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Pharmaceutical regulation and innovative performance: a decision-theoretic model

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Pharmaceutical regulation and innovative performance: a decision-theoretic model*

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Abstract

In this paper we develop a model of the impact of the drug approval process on the terms of a contract between a pharmaceutical company that requires the services of a contract research organization (CRO) to carry out testing of new drug molecules. Results show that if the equilibrium contract includes a variable payment (royalty), the CRO gives more effort to create a more accurate result, the more strict the FDA approval process. We also find that given the royalty shares in the contract if the FDA demands more accuracy in results as a condition of approval, then the CRO will generate more accurate results from late stage tests. However, greater FDA stringency in the approval process benefits pharmaceutical companies because the greater is FDA stringency, the less is the risk of a drug recall. We also find that in order to employ a CRO in the testing process, the pharmaceutical company's prior probability that the drug is of high quality must be very high.

JEL categories: L24, L65

Keywords: Pharmaceutical regulation, Food and Drug Administration, R&D outsourcing, contract research.

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1 Introduction

The increasing cost of health care and pharmaceutical products make understanding the determinants of market performance in the pharmaceutical industry a topic of persistent policy interest. The pharmaceutical industry is R&D intensive, and pharmaceutical industry R&D, with much testing between the laboratory and the marketplace, is difficult and costly. The number of new drug molecules successfully brought to market is declining, and R&D cost per new drug molecule is increasing.[1] The cost of pharmaceutical industry R&D is reflected in the price of the pharmaceutical products. This makes understanding the R&D process is important for understanding pharmaceutical market performance.

Pharmaceutical companies face stiff competition and pressure to introduce new drugs. Many pharmaceutical companies pursue R&D joint venture and outsourcing strategies, seeking to reduce the cost and time of drug development, to broaden their drug pipeline, and to stay competitive. They increasingly rely on Contract Research Organizations (CROs) to complete testing required by the Food and Drug Administration as part of a New Drug Application (NDA).[2]

Drug development is expensive because extensive testing is required before a pharmaceutical product can be approved for use in the general population. Drug development is risky in at least three senses. It is risky in the sense that attaches in general to technical success: the path from idea to application is like a path through a maze, with twists and turns, dead ends that require new starts, and the real possibility of failure.[3] Drug development is risky from a commercial point of view because of uncertainty about the profitability of a drug, if it goes to market — a drug, once marketed to the general public, may be revealed to be ineffective; it may turn out to have harmful-side effects. Finally, drug development is risky because the outcome of the regulatory process through which a drug must pass before it is permitted to go to market is uncertain. For the U.S. market, Food and Drug Administration procedures are known, but the FDA response to any particular New Drug Application (NDA) can be foreseen only imperfectly.

There is a huge literature on R&D joint ventures and outsourcing, but few studies that focus on the economic forces that influence a pharmaceutical company's decision to outsource parts of the R&D process and the way such outsourcing impacts the approval process. Food and Drug Administration procedures aim to ensure that drugs are safe. The way firms respond to those procedures has implications for the drug development process and, ultimately, the information that reaches the FDA and upon which it bases its decisions. The starting point of our research is that drug approval procedures, designed to ensure drug safety, affect the private profitability of outsourcing, the way pharmaceutical companies design contracts with contract research organizations, and the way CROs respond to those contracts. The decisions firms make in response to drug approval procedures are important for drug market performance, and it is the nature of these decisions that we wish to explore.

As emphasized by Mirowski and Van Horn (2005), the CRO is a novel entity in the pharmaceutical sector, one that dominates the outsourcing and commercialization of science. CROs have been a subject

[1] See, for example, Duff Wilson, "Patent Woes Threaten Drug Firms," *New York Times*, internet edition, March 6, 2011.

[2] For discussions of the drug approval process, see Dranove and Meltzer (1994), Olsen (1995, 1996), Hadler (2003, pp. 188-190).

[3] Tapon and Cadsby (1996, pp. 389–390) quote a drug industry researcher:

> I think that rational drug design is obviously very admirable. It's more than a great idea, it's a move in the right direction. It applies as much rationality to your programs as possible. But, you're not going to be able to predict 100% ... of the outcome. You're always going to have things that happen that nobody really foresaw and you look back in hindsight and say that there is no way that we could have predicted that outcome... There is a certain amount of good luck involved ... you have to have the breaks; if you don't have the breaks in drug development you may have great difficulty in getting any compound.

of study for medical literature for some time due to the growing nature of the business and the increasing influence of CROs in the biopharmaceutical innovation. It is important for the policy makers, regulators and medical researchers to understand how pharmaceutical company-CRO contracts are formed and how these contracts affect drug market performance. Understanding the influence of the FDA's safety standards on the outsourcing contract is important to permit the FDA and other regulators to influence outsourcing contracts in a way that promotes drug safety. On the other hand, understanding contract terms and the interaction of contract terms with FDA's approval process helps both CROs and pharmaceutical companies, the parties directly involved in contract design. This paper contributes to the economic analysis of contracts by showing how the presence of a regulator influences the outsourcing R&D contract and the R&D effort of interested parties. The paper also contributes to the medical literature on CROs.

CROs have attracted increasing attention in the medical literature in the last 18 years, but they are not limited to the biopharmaceutical industry. We also observe outsourcing of R&D activities to specialized research organizations and to universities in other sectors, such as software, defense, chemicals, and engineering sectors. CROs and regulation both have wide application in other industries wherever we observe the outsourcing and commercialization of scientific research. Understanding the impact of regulation on the incentives of CROs and, ultimately, product quality is important for citizens, the regulator, and firms in the increasingly large parts of the economy where contract research takes place.

In this paper, we develop a model of the impact of the drug approval process on the terms of a contract between a pharmaceutical company that uses the services of a contract research organization (CRO) to carry out testing of a new product that will be submitted to the Food and Drug Administration (FDA) as part of an application for approval to use the product with the general public.

Results show that for a given level of FDA strictness in New Drug Application (NDA) approvals, if the royalty (variable) payment in an outsourcing contract is increased, the CRO makes a greater effort to obtain more accurate results. We also find that for a given royalty rate, if the FDA toughens its approval criteria, the CRO will generate more accurate test results. Increased FDA stringency in the approval process decreases the probability of approval. But such stringency benefits the pharmaceutical company, to the extent that it lowers the risk of a drug recall. We also show that for it to be profitable for a pharmaceutical company to employ a CRO, the pharmaceutical company's prior probability that the drug is of high quality must be sufficiently high. The net effect of an increase in FDA's demand for accuracy is that the CRO will produce more accurate results, and that this will decrease the CRO's profit but benefit the pharmaceutical company.

In Section 2 we provide a description of the drug development process and R&D outsourcing in the bio/pharmaceutical industry. In Section 3 we highlight the related literature. In Section 4 we outline the analytical framework used in the paper. In Section 5 we analyze the determinants of the CRO's equilibrium effort, with particular attention to the way that effort is affected by the terms of the pharmaceutical company-CRO contract and by FDA regulatory policy. In Section 6 we examine the pharmaceutical company's choice of contract terms and the way that choice is affected by FDA regulatory policy. Section 7 concludes. Proofs are given in the Appendix.

2 Industry Background

The pharmaceutical industry is rapidly growing, with prospects for growth in developing economies exceeding this in developed economies (Thomas, 2013). It is research intensive — pharmaceutical companies continuously invest in R&D to maintain a flow of products in their drug pipeline. It is also heavily regulated by

public authorities, which seek to ensure that medicines certified for use by the general public are medically safe.[4] Drug development is a lengthy and expensive process. Major R&D expenses occur during clinical trials, and the failure rate of this later stage is also very critical (Kermani and Bonacossa 2003).

A pharmaceutical company seeking to develop a new medicine first performs research on new chemical compounds. It might conduct the research in its own laboratories, or it might form a research alliance with a biotechnology company. It might acquire a license to use a compound developed elsewhere. These early research stages involve developing stable molecules for further research and development.

Depending on the outcomes of pre-clinical test results, a pharmaceutical company prepare an Investigational New Drug approval application (IND) and seek FDA permission to perform trials on human subjects. The research phases are described in Table 1. Later stages (Phases I to III) involve testing the efficacy and safety of a drug. During Phase I, companies test the potential drug on a small group of healthy individuals. During Phase II they repeat the process on a relatively large group of patients who have the target disease. If the drug passes Phase I and II, then Phase III, where the drug is tested on a large group of patients, takes place.

A pharmaceutical company that seeks to market a new drug submits data from tests to the Food and Drug Administration as part of a new drug application. The FDA decides whether to allow the marketing of the drug. There is no guarantee that the NDA will be accepted by the FDA. We model pharmaceutical companies as avoiding the approval of a drug that proves to be of low quality not only because of the immediate losses that would result, but also because of the impact of such an event on the firm's reputation.[5] But pharmaceutical companies do face drug recalls, and this implies that neither the FDA nor the pharmaceutical company can predict the performance of a drug with 100% accuracy.

Different stages of pre-application testing are increasingly outsourced to Contract Research Organizations that specialize by therapeutic area and can offer advantages in terms of cost, speed, accuracy, and data-management compared with in-house testing (Frost and Sullivan, 2006). Depending on the outcomes of its own and CRO testing, a pharmaceutical company decides whether to submit a NDA. The terms of the pharmaceutical company-CRO contract affect the CRO's incentive to produce accurate results, and this in turn affects the pharmaceutical company's expected profit from the project. Pharmaceutical company-CRO contracts typically involve a sequence of payments in the form of lump-sum startup payment and a variable royalty payment. The analysis of the payment structure in these kinds of contracts, and the effect of FDA regulatory policy on that structure, is the primary focus of this paper.

3 Literature review

Within the broad literature on contract R&D,[6] the effects of regulation on the terms and performance of R&D contracts have not been widely studied. Lerner and Merges (1998) conclude that the extent to which control rights are allocated to a financing firm are inversely related to the financial resources of the R&D firm. Two recent papers, Piachaud (2002) and Lowman *et al.* (2012) analyze the role of CROs in the pharmaceutical

[4] We focus on regulatory institutions in the United States; the economic relationships we highlight are general.

[5] We qualify this point in our conclusion.

[6] See Baldwin (1962), Balbien and Wilde (1982), Mowery (1983), Arora (1996), and Banerjee and Duflo (2000). Firms' make-or-buy decisions have been studied to determine the factors that influence outsourcing strategies and the relation between outsourcing and in-house R&D expenditures (Kurokawa 1997, Lai et al. 2004, Grimpe and Kaiser 2008). Tapon (1989) predicts that pharmaceutical firms will increasingly outsource R&D activities to university laboratories. Tapon and Cadsby (1996) conclude that firms outsource when they are weak in some areas of research, when transaction costs are low, or when the government wants research to be carried out in a particular location. Some papers use transaction cost analysis to explain the 'boundary' choice (Grimpe and Kaiser 2008, Veugelers and Cassiman 1999, Ulset 1996).

industry and identify CROs as key components of the pharmaceutical clinical development process. But the effect of regulation on the accuracy and precision of the contracting firm's R&D has been left unexplored. CROs contribute to the commercialization of drug development by specializing in different phases of drug development, as studied by Gad (2003). Milne and Paquette (2004) identify pre-clinical services as one of the fastest growing specialties of CROs in recent years. Lester and Connor (2003) argue that CROs are better equipped to deal with changing technologies and therefore can help pharmaceutical companies most in fast-changing technology areas. But how an FDA demand for greater assurance of safety affects the role of CROs is an unexplored topic, despite the fact that CROs are the prime agents for outsourcing of NDA testing in the pharmaceutical industry (Mirkowski and Van Horn, 2005; Azoulay, 2003; Pichaud, 2002). Carpenter et al. (2008) shows that the FDA's decision process affects the quality of approved drugs. But how FDA's regulatory process impacts pre-application testing, pharmaceutical-CRO contracts, and the quality of drugs put on the market are all important policy questions which are still unanswered to the best of our knowledge. This paper seeks to fill this gap in the literature.

4 Setup

We develop a stylized model of a pharmaceutical company that has developed a drug that it may wish to submit for approval to the regulatory agency. The drug is either of high quality (H) or low quality (L). The quality of the drug is not known unless and until the drug is introduced for use to the general public. If the drug is of high quality, the pharmaceutical company receives a lump-sum payment Π. If the quality of the drug is low, it incurs a lump-sum loss $-X$, with $X > 0$. Π and X can be thought of as the present-discounted values of income streams received over time in alternative states of the world.

Along with its new product, the pharmaceutical company develops a probability h that the drug is of high quality. The pharmaceutical company takes the drug and its quality estimate h to a contract research organization, which it hires to perform testing that is required by the FDA as part of a new drug application (NDA). The pharmaceutical company makes a take-it-or-leave-it contract offer to the CRO. The offer provides for a royalty rate ρ ($0 \leq \rho \leq 1$) to be received by the CRO if the drug is approved for release to the general public and, after release, proves to be of high quality.

The contract also provides for a lump-sum payment (M) to be received by the CRO in all states of the world. The lump-sum payment ensures that the CRO's participation constraint is met, and provided this is the case, reflects the relative bargaining power of the contracting pharmaceutical company and the CRO.[7]

Under the terms of the contract, CRO produces a signal σ of the drug's quality (H or L) and a probability $g \geq \frac{1}{2}$ that the signal is correct.[8] That is,

$g = \Pr(\sigma = H|H)$ = probability that the signal is H, given that the true but unknown quality of the drug is H

$= \Pr(\sigma = L|L)$ = probability that the signal is L, given that the true but unknown quality of the drug is L.

It follows that $1 - g$ is the probability the signal is incorrect, that is,

[7] Since it is a payment received in all states of the world, the amount of the lump-payment does not affect CRO's effort, provided the participation constraint is met. The payoffs reported for the numerical examples, below, are for $M = 0$, that is, they are CRO and pharmaceutical company payoffs before taking the lump-sum payment into account.

[8] A signal with reliability $g = \frac{1}{2}$ is uninformative — it is just as likely to be wrong as to be right. A signal that the drug is of high quality that is more likely to be incorrect than correct is a signal that the drug is of low quality.

$1-g = \Pr(\sigma = L|H) =$ probability that the signal is L, given that the true but unknown quality of the drug is H

$= \Pr(\sigma = H|L) =$ probability that the signal is H, given that the true but unknown quality of the drug is L.

The CRO's cost function is $y(g)$, with $y'(g) > 0$, $y''(g) > 0$, and $\lim_{g \to 1} y(g) = \infty$. For illustrative purposes, we will assume

$$y(g) = k\frac{g - \frac{1}{2}}{1-g}, \tag{1}$$

where k is a positive constant.

CRO picks g to maximize its expected payoff. g is used to update h, using Bayes' rule, to produce a post-testing probability that the drug is of high quality. The updated probability that the drug is of high quality is s_H if the signal is H, s_L if the signal is L. If $\sigma = H$, the updated signal is

$$s_H = \Pr(H|\sigma = H) =$$

$$\frac{\Pr(\sigma = H|H)\Pr(H)}{\Pr(\sigma = H|H)\Pr(H) + \Pr(\sigma = H|L)\Pr(L)} = \frac{gh}{gh + (1-g)(1-h)}. \tag{2}$$

If $\sigma = L$, the updated signal is

$$s_L = \Pr(H|\sigma = L) =$$

$$\frac{\Pr(\sigma = L|H)\Pr(H)}{\Pr(\sigma = L|H)\Pr(H) + \Pr(\sigma = L|L)\Pr(L)} = \frac{(1-g)h}{(1-g)h + g(1-h)} \tag{3}$$

After CRO produces its signal, the pharmaceutical company decides whether or not to submit the drug for FDA approval. As discussed below, we assume that payoffs are such that if $\sigma = L$, the pharmaceutical company's privately optimal decision is not to submit the drug for approval.

If the drug is submitted for approval, the FDA receives a signal $s_H = \Pr(H|\sigma = H)$ from the pharmaceutical company. We model the FDA approval standard as an approval threshold probability, τ. The FDA approves the drug if s_H is at least as great as the FDA approval threshold probability, $s_H \geq \tau$. To capture private-sector uncertainty about the outcome of the regulatory process, we suppose that the pharmaceutical company and the CRO do not know the approval threshold. We treat them as modelling τ as a random variable on an interval $T \leq \tau \leq 1$. For analytical simplicity, we assume that their beliefs are that τ is uniformly distributed on $T \leq \tau \leq 1$, that is, with density and distribution

$$f(\tau) = \frac{1}{1-T} \text{ and } F(\tau) = \frac{\tau - T}{1-T}, \tag{4}$$

respectively. After CRO has completed its testing, therefore, the probability the drug is approved is

$$P^A(s_H) = \int_{\tau=T}^{s_H} f(\tau)\, d\tau = \frac{s_H - T}{1-T}. \tag{5}$$

The pharmaceutical company writes the contract with the CRO and it receives a value of g as a report from the CRO. The pharmaceutical company structures the terms of the contract to prompt the best result possible from the CRO, given that it is outsourcing the testing to the CRO. We assume that g is not contractible due to the inherently uncertain nature of the drug testing process. Pharmaceutical companies can only influence the effort level of the CROs, but not the resulting assessment of the drug's true quality.

The FDA receives the NDA, which includes testing results from all the drug development phases, observes s_H. s_H combines the information g and h in an efficient way, in the Bayesian sense as described above.

We also assume that contracts do not specify large payments to CROs, conditional on generating a favorable report. Such contracts are such then this would create an incentives for the CRO that would invalidate the testing process and undermine the validity of the documentation submitted to the FDA as part of the new drug application.[9]

5 CRO's problem

5.1 Objective function

We model CRO as making its choice of precision g to maximize its expected payoff according to the terms of its contract with the pharmaceutical company. We assume the CRO reports its findings accurately.[10] Table 2 shows the probabilities of different states of the world, and associated payoffs, at the moment the contract offer is received, if, after CRO generates its signal, the pharmaceutical company submits the drug to the FDA for approval.

Thus row 1 of Table 2 shows the prior probability that the drug is of high quality, h. With probability g, CRO's signal will be accurate. h will be updated to s_H. If the pharmaceutical company submits the drug for approval, it receives approval with probability $P^A(s_H)$. In this state of the world, the quality of the drug is revealed to be high. The pharmaceutical company's payoff is the expected payoff to marketing a high-quality drug, $P^A(s_H, T)\,\Pi$, net of royalty payments to CRO (the factor $1-\rho$), and minus the lump-sum payment M. Correspondingly, CRO's payoff in this state of the world is expected royalty income, $P^A(s_H, T)\,\rho\Pi$, plus the lump-sum payment M, minus the cost $y(g)$ of generating the signal.

Moving to row 2 of Table 2, with prior probability $1-h$ the drug is of low quality and with probability $1-g$, CRO's signal, inaccurate, is that the drug's quality is high. If the pharmaceutical company submits the drug for approval, it is approved with probability $P^A(s_H, T)$. After release to the public, the quality of the drug is revealed to be low. The pharmaceutical company's payoff is the expected loss, $-P^A(s_H, T)\,X$, minus the lump-sum payment to CRO. CRO's payoff in this state of the world is the lump-sum payment minus the cost of generating the signal. The other rows of Table 2 are read in the same way.

As noted above, we assume that payoffs are such that if CRO's signal is that the drug is of low quality, the pharmaceutical company does not submit the drug for approval. At the moment the contract is negotiated, the probability that the signal will be H is

$$hg + (1-h)(1-g) \tag{6}$$

(see the first two rows of column 3 of Table 2). This is the prior probability that the drug is of high quality

[9] Further, it would not be in the CRO's own interest to generate a false report, to the extent that it is in a repeated game with respect to the market. If there is an appearance that its findings are influenced by "what the client wants," its reputation as a testing agency will suffer and future business will be lost.

[10] If the CRO finds that the drug is likely to be of high quality, it would have no incentive to misreport its results; to do so would involve loss of expected royalty income. If the CRO finds that the drug is likely to be of low quality and it makes a contrary report (a) with some probability the drug is submitted for but does not receive approval, in which case CRO's payment is what it would receive by reporting correctly; (b) with some probability the drug is approved and revealed to be of high quality, so the CRO receives royalty income; and (b) with some probability the drug is approved and revealed to be of low quality. In this last state of the world, CRO's payment is what it would receive by reporting correctly. It would further expose itself to possible legal damages if subsequent investigation were to reveal misreporting, as well as loss of reputation with other potential clients. The expected payoff from misreporting may be negative; we assume it is less than the expected payoff from reporting accurately.

times the probability that CRO's signal is accurate, plus the prior probability that the drug is of low quality times the probability that CRO's signal is inaccurate.

If $\sigma = H$, CRO's expected payoff is the probability that the drug is of high quality, given that $\sigma = H$, times the probability that the drug is approved if the signal to the FDA is s_H, times the corresponding payoff $\rho\Pi$, plus the lump-sum payment, minus cost:

$$\Pr(H|\sigma = H)\left[P^A(s_H, T)\rho\Pi + M - y(g)\right] + \Pr(L|\sigma = H)\left[M - y(g)\right] \tag{7}$$

or (substituting $s_H = \Pr(H|\sigma = H)$, $1 - s_H = \Pr(L|\sigma = H)$ and combining terms)

$$s_H P^A(s_H, T)\rho\Pi + M - y(g). \tag{8}$$

This is the probability that the drug is of high quality, given that $\sigma = H$, times the probability that the drug is approved if the signal to the FDA is s_H, times the corresponding payoff $\rho\Pi$, plus the lump-sum payment, minus cost.

The probability the signal will be L is one minus (6). In this case the pharmaceutical company does not submit the drug for approval, and CRO's payoff is $M - y(g)$. Multiplying CRO's payoff for different signals by signal probabilities, adding, and simplifying, CRO's objective function is its income if the drug is of high quality, if its signal is accurate, and the drug is approved, plus the lump-sum payment, minus the cost of signal generation:

$$\pi^{CRO} = hgP^A(g, h, T)\rho\Pi + M - y(g). \tag{9}$$

5.2 Choice of g

The first-order condition to maximize π^{CRO} is

$$\frac{\partial \pi^{CRO}}{\partial g} = h\rho\Pi\frac{\partial gP^A(g, h, T)}{\partial g} - y'(g) \equiv 0. \tag{10}$$

We assume that the second-order condition is met.[11]

From (10) and the second-order condition, we obtain comparative-static results for the impact of the royalty rate, FDA policy, and Π on g (Lemma 1). Increases in ρ, holding T constant, and increases in T, holding ρ constant, increase CRO's profit-maximizing choice of the precision g of its estimate. Similarly, an increase in Π, which is the same as an increase in CRO's payoff, $\rho\Pi$, all else equal, increases g. The comparative static effect of h on g is of ambiguous sign. The lump-sum payment M, which is determined so the contract research organization earns zero economic profit,[12] has no impact on CRO's choice of g.

Lemma 1:

$$\frac{\partial g}{\partial \rho} > 0; \tag{11}$$

$$\frac{\partial g}{\partial \Pi} > 0; \tag{12}$$

$$\frac{\partial g}{\partial T} > 0 \tag{13}$$

Proof: See Appendix.

[11] See equations (24), (25) in the Appendix.

[12] That is, the terms of the contract offer CRO a normal rate of return.

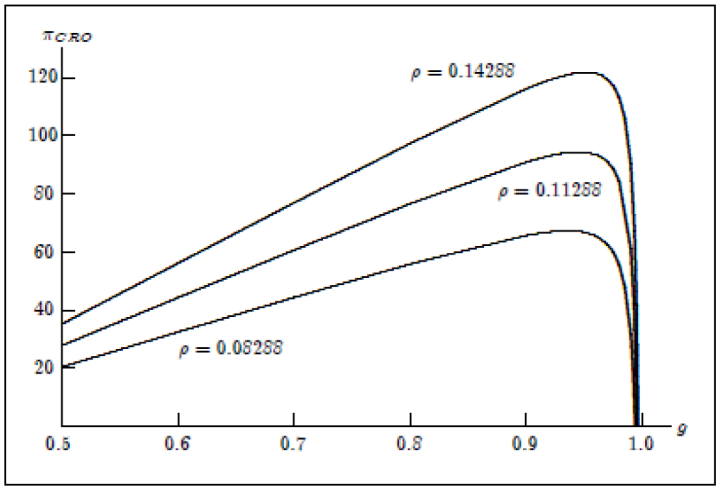

Figure 1: CRO's payoff function, alternative royalty rates ($h = 0.99$, $T = 0.98$, $k = 1$, $\Pi = 1000$, $X = 200000$.

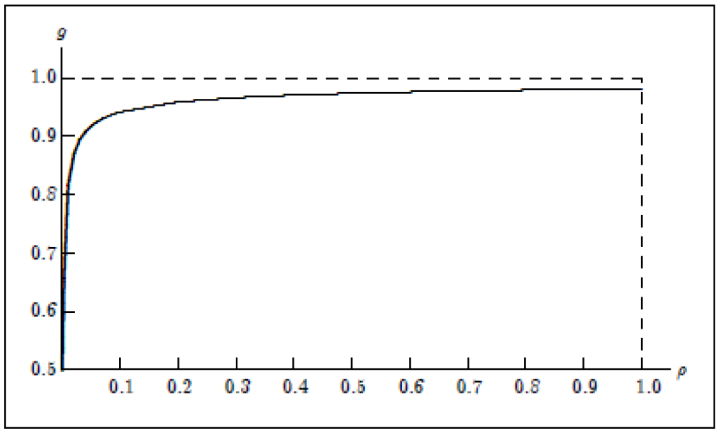

Figure 2: CRO's choice of g, $0 \leq \rho \leq 1$ ($h = 0.99$, $T = 0.98$, $k = 1$, $\Pi = 1000$, and $X = 200000$).

5.3 Illustration

For precision cost function (1), CRO's objective function (excluding the lump-sum payment) is

$$\pi^{CRO} = hgP^A(g, h, T)\,\rho\Pi - k\frac{g - \frac{1}{2}}{1 - g}. \tag{14}$$

This is drawn in Figure 1 for specific parameter values and three different royalty rates.[13]

It is clear from (14) that for ρ sufficiently small, CRO's payoff before receiving the lump-sum payment could be negative. Higher royalty rates lead to higher payoff functions and a larger maximum payoff.

CRO's payoff-maximizing choice of g rises with ρ, as stated in the first part of Lemma 1. This also appears in Figure 2, which shows the g, ρ relationship implied by CRO's first-order condition. For precision cost function (1), CRO's choice of g rises sharply with ρ as ρ rises from low levels. For these parameter values, further increases in precision are small for royalty rates above 10 per cent.

[13] $\rho = 0.11288$ is Pharma's equilibrium offer for the parameters used for the numerical example. The two other values of ρ are the equilibrium value plus and minus 3 percentage points.

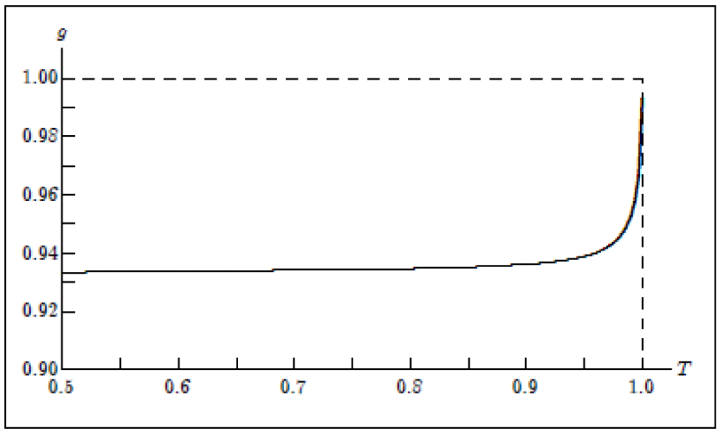

Figure 3: CRO's choice of g, $0.5 \leq T \leq 1$ ($h = 0.99$, $\rho = 0.11288$, $k = 1$, $\Pi = 1000$, and $X = 200000$).

Stricter FDA approval policy — a narrower range over which the approval threshold is distributed — also induces greater precision, holding ρ constant. This is part III of Lemma 1, and is illustrated in Figure 3, which shows the $T - g$ relationship for illustrative parameter values.

6 The pharmaceutical company's problem

6.1 Objective function

From Table 2, at the moment it makes a contract offer, the pharmaceutical company's expected payoff if $\sigma = H$ and it submits the drug to the FDA for approval is

$$\Pr(H|\sigma = H)\left[P^A(s_H, T)(1-\rho)\Pi - M\right] + \Pr(L|\sigma = H)\left[-P^A(s_H, T)X - M\right] =$$

$$s_H\left[P^A(s_H, T)(1-\rho)\Pi - M\right] + (1-s_H)\left[-P^A(s_H, T)X - M\right] =$$

$$P^A(s_H, T)\left[s_H(1-\rho)\Pi - (1-s_H)X\right] - M. \tag{15}$$

The pharmaceutical company's payoff if $\sigma = H$ and it does not submit the drug to the FDA for approval is

$$-M. \tag{16}$$

We model the pharmaceutical company as an expected profit maximizer. If $\sigma = H$, the pharmaceutical company will submit the drug for approval if

$$P^A(s_H, T)\left[s_H(1-\rho)\Pi - (1-s_H)X\right] - M \geq -M$$

$$s_H(1-\rho)\Pi - (1-s_H)X \geq 0. \tag{17}$$

We assume that condition (17) is satisfied. This implies some restrictions on the state-dependent payoffs — Π cannot be too small, X cannot be too large — and it implies some restrictions on equilibrium contract terms (ρ cannot be too large).

Similarly, the pharmaceutical company's expected payoff if $\sigma = L$ and it submits the drug to the FDA

for approval is

$$\Pr(H|\sigma = L)\left[P^A(s_L)(1-\rho)\Pi - M\right] + \Pr(L|\sigma = L)\left[-P^A(s_L)X - M\right] =$$

$$s_L P^A(s_L)(1-\rho)\Pi - (1-s_L)P^A(s_L)X - M =$$

$$P^A(s_L)\left[s_L(1-\rho)\Pi - (1-s_L)X\right] - M$$

The pharmaceutical company's expected payoff if $\sigma = L$ and it does not submit the drug to the FDA for approval is $-M$. If $\sigma = L$, the pharmaceutical company will not submit the drug to the FDA for approval if[14]

$$s_L(1-\rho)\Pi - (1-s_L)X \leq 0. \tag{18}$$

Once again, this implies some restrictions on the parameters.[15]

Then the pharmaceutical company's objective function, at the moment the contract is negotiated, is

$$[gh + (1-g)(1-h)]\left\{P^A(s_H, T)\left[s_H(1-\rho)\Pi - (1-s_H)X\right] - M\right\} +$$

$$+ \left[(1-h)g + h(1-g)\right](-M), \tag{19}$$

and omitting several steps, this becomes[16]

$$\pi^{Ph}(\rho, T) = P^A\left[g(\rho), h, T\right]\left\{g(\rho)h(1-\rho)\Pi - \left[1-g(\rho)\right](1-h)X\right\} - M. \tag{20}$$

6.2 T and the choice of ρ: analytics

We model the pharmaceutical company as selecting ρ to maximize (20), given that CRO sets g to satisfy the first-order condition (10).[17]

Differentiate the first-order condition to maximize (39) with respect to ρ,

$$\frac{d\pi^{Ph}}{d\rho} \equiv 0, \tag{21}$$

with respect to T to obtain the comparative static derivative

$$\frac{\partial \rho}{\partial T} = \frac{\frac{\partial}{\partial T}\left(\frac{d\pi^{Ph}}{d\rho}\right)}{-\frac{d^2\pi^{Ph}}{d\rho^2}}. \tag{22}$$

The denominator on the right is negative, by the assumption that the second-order condition for the pharmaceutical company's optimization problem is satisfied. It is apparent from (22) that $\frac{\partial \rho}{\partial T}$ has the same sign as the second-order cross-derivative $\frac{\partial}{\partial T}\left(\frac{d\pi^{Ph}}{d\rho}\right)$: if an increase in T increases $\frac{d\pi^{Ph}}{d\rho}$, then ρ rises as T rises, and vice versa.[18] $\frac{\partial}{\partial T}\left(\frac{d\pi^{Ph}}{d\rho}\right)$, however, is ambiguous sign. We therefore turn to numerical evaluation to

[14] We make tie-breaking assumptions that if $\sigma = H$ and (17) holds with equality, Pharma submits, and if $\sigma = L$ and (18) holds with equality, Pharma does not submit. These assumptions are without loss of generality.

[15] Both sets of conditions are satisfied for the numerical results we present below.

[16] Compare with CRO's payoff function, (9). On the left, we suppress the functional dependence of π^{Ph} on h, Π, X, and M for notational compactness.

[17] This is the first-order approach of the principal-agent literature; see Mirrlees (1999 [1975]), Rogerson (1985).

[18] This is similar to the notion of strategic substitutability, the main difference being that here ρ is a choice variable of the pharmaceutical company, T an FDA policy variable.

illustrate the properties of the model.

6.3 T, ρ, and g: numerical evaluation

Table 3 shows the impact of changes in the strictness of FDA approval policy on equilibrium outcomes for the precision cost function (1). The evaluations are for a high prior probability ($h = 0.99$) that the drug is of high quality. If the drug is released to the public and proves to be of high quality, the payoff is $\Pi = 1000$. If the drug is released to the public and proves to be of low quality, the penalty is $X = 200000$. These gross payoff amounts are chosen to represent the case that release of a drug that proves to be of low quality involves catastrophic losses.

As we have seen with Lemma 1, the partial effect of increases in T and ρ are to increase g. The pharmaceutical company's reaction to increases in T, which tends to increase g, is to lower the royalty rate ρ, but not so much that g falls with as T rises: the net impact of an increase in T is to increase the precision of CRO's signal. This increase in g is translated into an increase in the updated signal, s_H, that is sent to the FDA, if CRO's signal is that the drug is of high quality. Despite this increase in s_H as T rises, the net effect of an increase in T on the probability of approval (which rises as s_H rises but falls as T rises) is negative: $P^A(s_H)$ falls as T rises. The strategic interaction of T and ρ means that the pharmaceutical company's payoff rises and CRO's payoff falls as T rises.

These relationships continue as T increases to higher values, as shown in Table 4. The lesson of Tables 3 and 4 is that if the pharmaceutical company is confident that its product is of high quality, increasing FDA stringency favors the pharmaceutical company and disadvantages the independent contract research organization.

Tables 5 and 6 show the impact of changes in the pharmaceutical company's initial probability h that the drug is of high quality on s_H, ρ, g, π^{CRO} and π^{Ph}, holding the lower bound of the approval threshold constant. Values in Table 5 are computed for $T = 0.5$, values in Table 6 for $T = 0.9$. Payoffs are as for Tables 3 and 4. The same qualitative pattern appears in both tables.

As the pharmaceutical company becomes less confident in the quality of its drug (as h falls), all else equal, it must offer a CRO a higher royalty rate to induce the CRO to accept a contract. The precision of the CRO's estimate, g, rises as the royalty rate rises — CRO generates more accurate results. But the posterior probability s_H that the drug is of high quality falls as h falls, and with it the probability of approval, conditional on s_H. CRO's expected payoff rises, and the pharmaceutical company's payoff falls, as h falls. For a sufficiently low value of h, the pharmaceutical company's expected payoff if the drug is approved is negative, and the drug would not be submitted to the FDA for approval.

7 Conclusion

In this paper we model the terms of contracts between pharmaceutical companies and contract research organizations. Pharmaceutical companies employ CROs to conduct later-stage tests of drug molecules. Depending on their own evaluation of the probability with which a drug is of high quality and the CRO's evaluation, pharmaceutical companies decide whether to submit a drug for FDA approval. If the pharmaceutical company's prior probability that the drug is of high quality is not sufficiently high, it will not submit the drug for FDA approval and therefore will not employ a CRO to conduct late stage tests. We analyze the effect of the FDA's demand for precision in results on the choice of royalty rate in the CRO contract, if

the prior probability is sufficiently high. We also analyze the effect of royalty rates and FDA requirements for precision in test results on the CRO pursuit of research accuracy.

We find that for a given FDA approval threshold, as the royalty rate rises, a pharmaceutical company must pay a higher royalty rate, the lower its prior probability that the drug is of high quality. As the royalty rate rises, CRO's profit-maximizing choice of precision in its estimation rises as well. This result is consistent with the contract literature which states that royalties increases the unobserved effort level of the agent. We also find that given the royalty rate specified in the contract, if the FDA becomes more stringent in its accuracy requirements, then CRO will put more effort into obtaining accurate results. This has the important policy implication that a stricter FDA approval process improves the effectiveness of regulatory drug evaluation.

The analysis of the pharmaceutical company's problem indicates that if the FDA demands greater precision, the equilibrium royalty rate falls, but not so much that CRO's realized precision falls. The net impact of an increase in the lower limit of the range of the approval threshold is to increase the precision of CRO's signal. However, as the FDA's demand for precision rises, the probability of approval falls. The net impact is that as the FDA's demand for precision in results rises the pharmaceutical company's payoff rises and CRO's payoff falls.

The model presented here explores the impact of FDA approval standards on the terms of contracts between pharmaceutical companies and contract research organizations. It would be of interest to extend the analysis backward and investigate the impact of FDA approval standards on pharmaceutical company research decisions. It would also be of interest to examine the impact of FDA approval standards on R&D competition among pharmaceutical companies. Finally, we have assumed extreme risk aversion on the part of pharmaceutical companies, by assuming that a pharmaceutical company would not submit a drug known or expected to be of low quality for FDA approval. Enough possible counterexamples exist to make the exploration of alternative specifications interesting.[19] These topics must wait for future research.

8 Appendix

8.1 CRO's problem

8.1.1 CRO's objective function

Picking up from (6) and (8), the probability that $\sigma = H$ is $hg + (1-h)(1-g)$ and CRO's expected payoff if $\sigma = H$ is $s_H P^A(s_H, T)\rho\Pi + M - y(g)$. The probability that $\sigma = L$ is $1 - [hg + (1-h)(1-g)]$ and CRO's expected payoff if $\sigma = L$ is $M - y(g)$. CRO's expected payoff is then

$$[hg + (1-h)(1-g)]\left[s_H P^A(s_H, T)\rho\Pi + M - y(g)\right]$$

$$+\{1 - [hg + (1-h)(1-g)]\}(M - y(g)) =$$

$$[hg + (1-h)(1-g)]\, s_H P^A(s_H, T)\rho\Pi + M - y(g) =$$

[19] See among others Gina Kolata, "When drugs cause problems they are supposed to prevent," *New York Times* internet edition 16 October 2010; Duff Wilson, "Merck to Pay $950 Million Over Vioxx," *New York Times* internet edition November 22, 2011; Barry Meier and Katie Thomas, "Device Malfunction Casts Doubt on Industry Oversight Pledge," *New York Times* internet edition, April 18, 2012. The latter reference involves a heart implant, not a pharmaceutical, but seems reasonable to cite in the present context.

(and substituting for s_H)

$$[hg + (1-h)(1-g)] \frac{gh}{gh + (1-g)(1-h)} P^A(s_H, T) \rho\Pi + M - y(g) =$$

$$= hgP^A(g, h, T) \rho\Pi + M - y(g),$$

which is (9).

8.1.2 Lemma 1

The first-order condition to maximize (9) is (10). In more detail, this can be written

$$\frac{\partial \pi^{CRO}}{\partial g} = h\rho\Pi \frac{\frac{gh[gh+(2-g)(1-h)]}{[gh+(1-g)(1-h)]^2} - T}{1-T} - y'(g) \equiv 0 \tag{23}$$

The second-order condition, which we assume is met, is

$$\frac{\partial^2 \pi^{CRO}}{\partial g^2} = h\rho\Pi \frac{\partial^2 gP^A(g, h, T)}{\partial g^2} - y''(g) < 0. \tag{24}$$

or equivalently

$$\frac{\partial^2 \pi^{CRO}}{\partial g^2} = \frac{h\rho\Pi}{1-T} \frac{2h(1-h)^2}{[gh + (1-g)(1-h)]^3} - y''(g) < 0. \tag{25}$$

To investigate comparative static relationships, differentiate the first-order condition

$$\frac{\partial \pi^{CRO}}{\partial g} \equiv 0$$

with respect to any parameter x (where x can be ρ, Π, T, or h) to obtain

$$\frac{\partial^2 \pi^{CRO}}{\partial g^2} \frac{\partial g}{\partial x} + \frac{\partial^2 \pi^{CRO}}{\partial x \partial g} = 0$$

$$\frac{\partial g}{\partial x} = \frac{\frac{\partial^2 \pi^{CRO}}{\partial x \partial g}}{-\frac{\partial^2 \pi^{CRO}}{\partial g^2}}. \tag{26}$$

The denominator on the right is positive by the second-order condition.

Hence $\frac{\partial g}{\partial x}$ has the same sign as the numerator on the right.

ρ, Π For notational compactness, write

$$A(g, h) = \frac{gh[gh + (2-g)(1-h)]}{[gh + (1-g)(1-h)]^2} \tag{27}$$

for the first term in the numerator after the first equals sign in (23). The first-order condition implies that $A(g, h) > T$. Then differentiating (23) with respect to ρ gives

$$\frac{\partial^2 \pi^{CRO}}{\partial \rho \partial g} = h\Pi \frac{A(g, h) - T}{1-T} > 0, \tag{28}$$

and this gives (11). In the same way, we obtain (12).

8.1.3 T

Differentiate the first-order condition

$$\frac{\partial \pi^{CRO}}{\partial g} = h\rho\Pi \frac{A(g,h) - T}{1-T} - y'(g) \equiv 0 \tag{CROfoc4}$$

with respect to T to obtain

$$\frac{\partial^2 \pi^{CRO}}{\partial g \partial T} = h\rho\Pi \frac{\partial}{\partial T} \frac{A(g,h) - T}{1-T}. \tag{29}$$

First,

$$\frac{\partial}{\partial T} \frac{A-T}{1-T} = \frac{A-1}{(1-T)^2}. \tag{30}$$

The numerator on the right is (omitting several steps)

$$A - 1 = (1-h) \frac{g^2 h - (1-h)(1-g)^2}{[gh + (1-g)(1-h)]^2}. \tag{31}$$

On the right, $g^2 h - (1-h)(1-g)^2$ is positive for $\frac{1}{2} < g, h \leq 1$.[20] Hence $\frac{\partial^2 \pi^{CRO}}{\partial g \partial T} > 0$ and this gives (13).

8.2 The pharmaceutical company's problem

8.2.1 The pharmaceutical company's objective function

From (19), the pharmaceutical company's objective function is

$$\begin{aligned} &[gh + (1-g)(1-h)] P^A(s_H, T) s_H (1-\rho) \Pi \\ &- [gh + (1-g)(1-h)] P^A(s_H, T)(1-s_H) X - M. \end{aligned} \tag{32}$$

In the first term,

$$[hg + (1-h)(1-g)] s_H P^A(s_H, T) = \frac{gh}{1-T} \left[\frac{gh}{gh + (1-g)(1-h)} - T \right]. \tag{33}$$

Looking at the coefficient of X,

$$\begin{aligned} &[gh + (1-g)(1-h)] P^A(s_H, T)(1-s_H) = \\ &[gh + (1-g)(1-h)] \frac{\frac{gh}{gh+(1-g)(1-h)} - T}{1-T} \left(1 - \frac{gh}{gh + (1-g)(1-h)} \right) = \\ &\frac{gh + (1-g)(1-h) - gh}{1-T} \left[\frac{gh}{gh + (1-g)(1-h)} - T \right] = \\ &\frac{(1-g)(1-h)}{1-T} \left[\frac{gh}{gh + (1-g)(1-h)} - T \right]. \end{aligned} \tag{34}$$

[20] $g^2 h - (1-h)(1-g)^2 = 0$ for $g = h = \frac{1}{2}$; its partial derivatives with respect to g and h are positive for $\frac{1}{2} < g, h \leq 1$.

Substituting in (32), the pharmaceutical company's objective function is

$$\pi^{Ph} = \frac{gh}{1-T}\left[\frac{gh}{gh+(1-g)(1-h)} - T\right](1-\rho)\,\Pi$$

$$-\frac{(1-g)(1-h)}{1-T}\left[\frac{gh}{gh+(1-g)(1-h)} - T\right]X - M$$

$$\pi^{Ph} = \left[\frac{gh}{gh+(1-g)(1-h)} - T\right]\left[\frac{gh(1-\rho)\,\Pi - (1-g)(1-h)\,X}{1-T}\right] - M \tag{35}$$

$$\pi^{Ph} = \frac{\frac{gh}{gh+(1-g)(1-h)} - T}{1-T}\left[gh(1-\rho)\,\Pi - (1-g)(1-h)\,X\right] - M, \tag{36}$$

and this is (20).

$\frac{\partial \rho}{\partial T}$

$$\max_{\rho} \pi^{Ph}\left[\rho, g(\rho,T), T, h, \Pi, X\right]. \tag{37}$$

Suppress the last three parameters for notational compactness.

$$\max_{\rho} \pi^{Ph}\left[\rho, g(\rho,T), T\right] \tag{38}$$

The pharmaceutical company's problem can also be written, in successively greater detail, as

$$\max_{\rho} P^{A}(g,h,T)\left[gh(1-\rho)\,\Pi - (1-g)(1-h)\,X\right] - M. \tag{39}$$

$$\max_{\rho} \frac{s_H - T}{1-T}\left[gh(1-\rho)\,\Pi - (1-g)(1-h)\,X\right] - M. \tag{40}$$

$$\max_{\rho} \frac{\frac{gh}{gh+(1-g)(1-h)} - T}{1-T}\left[gh(1-\rho)\,\Pi - (1-g)(1-h)\,X\right] - M \tag{41}$$

Begin with (38): the first-order condition is

$$\frac{d\pi^{Ph}}{d\rho} = \frac{\partial \pi^{Ph}\left[\rho, g(\rho,T), T\right]}{\partial \rho} + \frac{\partial \pi^{Ph}\left[\rho, g(\rho,T), T\right]}{\partial g}\frac{\partial g(\rho,T)}{\partial \rho} \equiv 0 \tag{42}$$

or, using subscripts to denote partial derivatives,

$$\frac{d\pi^{Ph}}{d\rho} = \pi^{Ph}_{\rho} + \pi^{Ph}_{g} g_{\rho} \equiv 0 \tag{43}$$

(43) implicitly defines the pharmaceutical company's choice of ρ as a function of the FDA policy variable, T, and other parameters.

Differentiate (43) with respect to T: (writing $\frac{\partial \rho}{\partial T}$ since ρ is also a function of h, Π, and X):

$$\pi^{Ph}_{\rho\rho}\frac{\partial \rho}{\partial T} + \pi^{Ph}_{\rho g}\left[g_{\rho}\frac{\partial \rho}{\partial T} + g_T\right] + \pi^{Ph}_{\rho T} + \pi^{Ph}_{g}\left[g_{\rho\rho}\frac{\partial \rho}{\partial T} + g_{\rho T}\right]$$

$$+g_{\rho}\left[\pi^{Ph}_{\rho g}\frac{\partial \rho}{\partial T} + \pi^{Ph}_{gg}\left(g_{\rho}\frac{\partial \rho}{\partial T} + g_T\right) + \pi^{Ph}_{gT}\right] = 0. \tag{44}$$

Collect terms in $\frac{\partial \rho}{\partial T}$:

$$\left(\pi_{\rho\rho}^{Ph} + 2\pi_{\rho g}^{Ph} g_\rho + \pi_g^{Ph} g_{\rho\rho} + g_\rho^2 \pi_{gg}^{Ph}\right) \frac{\partial \rho}{\partial T} + \pi_{\rho g}^{Ph} g_T + \pi_{\rho T}^{Ph} + \pi_g^{Ph} g_{\rho T} + g_\rho \pi_{gg}^{Ph} g_T + g_\rho \pi_{gT}^{Ph} = 0 \tag{45}$$

In (45), we know from Lemma 1 that $g_\rho > 0$ and $g_T > 0$. The assumption that the second-order condition for the pharmaceutical company's problem is satisfied gives us that

$$\pi_{\rho\rho}^{Ph} < 0. \tag{46}$$

From (41),

$$\pi_\rho^{Ph} = -\frac{\frac{gh}{gh+(1-g)(1-h)} - T}{1-T} gh\Pi. \tag{47}$$

Then

$$\begin{aligned}
\pi_{\rho g}^{Ph} &= \frac{h\Pi}{1-T} \frac{\partial}{\partial g} \left[\left(\frac{gh}{gh + (1-g)(1-h)} - T \right) g \right] \\
&= \frac{h\Pi}{1-T} \left[\frac{gh}{gh + (1-g)(1-h)} - T + \frac{\partial}{\partial g} \frac{gh}{gh + (1-g)(1-h)} \right] \\
&= \frac{h\Pi}{1-T} \left\{ \frac{gh}{gh + (1-g)(1-h)} - T + \frac{h(1-h)}{[gh + (1-g)(1-h)]^2} \right\} > 0.
\end{aligned} \tag{48}$$

Further simplification of the expression in braces is possible, but the sign of the expression is clear, since the first two terms in braces are $s_H - T > 0$. Then in the coefficient of $\frac{\partial \rho}{\partial T}$ in (45), the first term is negative, the second term is positive. The coefficient of $\frac{\partial \rho}{\partial T}$ is thus of ambiguous sign, meaning that $\frac{\partial \rho}{\partial T}$ is of ambiguous sign.

Stage	Description
Discovery	Target identification, biochemical mechanism.
Formulation	Identifying drug's stability.
Lead Molecule	Identifying the lead molecule for the development.
Preclinical	On animals to find out various parameters.
Phase I	Small-scale, identify tolerance, repeated-dose studies.
	Healthy volunteers. Initial single-dose, dose increase.
Phase II	Small-scale, preliminary efficacy on patients.
Phase III	Large-scale clinical trials, safety and efficacy
	Large scale patients, Preparation for NDA.

Table 1: Description of Drug Development Stages. Source: http://www.pacificbiolabs.com/drug_stages.asp.

True	Signal	Probability	Pharma	CRO
H	H	hg	$P^A(s_H, T)(1-\rho)\Pi - M$	$P^A(s_H, T)\rho\Pi + M - y(g)$
L	H	$(1-h)(1-g)$	$-P^A(s_H, T)X - M$	$M - y(g)$
H	L	$h(1-g)$	$P^A(s_L)(1-\rho)\Pi - M$	$P^A(s_L)\rho\Pi + M - y(g)$
L	L	$(1-h)g$	$-P^A(s_L)X - M$	$M - y(g)$

Table 2: States, signals, probabilities, at moment contract is negotiated, and payoffs if Pharma submits.

T	ρ	g	s_H	$P^A(s_H)$	π^{CRO}	π^{Ph}
0.50	0.106937	0.931960	0.9992631	0.998526	92.17	743.92
0.60	0.106852	0.932100	0.9992647	0.998161	92.06	744.07
0.70	0.106712	0.932332	0.9992674	0.997558	91.87	744.30
0.80	0.106439	0.932790	0.9992727	0.996363	91.50	744.74
0.90	0.105680	0.934112	0.9992880	0.992880	90.45	745.94

Table 3: Equilibrium characteristics, low to high T ($h = 0.99$, $k = 1$, $\Pi = 1000$, and $X = 200000$). Payoffs are shown for $M = 0$, that is, before taking the lump-sum payment into account.

T	ρ	g	s_H	$P^A(s_H)$	π^{CRO}	π^{Ph}
0.90	0.105680	0.934112	0.9992880	0.992880	90.45	745.94
0.91	0.105522	0.934396	0.9992913	0.992125	90.22	746.18
0.92	0.105331	0.934746	0.9992953	0.991191	89.95	746.48
0.93	0.105093	0.935189	0.9993004	0.990006	89.61	746.83
0.94	0.104792	0.935766	0.9993071	0.988452	89.18	747.28
0.95	0.104395	0.936551	0.9993161	0.986323	88.58	747.85
0.96	0.103853	0.937680	0.9993291	0.983228	87.76	748.60
0.97	0.103075	0.939445	0.9993493	0.978311	86.52	749.59
0.98	0.101903	0.942602	0.9993853	0.969265	84.45	750.80

Table 4: Equilibrium characteristics, high T ($h = 0.99$, $k = 1$, $\Pi = 1000$, and $X = 200000$). Payoffs are shown for $M = 0$, that is, before taking the lump-sum payment into account.

h	ρ	g	s_H	$P^A(s_H)$	π^{CRO}	π^{Ph}
0.99	0.10694	0.93196	0.99926	0.99852	92.172	743.30
0.98	0.15020	0.94287	0.99877	0.99754	130.70	601.27
0.97	0.18812	0.94920	0.99835	0.99670	163.79	478.95
0.96	0.22279	0.95354	0.99797	0.99594	193.35	368.13
0.95	0.25521	0.95679	0.99763	0.99526	220.30	267.74
0.94	0.28599	0.95938	0.99730	0.99460	245.21	171.15
0.93	0.31549	0.96150	0.99699	0.99398	268.42	79.97
0.925	0.32985	0.96243	0.99684	0.99368	279.48	35.80

Table 5: Equilibrium characteristics, $T = 0.50$ ($k = 2$, $\Pi = 1000$, and $X = 200000$). Payoffs are shown for $M = 0$, that is, before taking the lump-sum payment into account.

h	ρ	g	s_H	$P^A(s_H)$	π^{CRO}	π^{Ph}
0.99	0.10568	0.934118	0.99929	0.99288	90.45	745.94
0.98	0.14500	0.94593	0.99883	0.98835	124.60	613.74
0.97	0.17752	0.95289	0.99847	0.98473	151.96	508.00
0.969	0.18051	0.95345	0.99844	0.98440	154.42	498.38

Table 6: Equilibrium characteristics, $T = 0.90$ ($k = 2$, $\Pi = 1000$, and $X = 200000$). Payoffs are shown for $M = 0$, that is, before taking the lump-sum payment into account.

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