

Summer 2017

Syncing The Unsyncable: Legal and Policy Implications of Paperless Clinical Trials

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Recommended Citation

Kimberly Rhodes, *Syncing The Unsyncable: Legal and Policy Implications of Paperless Clinical Trials*, 9 HASTINGS SCI. & TECH. L.J. 185 (2017).

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Syncing The Unsyncable: Legal and Policy Implications of Paperless Clinical Trials

by KIMBERLY RHODES* & MICHAEL ROMEO**

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* Kimberly Rhodes serves as Chief Legal Officer (CLO) at the WIRB-Copernicus Group (WCG). WCG delivers transformational solutions that stimulate growth, foster compliance, and maximize efficiency for those who perform clinical trials. Kim's professional experience includes complex negotiations, M&A, corporate governance, intellectual property and litigation management in the healthcare, technology, and financial services industries. Her career highlights include serving as General Counsel to several technology companies including, Quintiq, Fiberlink, and eCount/CitiPrepaid, as well as Senior Corporate Counsel at SAP and Senior Counsel at IBM. Kim graduated from Villanova School of Law and received her undergraduate degree from the University of Pennsylvania.

** Michael Romeo is a third-year law student at Villanova University Charles Widger School of Law, where he is expecting to receive his J.D. in May 2017. Michael is a managing editor of outside articles for the *Jeffrey S. Moorad Sports Law Journal*, and attended Niagara University for his undergraduate education.

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I. The Wonders of Modern Medicine and the Rise of the Pharmaceutical Industry

Medical advances have altered the landscape of society in western nations. Today, some diseases that were fatal just 70 years ago are now either easily curable or completely eradicated.¹ Other illnesses that were considered incurable just 25 years ago, like AIDS, are now treatable, chronic conditions.² The Western world no longer fears contracting once deadly diseases like smallpox or measles.³ Fortunately, many of the dangerous diseases of our ancestors are curable with prescription medicine or other forms of advanced treatment. In fact the population of individuals over the age of 85 is expected to increase by roughly 350% between 2010 and 2050.⁴

Although it is remarkable to consider how far medicine has come, it is equally as exciting to consider where medicine is headed. Some medical professionals think that the children of Generation Z will regularly live to be about 100 years old thanks in large part to the exponential advancement of

1. See Kevin Berman, *Smallpox*, MEDLINEPLUS, <https://medlineplus.gov/ency/article/001356.htm> (last updated Apr. 14, 2015), (noting smallpox is essentially eradicated today); see also Erin Brodin, *Seven Human Diseases the World is on the Cusp of Eradicating*, BUSINESS INSIDER (May 14, 2015, 11:48 AM), <http://www.businessinsider.com/diseases-that-are-almost-eradicated-2015-5/#measles-1> (listing seven diseases that are close to eradication thanks to modern medicine). Specifically, the author notes that measles, rubella, polio, guinea worm, lymphatic filariasis, onchocerciasis, and mumps as diseases that are close to being wiped out by medicine.

2. See *Living with HIV*, CTR. FOR DISEASE CONTROL & PREVENTION, <http://www.cdc.gov/actagainstaids/basics/livingwhiv.html> (last updated Aug. 24, 2016) (discussing tips and responsibilities associated with living with HIV); see also *A Timeline of HIV/AIDS*, AIDS.GOV, <https://www.aids.gov/hiv-aids-basics/hiv-aids-101/aids-timeline/> (last visited Mar. 26, 2017).

3. See *Smallpox*, COMMUNICABLE DISEASE CONTROL & PREVENTION, <http://www.sfdcp.org/smallpox.html> (last visited Mar. 26, 2017). Specifically, it is noted that the last case of smallpox in the U.S. was in 1949, and the last case of smallpox in the world was in 1977 in Somalia.

4. See Laura F. Friedman, 'One of Societies Greatest Achievements' – In a Simple Chart of The Past 175 Years, BUSINESS INSIDER (June 19, 2015, 4:40 PM), <http://www.businessinsider.com/how-has-life-expectancy-changed-throughout-history-2015-6> (citing the management of infectious diseases as a main cause for increased life expectancy).

medicine.⁵ In 2016, a man was successfully given two new arms that are expected to become functional.⁶ Frequently it is reported that a cure for cancer is imminent and life expectancies are increasing for almost all forms of cancer.⁷ There is evidence to suggest that a vaccine to treat Ebola is closer than most people might expect.⁸

Notwithstanding incredible progress, medical advancements continue and it is clear more can be done to ease suffering and prolong life. Developing, testing and researching new treatments for patient use in the United States is an arduous process, and it is both expensive and time consuming.⁹ Every prescription drug that is available to the masses has to first pass through the clinical trial process.¹⁰

Generally, a clinical trial in the United States subject to FDA guidelines is a four-step phase or process.¹¹ Phase one of a clinical trial consists of highly controlled tests with a very small number of people, which is aimed at evaluating safety, dosage, and potential side effects.¹² Phase two increases the number of people in the study, and further assesses safety and

5. See Joseph Brownstein, *Most Babies Born Today May Live Past 100*, ABC NEWS, <http://abcnews.go.com/Health/WellnessNews/half-todays-babies-expected-live-past-100/story?id=8724273> (Oct. 1, 2009) (discussing how children born in 2009 will most likely live to be older than 100).

6. See Jacqueline Howard, *Double Arm Transplant Will Allow Veteran 'To Pursue My Dreams'*, CNN (Oct. 5, 2016 7:44 PM), <http://www.cnn.com/2016/10/05/health/double-arm-transplant-veteran-john-peck>.

7. See Anna Magee, *How Close Are We To Curing Cancer?*, THE TELEGRAPH (Mar. 21, 2016, 7:00 AM), <http://www.telegraph.co.uk/wellbeing/health-advice/how-close-are-we-to-curing-cancer/>; see also Anna Hodgekiss, *Are We Nearing A Cure For Cancer? Holy Grail is Closer Than Ever, Oncologist Claims*, DAILY MAIL (May 30, 2016 9:38 AM), <http://www.dailymail.co.uk/health/article-3616249/Are-nearing-cure-cancer-Holy-grail-closer-oncologist-claims.html>; Greg Jones, *Why Are Cancer Rates Increasing?*, CANCER RESEARCH CTR (Feb. 4, 2015), <http://scienceblog.cancerresearchuk.org/2015/02/04/why-are-cancer-rates-increasing/> (noting that "more people are beating cancer today than ever before. Survival has doubled in the last 40 years. And half of people diagnosed will survive their cancer for more than 10 years, an all-time high.").

8. See *Sierra Leone Trial to Introduce a Vaccine Against Ebola (STRIVE) Q&A*, CTR. FOR DISEASE CONTROL & PREVENTION, <http://www.cdc.gov/vhf/ebola/strive/qa.html> (last updated Apr. 20, 2016); see also German Center for Infection Research, *Ebola Vaccine: Promising Phase I Trials*, SCIENCE DAILY (May 3, 2016), <https://www.sciencedaily.com/releases/2016/05/160503131401.htm>.

9. See Yevgeniy Feyman, *Shocking Secrets of FDA Clinical Trials Revealed*, FORBES (Jan. 24, 2014), <http://www.forbes.com/sites/theapothecary/2014/01/24/shocking-secrets-of-fda-clinical-trials-revealed/#7d5a08f92279>.

10. See *Clinical Trials*, PHARMA, <http://www.phrma.org/advocacy/research-development/clinical-trials> (last visited Mar. 28, 2017) (discussing the process and steps of the clinical trial process).

11. See *Step 3: Clinical Research*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/ForPatents/Approvals/Drugs/ucm405622.htm> (last updated Oct. 14, 2016).

12. *Id.* (noting first step of clinical trial process).

effectiveness.¹³ During phase three, the experimental drug is administered to large groups of people, and is aimed at confirming effectiveness through monitoring and trial data collection.¹⁴ Lastly, phase four occurs after the drug is on the market to monitor risks associated with long-term use and the drug's effectiveness in various populations.¹⁵

According to the FDA, 70% of drugs pass phase one, 33% pass phase two and 25% to 30% pass phase three.¹⁶ To put those numbers into more understandable terms, according to the FDA, roughly six out of every one hundred drugs that begin the clinical trial process make it past phase three. Moreover, some sources suggest that the time from lab to market for a new drug is about 15 years,¹⁷ and costs can be upwards of \$30 to \$40 million *just* for the first three phases of a clinical trial, and then another \$30 to \$40 million if the drug makes it to phase four.¹⁸ Some studies even suggest that when accounting for all the “behind the scenes” costs, the average cost of getting a drug from lab to market could be as high as \$1.3 billion.¹⁹

These high costs and lengthy processes naturally raise questions — how can this process be improved? Under the construct of the burdensome regulations and requirements, how can medicine and the pharmaceutical industry meet the needs of patients and future generations faster, safer, and more economically? How can the sponsoring pharmaceutical companies, contracted research organizations, site investigators, and others reduce the time it takes a treatment or drug to go from lab to market? One option is to expand the use of software platforms to reduce cycle times throughout the clinical trial process.

Commensurate, and even surpassing the profound advancements in Western medicine in the last century, software, communication, imaging and related technologies have been exponentially advancing in the last several

13. *Id.* (noting second step of clinical trial process).

14. *Id.* (noting third step of clinical trial process).

15. *Id.* (noting fourth step of clinical trial process).

16. *See id.* (stating what percentage of drugs pass through each phase).

17. *See Clinical Trials 101*, CROHNS & COLITIS FOUND. OF AM., <http://www.cafa.org/resources/clinical-trials-101> (last visited Mar. 28, 2017) (noting length of average clinical trial).

18. *See* Aylin Sertkaya et al., *Examination of Clinical Trial Costs and Barriers for Drug Development*, E. RESEARCH GRP. (July 25, 2015), <https://aspe.hhs.gov/report/examination-clinical-trial-costs-and-barriers-drug-development>.

19. *See* Avik S. A. Roy, *Stifling New Cures: The True Cost of Lengthy Clinical Drug Trials*, 5 PROJECT FDA REPORT, (March 2012) (discussing the behind the scenes costs associated with clinical trials, and how those costs can drive the total cost to over \$1 billion).

decades.²⁰ Technological and medical advancements go hand in hand.²¹ Other industries that are of similar size to healthcare and pharmaceuticals have evolved their business models to incorporate and accelerate growth and success using technological advances. For example, in the financial services industry, virtually all major banks have some form of online banking, and according to recent research, about 50% of United States adults use online banking.²² Further, about 35% of cell phone users use their smart phones to bank online.²³ There are even some banks that are exclusively online and have no physical, brick and mortar branches.²⁴

So, with technology permeating so many facets of other industries, why has the medical and pharmaceutical industry lagged in matching the pace of technological advancement? Specifically, what are the legal and policy risks associated with hastening the clinical trial process by utilizing technology based clinical trial platforms versus traditional paper-based methods? That is the question this article seeks to answer.

First, this article will look to the recent legal trends surrounding technology in healthcare and the pharmaceutical industry generally. Then, this article will analyze traditional paper intensive approaches to key elements of clinical trials including; site feasibility, document distribution, and informed consent and discuss how those areas could be improved by the use of technology. Potential new liability exposures will be analyzed in light of the expanded use of technology in the clinical trial process. The policy section will discuss steps regulatory bodies have taken to embrace technological advances, and project where technology and medicine are headed. Finally, this article will conclude with a policy discussion that compares the benefits of new technologies to possible risk increases and suggest ways that the laws and regulations can continue to evolve to harness, expand, and encourage new technologies.

20. See Max Roser, *Technological Progress*, OUR WORLD IN DATA (2016), <https://ourworldindata.org/technological-progress/> (discussing the exponential growth of technology).

21. See Bianca Banova, *The Impact of Technology on Healthcare*, AM. INST. OF MED. SCI. & EDUC. (Mar. 28, 2013), <https://www.aimseducation.edu/blog/the-impact-of-technology-on-healthcare>.

22. See Susannah Fox, *51% of U.S. Adults Bank Online*, PEW RESEARCH CTR. (Aug. 7, 2013), <http://www.pewinternet.org/2013/08/07/51-of-u-s-adults-bank-online>; see also Evan Bakker, *Technology is Disrupting the Financial Services Industry – Here's How*, BUS. INSIDER (Feb. 22, 2016), <http://www.businessinsider.com/technology-is-changing-the-financial-services-industry-2016-1>.

23. See *id.*

24. See ALLY FINANCIAL, <https://www.ally.com/about/> (noting that Ally is a completely online bank); see also Marycela Diaz-Unzalu, *Technology Trends Affecting the Banking Industry*, FED. RESERVE BANK OF ATLANTA (Mar. 28, 2014), <https://frbatlanta.org/education/publications/extra-credit/2014/spring/technology-trends-affecting-banking-industry>.

II. Background: The Intersection of Law, Technology, Medicine, and Business

Since the late 1990s, policy and legislative steps have been taken in the United States to promote the implementation and adoption of electronic business practices. In 1999, the National Conference of Commissioners on Uniform State Laws (NCCUSL) promulgated the Uniform Electronic Transactions Act (UETA).²⁵ According to the NCCUSL, the goal of the UETA was to make a “comprehensive effort to prepare state law for the electronic commerce era.”²⁶ As of 2016, the UETA has been adopted by 47 states,²⁷ and governs “electronic records and electronic signatures relating to a transaction.”²⁸

One year later, the federal government joined the e-commerce movement by enacting the Electronic Signatures in Global and National Commerce Act (hereafter “ESIGN”).²⁹ Effectively, this act assured that electronic signatures and agreements would be given the same enforceability as paper agreements.³⁰ Although neither the ESIGN Act nor the UETA are directly implicated in the discussion relevant to this article, they gave electronic agreements and signatures the same legal force as paper agreements and signatures.³¹ Without the backbone of these acts, e-commerce and e-business (and thus, e-clinical trials) would carry no legal weight at all.³²

25. See *Electronic Transactions Act Summary*, NAT’L CONFERENCE OF COMM’RS ON UNIF. STATE LAWS, <http://www.uniformlaws.org/ActSummary.aspx?title=Electronic%20Transactions%20Act> (last visited Mar. 28, 2017).

26. See *id.* Although every state that has adopted the UETA has codified it in their own way, an example of how the UETA was written into law can be seen in FLA. STAT. ANN. § 668.50 (LexisNexis 2016).

27. See *Electronic Transactions Act*, NAT’L CONFERENCE OF COMM’RS ON UNIF. STATE LAWS, <http://www.uniformlaws.org/Act.aspx?title=Electronic%20Transactions%20Act> (last visited Mar. 28, 2017) (showing map of what states have adopted the UETA).

28. NAT’L CONFERENCE OF COMM’RS ON UNIF. STATE LAWS, *supra* note 25.

29. See 15 USCS § 7001 (discussing provisions of the ESIGN Act).

30. See 15 USCS § 7001(a)(1) (“a signature, contract, or other record relating to such transaction may not be denied legal effect, validity, or enforceability solely because it is in electronic form”). Further, § 7001(a)(2) states “a contract relating to such transaction may not be denied legal effect, validity, or enforceability solely because an electronic signature or electronic record was used in its formation.”

31. See *id.*

32. See Howard Burde, *The HITECH Act – An Overview*, 13 AMA J. OF ETHICS, (VIRTUAL MENTOR) no. 3, 2011 at 172–75.

A. The Dynamic Duo of HIPAA and HITECH

1. *The Health Insurance Portability and Accountability Act*

In 1996, congress passed the Health Insurance Portability and Accountability Act (hereinafter “HIPAA”).³³ Although HIPAA affected a number of areas of the law, it is most known for the impacts it has on patient and medical record privacy.³⁴ Specifically, Section 264 of the Administrative Simplification provisions is commonly referred to as the “Privacy Rule.”³⁵ The main goal of HIPAA and the Privacy Rule specifically is to “define and limit the circumstances in which an individual’s protected health information may be used or disclosed by covered entities.”³⁶

HIPAA’s Privacy Rule “[applies] to health plans, health care clearinghouses, and to any health care provider who transmits health information in electronic form.”³⁷ The Privacy Rule is focused on minimizing the release of individually identifiable health information (IIHI) by any of the abovementioned-covered entities.³⁸ In addition to obvious examples of IIHI, things like credit card numbers and telephone numbers are also considered to be sources of IIHI.³⁹ Further, the Privacy Rule enacted a “minimum necessary” standard for disclosing medical information, which requires that covered entities make “reasonable efforts to limit protected health information to the minimum necessary to accomplish the intended purpose of the use, disclosure, or request.”⁴⁰ In the early 2000s, the Office for Civil Rights (the branch of the Department of Health and Human Services responsible for investigating HIPAA violation claims) was regularly receiving “over one hundred privacy-related complaints per week.”⁴¹

In addition to the privacy components of HIPAA, the law also includes security measures. The purpose of the security rule is to require “appropriate administrative, physical and technical safeguards to ensure the

33. See *Summary of the HIPAA Privacy Rule*, U.S. DEP’T OF HEALTH & HUMAN SERV., <https://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations/> (last visited Mar. 28, 2017), (giving an overview of HIPAA).

34. See *The HIPAA Privacy Rule*, U.S. DEP’T OF HEALTH & HUMAN SERV., <https://www.hhs.gov/hipaa/for-professionals/privacy/> (last visited Mar. 28, 2017).

35. See U.S. DEP’T OF HEALTH & HUMAN SERV., *supra* note 33.

36. See Elizabeth Hutton & Devin Barry, *2004 Privacy Year In Review Annual Update: Medical: Privacy Year In Review: Developments in HIPAA*, 1 INFO. SOC’Y J.L. & POL’Y 347, 352 (2005).

37. See U.S. DEP’T OF HEALTH & HUMAN SERV., *supra* note 33 (discussing the HIPAA privacy rule).

38. See Hutton & Barry, *supra* note 36, at 352.

39. *Id.*

40. See 45 C.F.R. § 164.502(b)(1).

41. See Hutton & Barry, *supra* note 36, at 355.

confidentiality, integrity, and security of electronic protected health information.”⁴² In today’s world, the very real threat of computer hacking by third parties is a serious consideration for the healthcare industry, being hacked and the resulting exposure of PHI would open up a covered entity to liability under HIPAA.⁴³

2. *The Health Information Technology for Economic and Clinical Health Act*

In 2009, HIPAA, and technology in health and medicine took a further leap into the technology era with the enactment of the Health Information Technology for Economic and Clinical Health Act (HITECH Act).⁴⁴ The HITECH Act was passed as part of the American Recovery and Reinvestment Act, which was President Obama’s stimulus package aimed at pulling the country out of a significant and prolonged recession following the collapse of financial markets due to poor mortgage loan practices and securitization.⁴⁵ The goal of the HITECH Act was to implement a national system of electronic record keeping for medical records.⁴⁶ The HITECH Act aimed to accomplish widespread adoption of Electronic Health Record Systems (EHRs) with the use of incentive payments to health care industry clinicians and participants.⁴⁷

Although the HITECH Act is predominantly aimed at the implementation of EHR systems across the United States, it also facilitates the enforcement of HIPAA.⁴⁸ In addition to expanding the definition of who must comply with HIPAA, the HITECH Act also created a security breach notification requirement.⁴⁹ In the event of a breach, the company responsible for holding the data must notify the affected customers and the government,

42. See *The Security Rule*, U.S. DEP’T OF HEALTH & HUMAN SERV., <http://www.hhs.gov/hipaa/for-professionals/security/> (last visited Mar. 28, 2017).

43. See Leon Rodriguez, *Privacy, Security, and Electronic Health Records*, HEALTH IT BUZZ (Dec. 12, 2011), <https://www.healthit.gov/buzz-blog/privacy-and-security-of-ehrs/privacy-security-electronic-health-records/>; see also Kevin McCarthy, *HIPAA and Hacking: What You Need to Know*, NUEMD (Apr. 14, 2016), <http://www.nuemd.com/news/2016/04/14/hipaa-hacking-you-need-know> (noting the increase in hacking attempts aimed at healthcare infrastructure).

44. See Kirk J. Nahra, *A New HIPAA Era Emerges*, 1005 PLI/PAT 467, 471 (2010) (Westlaw).

45. See *About the Recovery Act*, WHITE HOUSE, <https://www.whitehouse.gov/recovery/about> (last visited April 19, 2017).

46. See Kara J. Johnson, *HITECH 101*, AM. BAR ASS’N, http://www.americanbar.org/groups/young_lawyers/publications/the_101_201_practice_series/hitech_101.html (last visited Mar. 28, 2017).

47. See *id.* (positing that the HITECH Act “was passed as a monetary incentive plan for hospitals to begin converting to electronic records.”).

48. See *id.* (reasoning that “HITECH significantly changes both enforcement and sanctions with regard to health care privacy and security requirements under HIPAA.”).

49. See Nahra, *supra* note 44.

and if the breach affects more than 500 people, the media must also be notified.⁵⁰ By requiring notification to affected parties, the HITECH Act not only holds record holders more accountable but also aims to increase and preserve the trust between patients and entities holding their health information in electronic format.⁵¹

Prior to the implementation of HITECH, third-party service providers were not directly subject to liability for violations of HIPAA; instead they could be held liable privately to the covered entity utilizing their services under a breach of contract claim.⁵² However, pursuant to HITECH, “business associates are now directly subject to civil and criminal penalties under HIPAA if they violate . . . security safeguard requirements or the terms of their business associate agreements.”⁵³ Thus, HITECH increased the scope of HIPAA by allowing business associates to be held directly liable for violations of the privacy rule.⁵⁴

Additionally, HITECH dramatically increased the possibility of enforcement of HIPAA because it allows a state attorneys general to bring HIPAA enforcement actions, in addition to ramping up the penalties violators can face.⁵⁵ Prior to the HITECH Act, HIPAA violators were subjected to penalties of \$100 per known violation, with a damages cap of \$25,000 per year.⁵⁶ Considering that the size of the United States healthcare industry where many large players have revenues in the tens of billions or more,⁵⁷ with a total market size of upwards of \$3 trillion, the \$25,000 fine levels may have been inadequate to act as a deterrent.⁵⁸ The stakes are higher under the

50. See *HITECH Breach Notification Rule*, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, <https://www.hhs.gov/hipaa/for-professionals/breach-notification/> (last visited Mar. 28, 2017) (analyzing the breach notification requirement implemented by the HITECH Act).

51. See *id.*

52. See Norbert F. Kugele, *HIPAA Goes HITECH: How the HITECH Amendments to HIPAA Impact Employer-sponsored Health Plans*, 35 *MI TAX L.* 19, 20 (2009).

53. See *id.*

54. See *id.*

55. Health Information Technology for Economic and Clinical Health Act, § 13410, amending Social Security Act § 1176, codified at 42 U.S.C. § 1320d-5; see also Health Information Technology for Economic and Clinical Health Act, § 13410(e)(1); see also *HIPAA Violations and Enforcement*, AM. MED. ASS'N, <http://www.ama-assn.org/ama/pub/physician-resources/solutions-managing-your-practice/coding-billing-insurance/hipaahealth-insurance-portability-accountability-act/hipaa-violations-enforcement.page?> (last visited Mar. 28, 2017).

56. See Kugele, *supra* note 52, at 19-20.

57. See Laura Lorenzetti, *The 10 Biggest Health-Care Companies in the Fortune 500*, *FORTUNE* (June 20, 2015), <http://fortune.com/2015/06/20/fortune-500-biggest-healthcare-companies/> (noting several healthcare companies listed in the Fortune 500 with annual revenues between \$50 to \$140 billion).

58. See Dan Munro, *U.S. Healthcare Hits \$3 Trillion*, *FORBES* (Jan. 19, 2012, 11:52 PM), <http://www.forbes.com/sites/danmunro/2012/01/19/u-s-healthcare-hits-3-trillion/#66b0f34c2f67>.

HITECH Act, with penalties for HIPAA violations ranging from \$100 per violation to \$50,000 per violation, with an annual cap of \$1.5 million in penalties.⁵⁹

a. The Impact of HIPAA and HITECH on the Clinical Trial Ecosystem

Although HIPAA and HITECH are Acts aimed at the implementation, security, and privacy of EHRs, they both have substantial impacts throughout the entire healthcare system. Recently, the impact of these laws has become even more pronounced as the clinical trial process is, albeit slowly, going digital.⁶⁰ The shift from paper to digital clinical trials provides the framework for speeding up the time from lab to market and will also save companies who sponsor clinical trials large sums of money. Some research suggests that life science and other pharmaceutical companies could save as much as 25% of their annual operating expenditures by working with a clinical IT system.⁶¹ Thus, it comes as no surprise to discover that 66% of the top 50 pharmaceutical companies are currently digitizing certain parts of their clinical trial process.⁶²

Throughout the clinical trial process, PHI is exchanged between companies, clinicians, and patients. As a result, successfully navigating the clinical trial process requires compliance with a number of federal laws, like HIPAA and HITECH. Although there are serious financial and humanitarian incentives to digitizing the clinical trial process, pharmaceutical companies are hesitant to fully embrace digital clinical trials because of the potential compliance issues and the possible increase in liability exposure.⁶³

59. See Kugele, *supra* text accompanying note 52.

60. See *eClinical Solutions Market to Surpass \$13 Billion by 2024*, DIGITAL JOURNAL (Oct. 24, 2016), <http://www.digitaljournal.com/pr/3115602>.

61. See Elly Earls, *Ahead In The Cloud – A New home For Clinical Trial Data*, PHARMACEUTICAL-TECH. (Jan. 31, 2012), <http://www.pharmaceutical-technology.com/features/feature-ahead-in-the-cloud-a-new-home-for-clinical-trial-data/> (stating “IBM’s research suggests that many life sciences organizations could save as much as 25% of their annual operating expenditure on clinical IT systems by using cloud computing”).

62. See Glenn Keet & Eric Morrie, *Top eClinical Trends in 2016*, CLINCAPTURE, eCLINICAL TREND (Mar. 9, 2016), <http://www.clincapture.com/blog/top-eclinical-trends-in-2016-12-2/>. The statistics from this article are specific to eConsent adoption, not total eClinical trial adoption. However, eConsent adoption is one of the biggest hurdles many companies need to overcome in order to entirely digitize their clinical trial process. See also *Electronic Consent Management: Landscape Assessment, Challenges, and Technology*, HEALTHHIT.GOV (Oct. 29, 2014), available at https://www.healthit.gov/sites/default/files/privacy-security/ecm_finalreport_forrelease62415.pdf.

63. For a discussion pertaining to potentially increased liability by digitizing the clinical trial process, see *infra*, notes 86–99, 108–122, and 135–149.

b. A Primer on the Terminology and Business of Clinical Trials

As was discussed at length in Section I of this article, clinical trials are one of the driving forces behind the advancement of medicine.⁶⁴ Thus, a number of entities from the medical industry are involved in some form or another.⁶⁵ For example, a clinical trial is led by a principal investigator who is usually a medical doctor.⁶⁶ Further, the principal investigator is supported and assisted by a research team, usually consisting of nurses, other doctors, social workers, and health care professionals.⁶⁷

Clinical trials are often paid for (or sponsored) by pharmaceutical companies or university medical centers.⁶⁸ However, some federal agencies will fund clinical trials for specific diseases that are widespread. For example, federal agencies fund a large proportion of cancer related clinical trials.⁶⁹

When a sponsoring party wants to begin work on a clinical trial, they can either perform the research and work themselves, or they can recruit a contract research Organization or CRO.⁷⁰ A CRO is a company that is recruited and contracted by the sponsor “to manage and lead the company’s trials, duties, and functions.”⁷¹ A CRO acts as an agent for the sponsor, providing expertise and experience in the clinical trial process, while the sponsor does not need to hire permanent staff for the position.⁷² CRO’s can fill many roles throughout the clinical trial process, with some CROs handling a specific part of the clinical trial and others managing the trial from

64. See *supra* text accompanying notes 16–24.

65. See *Learn About Clinical Studies*, U.S. NAT’L INST. OF HEALTH, <https://clinicaltrials.gov/ct2/about-studies/learn> (last updated Jan. 2017).

66. See Jeff Kingsley, *What is a PI?*, ACRP, <https://www.acrpnnet.org/professional-development/certifications/pi-certification/> (last visited Mar. 28, 2017) (stating that a “[principal investigator] holds a doctoral-level degree (PhD, PharmD, DNP, DO, MD, DDS or equivalent degree) and serves as the principal, sub- or co-investigator[.]”)

67. See *Responsibilities of the Research Team*, OHIO STATE UNIV. CTR FOR CLINICAL & TRANSLATIONAL SCI., <https://ccts.osu.edu/education-and-training-programs/research-education-and-training-programs/clinical-research-coordinator-resources/responsibilities-of-the-research-team/> (last visited Mar. 28, 2017) (noting that “the research coordinator/nurse oversees and coordinates the daily activities of clinical research studies”).

68. See *id.*; see also Freemantle, N. and Stockten, D., *The Commercialization of Clinical Research: Who Pays the Piper, Calls the Tune?*, OXFORD JOURNALS (Aug. 1, 2004), <http://fampra.oxfordjournals.org/content/21/4/335.full>

69. See *Who Conducts Clinical Trials and Who Pays for Them?*, BREASTCANCER.ORG, http://www.breastcancer.org/treatment/clinical_trials/conduct_pay (last updated Aug. 10, 2016) (noting that many cancer related clinical trials are funded by United States Federal Agencies).

70. See Kathlyn Stone, *Contract Research Organization*, THE BALANCE (May 2, 2016), <https://www.thebalance.com/contract-research-organizations-cro-2663066>.

71. See *id.*

72. See *id.*

site selection to FDA approval.⁷³ As a result, CROs are becoming increasingly popular in the clinical trial world, and can be involved at every stage of the research and development process in a clinical trial.⁷⁴

3. *What Steps of the Clinical Trial Process Can be Digitized?*

As mentioned in the introduction, the clinical trial process is rather lengthy, consisting of a number of steps over several years.⁷⁵ Addressing the impact of digitizing every single step of the clinical trial process is beyond the scope of this article, which will focus on a discussion of three separate steps in the process that are digitizable and examine the impact of digitizing these three specific steps in terms of benefits to patients and the process generally, and the effect on possible liability exposure. The specific processes that will be discussed are the site selection process, document distribution, and informed consent.

a. Site Selection

When conducting a clinical trial, one of the preliminary steps is finding an appropriate site to recruit, interact with and monitor patients participating in the trial. Locating a site consists of finding the right demographics, patients, clinicians, hospitals, facilities etc. and can be one of the most arduous aspects of the clinical trials process.⁷⁶ However, the current model for site feasibility planning is outdated, and relies on a “crowdsourcing approach” instead of data and analytics.⁷⁷

Generally speaking, site feasibility “is a process of evaluating the possibility of conducting a particular clinical program/trial in a particular geographic region with the overall objective of optimum project completion

73. *See id.*

74. *See* Ed Silverman, *Why Contract Research Organizations Are So Hot*, FORBES (Oct. 4, 2011), <http://www.forbes.com/sites/edsilverman/2011/10/04/why-contract-research-organizations-are-so-hot/#5da56611694b>.

75. *See supra* text accompanying notes 11–17.

76. *See* Melissa Fassbender, ‘Paradigm Shift Needed’ in *Trial Site Selection Process*, OUTSOURCING-PHARMA (Mar. 31, 2016), <http://www.outsourcing-pharma.com/Commercial-Services/Paradigm-shift-needed-in-trial-site-selection-process> (reasoning that “site selection has traditionally been performed using manual, and error prone processes, which use historical, siloed data — ultimately resulting in too many non-enrolling and under-enrolling sites being selected.”)

77. *See* Ed Miseta, *Proper Feasibility Planning is Critical for Clinical Trial Success*, CLINICAL LEADER (June 22, 2015), <http://www.clinicalleader.com/doc/proper-feasibility-planning-is-critical-for-clinical-trial-success-0001> (suggesting that data driven site feasibility processes will lead to better results); *see also* Kenneth A. Getz, *Is Investigative Site Feasibility Feasible?*, APPLIED CLINICAL TRIALS ONLINE (July 1, 2008), <http://www.appliedclinicaltrials.com/investigative-site-feasibility-feasible> (noting that “[s]ponsors, CROs and investigative sites widely agree that site feasibility assessments are frequently exercises in futility.”)

in terms of timelines, targets, and costs.”⁷⁸ This is usually accomplished by sending out feasibility surveys to potential sites, which ask about demographics and enrollment prospects.⁷⁹ However, the surveying method can be problematic, because surveys are subject to over and under estimations.⁸⁰ Further, it is not unheard of for potential sites to be purposefully overconfident in their enrollment projections in order to win the study grant and become a host site for the trial.⁸¹

Therefore, the current process of finding an adequate site to host a clinical trial is in many respects left up to chance.⁸² Depending on the complexity of the drug and associated illness that is the subject of a prospective clinical trial, finding an adequate site may be very difficult. As an extreme example, any sort of large-scale research pertaining to the Ebola outbreak would necessarily have to occur in West Africa, as that is where the outbreak of the disease has occurred.⁸³ Locating a site that has the technological capabilities to host a clinical trial in West Africa could presumably prove difficult.

Further, even if a site is found, and patients are recruited, it is reported that “less than half of studies completed enrollment within the planned timeline.”⁸⁴ Patient recruitment and retention has always been one of the biggest hurdles that sponsors and CROs need to overcome.⁸⁵ Thus, sponsors and CROs can be forced to restart the site evaluation process, with less time and money than was available at the commencement of the trial. Regardless of the problems that a sponsor could encounter while seeking a site for a

78. See Viraj Rajadhyaksha, *Conducting Feasibilities in Clinical Trials: An Investment to Ensure a Good Study*, NAT'L CTR FOR BIOLOGY INFO. (July-Sept. 2010), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3146075/> (discussing the importance of a properly performed site feasibility process).

79. See Miseta, *supra* note 77.

80. See Getz, *supra* note 77.

81. See *id.*

82. See Miseta, *supra* note 77 (noting that “there would also be questions around how the sites produced their answers, and whether there was any scientific evidence to back it up.”)

83. See *2014 – 2016 Ebola Outbreak in West Africa*, CTR FOR DISEASE CONTROL, <https://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/> (last updated June 22, 2016) (reasoning that “since march 2014, West Africa has experienced the largest outbreak of Ebola in history”).

84. See Kenneth A. Getz, *Enrollment Performance: Weighing the “Facts”*, APPLIED CLINICAL TRIALS, (May 1, 2012), <http://www.appliedclinicaltrials.com/enrollment-performance-weighing-facts?id=&sk=&date=&pageID=2>; see also Interview by Elisabeth Fischer interviewing Marta Rayo Lunar, *Trial and Error: Site Selection for Clinical Studies*, PHARMACEUTICAL-TECH., <http://www.pharmaceutical-technology.com/features/feature130340/>.

85. See Olivia Diamond, *Overcoming Patient Recruitment and Retention Hurdles*, MEDRIO (Nov. 23, 2015), <http://medrio.com/partners/overcoming-patient-recruitment-and-retention-hurdles/> (reasoning that “Phase I through Phase III trials are, on average, 30% longer than planned due to patient recruitment issues and low patient retention”).

clinical trial, the current process is undoubtedly a driving force in the exploding time and cost associated with drug development.

i. Site Selection and the Impact of Technology

Utilizing a digital site selection program could likely save a huge amount of time and money. The utilization of a digital database for site selection is well within the limits of technology and the law and is already being used in the industry.⁸⁶ Specifically, a central database can store information gathered from prior trials and site-reported experience and competencies. This data can include information about investigators, patients, disease, or conditions and the success rates of sites that hosted trials in the past. With this wealth of information, computer generated algorithms compute and predict which sites would most likely have the optimum results for a specific clinical trial.⁸⁷

This process would save time and money for both the sponsor and the site. Traditionally, every time a site is considered to host a clinical trial, the site must fill out and complete a feasibility survey.⁸⁸ However, in a digital process, a survey would only need to be completed one time, and the answers could be stored in a database. Even Better, potential sites could have access to an online application or profile that they can continually update as the site's specific information changes.⁸⁹

Utilizing a digital process for site feasibility reduces not only time, but also costs associated with printing and mailing surveys required for site selection. Employing a traditional, paper based method, the CRO would send potential sites a survey, wait several days for the site to send it back, and then transform the answers into useful data.⁹⁰ However, if a digital process was utilized, potential sites could answer a survey one time, and then an algorithm would compute the data and suggest the sites that are most likely to be successful for each specific clinical trial.⁹¹

86. See Craig Morgan, *It's Site Selection, Not a Toss of the Dice*, CLINICAL INFORMATICS NEWS (June 28, 2016), <http://www.clinicalinformaticsnews.com/2016/6/27/its-site-selection-not-toss-dice.aspx>.

87. See *id.*

88. See Ed Miseta, *Bring Down The Cost Of Clinical Trials With Improved Site Selection*, CLINICAL LEADER (Dec. 19, 2013), <http://www.clinicalleader.com/doc/bring-down-the-cost-of-clinical-trials-with-improved-site-selection-0001>.

89. See *id.*

90. See Morgan, *supra* note 86.

91. See Miseta, *supra* note 88.

A digital site selection process would result in more accurate data.⁹² If a site is asked to fill out a selection survey once, without the potential reward of a specific clinical trial, the site is more likely to be candid in their responses.⁹³ An approach like this could dissuade a site from responding to selection surveys with an eye toward participating in a specific clinical trial, because inflating numbers in the hopes of getting one trial may be detrimental to getting a better trial in the future.⁹⁴ By utilizing a fully technology based method of site selection, potential sites would only respond to one survey, and would be unable to tailor their responses to a specific clinical trial.⁹⁵ Thus, responses could be more reliable, and thus provide sponsors and CROs with more accurate data, which would hopefully minimize the inclusion of sites that under recruit or are not successful in recruiting any participants.⁹⁶

Further, neither HIPAA nor HITECH would act as a barrier to the industry adopting a digital site selection process. The data needed to create a site selection database would not implicate individually identifiable health information; only specific data points are required. Thus, because the data would not be tied to specific people, and all identifying information could be stripped away, HIPAA's privacy rule would not be implicated.⁹⁷

The logical endpoint of this approach could be a ranking of different sites based on patient recruitment outcomes and success in past clinical trials. However, ranking of sites would necessarily be based only on past performances, and thus would only include the specific trials that the sites had previously hosted. Accordingly, some site representatives agree that this technology would be beneficial to sites too, because it can help determine "which data should be viewed as reliable in predicting future behavior,

92. See Morgan, *supra* note 86 (noting that electronic site selection methods can provide sponsors "with intelligence based on data documenting sites' past performance, size of patient database, staff expertise in certain therapeutic areas, and ability to produce quality data and manage a clinical trial").

93. See Miseta, *supra* note 88.

94. See *id.*

95. See Miseta, *supra* note 88.

96. For a discussion of problems with the current survey method of identifying sites for clinical trials, see *supra* notes 76-85. For a discussion specific to fabrication of survey answers and how technology can improve the process of site selection, see Sameer Tandon, *The State of Feasibility Assessments and Strategies to Improve Your Methodology*, PHARM. OUTSOURCING (Jan. 29, 2014), <http://www.clinicaltrialsarena.com/news/operations/the-state-of-feasibility-assessments-and-strategies-to-improve-your-methodology-4986833> (noting that "[s]ites frequently tell sponsors what they want to hear and this is often in response to the types of questions being asked.>").

97. For a discussion of HIPAA's privacy rule, and how it is implicated by Individually Identifiable Health Information (IIHI), see *supra* text accompanying notes 37-41.

versus which merely reflects the specifics of a particular study.”⁹⁸ Accordingly, a site selection database that is established with collaboration by the sites would include only accurate data, and thus would be beneficial to both sponsors and sites.⁹⁹

b. Document Distribution

Due to the large number of people and entities working together on a clinical trial, communication and information sharing is a critical part of a successful clinical trial. For example, the efficacy of the trial relies on proper distribution of trial related — clinical information.¹⁰⁰ Further, credentials and training materials must be shared among the healthcare professionals and pharmaceutical entities taking part in the trial.¹⁰¹

In small scale, localized, clinical trials, document distribution is not impossibly daunting — most paperwork can be exchanged via trackable delivery methods such as certified mail. However, increasingly in the modern era numerous clinical trials are big, multisite, global projects.¹⁰² These large, multi-site trials are placing new strains on the paper based document distribution framework that some industry participants continue to use.¹⁰³ Further, this problem is unlikely to go away, as clinical trials are steadily growing in size, geographic disbursement, and therefore complexity.¹⁰⁴

98. See Morgan, *supra* note 86.

99. See *id.*

100. See Vito Anthony Losito, *Manage Trial Master Files via Investigative Portals*, APPLIED CLINICAL TRIALS ONLINE (Feb. 1, 2011), <http://www.appliedclinicaltrialsonline.com/manage-trial-master-files-investigative-portals>.

101. See Nick Paul Taylor, *Digital Documents: Can Electronic Tools Ease Biopharma's Clinical Trial File Headaches?*, FIERCE BIOTECH (Jan. 27, 2014 6:57 AM), <http://www.fiercebiotech.com/r-d/digital-documents-can-electronic-tools-ease-biopharma-s-clinical-trial-file-headaches> (noting that “sponsors have formed deep collaborations with service providers” and that “sharing paper documents in an outsourced system is a headache for sponsors, and the problem is magnified by the globalization of late-phase trials”).

102. See *Global Clinical Research Market to Reach \$60 Billion in 2020*, CLINCAPTURE (Nov. 2, 2015), <http://www.clincapture.com/blog/global-clinical-research-market-to-reach-60-billion-in-2020/> (discussing the expected growth of global clinical trials).

103. See Wenle Zhao et al., *An Electronic Regulatory Document Management System for a Clinical Trial Network*, NAT'L CTR FOR BIOTECHNOLOGY INFO. (Jan. 1, 2011), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2829838/> (reasoning that global clinical trials create new challenges for document distribution including “the large number of documents to be collected and maintained, the complexity associated with simultaneous multiple project operations, [and] the need for document file sharing by multiple owners”).

104. See Taylor, *supra* note 101; see also *Global Trends in Clinical Trial Logistics: 2020 Perspective*, COREX, <http://corex-depot.com/expertise/white-papers/global-trends-in-clinical-trial-logistics-2020-perspective/> (last visited Mar. 15, 2017) (discussing the growth of clinical trials on a global scale).

Throughout the clinical trial process, the most important documents and information available to parties in the trial is commonly referred to as the Trial Master File (“TMF”).¹⁰⁵ The distribution of the TMF is crucial to the safety of participants, along with gathering and maintaining critical FDA reportable data throughout the process. Although TMF distribution seems to be a perfect candidate for a transition to electronic distribution, many of the industry leaders in the pharmaceutical arena are hesitant to vacate ink signature forms.¹⁰⁶ However, due to the expected growth of clinical trials, and the trend towards utilizing sites around the world, the traditional paper method of TMF distribution will need to make serious advances in methodology and logistics, or be replaced altogether.¹⁰⁷

i. Document Distribution and the Impact of Technology

The process of document distribution is in serious need of a digital overhaul. Digitizing the document distribution process would save both time and money, and would likely open communication channels between all the parties working on a clinical trial. Instead of sending documents in the mail, instant access is possible in at least two separate ways.

First, the TMF and other important documents can be securely stored on a specific server, which could be accessed remotely.¹⁰⁸ By doing document distribution by remote access, companies minimize the risk of the documents being improperly stored by third parties, lost in transit, or intercepted during transport.¹⁰⁹ Frankly, document distribution would be considered an antiquated term, because the documents are not actually being

105. See Losito, *supra* note 100.

106. See Cutting Edge Information, *By 2020, Global Distribution of Electronic TMF Documents is Projected to Increase 63% Over 2015*, MARKET WIRED (June 8, 2016), <http://www.marketwired.com/press-release/by-2020-global-distribution-electronic-tmf-document-s-is-projected-increase-63-over-2015-2132475.htm> (discussing that some companies “believed signatures shouldn’t be done electronically for their TMF”).

107. See Sheila Mahoney and Toni Lakin, *Moving From Paper to Electronic TMFs*, CONTRACT PHARMA (Oct. 9, 2013), http://www.contractpharma.com/issues/1013/view_features/moving-from-paper-to-electronic-tmfs (noting that when Paper TMFs are “locked away in a file room, other team members need to travel to access it or make special requests for copies to be made”).

108. For an overview and additional background information about remote server access, see *A Beginner’s Guide to Remote Access Software*, REMOTE ACCESS, <http://www.remoteaccess.org/> (last visited Mar. 15, 2017) (positing that “[c]omputing power and network bandwidth have made accessing and sharing data between a variety of different machines across vast distances not only easier but also more secure”).

109. See Kevin Jackson, *The Top 5 Benefits of Remote Network Monitoring*, HELPSYSTEMS (Dec. 14, 2016) <https://www.helpsystems.com/resources/articles/top-5-benefits-remote-network-monitoring> (noting the security benefits of remote access technology when end to end encryption is utilized).

distributed, the login credentials are.¹¹⁰ Instead of sending out copies of the TMF and other documents, one copy of the documents would be saved to a secure server. Then, the company holding the TMF could manage and circulate login credentials. That way, only one copy of the TMF actually exists, but that one copy can be viewed by multiple people simultaneously from around the world.¹¹¹

Further, the pharmaceutical industry's reluctance to adopt electronic signatures is shortsighted.¹¹² Within the TMF, various forms and releases need to be signed by patients and doctors.¹¹³ Since the passage of the E-SIGN Act in 2000, electronic signatures hold the same merit as their ink counterparts.¹¹⁴ Additionally, the E-SIGN Act bars state law from preempting the validity of electronic signatures.¹¹⁵ Although a state may enact their own law in place of the E-SIGN Act, the state statute must "[specify] the alternative procedures or requirements for the use or acceptance (or both) of electronic records or electronic signatures to establish the legal effect, validity, or enforceability of contracts or other records."¹¹⁶

Beyond the ambit of the E-SIGN Act, electronic signatures are also federally regulated.¹¹⁷ These regulations set out separate validation requirements for closed network and open network systems.¹¹⁸ Essentially, the regulations outline higher standards and requirements of authentication

110. *See id.*

111. *See* Jennifer Goldsmith, *Shredding Paper, Saving Cash: Going Digital with a Cloud-Based eTMF*, CLINICAL INFORMATICS NEWS (Oct. 30, 2014), <http://www.clinicalinformaticsnews.com/2014/10/30/shredding-paper-saving-cash-going-digital-cloud-based-etmf.html> (reasoning "cloud-based eTMFs are easily and securely accessible by all parties") (The author also notes that an additional benefit of cloud-based TMF systems is that it allows the sponsor to continually update the TMF and review the TMF to make sure that it stays in compliance with federal and state laws.). *Id.*

112. *See supra* text accompanying notes 100-106. For references to the pharmaceutical industries reluctance to adopt electronic signatures for TMFs, see *supra* text accompanying note 106.

113. *See* Losito, *supra* note 100. (stating that "a TMF consists of thousands of pages, and includes everything from regulatory documents, correspondence, and data to documentation that supports compliance with local regulations").

114. *See* 15 U.S.C. § 7001(a)(1) (2000) (stating that "a signature, contract, or other record relating to such transaction may not be denied legal effect, validity, or enforceability solely because it is in electronic form").

115. *See* 15 U.S.C. § 7002 (2000).

116. *See* 15 U.S.C. § 7002 (a)(2) (2000).

117. *See* 21 C.F.R. § 11.100 (2017).

118. *See* 21 C.F.R. § 11.10 (2017) for a list of the controls utilized for closed network systems; *see also* 21 C.F.R. § 11.30 (2017) for a list of the controls utilized for open network systems. The only difference between the two lists of controls is that the open network systems require all of the protections of the closed system plus "additional measures such as document encryption and use of appropriate digital signature standards to ensure, as necessary under the circumstances, record authenticity, integrity, and confidentiality."

and security for any electronic signatures relating to the Food and Drug Administration and the Department of Health and Human Services.¹¹⁹ However, the regulations clearly state that “persons may use electronic records in lieu of paper records or electronic signatures in lieu of traditional signatures” so long as the requirements of the regulations are met.¹²⁰ Thus, electronic signatures and records are accepted as valid by multiple sources of authority from the federal government, and there is no requirement for pharmaceutical companies to continue to utilize paper-based methods.

Another valid concern with electronic document distribution and storage is the possibility of being the victim of a cyber-attack, or what is more colloquially referred to as hacking. According to the Department of Health and Human Services, since 2010, there have been 240 HIPAA violations resulting from hacking that have affected 500 or more people.¹²¹ Although that seems like a high number, when compared to the 764 incidences of paper, laptop, and desktop computer theft resulting in HIPAA violations during the same time frame,¹²² the risk of being hacked is lower. Additionally, by using proper security software, encryption and protocols, the risk of being hacked can be substantially reduced. Most sophisticated businesses employ appropriate avoidance tactics such as continually updating passwords, utilizing malware-scanning software, and keeping software up to date which drastically minimizes the risk of being hacked.¹²³ So long as affirmative steps are taken to minimize the threat of cyber-attacks, electronic document distribution is an excellent way to minimize costs and save time throughout the clinical trial process.

c. Informed Consent

The most important part of the clinical trial process from a subject protection and ethical viewpoint is obtaining informed consent from the individuals who are participating in the clinical trial. Since the horrors of medical experiments during the Nazi era, and the subsequent adoption of the Nuremberg Code, informed consent has been the touchstone of ethical research.¹²⁴ However, acquiring consent is much more involved than getting

119. See 21 C.F.R. § 11.1 (2016).

120. See 21 C.F.R. § 11.2 (2016).

121. See *Breaches Affecting 500 or More Individuals*, U.S. DEP'T OF HEALTH & HUMAN SERV. OFFICE OF CIVIL RIGHTS, https://ocrportal.hhs.gov/ocr/breach/breach_report.jsf;jsessionid=8E03A0B57574BDB35FF1AEFE5DE51A95 (last visited Mar. 29, 2017).

122. See *id.*

123. See Jason Karn, *The Top 10 HIPAA Violations and How to Prevent Them*, NUEMD (June 16, 2015), <http://www.nuemd.com/blog/top-10-hipaa-violations-prevent-them>.

124. See *History of Research Ethics*, UNIV. OF MISSOURI-KANSAS CITY, <http://ors.umkc.edu>

a signature on a consent form.¹²⁵ Obtaining informed consent requires “full disclosure of the nature of the research and the participant’s involvement; adequate comprehension on the part of the potential participant; and the participants voluntary choice to participate.”¹²⁶ Accordingly, obtaining informed consent should be viewed as a bi-directional and ongoing communication process, not a one-time meeting and one-way disclosure resulting in a signed piece of paper.¹²⁷

Prospective participants of a clinical trial must be fully informed about the potential risks and rewards of participating in the clinical trial, and be given “sufficient opportunity to consider whether or not to participate” in the study.¹²⁸ Unfortunately, explaining the intricacies of a clinical trial may become exponentially more difficult as medicine continues to advance. For example, even the best of clinicians could have a hard time explaining to a patient with no medical background or knowledge how a new, cutting edge medicine is interacting with the body.¹²⁹

Additionally, participants in the clinical trial process must be given the opportunity to ask questions about the treatment, and should be encouraged to seek clarification if they do not comprehend something relevant to the clinical trial.¹³⁰ Unfortunately, providing participants with the opportunity to ask questions can be stifled by two factors. First, some patients may not know what to ask; depending on the complexity of the treatment; individuals may lack the requisite comprehension of the material to ask relevant questions. Second, individuals may be too intimidated or embarrassed to ask

/research-compliance-(iacuc-ibc-irb-rsc)/institutional-review-board-(irb)/history-of-research-ethics (last visited Mar. 29, 2017).

125. See 21 C.F.R. § 50.20 (2017) (listing the requirements for informed consent); see also *Informed Consent for Clinical Trials*, <http://www.fda.gov/ForPatients/ClinicalTrials/InformedConsent/default.htm> (last visited Mar. 26, 2017).

126. See *Required Components of Informed Consent*, CORNELL UNIV., <https://www.irb.cornell.edu/forms/consent.htm> (last visited Mar. 29, 2017) (analyzing the requirements for fully informed consent); see also 21 C.F.R. § 50.25 (2011) (discussing the elements of informed consent specific to clinical trials).

127. See Helen L. Stiffler, *Guidelines for Obtaining Informed Consent for Clinical Research*, APPLIED CLINICAL TRIALS ONLINE (Nov. 2, 2003), <http://www.appliedclinicaltrialsonline.com/guidelines-obtaining-informed-consent-clinical-research>.

128. See 21 C.F.R. § 50.20 (2017).

129. See Jennifer Fong Ha and Nancy Longnecker, *Doctor-Patient Communication: A Review*, 10 OCHSNER J., 38 (Spring 2010), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3096184/#i1524-5012-10-1-38-DiMatteo1> (finding that “75% of orthopedic surgeons surveyed believed that they communicated satisfactorily with their patients, but only 21% of the patients reported satisfactory communication with their doctors. Patient surveys have consistently shown that they want better communication with their doctors”).

130. See *Informed consent for clinical Trials*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/ForPatients/ClinicalTrials/InformedConsent/default.htm> (last updated Feb. 25, 2016).

the research team a question.¹³¹ While these barriers to informed consent seem like speculation, some studies suggest that nearly one out of every five prospective participants in a clinical trial had difficulty understanding the informed consent document, and “15% were not satisfied that their question has been answered during the consent process.”¹³²

As discussed above in connection with trial related document distribution — large scale, global clinical trials are increasing in number.¹³³ As participants and doctors begin clinical trials that cross the globe, increased confusion and lack of comprehension is likely to proliferate commensurate with an international focus which will also bring mounting language barriers.¹³⁴

Although informed consent seems like a minor part of the clinical trial process, it is undeniably a critical aspect of ethical trials and patient care. Unlike a traditional doctor patient relationship, the research team in a clinical trial has a primary goal of scientific and medical advancement, which *can* be at odds with the best interests of the patient.¹³⁵ Thus, for the sake of patient protection, fully informed consent and comprehension of the clinical trial is paramount.

i. Informed Consent and the Impact of Technology

As mentioned previously in this article, some pharmaceutical industry leaders have already begun to adopt electronic informed consent, or “eConsent” systems.¹³⁶ Additionally, in March 2015, the FDA issued draft guidance on the use of electronic informed consent systems, which the FDA defined as “[using] electronic systems and processes that may employ multiple electronic media . . . to convey information related to the study and

131. See *Are You Too Embarrassed to Ask Your Doctor?*, WEBMD (May 9, 2005), <http://www.webmd.com/fitness-exercise/features/are-you-too-embarrassed-to-ask-your-doctor#1> (noting that fear of asking a doctor an embarrassing question is a common phenomenon).

132. See Beverly H. Lorell et al., *Informed Consent in Clinical Research: Consensus Recommendations for Reform Identified by an Expert Interview Panel*, SAGEPUB (July 15, 2015), <http://ctj.sagepub.com/content/12/6/692.full.pdf+html>.

133. See *supra*, text accompanying note 102.

134. See Lokesh P. Nijhawan et al., *Informed Consent: Issues and Challenges*, 4 J. ADV. PHARM. TECH. RES. 134 (2013), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3777303/> (citing language barriers as a challenge in obtaining informed consent).

135. See Benjamin Mason Meier, *International Protection of Persons Undergoing Medical Experimentation: Protecting the Right of Informed Consent*, 20 BERKELEY J. INT’L L. 513, 516 (2002) (noting that “informed consent levels the playing field, providing the subject with the tools necessary to make a decision contrary to the wishes of the physician.”).

136. See Keet and Morrie, *supra* text accompanying note 62.

to obtain and document informed consent.”¹³⁷ Although nothing in the draft guidance is legally binding authority, it sheds light on where the FDA unofficially stands in regards to eConsent adoption.¹³⁸ In fact, the FDA’s draft guidance on the issue suggests that the FDA supports and will permit the use of electronic media in the informed consent process.¹³⁹

Throughout the draft guidance, and in the federal regulations governing consent, the FDA stresses the importance that patients understand the information that is being conveyed to them.¹⁴⁰ This is where the industry can harness the positive potential of eConsent. Instead of a piece of paper with writing on it, a complete eConsent package could be a downloadable file that a potential patient can review at their own pace in the comfort of their home or with their clinician, at the office or via video or telephone.¹⁴¹ Instead of black and white text, the eConsent platform could include videos and interactive charts to keep the patient interested in the material.¹⁴² Additionally, hyperlinks could be utilized to give simple definitions for complicated medical terminology.¹⁴³

Further, it is fully within the realm of technological possibility for real-time chatting to occur between a patient and a medical professional. Subjects could even submit questions anonymously to a centralized database, where they would be stored until an in-person meeting between a group of patients and medical professionals. Doing so could help alleviate anxiety that may come with asking a question in person, and could even help address a common dilemma; patients not knowing what to ask - because of the belief that another patient will ask a question for them.

For confirmation of patient consent review, there is currently technology in development that tracks the eyes of individuals as they read

137. See *Use of Electronic Informed Consent in Clinical Investigations*, U.S. FOOD & DRUG ADMIN. (Dec. 2016), available at <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm436811.pdf>.

138. See *id.* at 5.

139. See *id.*; see also Alexander Gaffney, *FDA Says it’s OK With Modernizing the Clinical Trial Informed Consent Process*, REGULATORY AFFAIRS PROF’L SOC’Y (Mar. 9, 2015), <http://www.raps.org/Regulatory-Focus/News/2015/03/09/21673/FDA-Says-its-OK-With-Modernizing-the-Clinical-Trial-Informed-Consent-Process/>.

140. See U.S. FOOD & DRUG ADMIN., *supra* note 137.

141. See Keet & Morrie, *supra* note 62 (noting the use of text, video, audio, podcasts and interactive web sites disseminate information about the study to patients).

142. See *The Definitive eConsent Solution*, DRUGDEV, <https://www.drugdev.com/solutions/drugdev-econsent/> (last visited Mar. 29, 2017) (noting the use of “explanatory videos, audio narration, and glossary terms to put ‘informed’ back into informed patient consent”).

143. See *id.*

on a tablet or computer screen.¹⁴⁴ Some eye tracking technology “is capable of monitoring your eyes in order to define words if you stare at them puzzled, eliminating non-essential information when you’re skimming” and can even remind the reader of exactly where he or she previously stopped reading.¹⁴⁵ This showcases how eConsent systems can continue to utilize technological advances for the benefit of patients.

Similarly, eConsent management systems can be used to limit the possibility of accidentally sharing a patient’s health records with a party that the patient did not consent to viewing the records.¹⁴⁶ Through the use of “structured data”, or data that a computer can understand and extract discrete elements of, eConsent management systems can control what sections of a patient’s health records may be disseminated to specific parties.¹⁴⁷ For example, the eConsent system can bar one clinician from seeing drug abuse history of a patient, but could allow another clinician to see it if the patient consents.¹⁴⁸ Accordingly, this type of eConsent management system can “ensure[] the sender and receiver are authorized to engage in the exchange” while enforcing applicable federal, state, and local law.¹⁴⁹

III. Policy

Since President Obama’s passage of the American Recovery and Reinvestment Act (ARRA), the digitization of medicine has been on the forefront of the changing legal landscape.¹⁵⁰ Although the ARRA was limited to the adoption of electronic health records in medicine, it set up the framework for technology to play a larger part in all stages of medicine, including clinical trials.

144. See *This is Eye Tracking*, TOBII, <http://www.tobii.com/group/about/this-is-eye-tracking/> (last visited Mar. 29, 2017).

145. See Eliot Van Buskirk, *Eye-Tracking Tablets and The Promise of Text 2.0*, WIRED (Mar. 25, 2010), <https://www.wired.com/2010/03/eye-tracking-tablets-and-the-promise-of-text-20/>.

146. See *Electronic Consent Management: Landscape Assessment, Challenges, and Technology*, MITRE (Oct. 29, 2014), available at https://www.healthit.gov/sites/default/files/privacysecurity/ecm_finalreport_forrelease62415.pdf.

147. See *id.* at 6.

148. See *id.*

149. See *id.* at 6 (reasoning that an eConsent system can “negotiate the entire transaction in an automated way that enforces the patient’s electronic consent directive”).

150. See American Recovery and Reinvestment Act of 2009, Pub. L. No. 111-5, 123 Stat. 115 (2009); see also Sharona Hoffman & Andy Podgurski, 24 BERKELEY TECH. L.J. 1523, 1525 (2009) (listing one of the goals of the ARRA as “spurring technological advances in science and health.”).

In September 2013, the FDA released draft guidance regarding the use of “electronic source data in FDA-regulated clinical investigations.”¹⁵¹ This shows that the FDA is ready and willing to move the clinical trial process into the digital age. Although 21 CFR 11 is dedicated to controls for electronic records and electronic signatures, the references to closed and open systems show how dated these regulations are.¹⁵² Accordingly, although regulatory bodies have been willing to adopt electronic advancements in clinical trials, there is still work to be done.

However, this does not mean that the FDA is fighting an electronic revolution in medicine. To the contrary, they seem to be doing their best to embrace it. In 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) suggested that future FDA submissions for New Drug Applications should only be accepted in electronic format.¹⁵³ The FDASIA stated that this change should take place “no earlier than 24 months after the issuance of a final guidance issued” relating to the process for electronic submissions.¹⁵⁴ This final guidance was published on May 5, 2015,¹⁵⁵ meaning that after May 5, 2017, most drug submissions will need to be submitted to the FDA via electronic submission.¹⁵⁶ Thus, if the submissions need to be in electronic format, that suggests that the data and analytics of the associated clinical trials will be too.

Further, in June 2015, the FDA published a notice in the Federal Register, seeking “demonstration projects to test the capability and evaluate performance of using an end-to-end Electronic Health Record (EHR)-to-Electronic Data Capture (EDC) single-point data capture approach, using established data and implementation standards in a regulated clinical

151. See *Guidance for Industry Electronic Source Data in Clinical Investigations*, U.S. FOOD & DRUG ADMIN. (Sept. 2013), available at <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm328691.pdf>.

152. See 21 C.F.R. § 11.10, 11.30 (2017) (even the FDA has admitted that the references to closed and open systems showcase how dated their regulations are). See Leonard Sacks, *Electronic Technology in Clinical Trials*, U.S. FOOD & DRUG ADMIN. <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM441299.pdf> (last visited Mar. 29, 2017) (noting that the regulations “described an outdated model of open and closed electronic systems”).

153. See Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, § 1136, 126 Stat. 993 (2012).

154. See *id.*

155. See *Providing Regulatory Submissions in electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*, U.S. FOOD & DRUG ADMIN. (May 2015), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM333969.pdf>.

156. See Alexander Gaffney, *FDA to Require Electronic Submission of New Drug, Biologic Files in Next Two Years*, REGULATORY AFFAIRS PROF'L SOC'Y (May 7, 2015), <http://www.raps.org/Regulatory-Focus/News/2015/05/07/22116/FDA-to-Require-Electronic-Submission-of-New-Drug-Biologic-Files-in-Next-Two-Years/>.

research environment.”¹⁵⁷ In response to this notice, the FDA received 41 proposals from interested parties, seeking to “test standards-based technology solutions for collection of related healthcare and clinical research information.”¹⁵⁸ This shows two important developments in the growth of technology and healthcare. First, the FDA is interested in embracing the digital clinical trial process and they want to do so with the guidance of the industry.¹⁵⁹ Second, industry leaders are ready and willing to assist the FDA in establishing workable standards for adopting electronic processes in the clinical trial field.

Moreover, the technological advancements available to facilitate the drug development process are beneficial to all parties involved. As discussed at length above, increasing the use of technology saves time and money for the sponsors and CROs during the developmental stage.¹⁶⁰ Additionally, technology can help the FDA and other regulatory bodies speed up their approval process, by consolidating data into more manageable electronic formats.¹⁶¹ But most importantly, technological advances in clinical trials have the potential to impact patients by speeding up the time it takes new drugs to go from lab to market.¹⁶² The FDA already has guidelines for expediting the approval of new drugs for serious or life threatening diseases.¹⁶³ But the hope for the future is that this “fast-track” would be unnecessary, because technology would allow all drugs to make it through the clinical trial process faster and safer.¹⁶⁴

157. See Source Data Capture From Electronic Health Records: Using Standardized Clinical Research Data, 80 Fed. Reg. 36820, 36821 (June 26, 2015), available at <https://www.gpo.gov/fdsys/pkg/FR-2015-06-26/pdf/2015-15644.pdf>.

158. See *Source Data Capture from Electronic Health Records (EHRs)*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm464653.htm> (last updated Dec. 18, 2015).

159. See *Top eClinical Trends of 2015*, SASCOMMUNITY.ORG (2015), <http://www.sascommunity.org/planet/blog/category/fda/> (noting that the FDA is “embracing technology and opening up a dialogue with experts on how to best channel this revolution in order to advance clinical research.”).

160. See *supra* text accompanying notes 76–149.

161. See Ed Miseta, *The Future of Data and Technology In Clinical Trials*, CLINICAL LEADER (Mar. 22, 2016), <http://www.clinicalleader.com/doc/the-future-of-data-and-technology-in-clinical-trials-0001> (noting the importance of technology changing how data is managed).

162. See *infra* text accompanying notes 163–164.

163. See 21 U.S.C. § 356 (2016) (stating the process for “expedited approval of drugs for serious or life-threatening diseases or conditions”).

164. See Danielle Dupont, *The Future of Clinical Research: Developing New Drugs Faster Using Electronic Health Records*, ATLAS OF SCIENCE (Jan. 12, 2016), <https://atlasofscience.org/the-future-of-clinical-research-developing-new-drugs-faster-using-electronic-health-records/> (suggesting that the use of Electronic Health Records could speed up clinical trials in the future); see also Bill Gwinn, *Understanding Feasibility For Faster Clinical Trials*, CENTERWATCH (Jan. 1, 2016), <http://www.centerwatch.com/news-online/2016/01/01/understanding-feasibility-faster->

There is no doubt that technology is changing the healthcare industry.¹⁶⁵ The governing bodies charged with overseeing medicine and healthcare seem to be embracing the change, albeit rather slowly. However, slow change is better than no change, and as technological advancements continue to change the way humans address healthcare, those same changes can be adopted to speed up the process of clinical trials and drug development. Although there may be instances where parties risk exposure to greater liability by embracing technology — that is a risk that the industry as a whole should accept. The end goal of pharmaceuticals is to produce new treatments and cures for diseases, and any perceived, slight increased risk, if any, for achieving that end should not be a bar to the accelerated adoption of technology.

clinical-trials/ (noting that technological advances in site feasibility selection can speed up the time of clinical trials).

165. See *3 Ways Technology Has Changed Healthcare*, UNIV. OF ILL. AT CHI., <http://healthinformatics.uic.edu/resources/articles/3-ways-technology-has-changed-healthcare/> (last visited Mar. 29, 2017).