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FDA Regulation in the Data-Driven Economy

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INTRODUCTION

The shift to data-driven growth is one of the most important forces behind the strong performance of the U.S. economy in recent years. Online sales are up by 16% over the past year,[1] and Americans are getting more and more of their information online. Indeed, data-related products and services account for roughly 30% of real personal consumption growth since 2007, second only to the 40% coming from the growth of healthcare-related goods and services.[2]

Yet regulators are struggling to keep up with the digital age. The accumulation of regulations designed for a slower, information-poor age fail to take advantage of new opportunities to improve outcomes while still protecting consumers. The issue of how to regulate in the data-driven economy has been widely discussed, including in several policy papers by the Progressive Policy Institute. For example, our proposal for a Regulatory Improvement Commission, designed to relieve the build-up of outdated and duplicative regulations over time, has been written into legislation and introduced in both the House and Senate.[3]

The Food and Drug Administration (FDA), in particular, is facing a variety of regulatory issues which involve the intersection between the data-driven economy and the more traditional world of health-related regulations. For example, the FDA took a carefully balanced approach in its rulemaking on mobile medical applications, choosing to exercise enforcement discretion, instead of regulating apps that do not track medical information, such as counting calories.

At the same time, a new measure presented in this paper shows the amount of regulation on the pharmaceutical industry has increased 40% since 2000. Moreover, not all the increase in FDA regulations embrace data-driven innovation.

The FDA has recently issued several draft guidelines which would effectively restrict

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communication from drug and medical device manufacturers to both healthcare professionals and the general public. For example, a draft guidance issued in June would impose onerous requirements on companies that wish to use social media, such as Twitter, to provide consumers with information about prescription drugs or devices.

This paper focuses on one draft FDA guidance, issued in February 2014, entitled "Guidance for Industry: Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices."[4] The document lays out a lengthy list of rules and restrictions for how drug and medical device manufacturers are allowed to communicate with healthcare professionals and "healthcare entities," such as hospitals, on unapproved new uses. For example, the scientific or medical journal article distributed by a manufacturer should "[c]ontain information that describes and addresses adequate and well-controlled clinical investigations."

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In a world with an ever-increasing stream of information, the FDA's restrictions, however well-intentioned, have the air of King Canute trying to hold back the tide. In the past, news about unapproved uses was limited and hard to obtain. Now, just a few Google searches can bring vivid anecdotes. Moreover, the growing use of electronic health records and other "big data" is going to bring a flood of potentially useful information about patient outcomes that does not fit the classic model of controlled clinical studies.

Additionally, this paper argues that physicians and other healthcare professionals are likely to be "sophisticated users of information." That means they are able to use "truthful and non-misleading" information to improve patient outcomes. As such, the FDA would be better off embracing the broad range of information generated by the data-driven economy, rather than trying to pre-emptively restrict its dissemination. This paper analyzes the FDA's draft guidance and makes recommendations for how the FDA can modify the draft regulation in a way that takes full advantage of the power of data. The framework for the FDA's regulatory approach should be to treat healthcare professionals as sophisticated users of information.

This paper begins with an overview of the rise of the data-driven economy and its impact on regulation. It then examines the broad trend of regulatory accumulation, as it applies to the pharmaceutical industry.

Next, the paper discusses the FDA's draft guidance and explains why it is not adequate for the digital age. Finally, recommendations for the draft guidance are provided, and the paper concludes with an expansion of the discussion to how this case study can serve as an example for regulators struggling with rulemaking in this time of unprecedented economic transformation.

THE DATA-DRIVEN ECONOMY

We live in a data-driven economy. Innovations in high-speed Internet connectivity, smart devices, and large-scale data storage have transformed how we do business, consume goods and services, and communicate. And by many accounts, this is only the beginning. We are headed for a future world that is interconnected, where traditional boundaries between industries—and nations—become blurred.[5] Every aspect of our lives, from our homes to our cars, will be completely integrated.

Previous PPI research has documented the data-driven economy as the driving force behind the economic recovery and corresponding job creation since the Great Recession.[6] For example, PPI Chief Economic Strategist Michael Mandel estimated that more than 750,000 jobs have been created in the United States as part of the "App Economy," since the iPhone first hit the market in 2007.[7] This includes direct and indirect jobs tied to the design and development of mobile applications.

Moreover, forthcoming PPI research will demonstrate that the data-driven economy has tremendous power to educate, lift incomes, and be an engine of social and economic mobility. Starting a business can be as simple as having a computer and an Internet connection.

There is little question that the United States has been a leading force for data-driven innovation, fueled by consumer demand. At the end of 2013, there were over 335 million wireless subscriptions in the United States,[8] more than the national population. Data consumption on mobile devices doubled from 2013 and is forecast to increase by another 650% through 2018.[9]

PPI's work on the data-driven economy also includes informing the policy conversation surrounding the economic potential of data. We believe that with so much at stake, it is essential to make sure that legislators and regulators have the best information. This is especially true since, as an intangible good, the economic footprint of data is not easy to measure.

REGULATION IN THE 21ST CENTURY

The rise of the data-driven economy has raised many questions for federal regulators. Major controversies on issues like data privacy, data localization, and even data taxation have grabbed national headlines with regulators scrambling to respond.

The problem, however, cannot be blamed merely on out of touch regulators. It is the unprecedented pace of data-driven innovation that our regulatory system is not equipped to deal with. Regulation in the 21st century requires an entirely new way of thinking: an approach to rulemaking that is dynamic and adaptive. It must recognize that traditional definitions of "industries" and "competition" are evolving into "ecosystems" and "connectedness." Our current system is designed for a different era of rulemaking, working off processes and definitions that harken back to the days of telephones, railroads, and big oil.

Yet it is up to regulators to modernize our regulatory system to embrace the data-driven economy. As part of this effort, PPI has undertaken extensive research on regulation in the 21st century, aimed at guiding regulators and policymakers through this transition. Our work strives to strike the right balance between protecting consumers and encouraging innovation in an interconnected world.

The natural buildup of regulations over time threatens to block the future flow of investment and innovation. Yet nowhere in our regulatory system is there a mechanism in place to objectively review and either remove or improve outdated, conflicting, or duplicative rules. To address this problem—what we call 'regulatory accumulation'—we proposed the creation of an independent Regulatory Improvement Commission (RIC).[10] The RIC would be authorized by Congress on an as-needed basis, taking suggestions from the public on which regulations to review, before sending back to Congress a package of recommendations for an up-or-down vote. The RIC proposal has been introduced as bi-partisan legislation in both the House and Senate.

The rise of the data-driven economy has raised many questions for federal regulators.

PPI has also written on how regulators should approach the so-called 'Internet of Everything'—the expansion of Internet-connectivity to physical objects.[11] In a future defined by the Internet of Everything, devices will become increasingly interconnected. The established jurisdiction of individual regulatory agencies will become blurred as physical objects and the services and data they provide become intertwined. This will require cross-collaboration and coordination across agencies.

Our research has even explored specific cases of regulators struggling to meet the demands of 21st century rulemaking. A previous PPI paper explored the case of the Food and Drug Administration's (FDA) review of MelaFind.[12] MelaFind, a device

that assists in the detection skin cancer, is an innovative and cost-saving approach to diagnosing skin lesions. However, upon its initial review, the FDA rejected MelaFind's application for approval. PPI argued at the time that the FDA failed to consider the productivity-enhancing potential of MelaFind, and should reconsider their decision. The potential for cost-saving technological innovation should always be a positive factor in the consideration of an application for approval.

Ultimately, the FDA reversed course and approved MelaFind, an important step in acknowledging the value of data-driven innovation. The MelaFind case highlights the need for regulators at the FDA and across all regulatory bodies to adapt to the realities of the digital age. MelaFind was not the first such regulatory skirmish, and, until regulators adopt a consistently pro-innovation approach to rulemaking, it will not be the last.

FDA REGULATION OF PHARMACEUTICAL COMPANIES

Few sectors of the economy stand to benefit more from data-driven innovation than healthcare. In fact, ongoing innovation in the design and delivery of patient treatment could transform the entire healthcare system, dramatically reducing healthcare costs while bringing enormous improvements to public health. For example, a new initiative from The Science Coalition, Science 2034, sees a future where clinical medicine and customized diagnosis come together to create an entirely new model of healthcare delivery—calling it nanomedicine.[13] A 2013 McKinsey study estimated that data-driven innovation in healthcare could reduce annual spending by up to $450 billion.[14]

Yet part of regulating healthcare in the data-driven economy means making sure that outdated, duplicative, and conflicting rules are not getting in the way. That means being mindful when rulemaking about the possible interaction with existing rules and evaluating whether the older rules are still necessary and applicable.

Consider the FDA's regulation of pharmaceutical companies. The FDA and its rulemaking will play a major role in realizing the potential of the data-driven economy.

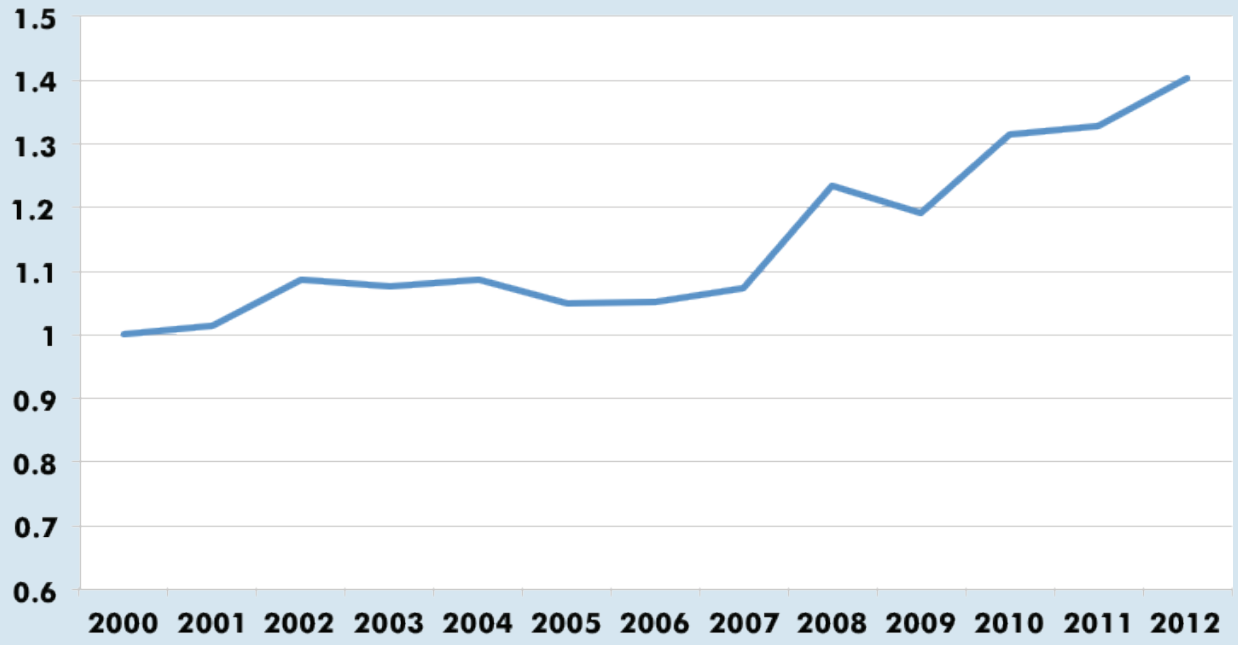
Our analysis shows the pharmaceutical industry has experienced a significant rise in FDA-imposed regulation since 2000. As evidenced in Figure 1, the number of 'restrictions' on drug companies increased by 767, or 40% since 2000. This represents a substantial rise in the overall regulatory burden of pharmaceutical companies, which must allocate resources to ensure regulatory compliance. The word "restriction" refers to command clauses such as "shall" and "must," as contained in sections of the Code of Federal Regulations related to the FDA.

Few sectors of the economy stand to benefit more from data-driven innovation than healthcare.

This analysis employs metrics derived from a novel dataset from the Mercatus Center.[15] It uses a semantic analysis of regulatory language in the Code of Federal Regulations (CFR), looking at the number of FDA-imposed restrictions on the pharmaceutical industry. We then index the number of restrictions over time, using each issue of the CFR since 2000.

The significant—even if unintentional—regulatory accumulation for pharmaceutical companies over time could have a negative effect on healthcare costs and productivity. That's because healthcare is a notoriously low-productivity sector, which has not taken full advantage of cost-saving technological advancements. In fact, PPI research has shown that the number of healthcare employees has been growing faster than the patient population, so that what we call 'gross medical productivity'—the number of potential patients per healthcare worker—is falling.[16] Adoption of labor-saving technology is the best way to reverse this trend, freeing up valuable resources while improving patient outcomes. But our regulatory environment must encourage such adoption.

FIGURE 1: INCREASE IN FDA REGULATORY RESTRICTIONS ON PHARMACEUTICAL COMPANIES* (2000=1)



**Defined as Pharmaceutical and Medicine Manufacturing Companies, NAICS 3254*
Note: Restriction refers to command clauses such as "shall" and "must," as contained in sections of the Code of Federal Regulations related to the FDA.
Source: Mercatus Center RegData 2.0, PPI

CURRENT RULEMAKING: A CASE STUDY OF FDA GUIDANCE

In 2014, the FDA issued several draft guidelines related to pharmaceutical and medical device companies' ability to communicate with healthcare professionals, researchers, and the general public. This included guidance about medical and scientific reprints for healthcare professionals, social media communications criteria, and reporting requirements regarding certain types of communication with the public.

Although all of these draft guidelines raise concerns about regulating the data-driven economy, this paper focuses on recently proposed guidelines for how drug and medical device companies communicate with healthcare professionals. In addition to doctors and medical professionals, this guidance also include insurance professionals, pharmacists, benefits managers, and federal and state government agencies.

Called "Distributing Scientific and Medical Publications on Unapproved New Uses," the FDA draft guidance focuses on the distribution of scientific and medical research on new or alternative uses for previously approved drugs and devices.[17] The guidance covers the circumstances by which pharmaceutical and medical device companies can share relevant medical and scientific journal articles, texts, and clinical practical guidelines (CPG), with healthcare professionals, either in-person or electronically.

Issued in February 2014, the draft guidance is expected to be finalized later this year.[18] The

intention behind the draft guidance is to provide a framework—a "safe harbor"—for sharing new research on unapproved uses in a way that frees drug and medical device companies of liability. If drug and medical device companies meet the criteria laid out in the guidance when sharing information with healthcare professionals, the FDA will not deem that an effort to market the drug or device for an unapproved use.

The FDA considers scientific or medical journals articles, texts, and CPGs separately. It gives a lengthy, although similar, set of criteria for each regarding required content and delivery methods. It also lists criteria for what constitutes ineligible scientific and medical publications for distribution.

> The February 2014 draft guidance lays out a similar set of requirements as the 2009 rules. However, it deviates from them in one critical way.

The guidance begins by requiring that all information-sharing within its scope must be truthful and non-misleading. There are also some standard requirements; for example, the research must be peer-reviewed and unabridged. It also cannot contain information that would result in harm if the medication was used in the manner described.

From there, it gets a bit more complicated—and restrictive. For example, the guidance requires that the research be based on "adequate and well-controlled clinical investigations," excluding studies based on real-world observational data. It also requires the publication not be "written, edited, or significantly influenced by" anyone having a financial relationship with the drug or medical device company whose product is being discussed.

The draft guidance also requires a slew of information be distributed alongside each medical or scientific publication. This includes a comprehensive bibliography of related publications and other research on the unapproved use that reaches a different finding or conclusion. It also requires that "permanent affixed statements" cover the shared publication, which includes disclosures on the drug or medical device company and the possibility of financial conflicts of interest.

Yet another restriction contained in the draft guidance applies to dissemination of scientific or medical reprints at medical conferences. Specifically, it bars sharing such material in exhibit halls or during any promotional speakers' programs, regardless of whether such information-sharing can be reasonably or easily partitioned.

For example, consider a study funded by a pharmaceutical company using real-world "big data," collected through apps, that documented vital statistics and mobility after patients use a medication developed by the company. Suppose the medication was intended to prevent high cholesterol, but the study also found patients had lower blood pressure after adjusting for exercise. The draft guidance would not allow this study to be shared with healthcare professionals, because it was not based on a clinical trial, in addition to being funded by the pharmaceutical company—even if it meets the criteria for being truthful and non-misleading.

We note there are several narrow exceptions to the restrictions listed in the draft guidance. Namely, pharmaceutical companies can provide a limited amount of off-label pharmacoeconomic data to drug formulary committees—committees that determine the drugs covered under a given healthcare insurer—even if it is not based on adequate and well-controlled clinical investigations.[19] There is also an exception for doctors who initiate off-label questions to a pharmaceutical company, which can only be answered one-on-one. However, it is not clear it if or how frequently these exceptions are used given their limitations. Moreover, is not clear if the guidance will supersede these exceptions once finalized.

The draft guidance is a follow-up to rules originally issued in 2009 but never finalized. Those rules followed the sunset of legislation in 2006 that had previously governed the transferal of medical and scientific information from drug and medical device companies to the healthcare community.

The February 2014 draft guidance lays out a similar set of requirements as the 2009 rules. However, it deviates from them in one critical way. The 2009 draft guidance explicitly emphasized the positive impact on public health from health professionals having access to research on alternative or unapproved uses. Consider this excerpt from the 2009 guidance not included in the 2014 version:

> "FDA does recognize … These off-label uses or treatment regimens may be important and may even constitute a medically recognized standard of care. Accordingly, the public health may be advanced by healthcare professionals' receipt of medical journal articles and medical or scientific reference publications on unapproved new uses of approved or cleared medical products that are truthful and non-misleading."[20]

The prevailing presumption in the 2009 rules was that more data can empower healthcare professionals and improve public health. The guidance genuinely provided an environment that enabled the exchange of information.

> Physicians are the closest equivalent to "sophisticated users of information."

Now the prevailing presumption seems to question the motives of drug and medical device companies. The FDA appears to pre-emptively regulate with suspicion. This attitude makes information-sharing seem risky and unattractive. It does little to show support for the power of information in a data-driven world.

POTENTIAL IMPACT OF THE GUIDANCE

Is the draft guidance right to pre-emptively limit the potential for information-sharing in healthcare? In order to provide a theoretical framework for this analysis, let us define what it means to be a **sophisticated user of information**:

> A sophisticated user of information has sufficient experience and knowledge to correctly use new truthful and non-misleading information to improve average outcomes.

This definition is analogous to the concept of a "sophisticated investor" in financial services, as defined by the Securities and Exchange Commission (SEC). A sophisticated investor:

> must have sufficient knowledge and experience in financial and business matters to make them capable of evaluating the merits and risks of the prospective investment.[21]

Financial services are allowed to offer a wider range of investments to sophisticated investors, under the assumption that they are capable of making informed decisions. There is extensive literature about the importance of sophisticated investors to soundly functioning financial markets. For example, in 2009 Jeremy Stein, then president of the American Finance Association, gave the annual presidential address on the topic of "Sophisticated Investors and Market Efficiency."[22]

In the U.S. healthcare system, physicians are clearly the closest equivalent to "sophisticated users of information." They have gone through many years of education and training, and typically have substantial experience practicing. More broadly, any healthcare professional involved in prescribing medication or devices must have a registration number issued by the Drug Enforcement Administration, which in turn requires applicants have a state-issued medical license.[23] The requirements for state licensure vary by state, but all require a medical degree, post-graduate training or residency, and the passing of the U.S. Medical Licensing Examination.[24]

From that perspective, does it make sense to restrict data flows from pharmaceutical and medical device companies to highly-trained physicians and other health care professionals as tightly as the guidance requires? There are three issues:

1. What does "truthful and non-misleading" mean?
2. Are physicians and other healthcare professionals truly "sophisticated users of information"?
3. If healthcare professionals are not sophisticated users of information, are patient outcomes improved more by restricting the flow of information or by training these professionals to be better users of information?

In today's data-rich economy, we now have access to stunningly large flows of relevant information that never existed before, generated in the ordinary course of doing business. For example, part of the benefit of the investment in electronic health records is that they allow broad collection of data on health events, treatments, and outcomes. This data by definition cannot meet the highest standards of clinical studies, since treatments are not randomized or double-blind and the patient pool is not random. However, analyzing the data for patterns is potentially very productive, both for improving patient outcomes and directing future clinical research.

> It is possible to incorporate changes into the FDA draft rules that both encourage greater information-sharing and promote improvements to public health.

Other types of potentially useful data could include pharmacoeconomic studies, clinical trials for sub-populations, meta-analyses, and real world observational data that do not currently meet the narrow set of requirements laid out in the FDA draft guidance. And although such information could not be shared under the draft guidance, healthcare professionals can already access many of these types of studies online.

From this perspective, "non-misleading" data would involve a sufficient description of the data to allow sophisticated users of information to correctly integrate it into their existing internal diagnostic and treatment models. That might include where it came from, the size of the sample, and potential biases.

Assuming that physicians and other healthcare professionals are sophisticated users of information, it makes sense to give them as much access to truthful and non-misleading information as possible. For example, according to the National Cancer Institute, the use of off-label drugs is very common in treating cancer patients.[25] This is because drugs are typically approved for one stage of a certain cancer, but research has shown these drugs to be effective across different types of cancers or in other stages. If new research, based on observational data, reveals a new use in treating or managing cancer for an already approved drug, such information should be shared with healthcare professionals. It would allow healthcare professionals to fully evaluate the costs and benefits across treatments, comparing an alternative drug therapy to surgery or other medical devices.

So the question of data restrictions, as proposed by the FDA, depends on whether physicians and other healthcare professionals are actually sophisticated users of information. Of course, since the healthcare system is currently built on diagnosis and treatment decisions by healthcare professionals, it is appropriate to point out that unsophisticated information processing by these professionals would pose a bigger problem for the healthcare system than simply whether they receive an extra email or two from a drug or medical device company.

If physicians and other healthcare professionals cannot handle new healthcare information correctly, a case could be made for restricting data

flows from pharmaceutical and medical device companies. But at the same, if these professionals are assumed not to be good gatekeepers, a case could also be made to allow drug and medical device companies to provide more information directly to consumers.

However, there is another solution. Rather than restricting information, pharmaceutical and medical device companies should be allowed to provide information as long as they provide training to the average working physician and other healthcare professionals on the best use of new information.

RECOMMENDATIONS

How can the FDA modify the draft guidance in a way that embraces data-driven innovation? We believe it is possible to incorporate changes into the draft rules that both encourage greater information-sharing between pharmaceutical and medical device companies and healthcare professionals and promote improvements to public health. We hope the FDA can use these recommendations in their efforts to finalize the draft guidance.

To start, we call for a change in the FDA's underlying presumptions. The FDA should recognize that healthcare professionals are sophisticated users of information, and craft rules accordingly. For healthcare professionals, more access to data and treatment information is better than less. In this regard, protecting patients and smart, digital age regulation go hand-in-hand.

Such a shift would enable the FDA to focus less on micromanaging how information is shared and more on ensuring that the information shared is truthful and non-misleading. The need for information quality control is constant, no matter how fast markets are changing.

Instead of pre-emptively restricting information, the FDA should enforce the standard of truthful and non-misleading information by acting upon cases where information is shown to be false, misleading, or to cause harm. Healthcare professionals would be empowered to make their own determinations about the usefulness of the information as it relates to their patients.

Of course, there is risk in putting fewer restrictions on information, especially information that could affect public health. However, if healthcare professionals are sophisticated users of information, this risk decreases. At the same time, there is a cost to not sharing potentially valuable information, especially if it could help manage a serious condition or maintain a certain quality of life for someone with a chronic disease.

The FDA should enforce the standard of truthful and non-misleading information by acting upon cases where information is shown to be false, misleading, or to cause harm.

The FDA is right to create a safe harbor for pharmaceutical and medical device companies that share information with healthcare professionals. Companies should not be sued for good-faith efforts to provide health professionals with information that could help them do their jobs better. But the FDA should consider changes in its safe harbor framework.

First, the FDA should broaden the safe harbor protections in the draft guidance by eliminating restrictions that medical research be based on "adequate and well-controlled clinical investigations" and not "written, edited, or significantly influenced by" anyone having a financial relationship with the drug or medical device company whose drug or device is being discussed. As long as the information is truthful and non-misleading, the FDA should not restrict it.

Broadening the safe harbor in this way also would permit other types of data and information to be shared. This includes pharmacoeconomic reports, meta-analyses, and other big data-

driven healthcare studies based on real-world or observational, structured or unstructured data.

Second, the FDA should make changes that enable information to be more easily shared digitally. The current draft guidance is full of requirements on what information must be provided alongside any medical or scientific research being shared, many of which are impractical for the digital age.

For example, instead of requiring that the full text of the approved labeling information be provided alongside shared research, a link to that information should be sufficient. It is worthwhile to also review whether requirements for "permanently affixed statements" of stickers or stamps denoting disclosures by the drug or medical device company, and the inclusion of a comprehensive bibliography of related research, are necessary or could be revised to be more Internet friendly.

Making such digital-friendly changes would also be consistent with Congress' 21st Century Cures initiative.[26] The initiative, launched in May 2014, seeks to encourage innovation in healthcare design and delivery by harnessing the power of the Internet to facilitate communication among doctors, patients, researchers, and industry professionals. It describes communication as "the free flow of data, research, and results related to what a therapy or combination of therapies does or does not do well and in what types of patients."

Finally, the FDA should explicitly affirm the principle in its 2009 rules that the interests of public health are served when healthcare professionals have access to information on unapproved new uses of approved drugs and medical devices. Acknowledging that the FDA supports such information-sharing will send a clear message to the healthcare community that the FDA is not "out to get them," but rather out to help them help patients.

Moreover, it will send a clear message to other regulators, both within and outside the FDA, on how to think about regulating in a data-driven economy. This would be a critical step in the right direction, taken at a time when the potential for data-driven innovation has never been greater.

As written, the draft guidance may actually harm consumers more than protect them. Too many restrictions could make pharmaceutical and medical device companies decide against sharing valuable information. The result would be to deny healthcare professionals the knowledge and power to provide the best treatments for their patients.

THE MESSAGE FOR REGULATORS

Regulating for the 21st century requires more than good intentions. It requires a change in mindset. The data-driven economy has the potential to transform every sector of the economy to the benefit of consumers, but only if the regulatory environment is right. That means regulating in a way that encourages data-driven innovation while protecting consumers.

Regulators should recognize that encouraging innovation does not necessarily come at the cost of consumer welfare—in fact, as argued in this paper, it could very well enhance it.

It's time to reframe the conversation about regulation in the 21st century. In a data-driven economy, regulators should encourage greater information-sharing, instead of pre-emptively regulating information in a way that controls and ultimately restricts it. Regulators should take the role of watchful guardians over data and information flows, taking action when there is evidence of harm or injury. In the case presented here, we believe healthcare professionals would best serve their patients through access to more information, not less.

We hope that regulators within the FDA and across other regulatory agencies will be able to use this example as a guide for approaching future regulatory questions surrounding data. Embracing the data-driven economy is the best way to promote future prosperity and well-being for all Americans.

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About the Progressive Policy Institute

The Progressive Policy Institute (PPI) is an independent research institution that seeks to define and promote a new progressive politics in the 21st century. Through research, policy analysis and dialogue, PPI challenges the status quo and advocates for radical policy solutions.

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