Choosing the right incentive strategy for research and development in neglected diseases

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Abstract For the first time in history, worldwide neglected disease budgets may be large enough to deliver a new drug every few years. That said, sponsors will only succeed if they extract maximum value from every dollar spent. This paper reviews possible cost-containment strategies and provides an evidence-based framework for choosing between them. Current proposals can be categorized as "end-to-end" proposals which require the sponsor to set a single reward for companies that complete the entire drug discovery process or "pay-as-you-go" schemes in which sponsors offer repeated rewards as drug candidates progress through the pipeline. A generic weakness of end-to-end proposals is that rewards are likely to be 20–30% higher than they would be in an equivalent pay-as-you-go programme. However, the benefits of pay-as-you-go programmes may be lost if commercial pharmaceutical companies are substantially better at choosing successful programmes than are their non-profit counterparts. The efficiency of pay-as-you-go methods depends on sponsors' willingness to withdraw funding from failed drug discovery programmes.

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Voir page 380 le résumé en français. En la página 380 figura un resumen en español.

يمكن الاطلاع على الملخص بالعربية في صفحة 381.

Introduction

We live in an era of hope. Ten years ago, worldwide spending on research and development (R&D) for tropical diseases was a paltry US$ 50 million.[1] In a world where per-drug R&D costs averaged US$ 802 million,[2] substantial progress was almost impossible. The situation today is very different; 5 years from now, R&D budgets are likely to reach US$ 500 million.[1] This figure is still only about a fifth of the total R&D budget of a large pharmaceutical company,[3] nevertheless, the dream of a new drug for tropical diseases every year or so could now become a reality. Whether or not governments and non-profit organizations (hereinafter collectively called "sponsors") achieve this goal depends on how wisely they spend the money.

In this paper, wisdom means cost containment. I assume that sponsors have already prioritized a list of desired R&D tasks. Given a fixed budget, how can sponsors accomplish as much of the list as possible? Unlike traditional calls for more funding for research into neglected diseases, this enquiry is not — and should not be — primarily political. Rather, it resembles a conventional business plan. Companies like Merck (with a budget of US$ 2 billion per year) [4] and Microsoft (US$ 6 billion) [5] routinely design R&D programmes much larger than those discussed here. Neglected disease sponsors should design funding strategies that are just as shrewd and evidence-based as those employed in business settings.

There are many schemes to choose from. Commentators have proposed a bewildering variety of strategies including advanced purchase commitments, prizes and private–public partnerships (Table 1).[6–8] While none of these schemes is perfect, some are surely better than others. In this paper, I present an evidence-based framework for sponsors to compare options and to help decide which incentive systems allow the desired level of R&D effort at the lowest cost.

All known incentive models are flawed in some way. No amount of discussion will produce an "ideal" mechanism and it would be both pointless and irresponsible to wait for one. Rather, sponsors must decide which mechanism is best (i.e. least flawed) for their specific R&D situation.[9]

The problem of choosing a method to provide incentives in research is particularly daunting in the area of drug discovery, which is actually a "pipeline" of about a dozen separate and distinct R&D activities.[3] Here sponsors face a basic choice: to create a single, end-to-end mechanism for drugs that complete the entire pipeline or else break the pipeline into short segments and offer different, pay-as-you-go rewards for each component.

End-to-end proposals

End-to-end ("E2E") incentives treat the drug development pipeline as an indivisible whole unit. In principle, E2E sponsors have a choice between purchasing R&D services in advance — for example through competitively bid contracts — and offering after-the-fact rewards. In practice, this model is problematic. Contract R&D is only feasible if sponsors are able to detect companies that try to shirk their obligations and/or continue working on failed programmes in an effort to pad out revenue. This type of monitoring is almost impossible in the early stages of drug discovery projects, where success relies on intrinsically unobservable characteristics such as inspiration and creativity — and where bad ideas may not be identified as such for 12–15 years.[2] For this reason, no one argues that E2E sponsors should pay companies in advance of drug discoveries (so-called "push" incentives). Instead, E2E strategies are automatically limited to "pull" incentives in which payment occurs only after a drug is delivered.

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There are two main problems when push mechanisms are removed from incentive models. First, sponsors must offer a premium to overcome drug company skepticism that the reward may never be paid. And second, that sponsors have relatively little information about how large a reward to offer. This suggests that sponsors will often overpay companies for their work. In practice, all E2E systems suffer from some mix of these difficulties.

Boosted demand

By far the simplest E2E proposal for accelerating R&D efforts is to give sponsors a bigger budget to buy drugs. No one doubts that this kind of "boosted demand" strategy will work if the boost is large enough — after all, government health spending already drives most rich nation R&D. On the other hand, drug companies are skeptical of schemes that require them to negotiate with sponsors after the company has spent its R&D money. Tough-minded sponsors can — and often do — argue that it is better for the company to accept a price that covers only part of its investment than to sell no drugs at all. Current drug budgets are too small for pharmaceutical companies to overcome their skepticism that they will not recover their R&D investment.

There is no question that boosted demand strategies would eventually work if sponsor budgets rose indefinitely. However, the idea that voters in rich nations would support indefinite increases in health spending for the developing world seems politically unlikely. The United Kingdom's International Finance Facility (IFF) proposal[10] tries a creative solution to this problem by asking rich nations to adopt modest long-term spending increases in order to finance a massive one-off spending surge in time to meet the UN Millennium Development Goals by 2015. While this strategy is not specifically aimed at stimulating drug discovery, this temporary form of boosted demand could well induce new R&D programmes in cases where drug companies expect to recoup their costs within a decade or so. Unfortunately, cases of companies recovering investments within 10 years are probably few and far between, with new drug discovery usually taking 12–15 years.

The basic problem with boosted demand is that sponsors only negotiate after the drug exists. Inherent in more sophisticated E2E strategies is the argument that sponsors can get by with smaller budgets if they specify prices in advance. The most popular proposals are prizes and advanced purchase commitments.

Prizes

Prizes are most effective when the sponsors cannot renege on their promises. In practice, this means reducing complex and nuanced questions (such as "what new drug would most benefit society?") to mechanical payment rules that courts can enforce. This strategy involves significant tradeoffs. Products that satisfy prize definitions will normally be at least slightly different from those that society needs. This suggests that sponsors will seldom receive full value for their money.

A sophisticated prize system has been proposed by Aidan Hollis.[8] He argues that prize amounts should be calculated with widely used variables such as disability-adjusted life years (DALYs) and quality-adjusted life years (QALYs). This approach, however, has drawbacks, since few people — least of all those who design and use such variables — believe that DALYs and QALYs are an adequate substitute for human judgment.[3] The problem, of course, is that drug companies are unlikely to trust after-the-fact rewards that are awarded at the discretion of a panel of experts. Hollis admits that using DALYs is a compromise, but argues that the resulting errors are still preferable to rich nation patent systems that are based on purchasing decisions by patients who neither understand nor pay for the drugs they use. This argument has much less force for neglected diseases, where priorities are usually set by public health experts.

A second and possibly more appealing strategy is to design prizes that preserve a role for human judgment but reduce the incentive for sponsors to avoid paying rewards. This can be done by promising to award a fixed sum of money by a particular deadline and then having a panel of experts allocate the money as they see fit. Since the sponsor's funds will be spent in any case, the panel cannot systematically underpay contestants.[8,9] Nevertheless, such schemes also have a drawback. If the drugs developed in a particular year are all disappointing, the sponsor will overpay for the research results.

Finally, proponents of advanced purchase commitments have also tried to invent clear rules for paying rewards. This work is directly applicable to prizes. The leading proposal consists of a short technical specification of the drug (for example: to prevent at least 50% of clinical episodes of malaria due to *Plasmodium falciparum*) and creates an Independent Adjudication Committee to decide whether or not new drugs comply. The Committee would also include industry-friendly members to reassure drug companies that their interests were being represented.[7] Whether or not this system represents an improvement over Hollis's suggestions is unclear.

Advanced purchase commitments

Advanced purchase commitments are similar to prizes, except that sponsors promise to buy fixed quantities of drugs at a predetermined price if and when R&D succeeds. Like prizes, they require rules that are both clear enough to administer and nuanced enough to be useful. However, there is also a deeper question: even if a perfect system could be designed, how would sponsors decide on the size of the reward (i.e. how many doses at what price) to offer?

Companies will only invest in R&D if the proposed reward would cover their expected R&D expenses. This fact suggests that a clever sponsor should offer a reward that is only slightly larger than the cost of the R&D effort that it hopes to elicit. One natural benchmark is provided by DiMasi et al.[2] who find that discovery costs (averaged over research failures) were US$ 802 million per drug for products approved in 1997. Unfortunately, this number, like all serious estimates, is actually a range. More specifically, DiMasi et al. claim that the true cost falls between US$ 684 million and US$ 936 million at 95% confidence. This poses an obvious problem: in order to be sure of eliciting R&D efforts, sponsors must set the reward at least equal to the high end of the range. But if the true cost is US$ 802 million, they can expect to overpay by US$ 115 million or 14% on average. Furthermore, this figure is probably an underestimate since DiMasi only tells us what per-drug costs were in 1997. Sponsors need to know the expected cost for products that may not be approved until 2018 or so. Since real R&D cost growth is large and uncertain (DiMasi et al. report that real annual growth for clinical testing costs since

Table 1. **Typical incentives for research and development (R&D)**

Incentive	Strengths	Weaknesses
Prizes	Elicits widely-scattered ideas.	Sponsor must estimate size of required reward; overpayment is likely.
Grants	Elicits widely-scattered ideas.	Sponsor must estimate size of required reward; overpayment is likely.
Advanced purchase commitments	Eliminates need to monitor researchers.	Sponsor must estimate size of required reward; overpayment is likely.
Open source	Volunteers supply labour and materials at no cost to sponsor.	Supply of volunteer labour and materials may not meet social need.
Contract R&D	Use of competitive bidding promotes cost-containment.	Hard to monitor researchers where tasks are highly creative; does not elicit ideas from widely scattered researchers.

the 1970s has varied between 6.1% and 11.8%; the range for pre-clinical testing is between 2.3% and 7.8%),[2] we expect the actual overpayment to be substantially larger. Most methods of calculating reward predict overpayments of 20–30%.[3]

Advocates of E2E schemes understand the need for accurate reward estimates. For now, the most complete analysis has been done by Berndt et al.[11] They start from the premise that companies try to set budgets (R&D plus marketing costs) equal to expected revenues. Since drug revenues are well known, R&D spending can be estimated once marketing costs are known. Berndt et al. review the literature and find two studies that bracket marketing costs at between 15% and 36% of revenue; they reject both studies, however, and use a figure of 10%. Thus, Berndt et al. calculate an advanced purchase commitment of US$ 2.56 billion. They then adjust the calculated figure a second time to US$ 3 billion remarking that "a malaria vaccine may be more difficult to develop than the typical new chemical entity."[11] While Berndt does not quote a formal range of possible values, the uncertainty in their calculation can be shown from the fact that a calculation based on the rejected 36% marketing study would have led to a much smaller US$ 1.8 billion reward. On the assumption that the actual reward lies midway between US$ 1.8 and US$ 3 billion, sponsors who offer the larger figure can expect to overpay by about 25%.

The search for a "bare-bones" programme

The preceding discussion implies that R&D costs are a single, well-defined number. This is untrue. While there is surely some base level of funding below which R&D is impossible (a "bare-bones" level), there is no limit to how much money companies can potentially spend. For sponsors, the problem is knowing how much money to spend above the bare minimum. While increased funding will almost always hasten discovery or make it more certain, the law of diminishing returns suggests that further spending will eventually be wasteful. Critics of the so-called US$ 800 million pill implicitly make this point by arguing that drugs for rich nations could be delivered more cheaply.[12,13] More importantly, the spending patterns of rich nations tell us very little about how sponsors should allocate scarce resources between programmes for neglected diseases. If the goal is to save the most lives, spreading funds over a large number of bare-bones projects could well be the wisest strategy.

If designers of E2E strategies for research in neglected diseases want to replicate rich nation research efforts, they can set rewards equal to rich nation per-drug R&D costs. Leading prize and advanced purchase commitment proposals usually follow this approach.[7,8] But, they can also offer smaller rewards designed to elicit a bare-bones programme or something in the middle. The problem, once again, is tying the reward to estimated R&D costs. The Global Alliance for TB Drug Development[14] argues that a bare-bones tuberculosis vaccine could be developed for about a quarter of the US$ 800 million figure for rich nations quoted by DiMasi et al. However, Global Alliance's quoted estimate ranges from US$ 115 and US$ 240 million, implying that a sponsor who chooses the upper figure will overpay by roughly 36%. Furthermore, Global Alliance's cost estimate is controversial[15] and the actual number could be higher.

Pay-as-you-go (PAYG) proposals

Few modern pharmaceutical companies view the drug discovery process as an indivisible series of actions. Instead, they follow a PAYG strategy by outsourcing individual R&D steps using contracts, prizes, and other incentives. Many large drug companies spend 30–40% of their R&D budgets on this kind of external innovation. A few so-called virtual pharmas buy almost all of their R&D from outside companies. These PAYG organizations consist of little more than an in-house drug development team that sets priorities and manages R&D purchases.[3]

Before the 1990s, non-profit entities lacked sufficient drug management expertise to implement a PAYG strategy. The Gates and Rockefeller Foundations have spent tens of millions of dollars to fill this gap. Today, about a dozen non-profit groups are capable of managing drug portfolios. Leading examples include the Institute for OneWorld Health (iOWH), Medicines for Malaria Venture (MMV), and Drugs for Neglected Disease Initiative (DNDi).

Designing a PAYG strategy

PAYG strategies open up new possibilities. Unlike E2E, PAYG sponsors are not limited to a single large pull incentive. Instead, they can offer a series of smaller rewards — some push, some pull — at various points along the drug discovery pipeline. This approach offers two advantages. First, small, frequent rewards are inherently more reassuring for the recipient than are large distant ones. Second,

some push incentives — notably contract R&D services — can be purchased on the open market, meaning that sponsors do not have to specify a reward in advance. They can sign a contract with whichever company offers the best price.

Designing a successful PAYG scheme means offering the right incentive at each point along the drug discovery pipeline and realizing that early R&D tasks differ vastly from those that happen towards the end of the drug discovery process. Early steps in drug discovery rely on assembling information that may be widely scattered across researchers. To find and optimize drug candidates requires researchers to be intensely creative and exercise discretion — i.e. make unsupervised decisions about how to conduct research. Mechanisms like prizes, grants, and open source[18] work best in this environment. However, towards the end of the discovery pipeline during pre-clinical and clinical testing, different qualities and incentives are required. Now, creativity is concentrated in the drug management team while the actual testing becomes increasingly protocol-driven and routine. Cost-containment is also much more important — about three quarters of all R&D costs are incurred after drugs enter pre-clinical testing,[14] making contract R&D an attractive option. Table 2 shows the main steps in the drug discovery process and what a typical PAYG strategy might look like.

Table 2. **A model pay-as-you-go strategy**

Discovery phase	Main social challenges	Preferred incentives
Basic research	Monitoring is difficult; advances may depend on widely-scattered knowledge and ideas	Grants, prizes, open source
Early-phase drug discovery	Monitoring is difficult; advances may depend on widely-scattered knowledge and ideas	Grants, prizes, open source
Pre-clinical and human testing	Research is costly. Work by researchers tends to be routinized and easy to monitor	Competitively-bid contracts for research and development services
Manufacture	Research is costly. Process design is difficult to monitor	Contracts to purchase products if and when produced

Drawbacks

Purchasing power and related issues

The preceding discussion suggests that sponsors can contain costs by offering multiple, frequent rewards and purchasing some services on the open market, and some large drug companies already do this. Nevertheless, there are drawbacks to this type of scheme. R&D providers typically give bigger discounts to companies that can offer substantial repeat business. Once a contract has been signed, R&D providers may pad bills or hide unfavorable test results in order to keep contract payments flowing. Big drug companies employ a large staff of people to liaise with research suppliers and use the prospect of repeat business to minimize the dangers of exploitation.[16] It is reasonable to think that neglected disease sponsors might derive fewer benefits from outsourcing because they lack this financial leverage.

However, it is worth asking how large this effect actually is. Providers of contract chemistry services reportedly enjoy typical profit margins of 10–15%.[17] Assuming a 10% return to capital, this implies that they are able to overcharge by, at most, about 5%. Sponsors should keep outsourcing as efficient as possible by imitating commercial methods. These methods include careful contract administration and maximizing repeat business incentives by concentrating purchases on a handful of trusted vendors.

Finally, sponsors can sometimes be more efficient outsourcers than industry. Because of intellectual property concerns, many drug companies avoid doing business in Asia despite reported cost savings of about 5%.[17] Non-profit sponsors have no such limitations. They may also be better placed to take advantage of novel mechanisms based on open source and the services of volunteers.[18]

Can non-profit drug development teams pick winners?

The main reason why PAYG solutions might not be cost-effective is bad management. This is not a question of scientific competence. After all, most private–public partnerships recruit drug development teams from the private sector. The problem, if it exists at all, is more subtle. In the private sector, corporations maximize profits because they believe that shareholders will withdraw funds from them if they fail. If private–public partnerships are less efficient, it must be because their shareholders — sponsors — are more willing to tolerate failure and inefficiency. Definitive empirical studies will not be available until private–public partnerships begin to deliver completed drugs. Nevertheless, recent detailed analyses of private–public partnerships find no evidence that they manage their drug portfolios less efficiently than a commercial company.[19,20] The track record of older institutions (e.g. the Pasteur Institute,[21] the US Army,[22] and the March of Dimes[23]) in developing vaccines similarly suggests that non-profit organizations are reasonably efficient.

Mixed models

So far in this paper, I have described the choice faced by sponsors between E2E and PAYG. One can, however, imagine options that blend E2E and PAYG, for example by funding private–public partnerships which then compete for an advanced purchase commitment. This type of blended scheme could make sense in certain, somewhat artificial, scenarios; for instance, where both public and private partners have important knowledge that the other lacks. In general, it would be difficult to justify investment in E2E and PAYG simultaneously if one method was known to have a clear cost advantage over the other.

Alternatively, some observers argue that sponsors should continue funding E2E and PAYG methods as simultaneous experiments. Given the costs involved in drug discovery, such experiments are bound to be expensive. Once the evidence is clear, sponsors can and should save money by halting experiments as soon as possible. Experiments may also be unwise when the evidence is ambiguous. It is reasonable to think that E2E and PAYG both have substantial economies of scale. Dividing funds can only weaken both programmes.

Is there a role for patents?

None of the rewards discussed so far requires patents. If sponsors want to, they can insist that companies give up some or all of their patent rights in order to claim a reward. Whether they should do so is another matter.

Private–public partnerships often argue that giving industrial partners patent rights encourages them to contribute R&D resources. However, R&D is only half the battle. To make a difference, drugs must also be affordable. The purpose of patents is to raise prices. This may be acceptable when costs fall on rich nation citizens or middle-class patients in the developing world. The problem arises when higher prices hit poor patients and sponsors. Agreements that give private partners patent rights should always be structured so that these normally "hidden costs" become visible. One particularly straightforward solution is to draft agreements that specify firm and guaranteed price caps for governments, sponsors, and low-income patients.

Back to basics

In this paper, I have argued that designing a funding strategy for neglected disease R&D is not very different from choosing a business plan. In the private sector, CEOs routinely demand to know evidence, options and tradeoffs. Leaders of large sponsors like the Gates and Rockefeller Foundations should do the same. It is no longer enough for scholars to point out that their favoured strategy offers benefits or that competing plans have drawbacks. After all, we have seen that every plan has benefits and drawbacks. Sponsors need to choose, and scholars should do a better job of helping them.

For many years, the neglected disease community focused on a single strategy: asking for more money. Massive investments by The Gates Foundation and others have fundamentally transformed the problem. This paper has shown that the choice between incentive schemes can be made rationally with the use of detailed logic and evidence (Table 3). Commentators sometimes argue that various multi-billion dollar proposals should be funded on the principle of "let's just try it!".[24] That is not good enough. Neglected disease R&D — which receives vast funds from The Gates Foundation — should be run just as carefully as Microsoft itself. ■

Table 3: **Drawbacks in incentive strategies: end-to-end (E2E) versus pay-as-you-go (PAYG)**

Drawback	E2E	PAYG
Researchers deliver drugs based on formal specifications that may not reflect true needs of patients	Unknown	Not applicable
Researchers demand premium in case sponsor reneges	Unknown but probably large	Unknown but probably small
Sponsor sets excessive reward	20–30%	5–6%
Companies may not perform promised work	Not applicable	<5%
Companies may not outsource efficiently	<5%	Not applicable
Non-profit drug portfolio management teams may be less efficient	Not applicable	Unknown but probably small [19,20]

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Résumé

Choisir la bonne stratégie d'incitation pour la recherche et le développement en faveur des maladies négligées

Pour la première fois dans l'histoire, les budgets mondiaux alloués aux maladies négligées pourraient être suffisants pour mettre sur le marché un nouveau médicament à intervalles de quelques années. Ceci dit, les organismes parrainants ne réussiront dans cette entreprise que si le maximum est tiré de chaque dollar dépensé. Le présent article examine les stratégies potentielles de limitation des coûts et propose un cadre reposant sur des éléments factuels pour guider le choix entre ces stratégies. Les solutions proposées actuellement peuvent être classées en options «bout en bout», qui impliquent que l'organisme parrainant fixe une rémunération unique pour les entreprises qui achèvent le processus complet de découverte d'un médicament et ou en schémas de rétribution à mesure des réalisations, dans le cadre desquels les organismes parrainants rémunèrent chaque étape du parcours réalisée par le candidat médicament. D'une manière générale, le point faible des options bout en bout est que leur rémunération est 20 à 30 % supérieure à celle dont bénéficierait un programme équivalent rémunéré par étapes. Cependant, ces derniers peuvent perdre leur avantage dans le cas où les entreprises pharmaceutiques commerciales parviennent à une sélection nettement meilleure des programmes susceptibles de réussir que leurs homologues à but non lucratif. L'efficacité des méthodes de rémunération par étape dépend de la volonté des organismes parrainants de retirer leur financement des programmes de découverte de médicaments en échec.

Resumen

Elección de la estrategia idónea de incentivos para la investigación y el desarrollo relacionados con las enfermedades desatendidas

Por primera vez en la historia, los presupuestos mundiales para enfermedades desatendidas son quizá suficientes para poder desarrollar un medicamento nuevo cada pocos años. Ahora bien, los patrocinadores de esos proyectos sólo conseguirán sus objetivos si logran extraer el máximo valor de cada dólar invertido. En este documento se examinan las posibles estrategias de contención de los costos y se proporciona un marco basado en la evidencia para elegir entre ellas. Las propuestas actuales pueden clasificarse

como propuestas de «principio a fin», en las que el patrocinador establece una suma fija para recompensar a las empresas que finalicen todo el proceso de descubrimiento del medicamento, y sistemas de «pago en función de los progresos», en los que los patrocinadores recompensan los esfuerzos de forma escalonada a medida que los medicamentos experimentales superan las sucesivas fases de desarrollo. Un inconveniente general de las propuestas de «principio a fin» es que las recompensas tienden a ser un 20% - 30% superiores a las correspondientes a un programa equivalente de «pago en función de los progresos». Sin embargo, los beneficios de estos últimos programas pueden no materializarse si las empresas farmacéuticas comerciales demuestran ser considerablemente más hábiles que sus homólogos sin fines lucrativos a la hora de elegir los programas con buenos resultados. La eficiencia de los métodos de pago en función de los progresos depende de la voluntad de los patrocinadores para retirar la financiación a los programas de descubrimiento de medicamentos que fracasen.

ملخص

اختيار استراتيجية للحوافز المناسبة للبحوث والابتكارات في الأمراض المهملة

ستكون الميزانية المخصَّصة لمكافحة الأمراض المهملة على الصعيد العالمي ولأول مرة في التاريخ ضخمة لدرجة تكفي لتقديم دواء جديد كل بضعة أعوام؛ وهذا يعني أن من يقوم برعاية الابتكارات لن ينجح بعمله ما لم يحصل على القيمة العظمى مقابل كل دولار يدفعه. ونستعرض في هذه الورقة بعض استراتيجيات احتواء التكاليف، كما نقدِّم إطاراً مُسْنداً بالبيِّنات لاختيار واحدة منها. ويمكن تصنيف المقترحات الحاضرة بأنها مقترحات استكمالية تتطلَّب أن يضع من يقوم برعاية الابتكارات جائزة واحدة للشركات التي تستكمل عملية اكتشاف الدواء بكاملها، أو أن يتبع خطط الدفع مع الاستمرار بالعمل، حيث يدفع القائمون على رعاية الابتكارات مكافآت متكرِّرة تتماشى مع تطوُّر الدواء المرشَّح للظهور ضمن مسيرة التصنيع. ومن نقاط الضعف الواضحة في المقترحات الاستكمالية أن المكافآت ستزيد في قيمتها عما كان ينبغي أن تكون عليه في برامج خطط الدفع مع الاستمرار بالعمل بمقدار 20 – 30%. إلا أن برامج الدفع مع الاستمرار بالعمل قد تتلاشى عندما تكون الشركات الصيدلانية التجارية على حالة تمكِّنها من اختيار البرامج الناجحة بشكل أفضل مما يتاح لنظرائها غير الهادفين للربح. وتعتمد كفاءة طرق الدفع مع الاستمرار بالعمل على رغبة القائمين على رعاية تلك الطرق بسحب التمويل من البرامج التي تفشل في ابتكار الأدوية.

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