which says little about the historic importance of the underlying right of a person to save her own life. Likewise, in its treatment of the common law doctrines of necessity, interference with rescue, and self defense, the court points to evolved limitations on those doctrines while ignoring the core concerns that animate them, namely the special importance of life and attempts to preserve it. That the ultimate protection of such varying attempts to save life is cabined by the precedents—regarding what constitutes "necessity," the related "necessity" of any aid being given to a third party, and the "reasonable" and "necessary" limitations on any force used in self-defense—does not suggest the absence of an underlying right to attempt to protect life, but rather the recognition of competing governmental interests that in various circumstances justify the deprivation of or a limitation upon the right. . . .

In the end, it is startling that the oft-limited rights to marry, to fornicate, to have children, to control the education and upbringing of children, to perform varied sexual acts in private, and to control one's own body even if it results in one's own death or the death of a fetus have all been deemed fundamental rights covered, although not always protected, by the Due Process Clause, but the right to try to save one's life is left out in the cold despite its textual anchor in the right to life. . . . It bears outlining the history and common law basis for the Alliance's claim in order to demonstrate, once again, that the history and traditions of this Nation support the right of a terminal patient, and not the government, to make this fundamentally personal choice involving her own life. Because judicial precedents and the historical record require strict scrutiny before upsetting rights of this magnitude, the FDA must demonstrate a compelling governmental interest before its policy restricting access can survive. Accordingly, I would remand the case to the district court to make the initial determination as to whether FDA has met its burden, and I respectfully dissent. . . .

III.

For these reasons, I have serious disagreements with the court's assessment of the Alliance's claim to a fundamental right protected by the Fifth Amendment to the Constitution. It is no more than tragic wordplay to suggest that the Alliance's liberty claim to potentially life prolonging medications, when no other government approved alternatives exist, does not involve a corollary to the right to life enshrined in the Fifth Amendment to the Constitution. Denying a terminally ill patient her only chance to survive without even a strict showing of governmental necessity presupposes a dangerous brand of paternalism. As the court phrases it, because "*[w]e* . . . cannot know until the clinical testing process has been completed that these drugs are

necessary," the terminally ill patient, informed by her physician, is denied a right to decide whether to bear those risks in an attempt to preserve her life. Such intervention is directly at odds with this Nation's history and traditions giving recognition to individual self-determination and autonomy where one's own life is at stake and should extend no further than the result in this case. Because the right of a terminally ill patient to access potentially life-saving investigational medications satisfies the *Glucksberg* test, I would remand this case for the district court to assess in the first instance whether there exists a compelling governmental interest, narrowly tailored, to overcome the Alliance's interest. Accordingly, I respectfully dissent.

NOTES AND QUESTIONS

1. *What Is the Fundamental Right Involved?* As we learned in Chapter 1 when we read *Glucksberg*, and as the majority and dissent insist here, substantive due process analysis requires that the claimed constitutional right be identified with specificity. The majority and dissent argue about the constitutional right alleged here by Abigail Alliance. How does the majority characterize the right? How does the dissent characterize it? Do you agree with the majority that there is no "right of access to experimental drugs that have passed limited safety trials but have not been proven safe and effective"? Do you agree with the dissent that the right to life is more fundamental than many other rights that the Supreme Court has recognized?

2. *Common Law*. Review the common law arguments about necessity, rescue and self-defense. Did you find those arguments persuasive here? Is any one of those arguments more persuasive than the others? How did the majority and the dissent disagree about the application of the common law in *Abigail Alliance*?

3. *Remand*. If the case had been remanded to apply strict scrutiny, as the dissent argued, what would have been the result in the district court? Could the government's arguments about not making these drugs available to terminally ill patients survive strict scrutiny?

4. *Bioethical Principles.* The dissent speaks frequently about protecting individual autonomy to make choices about staying alive. What bioethical principle, if any, guided the majority's reasoning? Is the dissent correct that the majority demonstrated "a dangerous brand of paternalism"?

5. *Canterbury*. The dissent referred to *Canterbury*, which we read at the beginning of this chapter. Which opinion is more faithful to *Canterbury*, the majority or the dissent? Is the lesson of *Canterbury* and this chapter that the Abigail Alliance deserves access to these drugs as long as they give full informed consent?

6. *Right to Try Laws.* The federal Right to Try Act, 21 USC §§ 360bbb–0a, was passed in May 2018. Unlike for drugs made available under FDA "compassionate use" provisions (now renamed "Expanded Access," *infra*), the FDA does not approve or deny right to try requests. It "recommends that patients first consult with their physician and that physicians consult with the sponsor of the investigational drug or biological product. The sponsor is in the best position to provide information about whether the drug or biological product meets the criteria to be considered an eligible investigational drug for use under the Right to Try Act." FDA, Right to Try, https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try. As of 2020, 41 states have passed right-to-try laws. The federal law applies to everyone, but you can also find out your state's laws identified at https://righttotry.org/in-your-state/.

Practice Exercise: Draft a sample right to try law. Then go to the website and compare your version to the federal Right to Try Act. Would you make any changes to the proposed language? What would you tell a pharmaceutical manufacturer to do if confronted with a request?

In response to these concerns, the FDA has amended its own "Expanded Access" provisions to streamline the process. See Food & Drug Administration, Expanded Access, https://www.fda.gov/news-events/public-health-focus/expanded-access. Regardless of whether access is sought through the FDA process or the Right to Try avenue, however, patients cannot access experimental medications without the manufacturers' consent. Why might a manufacturer decline to make such drugs available outside of recognized clinical trials?

In the next section, we identify five issues that challenge the current system and that you can expect to confront in practice.

C. LOOKING AHEAD: IMPROVING CONSENT IN NEW CIRCUMSTANCES

1. CAN TECHNOLOGY IMPROVE INFORMED CONSENT?

Do you think informed consent is satisfied if every item of the following checklist is met?

1) that the subjects are not only patients and, to the extent to which they are patients, that their therapeutic interests, even if not incidental, will be subordinated to scientific interests;
2) that it is problematic and indeterminate whether their welfare will be better served by placing their medical fate in the hands of a physician rather than an investigator;
3) that in opting for the care of a physician they may be better or worse off and for such and such reasons;

4) that clinical research will allow doctors to penetrate the mysteries of medicine's uncertainties about which treatments are best, dangerous, or ineffective;

5) that clinical research may possibly be in the patient's immediate best interest, perhaps promise benefits in the future, or provide no benefit, particularly if the patient is assigned to a control (placebo) arm of a study;

6) that research is governed by a research protocol and a research question and, therefore, his or her interests and needs will yield to the claims of science; and

7) that physician-investigators will respect whatever decision the subject ultimately makes;

8) that much of this information should be included in a video shown at the beginning of the informed consent process;

9) that the video should explain the difference between research and therapy;

10) that the investigator or a research nurse should orally discuss all aspects of the clinical trial with the subject;

11) that participants will be quizzed on their understanding of the protocol;

12) that protocols should be adapted to an eighth grade reading level;

13) that every IRB should include an expert in reading comprehension and elementary education.

Hoffman, *supra*, at 88–89 (incorporating list of ideas suggested by Professor Jay Katz).

One study found that informed consent increased considerably if five communications strategies were followed: keep forms at an eighth-grade level; use larger font size (14), more white space, bulleting, bolding, and underlining; use graphic displays instead of text; add a verbal description of the project; and keep the form short.

Practice Exercise: Go to the website and watch the video on informed consent prepared by the National Institutes of Mental Health (NIMH). Do you think it is a good model of informed consent?

One study found that informed consent increased considerably if five communications strategies were followed:

— keep forms at an **eighth-grade** level;

— use larger **font size** (14), more white space, bulleting, bolding, and underlining;

— use **graphic displays** instead of text;

— add a **verbal description** of the project;

— and keep the form **SHORT**.

What do you think? See Alan R. Tait et al., Informing the Uninformed: Optimizing the Consent Message Using a Fractional Factorial Design, 167(7) JAMA Pediatr. 640–46 (2013).

Go to the website and watch the four videos regarding the necessary education level of human subjects.

Are the videos at the appropriate education level for human subjects? Compare videos 1 and 2 with videos 3 and 4. Which ones do you think are more appropriate for adults? Would you give all adults the same video or would you change videos based on the human subject's socioeconomic status, education level, age, race, etc.?

Could you improve the presentation of any of the informed consent forms you studied in this chapter?

2. APOMEDIATED CLINICAL TRIALS

Professor O'Connor explains that we are entering a new age of "apomediated" research: "apomediation is envisioned as a more horizontal, peer-to-peer style of information exchange in which no single apomediary is essential to the process." Such research is distinct from traditional intermediary research, where the researcher controls the proposal and the choice of subjects. Instead, today, thanks to social media, patients can begin their own research. A patient interested in the connection between Vitamin D and genetic mutations, for example, can go online, contact other persons similarly interested in the disease, and upload and review her data without the help of a researcher. Dan O'Connor, The Apomediated World: Regulating Research When Social Media Has Changed Research, 41 J.L. Med. & Ethics 470 (2013).

In one case described by Professor O'Connor, one patient came up with the idea that ALS patients report their use of lithium online so that readers could determine whether lithium was a safe and effective treatment for ALS. In that situation, who is the researcher? Who needs protection as a human subject? Should there be any regulation at all of these patient-sponsored initiatives?

Practice Exercise: Compare the PatientsLikeMe approach to research with the other companies listed on the website.

Numerous websites lend themselves to such uses by patients, including www.patientslikeme.com (makes money by selling patient information to companies that are developing products); http://diygenomics.net (brings tools and libraries together for small scale genomics labs for the process of sequence assembly); https://www.inspire.com (receives funding

by providing research for life science companies); and http://www.armyofwomen.org (focusing on breast cancer—receives funds from grants and donations).

Do you like this patient-started approach to research? Or would it be better if the researchers used these sites to contact people (see, e.g., http://trialx.com, http://bcpatientrecruitment.com/) instead of letting the research be decided by patients? Will people lose their privacy in a world of apomediated research? Or do most people understand how social media sites work and give up some privacy in order to enjoy the benefits?

Facebook changed its positive and negative news feeds to see how that input affected the tone of members' Facebook posts. Is this human subjects research that should be governed by the Common Rule? What do you think of applying the following ethical rule to Facebook: "If you're afraid to ask your subjects for their permission to conduct the research, there's probably a deeper ethical issue that must be considered?" Would ethical standards be met if Facebook had given people the option to opt into the research? What if it had debriefed them about the study only after it took place? Did Facebook members have a right to learn that they had been studied and what the results of the research showed? See Vindu Goel, As Data Overflows Online, Researchers Grapple With Ethics, N.Y. Times, Aug. 13, 2014, at B1.

3. INCIDENTAL FINDINGS

Incidental findings raise several bioethical concerns. The Presidential Commission for the Study of Bioethical Issues defined incidental findings as "findings that lie outside the aim of a test or procedure." Presidential Commission for the Study of Bioethical Issues, Bioethics Commission on Incidental Findings: Anticipate and Communicate, Dec. 12, 2013, at https://bioethicsarchive.georgetown.edu/pcsbi/node/3186.html. Generally, an incidental finding occurs when researchers are studying a participant for one issue and incidentally discover another issue. For example, a researcher conducts a memory study on a participant's brain and finds a brain tumor. See id. Does the researcher owe a duty to the participant to disclose the researcher's findings? Consider the following examples:

Go to the website and read the IRB Primer on Incidental Findings.

> A research subject gives informed consent to undergo an MRI examination in connection with a study of brain hemorrhages. The researcher sees a brain tumor on the subject's MRI.
>
> A research subject gives informed consent to undergo an MRI examination in connection with a study of brain activity and intelligence. The researcher sees an unusually-shaped blip on the subject's MRI.

> A research subject gives informed consent to have her genome sequenced in order to participate in a study of multiple sclerosis. The researcher finds that the subject has the BRCA gene, which indicates susceptibility to breast cancer. Another subject in the same study has the gene associated with Alzheimer's disease.
>
> A research subject gives informed consent to undergo a CT scan in a study of the appendix. The CT scan reveals a polycystic liver.
>
> A research subject gives informed consent to be a control in an Alzheimer's imaging trial, and her scan reveals two brain aneurysms.
>
> A research subject gives informed consent to have his genome sequenced as part of a project to better diagnose syndromes of developmental delay, intellectual disability, and seizures. Researchers find the aorta weakening of Marfan syndrome.
>
> A research subject gives informed consent to have his genome sequenced to evaluate heart disease; researchers find he has myoclonus dystonia, a neuromuscular disease.
>
> A research subject who says she has normal hearing gives informed consent to have her genome sequenced in a study to investigate atherosclerosis. Researchers notice a deafness mutation.

Ricki Lewis, Incidental Findings from Genome Sequencing—Nuances and Caveats, Scientific American, Mar. 22, 2013, at http://blogs.scientificamerican.com/guest-blog/2013/03/22/incidental-findings-from-genome-sequencing-nuances-and-caveats/. Should researchers tell the subjects about the discoveries listed above? Some believe that incidental findings should not be reported unless there is "strong evidence of benefit." See Robert Green, et.al, ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing, American College of Medical Genetics and Genomics (2013). Others believe that "variations in any and all disease-associated genes could be medically useful and should be reported." Id.

These situations all involve incidental findings (IFs), "a finding concerning an individual research participant that has potential health or reproductive importance and is discovered in the course of conducting research but is beyond the aims of the study." Susan M. Wolf et al., The Law of Incidental Findings in Human Subjects Research: Establishing Researchers' Duties, 36 J.L. Med. & Ethics 361 (2008). Although scans and other imaging techniques made it possible for researchers to discover many IFs, the ability to sequence the human genome has expanded the scope of IFs. "In the context of genetic research, the question is how to deal with the dozens or hundreds of disparate IFs that can potentially be uncovered in any individual research participant's genetic material." Elizabeth R. Pike et al., Finding Fault? Exploring Legal Duties to Return

Incidental Findings in Genomic Research, 102 Geo. L.J. 795, 800 (2014). We examine genetic testing in Chapter 6.

Which IFs should be revealed to human subjects? What do you think of the following four approaches:

1. No return of incidental findings;
2. Return all genomic data without interpretation;
3. Return results consistent with a compendium put together by scientific consensus;
4. Return IFs only when they are analytically valid, have significant health implications, and are clinically actionable.

Id. What policy would you draft for incidental findings?

4. COMPASSION IN PUBLIC HEALTH EMERGENCIES

Should drugs that have not been tested on human beings ever be given to people outside a clinical trial? The FDA allows "compassionate use" for those with "a serious or immediately life-threatening disease or condition and no comparable or satisfactory therapeutic alternatives." What circumstances do you think are serious enough to warrant compassionate use?

Dr. Sam Brisbane, a Liberian doctor, died after contracting the Ebola virus. He remained at the hospital to help patients, with the Ebola present, even though he risked contracting it himself. He was unable to escape the virus due to inadequate supplies, infrastructure, and training in infection control. Dr. Brisbane decided to remain at the hospital and risk his life to save others' lives. See Josh Mugele & Chad Priest, A Good Death—Ebola and Sacrifice, 371 N. Eng. J. Med. 1185 (2014).

The Ebola outbreak in Western Africa tested the limits of the principle of compassionate use. Ebola is a disease that historically has not affected a lot of people, and rarely affects people in the United States; prior to the recent outbreak, probably fewer than 3000 people had been infected since 1976. Because of the extensive research procedures described in this chapter, bringing a successful drug to market usually costs millions of dollars; manufacturers can be expected to focus on drugs needed for large numbers of people. Because of the lack of private market interest in Ebola, the U.S. government offered $100 million to drug companies to work on Ebola vaccines and treatment in preparation for Ebola's possible use by terrorists. The products available in 2014 have not yet been tested on human subjects. See Richard Harris, Why Is There No Drug to Treat Ebola?, NPR, Morning Edition, Aug. 12, 2014, at http://www.npr.org/2014/08/12/339752974/why-is-there-no-drug-to-treat-ebola.

After a serious outbreak of Ebola in West Africa, stories emerged about four people connected with ZMapp, one of the products that is hoped to treat the disease. In Sierra Leone, a medical team from Doctors Without Borders and the World Health Organization decided not to give ZMapp to Doctor Sheik Umar Khan, a prominent doctor who led the fight against the Ebola outbreak in Sierra Leone. Dr. Khan was never asked whether he wanted the drug. He died on July 29, 2014. On the other hand, after their sponsoring organization requested doses of ZMapp from the manufacturer—Mapp Biopharmaceuticals—two white American missionaries received doses after their return to United States. A seventy-five-year-old Spanish priest also received a dose of the serum. Then the company ran out of product. No Africans received the first doses of the serum. See Andrew Pollack, Opting Against Ebola Drug for Ill African Doctor, N.Y. Times, Aug. 12, 2014, at A1; David Greene, Use of Experimental Ebola Serum Raises Ethical Questions, NPR, Morning Edition, Aug. 11, 2014, at http://www.npr.org/2014/08/11/339485891/use-of-experimental-ebola-serum-raises-ethical-questions.

Practice Exercise: Write down your ethical assessment of this situation before reviewing the comments below.

Do you agree with bioethicist Arthur Caplan that "it is very troubling that the only people known to have gotten the drug to date are two Americans and a Spaniard?" Arthur Caplan, Bioethicist: Ebola Treatment to West is Troubling, Bad Science, NBC News, Aug. 12, 2014, at http://www.nbcnews.com/storyline/ebola-virus-outbreak/bioethicist-ebola-treatment-west-troubling-bad-science-n178026. Does the situation demonstrate that racism persists in human subjects research?

Do you agree with the judgment of the doctors in Sierra Leone, who said they didn't give Dr. Khan a dose because they "feared stoking the considerable suspicion of Western medical institutions in the country?" Pollack, *supra*. Or do you agree with bioethicist Alta Charo's commentary:

> No one can say that the optics here are not troubling. That is you have a very small amount of a drug that might work and the only people who get it are the Americans. But you need to also remember that if we had given it to non-Americans first there would be equally bad optics of testing drugs on people from developing countries before we're willing to test it on ourselves, which has usually been the complaint in the past.

Greene, *supra*.

Coming Attractions Bridal and Formal (CABF), a bridal shop in Akron, Ohio, was visited by Texas nurse Amber Vinson. Before her visit, Nurse Vinson had treated a patient with the Ebola virus at a Dallas hospital. The hospital told medical personnel that they were free to travel and intermingle with people after the Ebola treatment. Vinson was

diagnosed with Ebola after she returned home. CABF was closed for cleaning and then closed permanently because of its reputational damage associated with Ebola. Should CABF be allowed to sue the hospital for a health care liability claim? A Texas court of appeals said yes because the hospital's duties as a health care provider were involved. "[W]e conclude CABF asserts an action against a health care provider for a claimed departure from accepted standards of safety which proximately resulted in injury to a claimant." See Texas Health Resources v. CABF, 552 S.W.3d 335 2018 (Tex. Ct. App. 2018).

The World Health Organization (WHO) panel decided that experimentation with unproven treatments is ethical "in the particular circumstances . . . provided certain conditions are met." See Annette Reid & Ezekiel J. Emmanuel, Ethical Considerations of Experimental Interventions in the Ebola Outbreak, 384 Lancet 1896 (2014). The conditions that they take into consideration to conduct trials for experimental treatments are: collaborative partnership (involve local communities to plan, conduct, and oversee trials); social value (share the knowledge learned); scientific validity (adequate means and use of known data); fair selection of study population (transparency); favorable risk-benefit ratio (minimize risks); independent review (ensure public accountability); informed consent (allow participants to freely participate without coercion); and respect for recruited participants and study communities (protect patients in various aspects). Id.

Additionally, a working group at the NYU Langone Medical Center has released findings from its studies on the research ethics of compassionate use. The following are the major findings:

> 1. Biotechnology companies have no legal or regulatory obligation to provide access to unapproved treatments on the grounds of compassionate use.
>
> 2. The U.S. Food and Drug Administration (FDA) is not an obstacle to those seeking compassionate use. . . . The FDA almost always defers to the company that is developing the unapproved treatment to decide whether to grant compassionate use acces [sic].
>
> 3. Increasing access to unapproved therapies may prove detrimental in the long run to longstanding and effective research and clinical trial systems through which interventions are proven effective and safe, and given regulatory approval.

Petrie-Flom Center, NYULMC: Compassionate Use Could Impact Long-Term Medical Benefits, Sept. 18, 2014, at http://blogs.law.harvard.edu/billofhealth/2014/09/18/nyulmc-compassionate-use-could-impact-long-term-medical-benefits/.

After the anthrax attacks around the time of September 11, 2001, the government mandated anthrax vaccination of military personnel even though the Anthrax Vaccine Adsorbed (AVA) was an investigational

drug that had not been approved for that use by the FDA. Do you agree that in these circumstances giving the vaccine was more important than worrying about its status in the FDA? Should the military enjoy all the rights to informed consent identified in this chapter, or can the government treat them differently because of its concerns about national defense? See Doe v. Rumsfeld, 294 F.Supp.2d 119 (D.D.C. 2003) (vaccine program violated statute prohibiting administration of investigational drugs to service members without informed consent).

Practice Exercise: Would you approve this experiment and rule that it should be exempt from federal informed consent rules?

When there are emergency outbreaks and an unproven treatment exists, who should get the drug? The person closest to death? The person with the best chance of recovery? The person who is least sick? The youngest victim? The oldest victim? The health care workers who fight the disease? The military? Those more recently infected? Those who can be closely monitored? No one until the drug's use is successfully tested in a randomized clinical trial subject to the Common Rule and IRB review? How would you get informed consent from a patient in these circumstances?

Doctors at the University of Pittsburgh know that trauma patients with cardiac arrest have less than a ten percent chance of survival. They wanted to induce hypothermia in those patients to give them a better chance of recovery. As a first step, they must test whether their Emergency Preservation and Resuscitation for Cardiac Arrest from Trauma procedure (EPR-CAT) is safe and effective. In this procedure, emergency room personnel drain the blood of trauma patients suffering gun or knife wounds and replace it with freezing saltwater. The patients are then clinically dead because they lack heartbeat and brain activity. At that point doctors work to save the patients' lives and later resuscitate them, returning blood to their bodies. See Kate Murphy, Killing a Patient to Save His Life, N.Y. Times, Jun. 9, 2014, at D1; Acute Care Research, Emergency Preservation and Resuscitation for Cardiac Arrest from Trauma Procedure (EPR-CAT), at http://www.acutecareresearch.org/studies/current/emergency-preservation-and-resuscitation-cardiac-arrest-trauma-epr-cat.

The unconscious patients cannot consent to the procedure. Are you surprised that this project was sponsored by the U.S. Department of Defense? Or that the hospital provided yellow bracelets to residents of Pittsburgh so they could demonstrate if they wanted to opt out of this experiment? The project (University of Pittsburgh, Emergency Preservation and Resuscitation (EPR) for Cardiac Arrest from Trauma (EPR-CAT)) is described here: http://clinicaltrials.gov/ct2/show/NCT01042015?term=emergency+preservation+and+resuscitation&rank=1. Would you wear the yellow bracelet?

5. A NEW PUBLIC HEALTH EMERGENCY: COVID-19

The COVID-19 pandemic has reignited the discussion of Right to Try laws and whether such laws may help in the development of COVID treatments and vaccinations. In Spring 2020, as the pandemic was declared, the FDA used its "compassionate use" pathway to allow some patients to access proposed COVID treatments, including the Gilead drug remdesivir and the malaria drug chloroquine. Jacquie Lee, FDA Experimental Virus Drug Policy Highlights Right to Try Issue, Bloomberg Law, Mar. 19, 2020, https://news.bloomberglaw.com/pharma-and-life-sciences/fda-experimental-virus-drug-policy-highlights-right-to-try-issue. The Goldwater Institute has pushed to expand Right to Try even further amid the pandemic, allowing broader access to unapproved medications without the FDA's permission. Goldwater Institute, Right to Try Opens Door for Innovation in Coronavirus Crisis, https://goldwaterinstitute.org/article/right-to-try-innovation-and-the-coronavirus-crisis/ (posted Mar. 19, 2020). While such efforts might have a positive impact, there is still potential danger in allowing experimental treatments to be given to COVID patients without knowledge of appropriate dosing, side effects, or possible long-term impacts.

Perhaps the best example of expanding the use of drugs during the pandemic was the use of the anti-malarial drug hydroxychloroquine, which President Trump supported as a treatment for COVID. On February 4, 2020, the Secretary of HHS determined there was a public health emergency; on March 28, FDA issued an Emergency Use Authorization (EUA) for emergency use of oral formulations of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of COVID-19. On June 15, 2020, however, based on the FDA's continuing review of the scientific evidence, the agency determined that the drugs were unlikely to be effective and could cause serious cardiac and other adverse events, and revoked the EUA. See Food & Drug Administration, Authorizations and Revocation of Emergency Use of Drugs During the COVID-19 Pandemic; Availability, 85 Fed. Reg. 56231 (Sept. 11, 2020).

The global COVID-19 pandemic also spurred efforts to develop and produce a vaccine as quickly as possible. While the vaccine development process typically takes years to complete, both the government and private entities sought to expedite the process to develop and test COVID vaccine candidates. This push was highlighted by President Trump's announcement of "Operation Warp Speed," a public-private partnership aiming to have a vaccine available by January 2021. See United States Government Accountability Office, Operation Warp Speed: Accelerated COVID19 Vaccine Development Status and Efforts to Address Manufacturing Challenges (Feb. 2021), https://www.gao.gov/assets/gao-21-319.pdf. The program provided government assistance to support the development, manufacturing, and distribution of COVID-19 vaccines. Similarly, the World Health Organization, along with other global health actors such as the Wellcome Trust, announced the creation in April 2020

of the Access to COVID-19 Tools (ACT) Accelerator, designed to accelerate global development, production, and access to COVID-related health technologies. World Health Organization, Access to COVID-19 Tools (ACT) Accelerator: A Global Collaboration to Accelerate the Development, Production and Equitable Access to New COVID-19 Diagnostics, Therapeutics and Vaccines (Apr. 24, 2020), https://www.who.int/publications/m/item/access-to-covid-19-tools-(act)-accelerator. The FDA authorized a vaccine made by Pfizer for emergency use on December 11, 2020, followed a week later by authorization of one made by Moderna. Denise Grady, Abby Goodnough & Noah Weiland, F.D.A. Authorizes Moderna Vaccine, Adding Millions of Doses to U.S. Supply, N.Y. Times, Dec. 18, 2020, https://www.nytimes.com/2020/12/18/health/covid-vaccine-fda-moderna.html.

By May 3, 2021, more than 246 million vaccine doses had taken place in the United States. 40% of adults are estimated to have received two doses, while 56% have received one. President Biden hopes that by July 4, 2021, 70% of American adults would have received one dose, and thinks 160 million American adults will be fully vaccinated by then. Alana Wise, Biden Sets New Goal: At Least 70% of Adults Given 1 Vaccine Dose by July 4, NPR, May 4, 2021, https://www.npr.org/2021/05/04/993537622/biden-sets-new-goal-for-at-least-70-of-adults-to-be-vaccinated-by-july-4. Were you vaccinated? How did you get your vaccine? What would you recommend as the best way to distribute the vaccine across the United States? Across the world?

With the expedited start of Phase III trials for COVID vaccines, there was a prominent discussion regarding the ethics of testing a vaccine for a disease that does not have a cure. Much of the debate centered on "challenge trials," in which participants who receive a vaccine candidate are injected with a small amount of the virus and then monitored to see whether they become sick. The hope is that the amount of virus injected will be enough to spur the subjects to develop antibodies to the virus, but not enough for them to actually contract the disease. However, given the speed with which these trials have been proposed and the lack of knowledge about the virus itself, there are no clear guidelines regarding a safe dose. The ethical debate arises because there is (as of this writing) no known cure or treatment for COVID, which means that there is no clear way to treat any research subjects who do get sick. Whether the value of quickly developing a vaccine that could end the global pandemic can justify deliberately exposing healthy people to potential COVID infection is an ethical debate with no clear answer. Hannah Devlin, WHO Conditionally Backs Covid-19 Vaccine Trials That Infect People, The Guardian, May 8, 2020, https://www.theguardian.com/science/2020/may/08/who-conditionally-backs-covid-19-vaccine-trials-that-infect-people?CMP=share_btn_tw.

In Chapter 3, we explore the effects of new technology on traditional concepts of reproduction and parenthood, especially how technology affects the right to privacy.