

July 2015

# Protecting Patients: A Proposal For Codifying The Reasonable Innovation Rule

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## Recommended Citation

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## Protecting Patients: A Proposal For Codifying The Reasonable Innovation Rule

*Stephanie M. Mehle\**

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\* J.D., *cum laude*, The University of Akron School of Law, 2015. B.A. in Political Science and Justice Studies, *cum laude*, Kent State University, 2012. I would like to thank Professor Katharine Van Tassel for sharing her expertise, enthusiasm, and encouragement as my mentor. I would also like to thank the editors, editorial board, and staff of the *Akron Law Review* for providing invaluable suggestions in preparing this article for publication. I owe a special thanks to my family for always supporting my dreams.

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## I. INTRODUCTION

Medical progress in America is driven by innovation. Nevertheless, throughout American history, many have died as a result of human experimentation performed under the guise of innovation. Although the Food and Drug Administration (“FDA”) can easily regulate drugs, regulating physicians is a much more daunting task. Under current law, a doctor may try any treatment, regardless of whether it is objectively reasonable, as long as the doctor first obtains the patient’s informed consent.<sup>1</sup> The purpose of this Comment is to demonstrate that a patient’s informed consent is an inadequate protection from harm and a new rule, the reasonable innovation rule, must be codified. Codification of the reasonable innovation rule will balance the dual goals of medical innovation and patient protection.

First, a preliminary explanation of the reasonable innovation rule is required. Ordinarily, customary care, the standard practice established in the medical field in any given jurisdiction, meets the needs of most

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1. K.H. Satyanarayana Rao, *Informed Consent: An Ethical Obligation or Legal Compulsion?*, 1 J. CUTANEOUS & AESTHETIC SURGERY 33, 33 (2008), available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2840885/>. Informed consent hinges on the ethical principle of autonomy, which is the patient’s right to decide what happens to his or her body. *Id.* Informed consent can either be express or implied. *Id.*; see also Bryan Murray, *Informed Consent: What Must a Physician Disclose to a Patient?*, 14 VIRTUAL MENTOR 563, 563 (2012), available at <http://virtualmentor.ama-assn.org/2012/07/hlaw1-1207.html>. Prior to obtaining informed consent, physicians must explain any risks and benefits, as well as any information a reasonable person would find important to the decision-making process. *Id.*

patients.<sup>2</sup> Under the reasonable innovation rule, if customary care is unlikely to provide adequate treatment for one particular patient, a doctor may innovate to meet the patient's unique needs.<sup>3</sup> The rule demands that the innovative procedure be thoroughly researched before being implemented.<sup>4</sup> In other words, a physician may not implement *any* treatment, only one that is *reasonable*. "Reasonableness" is a higher standard than "informed consent" because it mandates a shared responsibility between doctor and patient to engage only in treatments that are considered objectively reasonable. This shifts some of the burden currently pressuring patients to consent to risky, inadequately researched procedures suggested by their physicians.<sup>5</sup>

Part II of this Comment will examine the history of human experimentation and how the current regime of experimenting developed then explore the gap between experimentation approved by an Institutional Review Board ("IRB")<sup>6</sup> and FDA oversight. Part III will consider the competing interests of individual patient protection and medical innovation in general and whether informed consent appropriately balances those interests. Part IV will evaluate the inadequacies of current reliance on informed consent by using two case studies, both involving novel microbial procedures, and discuss how codification of the reasonable innovation rule would address those inadequacies.

The two case studies involve (1) fecal microbiota transplants, which have been highly successful,<sup>7</sup> and (2) bacterial transplants performed in

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2. 1 STEVEN E. PEGALIS, *AMERICAN LAW OF MEDICAL MALPRACTICE* § 3.3 (3d ed. rev. 2014).

3. *Brook v. St. John's Hickey Mem'l Hosp.*, 380 N.E.2d 72, 76 (Ind. 1978).

4. *Id.*

5. Nancy M. Kettle, *Informed Consent: Its Origins, Purpose, Problems, and Limits* 64-65 (Aug. 9, 2002) (unpublished Master thesis, University of South Florida), available at <http://scholarcommons.usf.edu/cgi/viewcontent.cgi?article=2522&context=etd>.

6. *Institutional Review Boards Frequently Asked Questions*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/regulatoryinformation/guidances/ucm126420.htm> (last updated June 25, 2014) [hereinafter *IRB FAQs*]. "Under FDA regulations, an IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects. In accordance with FDA regulations, an IRB has the authority to approve, require modifications in (to secure approval), or disapprove research. This group review serves an important role in the protection of the rights and welfare of human research subjects. The purpose of IRB review is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in the research. To accomplish this purpose, IRBs use a group process to review research protocols and related materials (e.g., informed consent documents and investigator brochures) to ensure protection of the rights and welfare of human subjects of research." *Id.*

7. Maryn McKenna, *Swapping Germs: Should Fecal Transplants Become Routine for Debilitating Diarrhea?*, *SCI. AM.* (Dec. 6, 2011), <http://www.scientificamerican.com/>

an attempt to cure brain cancer, which had deadly consequences.<sup>8</sup> In both cases, as with human experimentation as a whole, informed consent played a crucial role. These cases, however, also raise the question whether consent should bar recovery. Vulnerable, ill patients may consent to dangerous experiments out of desperation. The inadequacies of informed consent will be discussed with this in mind.

Ultimately, this Comment will argue that the common law reasonable innovation rule must be codified to protect vulnerable patients who are willing to try anything. Current oversight and regulation of physicians who implement novel treatments on a regular basis do not offer enough protection to the desperate patient. It is time for the FDA to intervene in our current “wild west” system where physicians are free to deviate from common practice and implement novel and even dangerous procedures as long as they obtain patients’ informed consent.

The FDA must take action by incorporating the reasonable innovation rule into federal regulations instead of leaving it hidden in case law. This will set a minimum standard for physicians who wish to integrate novel treatments into everyday practice. Codifying the rule will not unreasonably restrict innovation because physicians will be able to try new procedures that meet patients’ unique needs, provided the procedures are well researched and reasonable.

## II. REGULATION IN THE UNITED STATES: A BACKGROUND

### A. *The History of Human Experimentation Without Regulation*

America has a dark history of human experimentation, even within the past 100 years.<sup>9</sup> This Comment maintains it is futile to believe that vulnerable populations can always provide true informed consent for treatment using experimental procedures. It asserts, instead, that the obtaining of informed consent for experimental treatment from certain patients, including those who are terminally ill, near death, and for whom approved treatments have failed, is problematic. The practice, in fact, provides disconcerting parallels, though on an individual basis, to

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article.cfm?id=swapping-germs.

8. See Marjie Lundstrom, *UC Davis Surgeons Resign After Bacteria-in-Brain Dispute*, SACRAMENTO BEE, <http://www.sacbee.com/2013/08/25/5678851/uc-davis-surgeons-resign-after.html> (updated Oct. 6, 2014, 2:38 PM).

9. Mike Stobbe, *Ugly Past of US Human Experiments Uncovered*, NBC NEWS, [http://www.nbcnews.com/id/41811750/ns/health-health\\_care/#.UtlxOIRDua8](http://www.nbcnews.com/id/41811750/ns/health-health_care/#.UtlxOIRDua8) (last updated Feb. 27, 2011, 6:14 PM).

prior human experimentation that we now consider unethical, regrettable, and of little benefit to the subjects involved.

Several case studies regarding medical research undertaken by American researchers involving human subjects demonstrate how vulnerable individual patients can be and support this Comment's thesis that regulation is essential to protect patients even from well-intentioned researchers. For instance, in 1932, the Public Health Service began an experiment called the "Tuskegee Study of Untreated Syphilis in the Negro Male."<sup>10</sup> The purpose of this study was to determine how syphilis affected African Americans as opposed to Caucasians.<sup>11</sup> The theory of the experiment was that Caucasians experienced more neurological complications from syphilis while African Americans experienced more cardiovascular complications.<sup>12</sup> How the results of the study would be used in clinical treatment remains unclear.<sup>13</sup>

This study had several problems. First, it lacked adequate informed consent.<sup>14</sup> Rather than revealing the true purpose of the experiment (to record the "natural history of syphilis in Blacks"),<sup>15</sup> the researchers informed the 600 participants, who were all black men, that they were being treated for "bad blood."<sup>16</sup> "Bad blood" was a colloquial expression used to describe a variety of illnesses such as anemia, fatigue, and syphilis.<sup>17</sup> The researchers did not disclose the study's true purpose because they wanted to ensure cooperation.<sup>18</sup> Furthermore, although no proven treatments for the disease existed when the study commenced, penicillin was found to be an effective treatment in 1947.<sup>19</sup> Nevertheless, the researchers withheld this treatment from the participants.<sup>20</sup> This study, which was projected to last a short six months, actually continued for forty years.<sup>21</sup> As a result, 28 men died from syphilis, 100 men died

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10. *The Tuskegee Timeline*, CTRS. FOR DISEASE CONTROL & PREVENTION, <http://www.cdc.gov/tuskegee/timeline.htm> (last updated Sep. 24, 2013).

11. Borgna Brunner, *The Tuskegee Syphilis Experiment*, INFOPLEASE (2007), <http://www.infoplease.com/spot/bhmtuskegee1.html>.

12. *Id.*

13. *Id.*

14. *Id.*

15. *About the USPHS Syphilis Study*, TUSKEGEE UNIV., [http://www.tuskegee.edu/about\\_us/centers\\_of\\_excellence/bioethics\\_center/about\\_the\\_usphs\\_syphilis\\_study.aspx](http://www.tuskegee.edu/about_us/centers_of_excellence/bioethics_center/about_the_usphs_syphilis_study.aspx) (last visited Jan. 7, 2014).

16. *Id.*

17. *Id.*

18. Brunner, *supra* note 11.

19. *The Tuskegee Timeline*, *supra* note 10.

20. *Id.*

21. *Id.*

from related complications, 40 men infected their wives, and 19 of their children were born with congenital syphilis.<sup>22</sup>

Another flagrant example of human experimentation involved the discovery and development of penicillin in the mid-1900s.<sup>23</sup> From 1946 to 1948, American public health doctors deliberately infected over 1,600 Guatemalans aged 10 to 72—prison inmates, children, mental patients, female prostitutes, and soldiers—with venereal diseases in order to test the efficacy of penicillin in treating or preventing sexually transmitted diseases.<sup>24</sup> In total, 696 were infected with syphilis, 772 with gonorrhea, and 142 with chancres.<sup>25</sup> After subjects contracted the disease, they were given penicillin.<sup>26</sup> Not surprisingly, the research failed to yield any medically useful information.<sup>27</sup> The study was well hidden and came to light only in 2011 when it was revealed that 83 of these patients died as a result of the experiment.<sup>28</sup>

During the same time, American doctors were performing another human experiment in Guatemala.<sup>29</sup> They injected seven women, residents of a Guatemalan insane asylum, with syphilis in the back of the skull.<sup>30</sup> The researchers hoped the syphilis infection would cure epilepsy, but instead, the women contracted bacterial meningitis, probably due to unsterilized injection needles.<sup>31</sup>

The 1940s through 1950s saw massive growth in the pharmaceutical industry, and as a result, the government and private

22. Brunner, *supra* note 11.

23. Donald G. McNeil, Jr., *U.S. Apologizes for Syphilis Tests in Guatemala*, N.Y. TIMES (Oct. 1, 2010), [http://www.nytimes.com/2010/10/02/health/research/02infect.html?\\_r=0](http://www.nytimes.com/2010/10/02/health/research/02infect.html?_r=0); *see also* Mariano Castillo, *Guatemalans to File Appeal Over STD Experiments*, CNN (June 15, 2012), <http://www.cnn.com/2012/06/15/us/guatemala-std-experiments/index.html>.

24. Castillo, *supra* note 23. Shockingly, “American tax dollars, through the National Institutes of Health, even paid for syphilis-infected prostitutes to sleep with prisoners, since Guatemalan prisons allowed such visits. When the prostitutes did not succeed in infecting the men, some prisoners had the bacteria poured onto scrapes made on their penises, faces or arms, and in some cases it was injected by spinal puncture.” McNeil, *supra* note 23; *see also* Kara Rogers, *Guatemala Syphilis Experiment*, ENCYCLOPÆDIA BRITANNICA, <http://www.britannica.com/EBchecked/topic/1805220/Guatemala-syphilis-experiment> (last visited Feb. 21, 2014).

25. Castillo, *supra* note 23.

26. *Id.*

27. *Shocking New Details of US STD Experiments in Guatemala*, ASSOCIATED PRESS, Aug. 30, 2011, available at <http://www.theguardian.com/world/2011/aug/30/guatemala-experiments>.

28. *Id.*; *see also* Susan Donaldson James, *Syphilis Experiments Shock, But So Do Third World Drug Trials*, ABC NEWS (Aug. 30, 2011), <http://abcnews.go.com/Health/guatemala-syphilis-experiments-shock-us-drug-trials-exploit/story?id=14414902>.

29. *Id.*

30. *Id.*

31. *Id.*

corporations began to fund prisoner experimentation.<sup>32</sup> “By the 1960s, at least half the states allowed prisoners to be used as medical guinea pigs.”<sup>33</sup> It was not until 1978 that the FDA stepped in to regulate human experiments conducted on prisoners.<sup>34</sup> These examples of horrific medical research performed on human subjects demonstrate that strict regulations designed to protect people who are participating in a study, or any type of experimental treatment, are necessary.

### B. *Experimental Treatment and the FDA: The Space Between*

This Comment argues that, while strong statutory protections are in place for human subjects, oversight by the FDA is lacking. Because of the gaps in oversight, it is inevitable that some vulnerable patients are being subjected to inappropriate experimental treatment. First, a preliminary explanation of the origin of statutory protections is required. Next, the intricacies of the FDA drug approval process will be detailed, and the FDA’s control over IRBs will be scrutinized. Finally, because of a lack of oversight of IRBs, patients have relied on tort law and medical malpractice actions to encourage physicians to use appropriate care in suggesting experimental treatments. Thus, a brief explanation of medical malpractice is provided for understanding the basis of those claims.

#### 1. The Origin of Statutory Protections

Most of the basic regulations concerning human subject research come from the Department of Health and Human Services (“DHHS”).<sup>35</sup> The DHHS is a cabinet-level department of the federal government that includes 11 agencies.<sup>36</sup> The FDA, one of the DHHS agencies, is tasked

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32. Stobbe, *supra* note 9.

33. *Id.* “Holmesburg Prison in Philadelphia made extensive use of inmates for medical experiments. Some of the victims are still around to talk about it. Edward ‘Yusef’ Anthony, featured in a book about the studies, says he agreed to have a layer of skin peeled off his back, which was coated with searing chemicals to test a drug. He did that for money to buy cigarettes in prison.” *Id.*

34. *Prisoners in Clinical Trials*, FIRST CLINICAL RES. (Nov. 21, 2007), <http://firstclinical.com/fda-gcp/?show=2007/RE%20Prisoners%20in%20clinical%20trials&format=fulllist>.

35. *Regulations*, DEPT. OF HEALTH & HUMAN SERV., <http://www.hhs.gov/ohrp/humansubjects/> (last visited Jan. 10, 2014). “In the United States, a series of highly publicized abuses in research led to the enactment of the 1974 National Research Act (Public Law 93-348), which created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the National Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines to assure that such research is conducted in accordance with those principles.” *Id.*

36. *About HHS*, U.S. DEPT. OF HEALTH & HUMAN SERV., <http://www.hhs.gov/about/> (last

with regulating “clinical investigations of products under its jurisdiction, such as drugs, biological products, and medical devices.”<sup>37</sup> The FDA, although under the DHHS umbrella, has its own specific rules for human subject research to protect participants in the clinical trials of new drugs and devices.<sup>38</sup> Any variation between DHHS and FDA rules reflect differences in the statutory scope or requirements.<sup>39</sup>

## 2. The Drug Approval Process

In response to a push for “legally mandated quality and identity standards for food, prohibition of false therapeutic claims for drugs, coverage of cosmetics and medical devices, clarification of the FDA’s right to conduct factory inspections, and control of product advertising,” Congress passed the 1938 Food, Drug, and Cosmetic Act (“FDCA”).<sup>40</sup> One of the most important provisions of this law was a mandate that drug manufacturers prove to the FDA that a drug is safe before it can be sold on the market.<sup>41</sup> This pre-market approval process forever changed the way that drugs are regulated in the United States.<sup>42</sup>

The FDA drug approval process for both prescription and over-the-counter drugs involves several steps. First, after obtaining promising clinical data, a drug manufacturer must apply for an Investigational New Drug Application (“IND”) from the FDA’s Center for Drug Evaluation and Research.<sup>43</sup> After submitting an IND, a manufacturer must wait 30 days before beginning clinical trials<sup>44</sup> to allow the FDA to research and review the prospective study.<sup>45</sup> “If [the] FDA finds a problem, it can

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revised Oct. 6, 2014).

37. *Regulations*, *supra* note 35.

38. *Comparison of FDA and HHS Human Subject Protection Regulations*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/EducationalMaterials/ucm112910.htm> (last updated Mar. 10, 2009).

39. *Id.*

40. *The 1938 Food, Drug, and Cosmetic Act*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/aboutFDA/WhatWeDo/History/origin/ucm054826.htm> (last updated Sep. 24, 2012).

41. *Id.*

42. *Id.*

43. *How Drugs are Developed and Approved*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/default.htm> (last updated Feb. 13, 2014). The Center for Drug Evaluation and Research “is the largest of FDA’s five centers. It has responsibility for both prescription and nonprescription or over-the-counter (OTC) drugs. The other four FDA centers have responsibility for medical and radiological devices, food, and cosmetics, biologics, and veterinary drugs.” *Id.*

44. “Clinical trials are experiments that use human subjects to see whether a drug is effective, and what side effects it may cause.” *Id.*

45. *Id.*

order a ‘clinical hold’ to delay an investigation, or interrupt a clinical trial if problems occur during the study.”<sup>46</sup> After clinical trials are complete and the manufacturer has determined that enough evidence exists to meet the FDA’s standards, the manufacturer must then submit a New Drug Approval Application (“NDA”).<sup>47</sup> The NDA is a detailed application containing information such as “manufacturing specifications, stability and bioavailability data, method of analysis of each of the dosage forms the sponsor intends to market, packaging and labeling for both physician and consumer, and the results of any additional toxicological studies not already submitted.”<sup>48</sup> Only after the NDA is approved may the drug be placed on the market.<sup>49</sup>

### 3. Regulation of Institutional Review Boards

The FDA has the power to regulate not only drugs and devices but also IRBs. “An IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects.”<sup>50</sup> Under current law, the FDA requires IRBs<sup>51</sup> to “review and monitor biomedical research involving human subjects.”<sup>52</sup> Each IRB that oversees FDA-regulated studies must register with the FDA.<sup>53</sup> All IRBs must assure that each human subject has given informed consent prior to commencement of the study.<sup>54</sup>

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46. *Id.*

47. *Id.*

48. *Id.*

49. *Id.*

50. *See IRB FAQs, supra* note 6.

51. For a description of IRBs, see *id.*

52. *See id.*

53. *Id.*

54. *Id.* “The fundamental purpose of IRB review of informed consent is to assure that the rights and welfare of subjects are protected. A signed informed consent document is evidence that the document has been provided to a prospective subject (and presumably, explained) and that the subject has agreed to participate in the research. IRB review of informed consent documents also ensures that the institution has complied with applicable regulations.” *Id.* The FDA sets out the following criteria for IRB approval of research in 21 C.F.R. § 56.111 (2013):

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

(1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which 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 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

IRBs have incurred a lot of criticism through the years, but perhaps the most serious concern is the FDA's lack of oversight.<sup>55</sup> In 2007, the Office of the Inspector General stated that the FDA's oversight of IRB clinical trials was "weak, disorganized, and thus unable to ensure the safety of clinical research participants."<sup>56</sup> The Office of the Inspector General further noted the FDA could not possibly supervise all clinical trials or IRBs tasked with overseeing the research involved in the trials

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benefits of therapies that 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 (for example, 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 and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, 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 part 50.

(5) Informed consent will be appropriately documented, in accordance with and to the extent required by 50.27.

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

(7) Where 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, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence additional safeguards have been included in the study to protect the rights and welfare of these subjects.

(c) In order to approve research in which some or all of the subjects are children, an IRB must determine that all research is in compliance with part 50, subpart D of this chapter.

55. David A. Hyman, *Institutional Review Boards: Is This the Least Worst We Can Do?*, 101 NW. U. L. REV. 749, 749 (2007). "Institutional Review Boards ('IRBs') are polarizing institutions. IRB supporters view them as the best thing since sliced bread. Detractors believe IRBs impose costs and have no benefits. Supporters point to the good faith and hard work of those who volunteer to serve on an IRB. Detractors suggest that IRBs emphasize bureaucratic busy-work. Supporters ask for more money and more staff so they can do an even more thorough job reviewing research protocols. Detractors point out that the IRB framework of research oversight would never be approved by an IRB. Supporters counter that notorious examples of abuse show that IRBs are necessary. Detractors respond with anecdotes of IRB stupidity and incompetence. Supporters argue that conducting research is a privilege, not a right. Detractors complain about censorship, restrictions on academic freedom, and the chilling of constitutionally protected free speech. Both sides then return to their respective camps, secure in the knowledge that they are right and those on the other side are self-righteous zealots." *Id.*

56. Jill Wechsler, *FDA Hit for Poor Clinical Trial Oversight*, SPECTROSCOPY (Nov. 1, 2007), <http://www.spectroscopyonline.com/spectroscopy/article/articleDetail.jsp?id=468088>.

because it “lacks an efficient information system for tracking clinical research activity, site inspections, and resulting corrective actions.”<sup>57</sup> The FDA, in fact, oversees less than 1% of all clinical trials.<sup>58</sup> As a consequence, patients may suffer serious delay in remedying issues that may arise during a clinical trial.<sup>59</sup> The FDA inspects less than 300 IRBs each year, “partly because the agency has no complete IRB database and thus cannot identify all review boards evaluating clinical trials for regulated products.”<sup>60</sup>

#### 4. Medical Malpractice

Given the FDA’s limited oversight of IRBs, patients have turned to tort law and actions premised on lack of informed consent. “Medical malpractice occurs when a health care provider renders treatment that deviates from the accepted standard of practice in the medical community.”<sup>61</sup> In other words, the care the doctor provided did not meet the level of care that should have been provided. Medical malpractice claims may be based either on deficient care in providing medical procedures or on failure to obtain informed consent prior to the procedure. The standard of care differs by jurisdiction and custom.<sup>62</sup> It may be acceptable for a doctor to use a certain treatment in one locale but not in another.<sup>63</sup>

Although the FDA cannot, and should not, micromanage all of the doctors in the United States to ensure compliance with established rules and regulations, these gaps in the oversight of medical care and research are more troubling when viewed in light of patient vulnerability to human experimentation. Understanding the FDA’s inability to oversee clinical trials and experimental treatments provides background for this

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57. *Id.*

58. *Id.*

59. Gardiner Harris, *Report Assails F.D.A. Oversight of Clinical Trials*, N.Y. TIMES (Sept. 28, 2007), [http://www.nytimes.com/2007/09/28/health/policy/28fda.html?\\_r=3&](http://www.nytimes.com/2007/09/28/health/policy/28fda.html?_r=3&).

60. See Wechsler, *supra* note 56.

61. Robert P. Valletti, *The Difficulty of Medical Malpractice: Deviation from Standard of Care*, GINARTE (Oct. 13, 2012), <http://www.ginarte.com/2012/10/difficulty-medical-malpractice-deviation-standard-care/>.

62. *Id.* “A major obstacle in medical malpractice claims, however, is proving there was an actual deviation from a standard of care because the medical community is replete with doctors who render their own ‘opinion’ as to what the requisite level of care should have been. In laymen terms, doctors give their opinions as to what procedures or treatment should have been done based on a given set of facts surrounding a person’s symptoms, and since there is no ‘bright line’ rule about what types of procedures or treatments should be given (hence why it is called a doctor’s ‘opinion’), proving a deviation from the standard is difficult.” *Id.*

63. *Id.*

Comment's argument that mere informed consent is not a sufficient safeguard for vulnerable patients.

### III. THE PROBLEM WITH INFORMED CONSENT

Medicine naturally seeks to balance a procedure's benefits against its risks. Physicians and patients must constantly evaluate whether the risks of a given treatment are worth its benefits. Requiring a patient's informed consent prior to a medical procedure attempts to protect both parties from making the wrong decision; but informed consent is often inadequate, given patients' limited knowledge of medicine and their level of desperation.<sup>64</sup> The law of informed consent was not developed to regulate use of experimental or innovative medicines or medical procedures, but it has been pressed into service in these areas. Accordingly, it provides an incomplete and often ineffectual solution.

#### A. *Should Informed Consent Bar Recovery?*

The doctrine of informed consent is premised upon the fundamental right of every person to determine what is done to his or her body in the course of medical treatment.<sup>65</sup> The patient must be provided with enough information to make an informed decision regarding whether to accept or decline treatment.<sup>66</sup> The elements of informed consent<sup>67</sup> include

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64. See King & Moulton, *infra* note 70, at 430.

65. Russell G. Thornton, *Informed Consent*, BAYLOR UNIV. MED. CTR. (Apr. 2000), available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1312305/>.

66. *Id.*

67. 45 C.F.R. § 46 (2005) currently reads as follows:

§46.116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

(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

competence, disclosure, understanding, voluntariness, and authorization.<sup>68</sup> A physician must explain the risks and benefits, as well as the purpose and duration of treatment, as part of the consent process.<sup>69</sup> Physicians obtain informed consent<sup>70</sup> prior to any procedure to safeguard against legal liability.<sup>71</sup>

There are two types of informed consent prevalent in America today.<sup>72</sup> Approximately half of the states utilize a physician-based standard where physicians are expected to inform the patient about the

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- procedures to be followed, and identification of any procedures which 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 which 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; and
  - (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.

68. See Kettle, *supra* note 5, at 60.

69. *Id.*

70. Jaime S. King & Benjamin W. Moulton, *Rethinking Informed Consent: The Case for Shared Medical Decision-Making*, 32 AM. J.L. & MED. 429, 430 (2006), available at <http://librarysource.uchastings.edu/repository/King/32AmJLMed429.pdf>. The American Medical Association explains that sufficient information sharing by the physician, including all probable risks and benefits, is paramount in the process of obtaining adequate patient consent. W. Eugene Basanta, *Communicating with Dying Patients*, Proceedings of the 18th World Congress on Medical Law 1 (2010), available at [http://www.law.siu.edu/\\_common/documents/publications/basanta/communicating-patients.pdf](http://www.law.siu.edu/_common/documents/publications/basanta/communicating-patients.pdf). The American Medical Association goes on to explain, "The patient's right of self-decision can be effectively exercised only if the patient possesses enough information to enable an informed choice. The patient should make his or her own determination about treatment. The physician's obligation is to present the medical facts accurately to the patient or to the individual responsible for the patient's care and to make recommendations for management in accordance with good medical practice. The physician has an ethical obligation to help the patient make choices from among the therapeutic alternatives consistent with good medical practice. Informed consent is a basic policy in both ethics and law that physicians must honor." *Id.*

71. *Patient Consent*, LAW, SCI. & PUB. HEALTH PROGRAM SITE, <http://biotech.law.lsu.edu/Books/aspn/Aspen-Patient.html> (last visited Jan. 11, 2014).

72. King & Moulton, *supra* note 70, at 430.

risks that a “reasonably prudent practitioner” would be aware of.<sup>73</sup> The other 23 states and the District of Columbia rely on a patient-based standard where physicians are expected to inform patients about the risks a “reasonable patient” would find valuable to the decision-making process.<sup>74</sup> Patients may bring a negligence action against a physician by alleging that they did not receive adequate information before consenting to the procedure.<sup>75</sup> A finding of informed consent, however, should not bar recovery when particular situations render the patient’s consent inadequate.<sup>76</sup>

In addition to possible shortcomings in information provided by the physician, other fundamental problems with informed consent must be considered. For instance, patients tend to strongly believe that their physician would not recommend anything unnecessary or ineffective.<sup>77</sup> Patients may also struggle with information overload regarding the treatment and non-treatment options provided by their physician.<sup>78</sup> Most patients are not familiar with medical terms and are unable to sift through complex and technical scientific information to understand what is important to their specific needs.<sup>79</sup>

Moreover, special consideration must be given to obtaining informed consent from what the DHHS has termed “vulnerable

73. *Id.*; Richard Weinmeyer, *Lack of Standardized Informed Consent Practices and Medical Malpractice*, 16 AM. MED. ASSOC. J. ETHICS 120, 121 (2014).

74. King & Moulton, *supra* note 70, at 430.

75. “The theory of negligence holds that the defendant is liable for a careless action or omission when the defendant had an obligation toward the plaintiff and careless action or omission causes an injury. The standard of reasonable care is the level of care that a common person would view as proper conduct. On the other hand, the profession is the group that sets the standards for determining the level of due care in professional negligence or malpractice. Medical malpractice occurs when a physician violates the standard of due care, including an omission to properly disclose information about a specific procedure. In case of physicians’ negligence in informed consent, an action would have to show that a physician violated a duty of ‘due care to inform a patient, that this breach resulted in a financially measurable injury, and that a reasonable person would not have consented.’” Kettle, *supra* note 5, at 57-58. “Listing ‘informed consent’ as an allegation of negligence, within a medical malpractice suit, often does not give rise to a plaintiff being awarded damages as the lack of ‘informed consent’ alone is not a basis for neglect except when the plaintiff can prove the decision to proceed, or not proceed, with a procedure would have been made differently, and solely, upon the accurate facts of an informed consent, had it been given prior to surgery.” Christine Cadena, *Medical Malpractice and the Informed Consent Doctrine* (Feb. 1, 2007), available at <http://tinytuna.com/medical-malpractice-and-the-informed-consent-doctrine/>.

76. See Kettle, *supra* note 5, at 69.

77. *Patient Consent*, *supra* note 71.

78. Kettle, *supra* note 5. Contributing to this problem is patients’ reliance on selective perception, making it difficult to figure out when words have a “special meaning for them, when preconceptions distort their processing of the information, and when other biases intrude.” *Id.* at 71.

79. *Id.* at 68.

subjects.”<sup>80</sup> Groups such as children, the undereducated, the mentally handicapped, the terminally ill, and pregnant women are considered vulnerable populations.<sup>81</sup> The common thread among these groups is that they may be more prone to coercion or undue influence while participating in experimental treatment.<sup>82</sup> The terminally ill, for example, are of particular interest to this Comment. The patients in the brain bacteria case, discussed in the following section, are considered a special group because all three patients were terminally ill.<sup>83</sup> Extra attention must be given to the terminally ill because they may be willing to try anything to improve their conditions and save their lives.<sup>84</sup>

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80. DEPT. OF HEALTH & HUMAN SERV., INSTITUTIONAL REVIEW BOARD GUIDEBOOK, ch. 6, available at [http://www.hhs.gov/ohrp/archive/irb/irb\\_chapter6.htm](http://www.hhs.gov/ohrp/archive/irb/irb_chapter6.htm) (last updated 1993).

81. *Id.* Alarming, these special groups frequently suffer from institutional failures because their unique needs are not adequately addressed prior to obtaining their informed consent. “In a cross-sectional survey of IRBs in U.S. institutions, investigators showed that IRBs rarely or never required procedures to determine capacity and also varied in their use of other safeguards, such as independent monitors, research proxies, and advance research directives.” Henry Silverman, *Protecting Vulnerable Research Subjects in Critical Care Trials: Enhancing the Informed Consent Process and Recommendations for Safeguards*, ANNALS OF INTENSIVE CARE, 2011, at 1, available at <http://www.annalsofintensivecare.com/content/pdf/2110-5820-1-8.pdf>. Although, the FDA has made exceptions for the terminally ill: it allows for “compassionate use” of a drug for those who are extremely desperate. “Expanded access,” sometimes called “compassionate use,” is the use of an investigational drug outside of a clinical trial to treat a patient with a serious or immediately life-threatening disease or condition who has no comparable or satisfactory alternative treatment options. *Expanded Access: Information for Patients*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm351748.htm> (last updated Oct. 4, 2013). “FDA regulations allow access to investigational drugs for treatment purposes on a case-by-case basis for an individual patient, or for intermediate-size groups of patients with similar treatment needs who otherwise do not qualify to participate in a clinical trial. They also permit expanded access for large groups of patients who do not have other treatment options available, once more is known about the safety and potential effectiveness of a drug from ongoing or completed clinical trials.” *Compassionate Use Programs*, ALS ASSOC., <http://www.alsa.org/als-care/resources/publications-videos/factsheets/compassionate-use.html> (last visited Feb. 24, 2015). “Just as in clinical trials, these investigational drugs have not yet been approved by the FDA as safe and effective. They may be effective in the treatment of a condition, or they may not. They also may have unexpected serious side effects.” *Id.*

82. Univ. of South Fla. IRB Training, *Identifying and Protecting Vulnerable Populations*, available at TAMPA GEN. HOSP., <https://www.tgh.org/PDFs/IdentifyingandProtectingVulnerablePopulations.pdf> (last visited Nov. 16, 2014).

83. Marjie Lundstrom & Sam Stanton, *Evaluation of UC Davis Medical Center's Handling of Neurosurgeons is Scathing*, SACRAMENTO BEE, <http://www.sacbee.com/2012/12/23/5072625/evaluation-of-uc-davis-medical.html> (updated Oct. 8, 2014, 10:39 AM).

84. Natalie L. Regoli, *Insurance Roulette: The Experimental Treatment Exclusion & Desperate Patients*, 22 QUINNIPIAC L. REV. 697, 697 (2004). This article describes an archetypal situation that closely mirrors the brain bacteria case. “During the last decade, the archetypal experimental treatment lawsuit has been one in which a gravely-ill patient petitions the court for an order directing his or her insurance company to authorize certain procedures. Such a case begins after standard medical treatment has failed, and the patient’s treating physician recommends newer

In summary, obtaining informed consent prior to an experimental procedure is not a sufficient safeguard for vulnerable patients. The law must intervene to protect patients who consent, as a last resort, to experimental treatments that may be ineffective or even unsafe.<sup>85</sup> This gap between inadequate informed consent by desperate patients and the need for medical innovation can be filled by codification of the reasonable innovation rule.

### B. *Autonomy Of Physician Decision Making*

As demonstrated by the previous sections of this Comment, regulation of medicine is necessary to protect patients. However, physician autonomy is a major concern when it comes to regulation of innovation and the medical profession. Advocates for greater physician autonomy maintain that greater autonomy and fewer regulations promote medical innovation.<sup>86</sup> Each patient presents a unique situation where physicians may need to implement new or different techniques to best treat the patient.<sup>87</sup> Excessive regulation and strict guidelines curb creativity crucial to physicians and the medical profession as a whole.<sup>88</sup> In order to attract talented professionals, the field of medicine must trust physicians to self-regulate.<sup>89</sup> Loss of autonomy is one of the most common complaints of physicians who report feeling disenchanting with their careers.<sup>90</sup>

Nonetheless, there must be a balance between regulation and autonomy to protect patients from consenting to procedures that are not yet approved for widespread use. The FDA continuously struggles with

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treatments out of the belief that they are the best opportunity to sustain the patient's health and life. In the patient's desperate efforts to procure whatever treatments may improve her condition, the patient decides to assume the risk of these new treatments." *Id.*

85. *Id.* at 699.

86. Richard L. Reece, *Government Regulation and Physician Autonomy*, MEDINNOVATION & HEALTH REFORM (Apr. 1, 2010), <http://medinnovationblog.blogspot.com/2010/04/thoughts-on-government-regulation-and.html>.

87. *Id.*

88. *Id.* The article argues, "Physicians struggle to improve quality, safety and efficiency in an imperfect world of clinical practice that is overwhelmed with information, laced with ambiguity and plagued by deepening physician shortages. From an organizational perspective, they require sufficient numbers of colleagues, a supportive infrastructure, adequate reimbursement and freedom from administrative and regulatory intrusion. High quality care depends on the autonomous exercise of clinical judgment by competent and empathic physicians who are accountable to their patients and society. No amount of regulation or incentives can substitute." *Id.*

89. David Orentlicher, *The Influence of a Professional Organization on Physician Behavior*, 57 ALB. L. REV. 583, 585 (1994).

90. *Id.*

this balance in deciding when and how to regulate.<sup>91</sup> As the fecal transplant portion of this paper will demonstrate, the FDA is hesitant to regulate when beneficial innovation is occurring. In that case, an innovative procedure—a fecal transplant—is resulting in an unusually high success rate: over 90% of patients who undergo the procedure experience complete elimination of symptoms.<sup>92</sup> Thus, the fine line between experimentation and innovation is once again tested.

#### IV. UNDERSTANDING THE SOLUTION TO INADEQUATE INFORMED CONSENT THROUGH CASE STUDIES

Now that this Comment has explored the problems with informed consent, it will shift focus to the solution for inadequate informed consent: codifying the reasonable innovation rule. This will be achieved by exploring instances where doctors used novel microbial experimental treatments that were not FDA-approved after obtaining informed consent.

First, subsection A will present a preliminary explanation of the microbiome. Next, subsections B and C will discuss two very different studies involving the use of microbial transplants. In the first study, surgeons introduced live bacteria to the brains of three patients in hopes of curing brain tumors, but this had deadly consequences. In the second study, physicians introduced healthy fecal bacteria to patients' colons to cure chronic diarrhea, and this treatment had a 90% success rate. Subsection D will compare the two studies to demonstrate why informed consent is an inadequate safeguard for vulnerable patients. Subsection E will introduce the reasonable innovation rule and explore its scope by comparing two cases. Subsection F will argue for codification of the reasonable innovation rule. Finally, subsection G will propose language for codification.

##### A. *Human Experimentation in the Context of the Microbiome*

The human body has over ten times more “bugs”—microbes that live in the guts, mouth, and skin—than human cells; the human body is “vastly more microbe than human.”<sup>93</sup> The microbiome was first

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91. MICHAEL MANDEL, PROGRESSIVE POLICY INST., HOW THE FDA IMPEDES INNOVATION: A CASE STUDY IN OVERREGULATION (2011), available at [http://progressivefix.com/wp-content/uploads/2011/06/06.2011-Mandel\\_How-the-FDA-Impedes-Innovation.pdf](http://progressivefix.com/wp-content/uploads/2011/06/06.2011-Mandel_How-the-FDA-Impedes-Innovation.pdf).

92. McKenna, *supra* note 7.

93. Karen Weintraub, *Microbiome: How Bugs May Be Crucial to Your Health*, BBC, <http://www.bbc.com/future/story/20120412-the-beasts-inside-you> (last visited Nov. 16, 2014).

discovered in 1683 when Antoine Van Leeuwenhoek scraped “gritty matter” off of his teeth and analyzed it under a microscope.<sup>94</sup> This experiment and its findings made him the first person to conceptualize bacteria in the mouth.<sup>95</sup> Over the centuries, the microbiomes that play such a crucial role in human health have remained mostly a mystery.<sup>96</sup> This is largely because it was nearly impossible to isolate and cultivate more than 95% of our microorganisms in simulated laboratory conditions.<sup>97</sup> However, recent advances in DNA sequencing have made it possible to study microbiomes without cultivating them in a laboratory.<sup>98</sup> Now that science is beginning to understand the effect that these microscopic bugs have on our health, coupled with the fact that a viable means of studying microbiomes now exists, the need for volunteer donors has skyrocketed.<sup>99</sup> As science enters this new realm of understanding how microscopic bugs interact with the human body and how to use this knowledge to treat or cure existing disease, society must decipher what constitutes innovative treatment and what constitutes human experimentation.

Two case studies involving microbial experimentation illustrate the conflict between the need for patient protection and the need for innovative medicine. The first highlights the inadequacies of informed consent, while the second demonstrates regulators’ hesitation to intervene where innovation is occurring.

### B. *The Bacterial Transplant Case*

In 2010 and 2011, three seriously ill patients at UC Davis Medical Center consented to have their skulls opened and live bacteria introduced to their brains.<sup>100</sup> Two highly regarded neurosurgeons believed that introducing *Enterobacter aerogenes*<sup>101</sup> to the patients’ brains would wipe

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94. Michael J. Cox, William O.C.M. Cookson & Miriam F. Moffat, *Sequencing the Human Microbiome in Health and Disease*, 22 HUMAN MOLECULAR GENETICS R88, R88 (2013), available at <http://hmg.oxfordjournals.org/content/22/R1/R88.full.pdf>.

95. *Id.*

96. Weintraub, *supra* note 93.

97. *The Human Microbiome Project*, BAYLOR COLL. OF MED., <https://www.bcm.edu/departments/molecular-virology-and-microbiology/research/the-human-microbiome-project> (last visited Nov. 16, 2014).

98. *Id.*

99. Faith Rohlke & Neil Stollman, *Fecal Microbiota Transplantation in Relapsing Clostridium Difficile Infection*, 5 J. THERAPEUTIC ADVANCES IN GASTROENTEROLOGY 403, 403 (2012).

100. See Lundstrom & Stanton, *supra* note 83.

101. *Enterobacter Aerogenes*, BIOQUELL, <http://www.bioquell.com/technology/microbiology/enterobacter-aerogenes/> (last visited Nov. 22,

out the patients' deadly glioblastomas after the bacteria colonized.<sup>102</sup> All three patients, however, died after their transplants.<sup>103</sup> Two died from entering a septic shock just 14 days after surgery, and the last patient lived a year but had to endure several more painful procedures due to surgical complications.<sup>104</sup>

The neurosurgeons were able to perform these procedures because they obtained informed consent from all three patients.<sup>105</sup> The consent forms were a mere 300 words that took up just one page, warning the patients of the procedure's dangers.<sup>106</sup> "There is no proof that such treatment (for brain cancer) might be beneficial,' the form read, 'nor are there animal data to support it.'"<sup>107</sup> The form went on to detail the consequences and risks of introducing the bacteria to the patients' brains, including "paralysis, inability to speak or understand speech, inability to swallow, vegetative state, coma or death."<sup>108</sup> The surgeon later claimed that, when the patients gave their express informed consent, they were all "of sound mind," and "their disease did not affect their judgment" or decision-making ability.<sup>109</sup>

The surgeons purchased the bacteria from a Virginia lab after the FDA ordered rigorous animal testing before "contemplating the bacteria's use in live patients."<sup>110</sup> Despite this, in a desperate attempt to prolong the patients' lives, the neurosurgeons circumvented the FDA and IRB regulations and approval and infected the patients.<sup>111</sup> It was reported that, after interviewing 27 doctors, nurses, and hospital staff, no

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2013). *Enterobacter aerogenes* is commonly found in the human gastrointestinal tract. *Enterobacter Aerogenes*, CUVERRO, <http://cuverro.com/tested-proven-trusted/scientific-proof/epa-tests/enterobacter-aerogenes> (last visited Dec. 27, 2014).

102. *Glioblastoma*, AM. BRAIN TUMOR ASS'N, <http://www.abta.org/understanding-brain-tumors/types-of-tumors/glioblastoma.html> (last visited Nov. 22, 2013). "Glioblastomas are tumors that arise from astrocytes—the star-shaped cells that make up the 'glue-like,' or supportive tissue of the brain. These tumors are usually highly malignant (cancerous) because the cells reproduce quickly and they are supported by a large network of blood vessels. . . . Glioblastoma can be difficult to treat because the tumors contain so many different types of cells. Some cells may respond well to certain therapies, while others may not be affected at all. This is why the treatment plan for glioblastoma may combine several approaches." *Id.*

103. Lundstrom, *supra* note 8.

104. Marjie Lundstrom, *Impact, Ethics of Surgery Slammed*, SACRAMENTO BEE, <http://www.sacbee.com/2013/02/11/5180237/impact-ethics-of-surgery-slammed.html> (updated Oct. 6, 2014, 2:38 PM).

105. Lundstrom, *supra* note 8.

106. Lundstrom, *supra* note 104.

107. *Id.*

108. *Id.*

109. *Id.*

110. *Id.*

111. *Id.*

one was willing or able to report unsafe care practices they witnessed.<sup>112</sup> The hospital personnel trusted the neurosurgeons so much as to not question the highly unusual procedure.<sup>113</sup> Both neurosurgeons have since resigned, and the families of the deceased patient-victims have settled their claims against the university.<sup>114</sup> Now, complex questions remain “about the nature of consent, what constitutes research[,] and how to safeguard vulnerable patients.”<sup>115</sup>

C. *The Fecal Transplant Case: An Increasingly Popular Cure for an Old Problem*<sup>116</sup>

Feces can save lives. Over 14,000 lives a year, to be exact.<sup>117</sup> Once one overcomes the initial “ick factor,” the prospect of safe, regulated, extremely effective fecal microbiota transplants (“FMT’s”) can bring hope to thousands of Americans who suffer from *Clostridium difficile* (“C. diff”) infections. Earlier this year, the FDA announced that it would require IND applications for fecal microbiota transplantations to treat C. diff infections for purposes of patient safety.<sup>118</sup> Shortly after the announcement, primarily due to negative pushback from advocates of FMT, the FDA backed away from regulating the procedure and decided that it would no longer require a physician to submit an IND application prior to performing a fecal transplant.<sup>119</sup> Instead, the FDA’s draft guidance merely requires physicians to obtain informed consent from patients before they undergo the transplant.<sup>120</sup> An examination of FMTs demonstrates the FDA’s reluctance to step in when physicians push for greater autonomy with respect to successful, novel treatments.

1. The Fecal Transplant Case

One-thousand seven-hundred years ago, a Chinese doctor first

112. Lundstrom & Stanton, *supra* note 83.

113. *Id.*

114. Lundstrom, *supra* note 8.

115. *Id.*

116. C. diff was discovered in 1935, yet scientists did not recognize it as the major cause of antibiotic-associated diarrhea until 1978. *Clostridium Difficile: An Intestinal Infection on the Rise*, HARVARD HEALTH PUBL’NS (June 1, 2010), [http://www.health.harvard.edu/newsletters/Harvard\\_Mens\\_Health\\_Watch/2010/June/clostridium-difficile-an-intestinal-infection-on-the-rise](http://www.health.harvard.edu/newsletters/Harvard_Mens_Health_Watch/2010/June/clostridium-difficile-an-intestinal-infection-on-the-rise).

117. *Clostridium Difficile Infection*, CTRS. FOR DISEASE CONTROL & PREVENTION, [http://www.cdc.gov/hai/organisms/cdiff/cdiff\\_infect.html](http://www.cdc.gov/hai/organisms/cdiff/cdiff_infect.html) (last updated Mar. 1, 2013).

118. *Investigational New Drug (IND) Application*, *infra* note 168.

119. Gaffney, *infra* note 175.

120. *Id.*

prescribed “drinking liquefied feces as a treatment for severe diarrhea and food poisoning.”<sup>121</sup> Subsequently, the use of fecal transplants was limited to veterinary medicine where the practice has been performed for over 100 years.<sup>122</sup> The first human fecal transplant was mentioned in a 1958 case series<sup>123</sup> where four patients were treated for their pseudomembranous enterocolitis.<sup>124</sup> It noted that three of the four patients were in critical condition when the fecal enemas were administered.<sup>125</sup> Surprisingly, all four patients’ symptoms resolved within hours of receiving the fecal transplant.<sup>126</sup> The first case confirming treatment of *C. diff* by means of a fecal microbiota transplant was documented in 1983.<sup>127</sup> The procedure, however, did not gain wide acceptance in the medical community due to the lack of controlled clinical trials.<sup>128</sup>

Thus, the notion of curing gastrointestinal problems with an FMT was nearly unheard of in 2011 when 79-year-old Marion Browning, a retired nurse, began suffering from painful, chronic diarrhea.<sup>129</sup> This ailment, which lasted nearly a year, occurred after she was prescribed antibiotics to treat her diverticulitis.<sup>130</sup> Unfortunately, the antibiotics also

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121. Diane Suchetka, *Ohio Hospitals Now Performing Fecal Transplants for Patients with Stubborn Cases of C. diff*, CLEVELAND PLAIN DEALER (Jul. 8, 2013, 6:20 AM), [http://www.cleveland.com/metro/index.ssf/2013/07/three\\_ohio\\_hospitals\\_now\\_perfo.html](http://www.cleveland.com/metro/index.ssf/2013/07/three_ohio_hospitals_now_perfo.html).

122. Lawrence J. Brandt, *Fecal Transplantation for the Treatment of Clostridium Difficile Infection*, 8 J. GASTROINTESTINAL & HEPATOLOGY 191, 191 (2012), available at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3365524/>.

123. Ryan Jaslow, *Fecal Transplants Beat Antibiotics for Curing Diarrhea Caused by C. Difficile*, CBS NEWS (Jan. 17, 2013, 11:10 AM), [http://www.cbsnews.com/8301-204\\_162-57564470/fecal-transplants-beat-antibiotics-for-curing-diarrhea-caused-by-c-difficile/](http://www.cbsnews.com/8301-204_162-57564470/fecal-transplants-beat-antibiotics-for-curing-diarrhea-caused-by-c-difficile/).

124. Johan S. Bakken et al., *Treating Clostridium Difficile Infection with Fecal Microbiota Transplantation*, 9 J. CLIN. GASTROENTEROLOGY & HEPATOLOGY 1044, 1044 (2011), available at <http://www.cghjournal.org/article/S1542-3565%2811%2900891-3/abstract>. “Pseudomembranous colitis is inflammation of the colon that occurs in some people who have taken antibiotics. Pseudomembranous colitis is sometimes called antibiotic-associated colitis or *C. difficile* colitis. The inflammation in pseudomembranous colitis is almost always associated with an overgrowth of the bacterium *Clostridium difficile*.” *Pseudomembranous Colitis*, MAYO CLINIC (Dec. 5, 2012), <http://www.mayoclinic.com/health/pseudomembranous-colitis/DS00797>.

125. Bakken et al., *supra* note 124, at 1045.

126. *Id.*

127. *Id.*

128. B. Guo et al., *Systematic Review: Faecal Transplantation for the Treatment of Clostridium Difficile-Associated Disease*, 35 ALIMENTARY PHARMACOLOGY & THERAPEUTICS 865, 873 (2012).

129. McKenna, *supra* note 7.

130. *Id.* Diverticulitis is a condition where “small pouches protrude from the walls of the colon. . . . Diverticulosis itself is really not a problem, as the pouches themselves are harmless and rarely cause symptoms. However, the situation becomes more serious if the pouches become infected from, for example, stool getting trapped in the pouch.” *Diverticulosis and Diverticulitis*,

killed the friendly bacteria in Browning's intestines, allowing a toxin-producing bacteria, *C. diff*,<sup>131</sup> to colonize and start "eating away at the entire lining of her gut."<sup>132</sup> Browning spent months visiting different doctors, searching for a cure.<sup>133</sup> Each visit resulted in a stronger antibiotic to attempt to cure the *C. diff*, and while her condition would improve at first, the antibiotics were ultimately unable to eliminate all of the infection.<sup>134</sup> After four rounds of powerful antibiotics, Browning's gastroenterologist informed her that he tried everything he could and referred her to Colleen Kelly, a clinical researcher at the medical school at Brown University.<sup>135</sup> Finally, a cure for Browning's painful *C. diff* was in sight.<sup>136</sup> What Kelly proposed sounded both "logical and strangely unmedical":<sup>137</sup> she wanted Browning to receive a fecal transplant.<sup>138</sup>

Healthy intestinal bacteria usually maintain a balance with pathogenic bacteria,<sup>139</sup> but in fragile individuals such as children, the elderly, or immunosuppressed people, the overuse of antibiotics can cause overgrowth of *C. diff*.<sup>140</sup> Once there is an overgrowth of *C. diff*, patients experience days of severe diarrhea, which is extremely dehydrating and can result in death if the condition persists.<sup>141</sup> In Browning's case, the powerful antibiotics prescribed to her upset the healthy balance of intestinal bacteria, resulting in a severe case of *C.*

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INT'L. FOUND. FOR FUNCTIONAL GASTROINTESTINAL DISORDERS, <http://www.iffgd.org/site/gi-disorders/other/diverticulosis> (last modified Sept. 16, 2014, 10:40 AM) (adapted from IFFGD Publication #153 by Cheri Smith, Medical Writer).

131. *Clostridium Difficile Infection*, *supra* note 117. *C. diff* causes inflammation of the colon due to prolonged use of antibiotics. "The main clinical symptoms of *C. difficile* infection (CDI) are watery diarrhea, fever, nausea, abdominal pain/tenderness, and loss of appetite. More serious conditions can also result such as pseudomembranous colitis (inflammation of the colon), perforations of the colon, and sepsis. It is possible to carry *C. diff* bacteria in your body but not show any symptoms; this is called colonization. After treatment, repeat testing is not recommended if the patient's symptoms have resolved, since many patients remain colonized with the bacteria." *Clostridium Difficile (C. Difficile) Infections*, VA. DEPT. OF HEALTH, <http://www.vdh.virginia.gov/epidemiology/surveillance/hai/cdiff.htm> (last updated Apr. 3, 2014).

132. McKenna, *supra* note 7.

133. *Id.*

134. *Id.*

135. *Id.*

136. *Id.*

137. *Id.*

138. *Id.* There are many names for fecal transplants. They are "variously called fecal transplant, fecal bacteriotherapy or fecal flora reconstitution." *Id.*

139. *Id.*

140. *Clostridium Difficile Infection*, *supra* note 117.

141. *Id.*

diff.<sup>142</sup> Kelly reasoned that, if she took a diluted stool sample from a healthy donor, the good bacteria could recolonize in Browning's intestine and wipe out the infection.<sup>143</sup> Browning, desperate to try anything after enduring months of gut-wrenching diarrhea, chose her son as her donor.<sup>144</sup> Kelly diluted the sample and used colonoscopy instruments to introduce the sample into Browning's large intestine.<sup>145</sup> The results were astounding: Browning's diarrhea was completely eliminated within two days and never recurred.<sup>146</sup>

## 2. Recent Developments in Fecal Transplants

Browning's success story did not go completely unrecognized: "in medical journals, about a dozen clinicians in the U.S., Europe, and Australia have described performing fecal transplants on about 300 *C. difficile* patients so far."<sup>147</sup> Although fecal transplants are not unheard of, their success rate is.<sup>148</sup> More than 90% of patients recover completely after receiving a fecal transplant.<sup>149</sup> This statistic is encouraging due to an increased occurrence of *C. diff* since a new epidemic strain emerged in 2004.<sup>150</sup> As a result of the antibiotic resistant *C. diff* strain, cases of those infected have "doubled from about 134,000 patients in 2000 to 291,000 patients in 2005."<sup>151</sup> Another study showed that mortality rates have increased "fourfold, from 5.7 deaths per million in the general population in 1999 to 23.7 deaths per million in 2004."<sup>152</sup> Furthermore, not only does *C. diff* pose an alarming threat to human life, but it also

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142. McKenna, *supra* note 7.

143. *Id.*

144. *Id.*

145. *Id.*

146. *Id.*

147. *Id.*

148. *Id.*

149. *Id.* "'There is no drug, for anything, that gets to 95 percent,' Kelly says. Plus, 'it is cheap and it is safe,' says Lawrence Brandt, a professor of medicine and surgery at the Albert Einstein College of Medicine, who has been performing the procedure since 1999." *Id.*

150. *Information About the Current Strain of Clostridium Difficile*, CTRS. FOR DISEASE CONTROL & PREVENTION, <http://www.cdc.gov/HAI/organisms/cdiff/Cdiff-current-strain.html> (last updated 2010). "Over the past several years nationwide, states have reported increased rates of *C. difficile* infection, noting more severe disease and an associated increase in mortality. *C. diff* infection remains a disease mostly associated with healthcare (at least 80%). Patients most at risk remain the elderly, especially those using antibiotics. Although the elderly are still most affected, more disease has been reported in traditionally 'low risk' persons such as healthy person in the community, and peripartum women." *Id.*

151. McKenna, *supra* note 7.

152. *Id.*

presents a startling economic cost.<sup>153</sup> Studies estimate the daily cost of C. diff treatment to be between \$17.6 million and \$51.5 million,<sup>154</sup> bringing “the national cost of C. diff treatment between \$1 billion and \$3.2 billion, conservatively.”<sup>155</sup> These figures illustrate the need for an effective, inexpensive treatment, which fecal transplants can fulfill.

Cases like Browning’s began to increase interest in FMT research. In January 2013, the New England Journal of Medicine published the results of a study that advocated for the use of fecal microbiota transplants.<sup>156</sup> The “52-patient study . . . compared the efficacy of treatment with vancomycin, an antibiotic, and FMT in patients who suffered from C. diff and had at least one relapse after antibiotics.”<sup>157</sup> The study found that subjects who were suffering from C. diff had decreased microbial diversity and introduction of healthy donor feces increased the diversity, eliminating the C. diff.<sup>158</sup> This study also emphasized that the best method for administering a fecal transplant remains unknown.<sup>159</sup> It explained, “Up until 1989, retention enemas had been the most common technique for FMT. However, alternative methods subsequently included fecal infusion via duodenal tube in 1991, rectal tube in 1994, and colonoscopy in 1998.”<sup>160</sup>

In October 2013, a new method of performing a fecal transplant was introduced: the pill form.<sup>161</sup> A Canadian disease specialist, Dr. Thomas Louie, performed a study on 31 patients suffering from C. diff.<sup>162</sup> Each subject took 24-34 capsules of fresh, healthy fecal bacteria, coated in gelatin to maintain integrity in the stomach before reaching the

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153. Syed Sayeed et al., *Hospital-Acquired C. Difficile Infections*, CONSUMERS UNION (Nov. 2008), <http://consumersunion.org/pub/Final%20Cdiff%20Policy%20Brief%2011-11-08.pdf>.

154. *Id.* “These figures do not take into account health care costs outside of the hospital or nursing home, lost productivity, pain and suffering of patients or the time that medical professionals must spend treating them.” *Id.*

155. *Id.*

156. Alexander J. Varond, *Fecal Microbiota Transplantation: FDA Announces Limited Enforcement Discretion*, FDA L. BLOG (Jul. 23, 2013), [http://www.fdalawblog.net/fda\\_law\\_blog\\_hyman\\_phelps/2013/07/fecal-microbiota-transplantation-fda-announces-limited-enforcement-discretion.html](http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2013/07/fecal-microbiota-transplantation-fda-announces-limited-enforcement-discretion.html).

157. *Id.*

158. Els van Nood et al., *Duodenal Infusion of Donor Feces for Recurrent Clostridium Difficile*, 368 NEW ENG. J. MED. 407, 414 (Jan. 31, 2013), available at <http://www.nejm.org/doi/full/10.1056/NEJMoal205037#t=articleBackground>.

159. *Id.*

160. Bakken et al., *supra* note 124.

161. Sarah Zhang, *Feces-Filled Pill Stops Gut Infection*, SCI. AM. (Oct. 7, 2013), <http://www.scientificamerican.com/article.cfm?id=feces-filled-pill-stops-gut-infection>.

162. *Id.*

intestines intact.<sup>163</sup> The pills cured 30 of the 31 patients.<sup>164</sup> Dr. Louie reported that lab-grown bacteria for the pills may be a future innovation, and he is currently experimenting with freezing donor fecal matter for later treatment.<sup>165</sup> These studies not only provided a modern-day test of the efficacy of fecal transplants, they also caught the attention of the FDA.<sup>166</sup>

### 3. The FDA's Attempt at Regulating Fecal Microbiota Transplants

In early May 2013, the FDA held a workshop to “provide a forum for the exchange of information, knowledge, and experience” regarding fecal transplants.<sup>167</sup> After gathering information from the workshop, the FDA announced that it would require doctors who were performing fecal transplants to submit an IND<sup>168</sup> application prior to the procedure in non-emergency situations.<sup>169</sup> This new regulation did not affect clinical trials because they were already subject to FDA approval.<sup>170</sup> The FDA guidelines provide that, “[o]nce the IND is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials. During this time, the FDA has an opportunity to review the IND for safety to assure that research subjects will not be subjected to unreasonable risk.”<sup>171</sup> However, the FDA explained that physicians could obtain approval via

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163. *Id.*

164. *Id.*

165. *Id.*

166. Varond, *supra* note 156.

167. *Public Workshop: Fecal Microbiota for Transplantation*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm341643.htm> (last updated Mar. 10, 2014).

168. *Investigational New Drug (IND) Application*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm> (last updated Oct. 27, 2014). “Current Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. Because a sponsor will probably want to ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The IND is the means through which the sponsor technically obtains this exemption from the FDA. During a new drug’s early preclinical development, the sponsor’s primary goal is to determine if the product is reasonably safe for initial use in humans, and if the compound exhibits pharmacological activity that justifies commercial development. When a product is identified as a viable candidate for further development, the sponsor then focuses on collecting the data and information necessary to establish that the product will not expose humans to unreasonable risks when used in limited, early-stage clinical studies.” *Id.*

169. Beth Mole, *FDA Comes to Grips with Fecal Transplants*, SCI. AM. (June 12, 2013), <http://www.scientificamerican.com/article.cfm?id=fda-comes-to-grips-with-fecal-transplants>.

170. *Id.*

171. *Investigational New Drug (IND) Application*, *supra* note 168.

phone or “other rapid means of communication” in an emergency.<sup>172</sup>

The move to regulate fecal transplants to ensure proper safety and oversight met with strong criticism from physicians.<sup>173</sup> Physicians argued that “the added burdens of adhering to clinical trials regulations would make the therapy more difficult, more expensive, more time-consuming, and, ultimately, drive more patients to engage in do-it-yourself fecal transplants.”<sup>174</sup> This criticism caused the FDA to quietly amend its previously issued guidelines regarding fecal transplants. In July 2013, just one month after the FDA announced that it would require IND applications from physicians, the FDA removed this requirement altogether.<sup>175</sup> “While maintaining its authority to require the submission of an IND in some cases, [the FDA] would resort to a policy of ‘enforcement discretion’ under which it would allow most practitioners to continue to conduct FMT procedures without an approved IND.”<sup>176</sup> This “enforcement discretion” merely requires the physician to obtain informed consent prior to performing a fecal transplant.<sup>177</sup> The FDA further instructed that the informed consent “should, at a minimum, include a statement that the FMT product is still investigational and involves assuming potential risks.”<sup>178</sup>

There are dangers associated with any procedure, and fecal transplants are not exempt from this. Despite the apparent success of FMTs, the procedure is still highly experimental. The human gastrointestinal tract is filled with bacteria—good and bad—and can be riddled with “viruses, fungi, protozoa and parasites.”<sup>179</sup> There is a possibility of transmitting “HIV, prion disease, e. coli 0157:H7, worms, shigella, and other dysentery-causing infectious agents.”<sup>180</sup> Since fecal transplants did not undergo the rigors of clinical trials, the best method

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172. Kristina Fiore, *Fecal Transplant: FDA Wants Regulation*, MED PAGE TODAY (May 15, 2013), <http://www.medpagetoday.com/InfectiousDisease/GeneralInfectiousDisease/39169>.

173. Alexander Gaffney, *FDA Fast Tracks Fecal Transplant Product Intended to Treat Clostridium Difficile Infections*, REGULATORY FOCUS (June 25, 2013), <http://www.raps.org/focus-online/news/news-article-view/article/3681.aspx>.

174. *Id.*

175. Alexander Gaffney, *Regulatory Approach for Fecal Transplant Product Finalized in Abrupt Guidance Document*, REGULATORY FOCUS (July 17, 2013), <http://www.raps.org/focus-online/news/news-article-view/article/3795/regulatory-approach-for-fecal-transplant-product-finalized-in-abrupt-guidance-d.aspx>.

176. *Id.*

177. *Id.*

178. *Id.*

179. Val Jones, *Fecal Transplants: Getting to the Bottom of the Matter*, SCIENCE-BASED MED. (Nov. 27, 2008), <http://www.sciencebasedmedicine.org/fecal-transplants-getting-to-the-bottom-of-the-matter/>.

180. *Id.*

for receiving a transplant (pill, colonoscopy, enema or nasoduodenal tube) and the best diluent (water or milk or other) are among the many questions that remain unanswered.<sup>181</sup> Thus, scholarship has concluded that more research is required before FMTs “can be widely advocated.”<sup>182</sup>

Furthermore, the loosening of restrictions regarding fecal transplants illustrates that the FDA does not want to regulate areas where new experiments are proving highly successful. Physicians continue to experiment with conducting fecal transplants on patients while merely obtaining informed consent.<sup>183</sup> At least three Ohio hospitals routinely offer the procedure to their patients.<sup>184</sup> The success rate of fecal transplants makes it tempting to view the new treatment as an exciting innovation; there is, however, a fine line between innovation and experimentation. The efficacy of fecal transplants came from “a long series of successful case studies in the course of treatment, not clinical trials.”<sup>185</sup> Most fecal transplants were performed without IRB approval or FDA oversight.<sup>186</sup> It can be argued that there is never innovation without experimentation, but this begs the question where should we draw the line.<sup>187</sup>

#### D. Comparing the Cases

These two cases—one involving fecal transplant and one involving bacterial transplants in the brain—are similar because the bacterial transplants in the brain were, and fecal transplants are, conducted without FDA or IRB oversight. Both procedures are experimental and require informed consent. Both procedures involve the novel concept of transplanting microbiomes in hopes that they would colonize and overcome the existing infection. The results, however, were strikingly different. One must wonder, “[I]f [the bacterial transplants in the brain]

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181. Judy Stone, *The S\*\*t Hits the Fan—FDA, INDs, and Fecal Microbiota Transplants*, SCI. AM. (May 20, 2013), <http://blogs.scientificamerican.com/molecules-to-medicine/2013/05/20/the-st-hits-the-fan-fda-inds-and-fecal-microbiota-transplants/>.

182. Zain Kassam et al., *Fecal Microbiota Transplantation for Clostridium Difficile Infection: Systematic Review and Meta-Analysis*, 108 AM. J. GASTROENTEROLOGY 500, 508 (2013).

183. Mole, *supra* note 169.

184. Suchetka, *supra* note 121.

185. Nicholson Price, *Experiment vs. Innovative Treatment in Bacterial Transplants*, BILL OF HEALTH (Aug. 27, 2013), <http://blogs.law.harvard.edu/billofhealth/2013/08/27/experiment-vs-innovative-treatment-in-bacterial-transplants/>.

186. *Id.*

187. See generally Nancy M. P. King, *The Line Between Clinical Innovation and Human Experimentation*, 32 SETON HALL L. REV. 573 (2002).

had worked, would the reaction have been the same, or would the surgeons have been hailed as innovators and heroes?"<sup>188</sup>

### E. *The Reasonable Innovation Rule*

Patients, however, would be safeguarded against unreasonable, inadequately researched treatments suggested by physicians if the reasonable innovation rule were codified. The doctors in the brain bacteria case would not have been permitted to perform the procedure under the reasonable innovation rule because adequate medical research was not conducted prior to the experiment. The reasonable innovation rule would set minimum standards higher than those required for informed consent. If this rule were codified, doctors would assume a larger role in providing reasonable treatment to their patients.

#### 1. The Common Law Rule

The reasonable innovation rule states that, if customary care is unlikely to provide an adequate treatment for a particular patient, a doctor may *reasonably* innovate to meet the unique needs of the patient.<sup>189</sup> Everyday medicine requires physicians to exercise quick decision-making skills, and therapeutic innovation is permissible when customary care does not work for a patient.<sup>190</sup> Each patient presents a different challenge, and reasonable innovation is necessary to meet the unique needs of each patient.<sup>191</sup>

#### 2. The Scope of the Rule

It is important to identify the proper scope of a rule that fills the gap between innovation and experimentation. The limits of the rule will be illustrated by contrasting two cases where doctors implemented a new technique with opposite results. The court in the *Brook v. St. John's Hickey Memorial Hospital* case, discussed in the following section, laid out factors to determine what constitutes a reasonable innovation.<sup>192</sup> The court found the physician in that case had compelling professional reasons for deviating from customary care by implementing an innovation.<sup>193</sup> First, he consulted medical journals and other professional

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188. Price, *supra* note 185.

189. Brook v. St. John's Hickey Mem'l Hosp., 380 N.E.2d 72, 76 (Ind. 1978).

190. *Id.*

191. *Id.*

192. *Id.*

193. *Id.*

articles that warned against using customary care.<sup>194</sup> Next, he successfully implemented the innovation on other similar patients.<sup>195</sup> Because of these two factors, the court concluded that his deviation from the standard of care was reasonable.

a. *Brook v. St. John's Hickey Memorial Hospital*

The first case illustrates how the reasonable innovation rule is applied in practice. In *Brook vs. St. John's Hickey Memorial Hospital*, a specialist diagnosed a two-year-old with a possible urological disorder.<sup>196</sup> The specialist ordered X-rays taken with a contrast medium<sup>197</sup> to confirm the diagnosis.<sup>198</sup> A radiologist injected the contrast medium into the child's calves because he was not able to find a vein in which he could inject the medium.<sup>199</sup> The contrast medium came in a package accompanied by the manufacturer's instructions for injection.<sup>200</sup> The instructions specifically recommended that the medium be injected into the gluteal muscles (buttocks).<sup>201</sup> The radiologist, however, was familiar with medical scholarship that warned against intramuscular injection into the buttocks of young children because of the potential for nerve and muscle damage.<sup>202</sup> The doctor decided to inject the medium into the child's legs because "they were the next largest muscle mass away from the trunk of the body."<sup>203</sup>

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194. *Id.* at 77.

195. *Id.*

196. *Id.* at 73.

197. "The contrast agent (also called contrast media, contrast material, X-ray dye, or gadolinium contrast) shows up white on X-ray, CT, and MR images. This makes . . . organs, blood vessels, and tissues more visible, which helps . . . interpret these imaging studies." *Contrast Injections for Imaging Studies*, UNIV. OF WASH. MED., available at [http://www.uwmedicine.org/services/radiology/Documents/Articles/Contrast\\_Injections\\_Imaging\\_Studies\\_2\\_10.pdf](http://www.uwmedicine.org/services/radiology/Documents/Articles/Contrast_Injections_Imaging_Studies_2_10.pdf) (last visited Feb. 16, 2015).

198. *Brook*, 380 N.E.2d at 73-74.

199. *Id.* at 74.

200. *Id.*

201. *Id.*

202. *Id.* The warning in the American Medical Association Journal specifically warned, "anyone concerned with infants and children must be aware that injection into the buttock may cause paralysis in the lower extremity. It is not often recognized that serious sciatic nerve injury can result from intragluteal administration of therapeutic and prophylactic agents. Injection injury of the sciatic nerve is more common than supposed and may be responsible for paralytic deformities which may be misdiagnosed as congenital club feet or the sequelae of poliomyelitis. The newborn infant, and especially the small premature infant, is more likely to suffer from this complication. Any age group is vulnerable, and injury may result from a solitary injection. By abandoning the intragluteal site and choosing another area for intramuscular injections, physicians may spare their patients unnecessary handicaps." *Id.* at 75.

203. *Id.* at 74.

Four months after the injection, the child's leg became stiff, and her heel began to lift off of the ground.<sup>204</sup> This problem was due to the shortening of her Achilles tendon and may have been caused by the intramuscular injection.<sup>205</sup> Fortunately, after two operations and extensive treatment, the child's condition was "substantially corrected."<sup>206</sup> The child's parents, however, sued the radiologist, along with the hospital and two other physicians, alleging that "[the radiologist] was negligent in choosing an injection site which had not been specifically recommended by the medical community and that this choice of an unusual injection site was a medical experiment."<sup>207</sup> The jury returned a verdict in favor of the radiologist,<sup>208</sup> but the appellate court reversed.<sup>209</sup> The Indiana State Supreme Court then affirmed the trial court's judgment.<sup>210</sup> In so doing, the Indiana Supreme Court reasoned that the radiologist had several compelling reasons to choose the calves as an injection site and deemed this method of injection a therapeutic innovation rather than a negligent human experiment.<sup>211</sup>

Further, the court reasoned that the radiologist was not negligent because he was trying to prevent the harm he had read about in journals by choosing an injection site further away from the sciatic nerve.<sup>212</sup> Additionally, the radiologist had used the injection site on other pediatric patients in the past with no adverse reactions.<sup>213</sup> The court warned that "[t]oo often [other] courts have confused judgmental decisions and experimentation. Therapeutic innovation has long been recognized as permissible to avoid serious consequences."<sup>214</sup> Doctors should be presumed to have the knowledge and skills to make judgments necessary to treat their patients' unique needs.<sup>215</sup> The reasonable innovation rule permits physicians to innovate in a limited scope if the patient is not responding to customary care.<sup>216</sup>

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204. *Id.*

205. *Id.*

206. *Id.*

207. *Id.* at 75.

208. *Id.* at 74.

209. *Id.*

210. *Id.* at 77.

211. *Id.* at 76.

212. *Id.* at 75.

213. *Id.* at 76.

214. *Id.*

215. *Id.*

216. *Id.* "(E)ven where there is an established mode of treatment, the physician may be permitted to innovate somewhat if he can establish that, in his best judgment, this was for the benefit of his patient and where the established modes of treatment have proved unsuccessful." *Id.*

b. *Felice v. Valleylab, Inc.*

*Felice v. Valleylab, Inc.*, by contrast, demonstrates that the reasonable innovation rule holds physicians accountable when they fail to follow reasonable practices. In that case, a two-year-old child complained of pain during urination.<sup>217</sup> A physician diagnosed the child with phimosis<sup>218</sup> and recommended a circumcision.<sup>219</sup> Dr. Goodger, a first-year family practice resident, and Dr. Glass, a third-year surgery resident, were the only doctors present at the surgery.<sup>220</sup> Dr. Glass instructed Dr. Goodger to perform the circumcision using the guillotine technique.<sup>221</sup> Dr. Glass further instructed Dr. Goodger to use the Valleylab Electrosurgical Unit (“ESU”) to perform the procedure.<sup>222</sup> ESU “operates by applying a high frequency electrical current through a ‘surgical pencil’ to the cutting area.”<sup>223</sup> The doctors had cut one-third the distance across the foreskin when they realized something was wrong.<sup>224</sup> The child’s penis retracted and became very pale, and the doctors soon determined that he had sustained a full thickness burn<sup>225</sup> from “excess electrical current running through the penis.”<sup>226</sup> The physicians removed the remaining foreskin with scissors, sutured by hand, and applied burn cream to the child’s penis.<sup>227</sup> Just a few days later, the child developed a high fever and was taken back to the hospital.<sup>228</sup> When he arrived,

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at 76, n.1

217. *Felice v. Valleylab, Inc.*, 520 So. 2d 920, 922 (La. Ct. App. 1987).

218. “Phimosis is a constriction of the opening of the foreskin so that it cannot be drawn back over the tip of the penis. This condition is a normal occurrence in the newborn boy, but over time, the skin that adheres to the tip of the penis can be retracted as the foreskin loosens. By age 17, 99 percent of males will be able to completely retract their foreskin.” *Phimosis and Paraphimosis in Children*, BOSTON CHILDREN’S HOSP., <http://www.childrenshospital.org/health-topics/conditions/p/phimosis-and-paraphimosis#sthash.9Q995J7v.dpuf> (last visited Feb. 16, 2015).

219. *Felice*, 520 So. 2d at 922.

220. *Id.* at 923.

221. *Id.* “In this technique the foreskin of the penis is stretched past the end of the penis and clamped with a hemostat to hold the foreskin in a position to be cut off. After the excess foreskin is cut away, the bleeding is controlled and the edges of the foreskin are sutured together. Generally the cutting in circumcisions is performed with a scalpel.” *Id.*

222. *Id.*

223. *Id.*

224. *Id.*

225. *Id.* “A third-degree burn is referred to as a full thickness burn. This type of burn destroys the outer layer of skin (epidermis) and the entire layer beneath (or dermis).” *Third Degree Burns*, CHILDREN’S HOSP. OF WIS., <http://www.chw.org/display/PPF/DocID/21911/router.asp> (last visited Nov. 18, 2013).

226. *Felice*, 520 So. 2d at 923.

227. *Id.*

228. *Id.*

doctors discovered that his penis was completely gone.<sup>229</sup>

The child's parents sued the Department of Health and Human Resources, based on *respondeat superior*, as well as the hospital for negligent training and supervision.<sup>230</sup> Valleylab was also named as a defendant for failure to warn of the dangers of the ESU device.<sup>231</sup> The court found the state to be 100% at fault and awarded damages to the child and his family.<sup>232</sup> The court reasoned that Dr. Glass was responsible for Dr. Goodger, but she simply assumed that Dr. Goodger had the requisite training and experience to perform a circumcision using the guillotine method with the ESU.<sup>233</sup>

Dr. Glass admitted that she had never been trained to use an ESU to perform circumcisions in medical school, and in fact, she started using this method only one week prior to the child's procedure.<sup>234</sup> Dr. Glass had spoken with another resident about the possible benefits of a circumcision performed with an ESU, and then she had used that procedure on another patient with no adverse effects.<sup>235</sup> The court noted that Dr. Glass did not inquire with her supervising doctors about the use of an ESU during circumcision.<sup>236</sup> She did not read any medical literature or review the ESU manual for any warnings regarding using the device for circumcision.<sup>237</sup> The patient did not even present a unique need that required a deviation from the standard practice for circumcision.<sup>238</sup> Instead, "Dr. Glass merely decided to try it and see what effect the ESU would have upon the surgery, since she considered it an improvement upon well-established technique."<sup>239</sup> Because of these lapses in the standard of care expected in a procedure like this, and because Dr. Glass modified a familiar technique without adequately researching its potential adverse effects, the court found the state was vicariously responsible for her negligence.<sup>240</sup>

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229. *Id.*

230. *Id.*

231. *Id.*

232. *Id.* at 929.

233. *Id.* at 928.

234. *Id.*

235. *Id.*

236. *Id.*

237. *Id.*

238. *Id.* at 929.

239. *Id.* at 928.

240. *Id.* at 928-29. "A hospital would be liable for the negligent act of a physician, nurse or any other 'employee' acting within the scope of his employment for the hospital under the doctrine of respondeat superior. In effect, the hospital is vicariously liable for the acts of its agent, servant or employee, whether he be physician, nurse, or technician where they have engaged in a negligent act

### 3. Comparing the Cases

Comparing these two cases illustrates the scope of the reasonable innovation rule. The *Felice* case is similar to the *Brook* case because both physicians deviated from the standard of care in their area.<sup>241</sup> Both doctors believed they were improving on established techniques to enhance their patients' care.<sup>242</sup> The *Felice* case, however, radically differs from the *Brook* case because use of the ESU was not considered a reasonable innovation.<sup>243</sup> In the *Felice* case, the patient did not present a unique need that required innovation and deviation from established standards of care.<sup>244</sup> Furthermore, Dr. Glass failed to adequately research the procedure.<sup>245</sup> She did not consult her supervising doctors and did not reference medical literature to explore potential consequences of what she thought was an innovative procedure.<sup>246</sup> Additionally, she had performed the technique on only one other patient before deciding to implement the technique regularly.<sup>247</sup> The gross deviation from customary care was a human experiment that left a boy permanently disfigured. The *Brook* case, on the other hand, illustrates the potential for appropriate innovation under the reasonable innovation rule: a doctor adequately researching and implementing an innovative, but reasonable, procedure based on a patient's unique needs.

The reasonable innovation rule is essential to medicine because we do not want to curb doctors' new methods, ideas, and procedures, but we do want to protect the patient. Without innovation, the medical field would become stagnant, and we would not see the growth that innovation provides to the field.<sup>248</sup> Each patient presents unique needs, and these needs can be met through reasonable innovation.<sup>249</sup>

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within the scope of their employment." PEGALIS, *supra* note 2, § 6:20.

241. See *Brook v. St. John's Hickey Mem'l Hosp.*, 380 N.E.2d 72, 77 (Ind. 1978); *Felice*, 520 So. 2d at 928.

242. *Brook*, 380 N.E.2d at 74; *Felice*, 520 So. 2d at 928.

243. See *Felice*, 520 So. 2d at 928-29 (discussing reasonable innovation).

244. *Id.* at 929.

245. *Id.* at 928.

246. *Id.*

247. *Id.* at 928.

248. Philip D. Noguchi, *From Jim to Gene and Beyond: An Odyssey of Biologics Regulation*, 51 FOOD & DRUG L.J. 367, 372 (1996).

249. *Id.*

F. *Why the Reasonable Innovation Rule Should be Codified:  
Balancing the Interest of Innovation with the Protection of Patient  
Safety*

The reasonable innovation rule must be codified because it successfully balances the interests of the law, physicians, patients, and innovation. First, the law will benefit from codification because the rule will no longer be hidden in case law. If the FDA codifies this rule, it will be concrete and accessible as a regulation. Informed consent will no longer be the minimum standard. The shortcomings and problems with obtaining true informed consent will be addressed because the physician will assume a shared responsibility in the medical decision-making process. The physician will be held to a standard of implementing only reasonable innovations. Having a reasonable standard balances the physician's interest in trying to save her patient by any means possible with what is reasonable based on the patient's unique needs.

Physicians will benefit from the codification of the reasonable innovation rule because their personal autonomy will be preserved. The rule is not so stringent as to eliminate freedom to deviate from common practices. It instead raises the minimum standard from being able to implement *any* procedure with informed consent to being able to implement any *reasonable* procedure. This will encourage researchers to focus on treatments that demonstrate success, like fecal transplants, while ensuring that physicians introduce only well-researched treatments to patients. Physicians will still find enjoyment and professional fulfillment in the latitude they are given in the decision-making process. Their knowledge, skills, training, and experience will be honored; their judgment, trusted.

Patients will also benefit from codification of the rule. When patients are in a dire situation that makes them more likely to consent to dangerous novel treatments, the rule will provide an extra safeguard. The physician will be required to implement only what is reasonable, and patients can fully trust their doctor's decisions. This will prevent results like those in the bacterial transplant case, where the physicians felt that they could side-step FDA regulations after obtaining their patients' informed consent. Thus, the solidarity of the patient-physician relationship (which is already quite strong)<sup>250</sup> will increase because the rule will foster trust.

Finally, the interest of medical innovation and growth will be

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250. *Patient Consent*, *supra* note 71.

preserved if the rule is codified. The rule recognizes that innovation is part of the medical profession and without innovation growth would be stunted. Innovative treatment based on the unique needs of the patient will still be permitted. This rule, however, will protect against unreasonable, poorly researched innovations not yet fit for human implementation regardless of whether patients have consented.

#### *G. Proposed Language for Codification*

The following language is proposed for codification:

A physician may innovate if it is reasonable under the circumstances. The decision to innovate should be driven by the unique needs of the individual patient that cannot be met by customary practice. If the physician seeks to incorporate the innovation into daily practice involving all patients, the physician must first obtain permission from the IRB in the hospital where the innovative procedure will occur or, if the procedure will not occur in a hospital, a stand-alone IRB.

Under this standard, the question of “reasonableness” is left to the jury to determine. Ideally, the jury will consider the same factors as in the *Brook* case: whether the doctor sufficiently researched the innovation by consulting professional literature prior to implementation, and whether there was evidence of prior success based on other patients.

### V. CONCLUSION

Codification of the reasonable innovation rule will help avoid tragedies like the deaths of the three patients who consented to bacterial injections out of desperation. Under the proposed reasonable innovation rule, the patients’ consent would not have been enough to commence the procedure. Instead, the physician would have had an obligation to implement only what was reasonable based on extensive research. Implementing the reasonable innovation rule would have prevented the physicians from circumventing FDA protocol. It recognizes that even physicians may be blinded by their desire to do whatever possible to save their patients. While this desire is admirable, it demonstrates the need for a minimum standard in the decision-making process.

The reasonable innovation rule will also foster innovation, as evidenced by the fecal transplant cases. This procedure, while not extensively studied in clinical trials, could be deemed reasonable based on the surrounding facts and evidence. The patients who underwent the fecal transplants presented a unique need that was not being met by customary practices. Novel innovations such as this are crucial, and the

rule will not curb the use of such treatments. Deeming an innovative treatment objectively reasonable is an important part of deciding whether to advise patients to undertake the potential risks of any given procedure.

The FDA should codify the reasonable innovation rule because of these reasons. The medical and legal professions, as well as society as a whole, will greatly benefit from the rule's codification. Most importantly, human experimentation masked as innovation will be reduced by codification of the rule.