

Editorial

A Clinical Trial for the Food and Drug Administration's Clinical Trial Process

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ABSTRACT

The U.S. Food and Drug Administration (FDA) is tasked with opposing goals which demand tradeoffs—the time and cost of clinical trials to assure safety and efficacy while also encouraging speedy drug advances and affordability. On top of that, there is no feedback mechanism to inform the FDA of the effectiveness of their tradeoff decisions. Dual Tracking is a proposed public policy field experiment that would provide needed feedback information. The proposal is rooted in the right of informed patients to choose among FDA-approved or new, experimental drugs still in clinical trials. All new drugs would continue along the FDA's clinical testing track. On a new track independent of the FDA (but only after successful FDA Phase I safety evaluations), drug development firms would have the option to legally contract with individual patients and their doctors to sell them a not-yet-FDA-approved drug. The contract would require ongoing Internet reporting in a specified format of all drug-related experiences. The results of the Dual Tracking process compared to the FDA's process would constitute the critical information now missing.

As many people know, before medical drugs and devices can be made available to the public in the United States approval is required from the U.S. Food and Drug Administration (FDA). The FDA's mission statement (www.fda.org) contains conflicting cost/benefit goals:

The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public

health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.

Daniel Klein and Alexander Tabarrok¹ have assembled a large body of research on the FDA at www.fdareview.org and, as to the FDA's effectiveness, they conclude:

We argue that FDA control over drugs and devices has large and often overlooked costs that almost certainly exceed the benefits. We believe that FDA regulation of the medical industry has suppressed and delayed new drugs and devices, and has increased costs, with a net result of more morbidity

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and mortality. A large body of academic research has investigated the FDA and with unusual consensus has reached the same conclusion.

The problem is a contemporary one because, prior to 1962, the FDA required only that developmental drugs pass a clinical trial for safety, allowing efficacy to be determined by experience in use. During the last four decades, the FDA's regulation requirements for efficacy testing have greatly expanded. Both Congress and the general public have been eager to give the FDA greater power whenever a highly publicized incident of harm attributed, rightly or wrongly, to drugs has occurred.

The potential "cost" to FDA officials *personally* via public humiliation from the media, affected patients, and politicians for approving a drug which subsequently proves to be "unsafe" far outweighs any *personal* "benefit" for more quickly approving an effective new drug. Henry Miller,² who has had extensive experience working at the FDA and has been a frequent FDA critic, noted an example of the risk-averse mindset so prevalent throughout the FDA:

In the early 1980s, when I headed the team at the FDA that was reviewing the NDA [new drug application] for recombinant human insulin, . . . we were ready to recommend approval a mere four months after the application was submitted (at the time when the average time for NDA review was more than two and a half years). With quintessential bureaucratic reasoning, my supervisor refused to sign off on the approval—even though he agreed that the data provided compelling evidence of the drug's safety and effectiveness. "If anything goes wrong," he argued, "think how bad it will look that we approved the drug so quickly."

Because the responsibilities Congress has assigned to the FDA are in conflict—safety and efficacy versus time and expense—a classic *trade-off dilemma* has been created for FDA officials tasked with implementing its mission. More extensive clinical testing increases the chances of identifying adverse side-effects and provides more reliable assessments of efficacy, but it also *raises prices* of approved drugs to compensate drug companies for highly expensive clinical trials on failed drugs, as well as the relatively few

approved ones. Additionally, society incurs a cost in the form of *time delays* before helpful/life-saving drugs become available to those who would benefit. This paper lays out a solution to resolve the FDA's tradeoff dilemma, which also overcomes various criticisms directed at the FDA.

Proposed solutions from FDA critics, for the most part, fall into two groups. One group believes that the FDA's extensive clinical testing for efficacy should be replaced with an unregulated, market process.^{2,3} These critics support a return to the pre-1962 era when the FDA was responsible for safety evaluations only. The other group accepts the full regulatory role of the FDA but recommends substantial restructuring to improve efficiency. A prime example is Henry Miller's⁴ plan to outsource clinical testing to nongovernmental, FDA-certified entities.

The approach taken in this paper rests on having identified Congress as the root cause of, yet solution to, the tradeoff dilemma. The basic problem is that Congress set into motion a bureaucratic agency without a *feedback mechanism* to evaluate operational efficiency. The basic solution is for Congress to legislate an appropriate feedback mechanism to provide the needed information.

Therefore, an argument is herein presented to justify legislation for a large-scale, public policy field experiment to implement a feedback mechanism which would function separately from the FDA, but as an integral part of the U.S. drug development and testing system.

A proposed Dual Tracking (DT) solution is rooted in the right of *informed* patients, along with their doctors, to choose among FDA-approved or new, experimental drugs still in clinical trials. On one track, a new drug would continue along the conventional FDA clinical-testing procedures. On a new, separate track independent of the FDA (but only after the successful completion of FDA Phase I, toxicity and safety evaluations), drug development firms would have the option to legally contract with consumers (individual patients) to sell them a not-yet-FDA-approved drug.⁵

Mandatory Internet posting of all in-process and final results of using a drug, including adverse side-effects, would continually inform patients and their doctors about potential risks, as well as potential benefits, so they could make sound decisions for their specific situations. Post-

ings would also block litigation based on claims that useful information was withheld.

Figure 1 below positions the Dual Tracking proposal as part of an expanded system for the development and testing of drugs. Regardless of one's political affiliation, *access and freedom of choice* to try to improve or save the life of oneself or a family member is an extraordinarily powerful rallying call, offering real potential for cross-party political cooperation.

The remainder of this paper analyzes the new components of the expanded system, its benefits, and explains how Dual Tracking can resolve the FDA's tradeoff dilemma. Section I describes the DT process and the information it would generate for better judging if the status quo FDA produces benefits in excess of costs and if the tradeoff choices might be improved. Section II analyzes how Dual Tracking would overcome the limitations of the current one-size-fits-all regulatory scheme. It explains how the tradeoff dilemma is dealt with by *segmenting* consumers (patients) based on their revealed preferences for risk. Section III focuses on drug innovations. Dual Tracking combines doctors' diagnostic skills and their motivation to improve the health of individual patients with drug developmental firms in a more flexible, collaborative learning experience. Section IV discusses major potential changes to the drug industry if Dual Tracking becomes a permanent part of the U.S. drug development and testing system. Section V discusses the advantages of DT legislation as an initial step along an evolutionary path of FDA improvement.

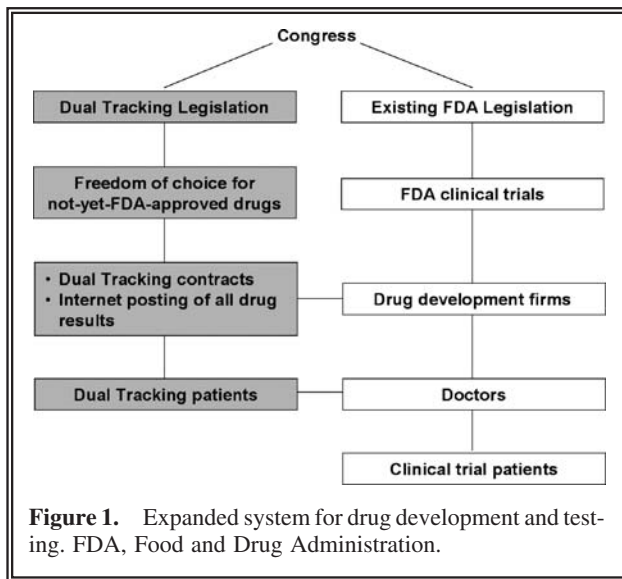


Figure 1. Expanded system for drug development and testing. FDA, Food and Drug Administration.

Dual Tracking is a Feedback Mechanism

Will FDA officials be likely to embrace Dual Tracking as a route out of its tradeoff dilemma? Dual Tracking seems to be at odds with a core assumption underpinning the FDA regulatory mindset that individuals (and their doctors) are not capable of deciding to use not-yet-FDA-approved drugs. In contrast, a core assumption of Dual Tracking is that some people (advised by their physicians) most assuredly are capable if pertinent usage information is available. If Congress will pass appropriate legislation, the Internet could be used to inform consumers about potentially useful drugs that are progressing through Phase II and III of FDA testing or have completed them and are awaiting a final NDA decision.

For example, let's assume a firm completes a Phase I clinical trial, satisfying the FDA's safety concerns for a drug to treat ALS (amyotrophic lateral sclerosis), the fatal neurological disease that killed baseball great Lou Gehrig. Let's further assume that clearly favorable results had been documented for a small sample of patients in the early portion of the Phase II trial addressing drug dosage. At that point, the firm could elect to use Dual Tracking and post data on the Internet covering Phase I and the ongoing Phase II trial.

It is important that as part of the legislation authorizing Dual Tracking, a government agency is assigned the task of specifying the required data, including, how the data must be recorded and presented. The data format should be configured to:

- (1) help consumers and their doctors evaluate the suitability and risk of the drug, and
- (2) serve as useful supplementary information for the FDA's approval process should the FDA choose to consider such information at any point along its own track.

There has been a genuine concern that drug companies have suppressed negative information about drug trials. In addition, the independence of academic investigators involved with clinical trials has been criticized. This entire issue is avoided with Dual Tracking, as all results would be required to be posted in a standardized, timely, and informative manner.

With government-specified standardized data and display formats, trial lawyers would lose the opportunity to sue developers over minor interpre-

tations of how best to communicate drug results. Instead, lawsuits would be restricted to serious instances in which the reporting of government-specified data was negligent or fraudulent.

Ensuring that data demands are not so horrendously complex as to deter drug firms from electing Dual Tracking for experimental drugs is essential if consumers are to have an effective freedom to choose. With its biased mindset, the FDA almost certainly would be wrong for this specification task.

Contracts between developers and consumers need to clearly communicate that the risk of adverse consequences, regardless of their form and severity, from using the DT drug are assumed by the consumer. Reasoning that the wide information disparity between doctors and patients inevitably disadvantages patients, courts have disallowed doctor/patient contracts that specify responsibilities of each party.⁶ One could anticipate a similar challenge to contracts between patients (consumers) and drug development firms. This hurdle could be overcome with DT legislation permitting developers and consumers to enter into legally binding contracts, because an information disparity would not exist as developers and consumers would share the same Internet-posted database of all the drug's treatment outcomes.

In the example of an experimental drug for treating ALS, revenues to the developer would be a function of the price charged and the volume sold, and it is reasonable to expect that these would be directly related to the ongoing safety and efficacy results displayed on the Internet. Consumers initially would not likely receive any reimbursement from their health insurance plans, as the drug would not be FDA-approved. But should ongoing results indicate dramatically better outcomes relative to costly, long, and futile best-practice treatments, insurers might become eager to provide reimbursement.

In summary, the proposed public policy field experiment would provide empirical information by which to weigh resulting medical benefits versus adverse consequences, and this, in turn, would serve as a basis for evaluating the extensive FDA testing and approval procedures. If an experimental test of the DT system demonstrates that the benefits from much quicker access to medical innovations clearly exceed adverse side-effects, it would underpin a case for making the DT mechanism permanent.

Segmenting Consumers by Risk Preference

It is reasonable to expect that consumers who contract for DT drugs will have a much higher tolerance for the risk of adverse consequences in order to possibly achieve otherwise unattainable favorable health outcomes. Regardless of the extent of adverse consequences to patients in any specific DT drug trial, an argument can be made that society at large would gain from this voluntary process because it accelerates the identification of new drugs as harmful, not beneficial, or highly beneficial.

There is a deeper behavioral aspect of consumer freedom of choice that extends beyond merely segmenting consumers into risk takers and risk avoiders. The critical point was made by Hayek and summarized by Vernon Smith⁷ as follows:

No one understood that [market] exchange process better than Frederick Hayek, when he said, . . . "Nobody can communicate to another all that he knows because much of the information he can make use of, he himself will elicit only in the process of making plans for action. As he will not merely make use of given knowledge, he discovers what he needs to know in order to make appropriate actions." This is the reason why survey instruments of opinion can only give you a very limited indication of what constitutes people's "knowledge": people don't know what it is they will do until they face particular circumstances and then they start to come up with solutions.

Individuals who have not experienced a heavy personal "cost" associated with the current FDA process are unlikely to be alarmed by growth in the FDA's power. Indeed, hearing news media reports of approved-drug recalls (Vioxx), they probably would support additional FDA testing if their opinions were sought in a survey.

Now put these individuals in a different context. If they or a member of their family became afflicted with ALS, such people would be faced with a deterioration of muscular functioning and death within 3 to 5 years, as there is no existing cure for ALS. They and their family members would experience an order-of-magnitude shift in their need to gain knowledge about ALS in general, and, in particular, about ongoing prospects for not-yet-FDA-approved treatments for ALS.

Their response to a survey on the FDA's current practices and an expansion of its power almost surely would be different. It seems safe to say they would eagerly consider an opportunity for a DT drug that might greatly extend and improve life.

The argument supporting a DT-type-freedom-of-choice option does not critically depend on a life-threatening illness situation. For example, patients faced with a future of inevitable worsening vision owing to macular degeneration presumably, with the support of their doctors, would carefully look for and consider DT treatments. A list of all similarly important but not life-threatening medical conditions would be long.

As noted earlier, what individuals want will become apparent when they encounter specific problems and have knowledge of available courses of action for dealing with them. Thus, what is "high" or "low" risk, and who has high- or low-risk preferences, is greatly determined by specific context. For those whose current needs are being met by available medical treatments, the low-risk FDA approval process may well be preferred, but that does not mean all of them have revealed some innate low-risk preference. Put anyone in a different context and they may well have a different risk preference. Dual Tracking allows that preference to be acted on and thus to be revealed.

Adaptive Efficiency and Drug Innovations

The importance of adaptive efficiency to society has been described by Douglas North⁸ as follows:

Adaptive efficiency is the willingness of a society to acquire knowledge and learning, to induce innovation, to undertake risk and creative activity of all sorts, as well as to resolve problems and bottlenecks of the society over time . . . Adaptive efficiency maximizes trials and eliminates errors. The society that permits the maximum generation of trials, as Hayek has persuasively argued, will have the best likelihood of solving problems over time. Adaptive efficiency, therefore, encourages the development of decentralized decision-making processes that will allow societies to explore alternative ways of solving problems.

An efficient process for developing innovative solutions to complex problems is promoted by as-

sembling people highly skilled in diverse specialties relevant to the problem, equipping them with appropriate technology, and experimenting early and often.⁹ A low-barrier "front-loaded" innovation process, although accompanied by frequent "failures," expedites learning and useful innovation in that hypothesized "best solutions" are more quickly found to be deficient, and this spurs efforts toward finding more effective ones.

Dual Tracking is grounded in the buildup of knowledge from front-loaded experimentation coupled to decentralized decision making. As to decisions, DT patients have a purpose different than the FDA's purpose. Patients want to improve their health and ideally be cured of their medical problems; the FDA's primary purpose is to maintain statistical rigor in the design and execution of clinical trials.

A DT environment also would likely promote interactions between physicians and drug development firms that are favorable to innovation. Doctors have a deep desire to help their patients and should be motivated to share their experiences with others, as a flow of information benefits everyone. One would expect DT firms to willingly act as a repository for doctors' accounts of experiences more extensive than required by the DT contract. The diversity and increased number of mini-experiments by doctors could provide a gold mine of useful information from which drug firms could learn a great deal. For instance, identification of genetic characteristics of patients and other variables could expedite learning to the immediate benefit of today's patients, to make fine-tuned adjustments for future clinical trials, and to inspire insights that lead to radically improved new formulations.

The existing FDA system is clearly at odds with the above-described desirable characteristics for speedily resolving society's problems and with the FDA's own mission statement to "speed" innovation. It surely does not reflect adaptive efficiency either—the "willingness of a society to acquire knowledge and learning, to induce innovation, to undertake risk and creative activity of all sorts (emphasis added)." And rather than promoting front-loaded innovation, the high cost and lengthy time in fulfilling the inflexible requirements of the clinical-testing process works to impede experimentation. Indeed, many criticisms of the existing FDA system are revealed to be characteristics of an inefficient structure as regards either speed or innovation:

1. The high cost of clinical trials and NDA submissions drives firms to:
 - A. submit fewer drug candidates to clinical testing;
 - B. eschew research on illnesses with small patient populations; and
 - C. avoid the higher risk associated with attempting large-scale improvement over existing therapies for a particular disease in preference for the lower risk associated with developing drugs that may achieve a small incremental improvement for a medical need of a large patient population.
2. From a diversity of specialties standpoint, it is highly desirable to have a large number of small drug development firms with high, focused scientific skill obtain needed resources, yet the existing system strongly favors large firms, owing to:
 - A. high capital costs of FDA testing requirements posing a particularly formidable obstacle to small firms, and
 - B. the importance of knowing how to deal with the FDA's administrative procedures, which large firms possess to a far greater degree than small firms.
3. Small firms, in particular, may have extraordinary skill in certain critical competencies that clearly justify a lot of experimentation. But the availability of capital to small firms depends on demonstrating success in passing FDA clinical milestones. Consequently, small firms oftentimes must "bet the farm" on a small number of drug candidates.
4. Although retrospective analysis of unique patient subsets within a clinical trial can be of utmost importance in learning how to develop an improved patient treatment, the FDA focuses on only the statistical significance of the entire set of clinical trial data. The core of personalized medicine is unique patient subsets. With rapidly advancing medical technology facilitating the trend towards individualized therapies, the FDA's blanket endorsement of the so-called gold standard of placebo-controlled, double-blind clinical trials can be seriously questioned.¹⁰

The point of this paper, that Dual Tracking will rapidly accelerate the trend of medical knowledge, suggests that a DT system, in addition to the FDA system, will make society better off over the long term compared to only a status quo FDA.

But without empirical evidence, it is only an abstract argument. The matter is important enough and the argument is compelling enough to deserve this large-scale, public policy field test.

Of course, DT results can be expected to show a higher incidence of adverse side-effects, almost surely including additional deaths, compared to the reported effects from the use of FDA-approved drugs. Any valid comparison, however, would have to include estimated deaths owing to delays in approving FDA drugs. Moreover, increased adverse side-effects for DT consumers who have a very short expected survival time under FDA-approved treatments should not be taken as strong evidence against Dual Tracking.

Yet, if a DT experiment clearly demonstrates substantial *net* benefits to consumers, this would support its use as a permanent feedback mechanism. The FDA may then use or not use DT data as part of its NDA analysis. The FDA may also use or not use the experiences of DT consumers to modify its testing procedures. Regardless of those decisions, the FDA is responsible to Congress and ultimately voters, and much more clear-headed thinking as to FDA effectiveness would likely result from the feedback of experimenting with the DT system.

A permanent DT environment would almost certainly exhibit the following system effects:

1. Phase I clinical submissions would increase, as firms would want to gain knowledge from expedited DT drugs.
2. Upfront experimentation with DT drugs in Phase II clinical trials would increase in order for firms to improve designs of Phase III trials; to develop insights for drug redesign/pre-clinical research leading to subsequent submission for IND (investigational new drug) status; and to more quickly cancel drugs with questionable efficacy based on receipt of additional information on DT usage.
3. Firms with high skill, as demonstrated by posted Internet results for successful DT drugs, would gain additional resources from these sources:
 - A. revenues from sales of DT drugs;
 - B. stock price appreciation and concomitant increased access to the capital market (especially important for small firms); and
 - C. more favorable partnership terms to share future royalties, because favorable DT consumer experiences reduced the uncertainty involved.

These benefits to society from adding a DT system do not require any changes to current FDA procedures.

DT System Dynamics

In a permanent DT environment and its evolving nexus among DT consumers, doctors, and drug development firms, two major changes in the drug industry landscape are predictable. One is a shift over time in market valuations of drug firms relative to their industry peers. A second is an increased involvement of doctors and a resulting flow of more information to drug development firms.

A shift in relative market valuations of drug firms would result from *a much faster recognition through a DT test of a high skill level of some firms in developing innovative drugs that greatly outperform existing FDA-approved treatments*. For example, consider a hypothetical situation where a small biotech company develops a radically different drug that shows complete remission of ALS symptoms in over 50% of Phase II clinical patients. The duration of its effectiveness is not yet known, nor has adequate time elapsed to rigorously test for adverse side-effects.

Nevertheless, as regards our ALS example, owing to the lack of a current effective ALS treatment coupled to the highly promising initial results, a biotech firm would likely elect to offer the drug through the DT option. Internet posting of such favorable efficacy results would grab the attention of ALS patients and their doctors, with many (particularly longer-afflicted patients) who would want to contract to purchase this drug. The firm would probably price the drug “low” in order to quickly expand the patient population and thereby expedite learning, including exchanges with the patients’ physicians. Greatly reduced legal costs owing to DT legislation that minimizes groundless lawsuits would enable drug development firms to do so.

For the ALS example, particularly promising early DT results would be a powerful signal to both the consumer (patient) market and the capital market. Absent Dual Tracking, information or rumors about phenomenal Phase II early results would be sketchy and have to warn that they are based on a *fixed*, and likely small, number of Phase II patients receiving the drug. In contrast, a DT drug of this hypothetical type would quickly generate an *increasing* number of users and additional *ongoing results* would be posted on the

Internet. This would provide better information as to the risk or reward from drug usage (and also as to the economic value to the developing firm). *Importantly, ALS patients and their doctors would have a direct readout of all ongoing treatment results, and they, not the FDA, would control the decisions affecting length and quality of the patient’s life.*

If the biotech firm in this example were publicly traded, its market valuation would greatly appreciate to reflect the increased probability of subsequent FDA approval and substantial economic value from marketing the ALS drug. The magnitude of price appreciation would be related to the quality of the efficacy and safety data posted on the Internet. If exceptionally strong results continued over time, the biotech firm would be in a much improved financial position to accelerate its clinical testing of the ALS drug, to secure more favorable partnership arrangements for the drug if that avenue were selected, and to increase its overall R&D spending.

In a DT world, demonstrated scientific skill in developing important drugs that work is highly valued by both capital suppliers and society. Which drug firms can be expected to oppose Dual Tracking? Those firms whose competitive advantage and skill resides more in the area of administrative capabilities in dealing with FDA complexities and less in the area of innovative science.

The second major change would be the role of doctors. To a far greater extent than doctors’ involvement with FDA clinical trials, DT doctors would be empowered to use their unique knowledge of their patients and their problem-solving skills to directly help their patients. In FDA clinical trials, doctors must strictly comply with specified procedures, so that test data will be suitable for the FDA’s statistical analyses. This means, among other things, that some doctors “treat” their patients with placebos, without it being known to either doctor or patient.

In a DT environment, a doctor’s sole purpose is to help specific patients with their specific health problems, and the doctors would have more latitude to do so. The opportunity to creatively utilize unique knowledge built up over their medical careers in an effort to help their patients and possibly assist in making better medical treatments widely available should make doctors enthusiastic for the proposed DT option. It is reasonable to expect that the diversity of their experiences will generate a greater diversity of insights relevant to developing new drugs.

Accelerating medical advances are equipping doctors with especially useful technology for observing how a change in variable X leads to different responses to a drug. Variable X may be some genetic trait of a patient or a descriptive biomarker that more distinctively categorizes a disease. Posting such information on the Internet may then lead to additional support or refutation as others investigate further. It also might cause a doctor or researcher at a drug developmental firm to pursue a new idea that leads to an important fundamental discovery.

Experience with “off-label” use of drugs supports the expectation that doctors would eagerly participate in a DT information-sharing network. An FDA approval of a drug applies to a specified, or “on-label,” use. Motivated by a desire to help patients, doctors often experiment with off-label uses of drugs when patients do not respond well to standard, on-label treatments. Doctors learn about the safety and efficacy of off-label uses through a network of informal avenues independent of FDA regulatory oversight. Thus, physicians have demonstrated a willingness to share what they learn about the usefulness of drugs.

As to the degree of physician enthusiasm for experimentation in a non-FDA-regulated environment (off-label use), David Klein and Alexander Tabarrok¹ orchestrated an insightful probing of doctors’ opinions about, among other issues, their support for off-label use. The finding was that 94% of doctors were opposed to adding FDA-proof-of-efficacy to off-label drugs because it would stymie their ability to experiment and communicate informally.

Also, Klein and Tabarrok¹ reported that, by a ratio of two to one, doctors supported maintaining the FDA’s existing clinical trials for on-label use. If applicable to the physician community in general, the results indicate that the DT proposal is aligned with the current mindset of most doctors—DT experimentation is beneficial as an add-on to existing FDA clinical trials. Thus, it would appear that the proposal of this paper to leave current FDA procedures in place while implementing an expanded freedom-of-choice option would be readily acceptable to doctors.

Dual Tracking is the First Step

The proposed DT field experiment would yield concrete information on actual consumer choices

and outcomes. This feedback would be useful for judging the merit of reasoned descriptions of FDA deficiencies, of abstract arguments for FDA reforms of various types, and of the effectiveness of the FDA’s current tradeoff decisions regarding its conflicting goals. While feedback measurement is an essential principle of any system design for improving effectiveness, it is often ignored in the design of government regulations and regulatory bodies.

The diverse political interests that surround the FDA would make it difficult to pass DT legislation. Yet its purpose is sound, its detailed mechanism of operation plausible, and, most importantly, it can be experimentally evaluated *without imposing a change in existing FDA procedures*. Adding Dual Tracking seems far less difficult to implement than, as suggested by many FDA critics, straightaway elimination of FDA clinical trials for efficacy and a return to the pre-1962 era of FDA responsibility solely for safety evaluation.

As to implementation, *specification of institutional detail* is a key component of experimental design.¹¹ One such detail of the DT proposal is the legal contract between consumers and firms, wherein consumers accept full responsibility for risks and rewards from drug usage and firms commit to promptly posting accurate data summarizing *all* treatment outcomes, including all adverse side-effects. Absent appropriate Congressional legislation authorizing such contracts, firms would most likely refrain from Dual Tracking out of fear of costly litigation.

The call for a public policy DT experiment in the medical arena via legislation is not novel. The Medical Liability Procedural Reform Act of 2005 (H.R. 1546) would authorize funding for states to create special health courts on an experimental basis. These courts would take only medical malpractice cases and would be run by full-time judges with health care expertise. The proposed experiments for special health courts and Dual Tracking share the same fundamental idea: obtain better information to help resolve a problem of national importance.

Dual Tracking might be opposed by FDA officials as being unnecessary because of the FDA’s efforts to “fast track” selected new drugs developed for “life threatening” illnesses. But the speed of the so-called fast track remains tightly controlled by the FDA, and it involves only a very small percentage of drugs. Thus, the FDA’s fast-

tracking “alternative” does not provide the type of early, easy, or rapid access available with Dual Tracking.

Another FDA objection might be that Dual Tracking could potentially dampen enrollment in placebo-controlled clinical trials, because some patients would elect to pay the costs of purchasing the DT drug and thereby avoid the chance of receiving a placebo. Logically, the more serious the illness, the more appealing would be the option of avoiding a placebo.

The real debate should not concern the extent that Dual Tracking might interfere with FDA clinical trials but whether this “interference” benefits society on balance. That requires experience/analysis of the full system effects of Dual Tracking. One effect could be an accelerated growth in statistical analyses of large-sample, nonplacebo-controlled experiments. A *Wall Street Journal* editorial (2005) argued as follows for the importance of using nonplacebo-controlled data:

Instead of restricted-access placebo trials, drug researchers could be using large, open-access trials in which everyone who wants the new drug can get it. They could then take advantage of advanced statistical methods to figure out whether the drug is working. Wall Street traders use these kinds of math tools all the time, and so do economists. So-called Bayesian statistics are already used in medical device regulation, where even the FDA recognizes that randomizing people into sham surgeries is simply beyond the pale.

Well, what about cancer and other terminal patients? They are now dying needlessly in placebo-controlled trials. And would-be patients like Kianna Karnes are dying outside of them because they make “compassionate use” all but impossible. Won’t Congress do something?

By giving *today’s patients* the freedom to choose what they and their doctors believe to be in their best interests, a Dual Tracking experiment would expedite a process of experimentation not only for drug development but also for drug testing.

The lack of freedom to choose medical treatments for those suffering from terminal diseases has prompted the Washington Legal Foundation and the Abigail Alliance for Better Access to De-

velopmental Drugs (www.abigail-alliance.org) to propose a “Tier 1 Initial Approval.” This proposal differs from Dual Tracking in that it seeks to *work within the FDA system* to gain early access to drugs. With this proposal, the FDA would decide whether or not to allow an experimental drug to be used for certain diseases that the FDA has categorized as life-threatening. Patients would need to show that they are not viable candidates for ongoing clinical trials. Furthermore, the FDA must agree that existing approved treatments are ineffective for the particular diseases. In that scheme, the *FDA controls the feedback mechanism* that could reveal its extensive clinical testing to be detrimental to seriously ill patients.

In sharp contrast to the Abigail Alliance proposal, Dual Tracking offers patients an alternative track that approximates a market process with FDA entanglements removed. Dual Tracking does not require any test of illness severity. Dual Tracking does not require the multitude of interactions with, and permissions from, the FDA as required by the Abigail Alliance proposal.

In summary, with Dual Tracking a drug development firm strictly follows the FDA-controlled clinical procedures on one track. On a separate track, a market process creates *a feedback mechanism that is independent of the FDA*.

Regardless of which group has the “best” solution to improving FDA efficiency, it is reasonable to suggest all groups coalesce behind Dual Tracking as the *initial* public policy goal. If DT legislation were passed, the general public would receive feedback results that plainly reveal the current effectiveness of the FDA. If those results indicated a need for change, the ensuing political debate would, in all likelihood, have one group argue for a return to the pre-1962 era of drastically reduced regulation and the other group offer to maintain the FDA’s regulatory scope but substantially reorganize how the FDA operates. Dual Tracking would set the stage but not determine the outcome.

REFERENCES

1. Klein DB, Tabarrok, A. “Do Off-Label Drug Practices Argue Against FDA Efficiency Requirements?” Working Paper, 2004.
2. Becker GS. Get the FDA out of the way, and drug prices will drop. *Bus Week* 2002;Sept. 16:16.
3. Tabarrok AT. Assessing the FDA via the anomaly of off-label drug prescribing. *Independ Rev* 2000;5:25.
4. Miller HI. *To America’s Health: A Proposal to Reform*

- the Food and Drug Administration*. Stanford, CA: Hoover Institution Press, 2000.
5. Madden BJ. Breaking the FDA monopoly. *Regulation* 2004;27(2):64.
 6. Epstein RA. Medical malpractice, imperfect information, and the contractual foundations for medical services. *Law Contemp Probl* 1986;49(2):201.
 7. Smith VL. Hayek and experimental economics. *Rev Austr Econom* 2005;18(2):135.
 8. North, Douglas C. Economic Development in Historical Perspective: The Western World. In: Myers RH, ed., *The Wealth of Nations in the Twentieth Century*. Stanford: Hoover Institution Press, 1996.
 9. Thomke SH. *Experimentation Matters*. Boston: Harvard Business School Press, 2003.
 10. Hampton JR. Evidence-based medicine, opinion-based medicine, and real-world medicine. *Perspect Biol Med* 2002;45(4):549.
 11. Smith VL. Theory, experiment, and economics. *J Econom Perspect* 1989;3(1):151.
 12. *Wall Street Journal*. Review & Outlook, "How About a 'Kianna's Law'?" 2005;March 24:A14.