

— The —  
**DISTRIBUTED  
PARTNERING  
MODEL**  
— for —  
Drug Discovery and Development



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# The Distributed Partnering Model for Drug Discovery and Development

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**Abstract:** The major contributors to therapeutic innovations in the 20th century have been the pharmaceutical companies, with biotechnology companies adding significantly over the last twenty-five years. However, these models increasingly have failed in translating the advances of biomedical sciences into innovative products. We suggest a modern-day paradigm for efficiently advancing new therapeutic products. This "distributed partnering" approach would involve four distinct, independent organizations to collaborate in a risk-adjusted manner to discover, define, develop, and deliver innovative products.

The new model would feature the formation of companies called product definition companies (PDC), which would focus solely on advancing innovation through the initial definition research phase. PDCs would consist of a team of experienced professionals who would raise funds to manage several projects simultaneously. PDCs would acquire early stage discoveries from research institutions and invest in defining product applications with a goal of selling the successful ones to pharmaceutical companies for further development and delivery.

### The Fully Integrated Pharmaceutical Co. (Pharma) Model

Once upon a time, the United States pharmaceutical industry was prolific in developing new and innovative medicines. One of this paper's authors recently described the conditions that made this model so successful over many decades. Throughout the 1970s, most large pharma companies had a president of research or vice president of research and development, who oversaw basic research (i.e., discovery). This person was given a budget and great freedom to pursue the science wherever it might lead. Once a discovery was made with the potential for becoming a new product, a development team was formed to better define a product under the supervision of the vice president of research and development. The development team had representation from all relevant disciplines, including marketing. These teams focused on accomplishing all the steps necessary to bring the product to market.

As the product moved through early clinical trials and the Food and Drug Administration process, the delivery team developed the marketing plan for sales teams to launch the product around the world. This model was productive by any measure and resulted in a steady stream of innovative products. However, this model, for many reasons, now is failing, resulting in a major threat to new drug innovation.<sup>3,4</sup>

#### What went wrong?

In the 1970s, industry leadership began to shift toward an emphasis on strict business practices.<sup>3</sup> Many large pharmas began to borrow these new business principles (e.g., management by objectives, etc.) from non-research-intensive corporations to manage discovery, product definition, and development. These management tools included rigid scrutiny and tight controls of research projects through quarterly reviews, timelines, and Gantt charts. However, this approach is inappropriate for basic scientific research in the biomedical sciences. Pharmas truly are unique research-intensive matrix organizations, ultimate adhocracies<sup>6</sup>, that operate through complex collaborations between professionals from multiple and diverse disciplines, such as chemistry, biology, development, regulatory affairs, patenting, marketing, information technology, statistics, manufacturing, finance, and

many others. Furthermore, these professionals must function in dynamic, changing, and complex environments.

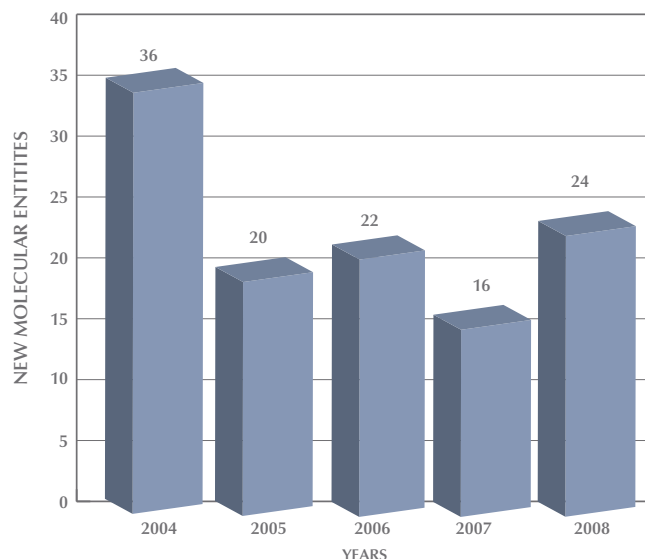
Proper functioning of the discovery/definition/development process requires that its management reside within the scientific staff. However, the increased dominance of the commercial side of pharmas (which demanded impossible degrees of predictability, tight controls of science and technology, and changing "choices" of which projects to pursue) ultimately led to a shift of control from research to marketing and commercial personnel. As suggested<sup>3</sup>, managing the research and development process in this way is counterproductive. Virtually every project is "killed" for one reason or another along the way, often rather arbitrarily. Thus, most pharmas essentially have become development companies managed by unimaginative marketing departments. Today, few would make the argument that the current pharma model of drug discovery and development is a productive model for advancing innovation. Despite billions of dollars of investment and numerous attempts to institute systems to encourage innovation, the current state of pharma discovery continues to decline (Figure 1).

### The Biotech Model

Biotech began in the late 1970s when leading scientists began to explore innovations in biology to develop new therapeutics. The concept became a reality with discoveries of the methods of producing proteins through genetic engineering (recombinant DNA) and of cloning antibodies (monoclonal antibodies).

In the early days, investments in biotech were made almost instinctively, based on the excitement of potentially applying new biological methods to produce therapeutics. Tom Perkins (founding partner at Kleiner Perkins Caufield & Byers) described his investment in Genentech Inc. as being based largely on the enthusiasm of Bob Swanson, an excited associate partner. Swanson proposed to start a new venture in an entirely new industry based on the discovery of Herb Boyer, a creative young academic scientist at the University of California, San Francisco. Perkins stated that after meeting with Swanson and Boyer, he and his partner, Eugene Kleiner, decided to fund a study to determine the feasibility of gene splicing (to produce proteins) and, if that worked, to fund Genentech. It did, and they did.

**Figure 1:  
R&D Expenditures are Increasing While  
FDA Approvals are Decreasing**



**R&D SPENDING**

2004.....	\$47.8
2005.....	\$51.8
2006.....	\$56.1
2007.....	\$58.5
2008.....	\$65.2

Source: Burrill & Company, US Food and Drug Administration

An important concurrent development was the passage of Bayh-Dole Act by the U.S. Congress in 1980. This legislation allowed research institutes to own the intellectual property derived from federally funded research (e.g., National Institutes of Health (NIH), National Science Foundation (NSF), etc.). This accelerated the formation of biotech startups to exploit the product definition and development of university-derived discoveries. Further enthusiasm for funding biotech startups was spurred by Genentech’s very successful initial public offering (IPO) in 1980.

The biotech model generally operated when entrepreneurs and venture capitalists organized to form a new company (i.e., a biotech) to pursue commercialization of a licensed scientific discovery that arose from publicly funded research. Much of the initial funding was used to recruit technical personnel and build infrastructure (i.e., laboratories, instrumentation, vivariums, pilot plants, etc.) similar to those existing in pharma, but on a smaller scale. These companies initially focused on product definition and development. As they advanced their lead product(s)

through development, they raised additional funds from venture capitalists or sold equity in the company through IPOs. As the product development advanced into late-stage clinical trials and the prospects of an FDA approval became realistic, most biotechs simply did not have the more extensive infrastructure or resources to conduct such studies

or to market the product. Thus, the early biotechs partnered with large pharmas to advance the potential of their lead product(s). This model became known as copartnering.

The goal of transitioning into an independent, fully integrated pharma rarely was achieved and copartnering with—or acquisition by—pharmas became the prevalent outcome.

During the past twenty-five years, the biotech model produced a number of successful products and companies. However, the evolution of biotech has been so drastic that, as described below, the existing model has become ineffective and anachronistic in modern

times. More than half a trillion dollars have been invested in the biotech model over the past twenty-five years and, as detailed by Pisano, the overall return on investment has been negative.<sup>7</sup>

**More than half a trillion dollars have been invested in the biotech model over the past twenty-five years and, as detailed by Pisano, the overall return on investment has been negative.**

### What went wrong?

The very early product definition and development success stories in biotech were nearly all based on the recombinant DNA protein engineering and monoclonal antibody technologies. In nearly all cases, the potential products were genetically engineered human proteins (some with slight variation) of known function and role in the pathophysiology of diseases and all had high potential for medical utility. The major challenge (other than intellectual property) was the large-scale production of a highly purified human protein or antibody. Thus, the successes were known hormones or growth factors, such as insulin, growth hormone, interferon, tissue plasminogen activator, erythropoietin and, later, monoclonal antibodies for transplant rejection and cancer.

The early successes of these products and companies created much enthusiasm in the investment and academic communities, which fueled hundreds of startup biotech companies. Over time, the general definition of biotech evolved to include a broad scope of technologies involving small molecules and diagnostics. The larger profitable companies are referred to as “big biotech” and function similarly to pharma. The term “biotech” describes a small (usually a startup), innovative company focused on a single (or limited) biological or technology product.

In more recent times, the technologies, discoveries, and potential novel products have been of a totally different nature in terms of “probability of success” when compared with the early biotech products. The projects have been highly innovative and, thus, unpredictable, risky, and very likely to involve long-term commitments. Many of the projects focus on small molecules, not proteins or antibodies. In effect, the research and development projects have become similar to those with which pharma deals. However, the small biotech only can tackle one project (or a few) at a time and within limited time horizons. The venture capitalists and investors do not have the resources or patience for these longer time horizons and the inevitable setbacks and delays. Pharma, on the other hand, has, in principle, the capabilities and resources [although currently not the right organizational procedures or willingness 3] to handle many of these kinds of long-term projects simultaneously, to pursue most things that look viable, and to re-work research when they experience impediments or delays. Virtually every major successful product has

been afflicted with serious problems or setbacks during development.<sup>3</sup> The biotech model simply does not allow for such difficulties.

Today, even the most promising discoveries made in research institutes are seen by venture capitalists as being too early and too risky for investing. Considerable efforts must be expended in analytical and upscale chemistry, safety pharmacology, toxicology, formulations, metabolism, and many other disciplines (preclinical development) before a specific candidate can be deemed ready to proceed to human testing or to pharma licensing. Therefore, today’s venture capitalists prefer to invest in technologies possessing well-identified lead compounds with high probabilities of success that are not far from entering clinical testing. Unfortunately, such opportunities almost never exist.

## A New Model for “Distributed Partnering” in the 21st Century

The future of financing life science innovations will require new, more efficient, sustainable models than those of the current pharma and biotech models.<sup>2,4</sup> We propose a new model that involves the concerted collaboration of multiple and varied organizational partners. Here, the economic and technical risks along the discovery and development paths are distributed and shared by independent partners that contribute differing but complementary expertise, culture, and value in a sequential process. The distributed partnering model includes four distinct, independent spheres that collaborate in a risk-adjusted manner to discover, define, develop, and deliver innovative products.

### Discovery research

As suggested by one of this paper’s authors and recently documented by Block and Keller<sup>1</sup>, federal and state research funding have become the primary sources for discovery research. Fortunately, in the United States, the importance of funding such research through federal agencies, such as the NIH, NSF, and Defense Advanced Research Projects Agency, now is accepted policy. In addition, many initiatives also are rising at the state level. For example, beginning in 2000, California was the first state to fund basic discovery research with the establishment of four publicly and privately financed institutes at the University of California and the

Governor Gray Davis Institutes for Science and Innovation. This investment was followed by voter approval of Proposition 71 in 2004, a \$3 billion effort led by Robert Klein to establish the California Institute for Regenerative Medicine to fund stem cell research. Currently, more than a dozen states are investing in biomedical innovation and infrastructure.

Numerous departments and centers of translational medicine and drug discovery now exist throughout the country. The nonprofit research community has responded with enthusiasm and energy. The seeds for the future exploitation of scientific advances for drug discovery already have been planted and the existing culture in academic settings is perfect for this type of work<sup>3</sup>, although the funding will have to be expanded significantly.

Once a grant has been awarded in a given area of research, the recipient essentially is free to pursue the science regardless of where it leads, unlike the pharma and biotech models. The “management” of the science by nontechnical managers and the administrative formalities are both minimal. Instead, the scientists are in charge. Oversight occurs primarily, as it should, through peer review and the granting agency. This culture cannot be duplicated in pharma or biotech. The unrestricted pursuit of basic science is essential to discovering the knowledge that can be the basis for new product innovation.

Academic laboratories, successful in making potential new drug discoveries, eventually are faced with technical and financial problems similar to those in biotechs when proceeding to the next stages of development, as described under “*What went wrong?*” NIH translational grants have helped, but their scope is too limited, too focused, and these grants rarely have extended to advance preclinical development needs. As described, venture capitalists simply will not fund this kind of early stage work. Academic laboratories have limited access to the funds or lack the expertise needed to do the advanced research and the early product definition required to move the project further. In addition, most academic researchers do not have the experience, temperament, or even interest in undertaking most of this work. Unfortunately,

pharmas, like biotechs, usually are not a reasonable option for handing off the work. They rarely are interested in pursuing these early discoveries in the absence of greater product definition. As a result, these potentially important early stage scientific discoveries are stifled by the absence of viable mechanisms for advancement.

### Definition research

Several approaches have been attempted to address a means of providing product definition and early development work (i.e., definition research) for innovative academic discoveries. A recent report from the Ewing Marion Kauffman Foundation described two academic models that have been successful in advancing early stage discoveries, the

Deshpande Center for Technological Innovation at the MIT School of Engineering and the William J. von Liebig Center at the University of California San Diego Jacobs School of Engineering.<sup>5</sup> Other approaches to fund early stage discoveries have been tried. They include incubators, accelerators, and virtual companies, most of which have the primary goal of starting new companies that face the same challenges and funding risks described above in the “*What went wrong?*” biotech model.

Similar opportunity needs for definition research also occur frequently in small biotechs. Here, potentially important discoveries are

abandoned because the biotech’s limited resources must be focused on clinical-stage or other advanced programs. Even in pharma, important discoveries are abandoned when they are not in sync with the current strategic plan. To fulfill these unmet needs for early product definition, we propose a new type of innovation organization called a product definition company (PDC).

The PDC combines an experienced management team with investment capital to advance a portfolio of discoveries through the product definition stage. An ideal example of a PDC would be one involving a small team of professionals highly experienced in areas, such as pharmaceutical research, clinical sciences, regulatory affairs, operations, and marketing. Some of these individuals would have extensive contacts and knowledge of universities’ early therapeutic discoveries for potential

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acquisition. The combination of expert personnel, specific possible projects, and the unique business model for the PDC would be the basis for raising sufficient initial capital to launch the operation. Much of the work could be done on a virtual basis, contracting the development tasks to Professional Service Providers (PSP) to perform the key tasks rather than building new infrastructure. The use of ad hoc scientific experts and consultants would be standard practice.

The PDC business model focuses on identifying and licensing promising discoveries from research institutes (and biotech/pharma). Licensees would receive traditional up-front fees, milestones, royalties, and equity ownership. The PDC then would progress by undertaking (via PSPs) and supervising the required product definition research for the acquired projects. The ultimate intention would be to **sell** the risk-reduced “asset packages” to third parties for further product development and delivery. Acquirers would include venture capitalists, pharmas, and big biotechs. The venture capitalists most likely would continue to fund advanced product development in a virtual mode, using PSPs rather than starting new biotech companies as in the previous model.

Typically, a PDC might invest between \$2 million and \$10 million in a given project, depending on the cost required to achieve proof of relevancy<sup>8</sup> for any given discovery within an average of three years. Proof of relevancy would be defined on a case-by-case basis when third parties judge progress to be sufficiently attractive for acquisition. Given the early stage nature of most discoveries under initial study, frequent technical failures during definition research would be expected; many would probably occur early and, thus, be less costly. Even product definition failures could create value through generation of valuable intellectual property.

The PDC would require initial investment funds sufficient to address multiple projects (i.e., ~ \$50 million to \$100 million). Depending on the funding and investment model selected, PDCs could be either private or public companies. Potential investors would include high net-worth individuals, hedge funds, strategic partners (including pharma/big biotech, PSPs, etc.) and venture

capitalists. The investment basis would value the expertise of the management team and its ability to evaluate and secure appropriate discoveries and translate them into potential products. The return on successful projects could range from two times to ten times that of invested funds upon completion of adequate definition research, making this a potentially profitable model. (See appendix A).

PDCs certainly would locate in regions that have significant concentrations of biomedical research institutions, such as San Diego, the San Francisco Bay area, and Boston, but they also could locate near state universities and private institutes with major research efforts and funding. PDCs in these regions could assist in advancing a culture that is compatible with commercializing innovation. In the

recently published book, *Start-Up Nation*, Dan Senor and Saul Singer describe Israel's remarkable success in technology innovation. They suggest the creation of an innovative culture is key to success on commercializing technology.<sup>9</sup>

Today, there are a multitude of excellent PSPs that can perform the required technical work, as well as or better than biotechs and pharmas, at greater efficiency and lower cost. Furthermore, many of these PSPs are so large, versatile, and experienced that they could tackle several different

aspects of the same project. Plus, all of the technical and development work for the PDC projects would be supervised and coordinated by experienced project managers.

Importantly, with the PSPs doing the development, technology transfer would occur in real-time as the knowledge would reside in the entities performing the work. Thus, these technologies or products could be even more valuable to those potentially interested in acquiring the asset in the future. In the pharma and biotech models, the data for advancing a technology/product come primarily from the company's assets (e.g., personnel, equipment, and facilities), which are expensive and inefficient. Today, the data could come from anywhere in the world, and the costs are only for the required technical work. Lastly, many other PDC functions can be performed on a virtual basis today, reducing unnecessary and expensive infrastructure and increasing organizational nimbleness and flexibility.

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**The PDC business model focuses on identifying and licensing promising discoveries from research institutes (and biotech/pharma).**

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## Development

To complete the “development” of a new product, delivery to the market still would require a number of additional tasks before marketing approval could be sought. Additional tasks include formulation and dosage-form development, advanced clinical trials, upscale chemistry, long-term toxicology, manufacturing technologies, and complex regulatory submissions, among other requirements. Venture capitalists could fund these activities either by forming a biotech, as in the existing model, or by operating in a virtual mode by use of PSPs as described above. For example, a venture capitalist may choose to fund advanced clinical trials (i.e., phase 2b, which is broadly described in the industry as proof of concept) before **selling** the asset to pharma or big biotech for final product development. Specialty funding companies, such as Symphony Capital, also could acquire PDC assets<sup>10</sup> and would develop them in a manner similar to the venture capitalists. Alternatively, pharma and big biotech would acquire the PDC asset at this stage and, in a similar approach, fund the PSP to the proof of concept stage.

## Delivery

Subsequently, among the activities required are marketing, manufacturing final product, distribution and sales, reimbursement arrangements, education of medical and health professionals, consumers (patients) and payers (insurance companies and government agencies), formulary registrations, global registrations, and post-marketing monitoring for safety and efficacy. These tasks already are conducted effectively and managed by pharmas and big biotechs. In fact, these tasks are the areas in which these corporations possess their greatest strengths.<sup>3,4</sup> The proposed model assumes that these types of companies would acquire the potential new products arising from PDCs and introduce the products into their delivery pipelines.

## Conclusion

The proposed new distributed partnering model offers the potential for a more productive and efficient advancement of innovation and will be applicable in any region with excellent research; it does not require legions of experienced entrepreneurs or local established venture capitalist firms to enact. The United States is well represented in each of the disciplines and cultures required in the model:

- *Discovery research* (federal, state, and philanthropic funding)
- *Product definition and early development* (large number of PSPs, vast industry experience, and entrepreneurial spirit)
- *Advanced product development and delivery* (extensive infrastructure, venture capitalists investment funds, and some of the best pharmas and big biotechs in the world)

This model focuses on advancing “products” as opposed to “companies” (i.e., we need thousands of products not thousands of companies). By combining the expertise of these distinct cultures and organizations, innovative products could be advanced efficiently, making the risks and investments more proportional to—and rational for—each partner. If successful, the United States might continue, and even accelerate, its global dominance in innovative medical products.

Finally, while this manuscript discusses the innovative biomedical sector of innovation, the model may well apply to other innovation sectors, including high-tech, information technology, cleantech, etc. As this early phase of innovation investment is crucial to the U.S. economy and to addressing the nation's most important challenges (e.g., higher quality, affordable healthcare; a cleaner environment; better security, etc.), the federal government should consider a follow-on matching investment to PDC private sector investors. The private sector limited partners would set the terms and conditions with the federal government serving as an additional limited-partner investor. The federal investment covenants would be that the investments be the first funding after seed, grants, etc. (i.e., pre-venture) in the technology and that a high percentage of the investments (~80 percent) be made in intellectual property technology that has a foundation in federal- or state-funded research project grants.

These investments will serve to grow our economy by immediately creating jobs in the crucial innovation economy sector. Furthermore, while investors may do well, society will be the greatest beneficiary in terms of better health care, a cleaner environment, a more plentiful food supply, better communications, and a safer world.

## Appendix A

The table below depicts potential Limited Partner economics for illustrative purposes. Actual results may vary.

### Accelerator Fund 1 (LP Economics at 32 percent return)

(\$ in thousands)	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
<b>Capital Related</b>							
GP	\$ 167	\$ 167	\$ 167	\$ -	\$ -	\$ -	\$ -
Outside LPs	49,500	-	-	-	-	-	-
<b>Total Capital Related</b>	<b>\$ 49,667</b>	<b>\$ 167</b>	<b>\$ 167</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ -</b>
<b>Fund Performance</b>							
LP Capital Invested	\$ (14,500)	\$ (14,500)	\$ (14,500)	\$ -	\$ -	\$ -	\$ -
LP Capital Returned	-	-	-	8,250	16,500	16,500	8,250
LP Profit	-	-	-	8,425	22,185	22,185	13,761
<b>Total Capital Returned/ (Invested)</b>	<b>\$ (14,500)</b>	<b>\$ (14,500)</b>	<b>\$ (14,500)</b>	<b>\$ 16,675</b>	<b>\$ 38,685</b>	<b>\$ 38,685</b>	<b>\$ 22,011</b>
Management Fees	(2,000)	(2,000)	(2,000)	(2,000)	(2,000)	(400)	(400)
GP Incentive Fees				(1,685)	(4,437)	(4,437)	(2,752)
Institution Incentive Fees				(1,264)	(3,328)	(3,328)	(2,064)
<b>Total Fees</b>	<b>\$ (2,000)</b>	<b>\$ (2,000)</b>	<b>\$ (2,000)</b>	<b>\$ (4,949)</b>	<b>\$ (9,765)</b>	<b>\$ (8,165)</b>	<b>\$ (5,216)</b>
<b>Total Cash Inflow/(Outflow)</b>	<b>\$ (16,500)</b>	<b>\$ (16,500)</b>	<b>\$ (16,500)</b>	<b>\$ 11,726</b>	<b>\$ 28,921</b>	<b>\$ 30,521</b>	<b>\$ 16,794</b>

IRR	17%
Cash Inflow	\$ 38,462
Multiple of Capital Invested	1.8x

### Assumptions

- Assumes that all funds are raised in Year 1.
- Management fee is reduced by 80 percent of the original amount (i.e., by \$1.6 million) beginning with the first fiscal quarter commencing six years from the initial closing, and continuing each year for the balance of the fund's term.
- Assumes total fund is invested in all investee companies by the end of Year 3 and dollars are invested ratably over the three-year investment period.
- Assumes that investments will be exited as a percentage of the aggregate as follows: 16.67 percent in Year 4, 33.3 percent in Year 5, 33.3 percent in Year 6, and 16.67 percent in Year 7.
- Compensation to fund employees assumes competitive market rates.
- Assumes fund makes twelve investments and realizes a gross IRR of 32 percent.
- GP incentive fees realized as carried interest equal to 20 percent.
- Institution incentive fees realized as carried interest equal to 15 percent.

The table below illustrates the support for the fund gross IRR assumption of 32 percent.

**Accelerator Fund 1** (*Assumptions for Gross IRR*)

Multiple	Number of Portfolio Companies Exited at Multiple	Gross Blended Return	Years	Invested/ Returned	Gross IRR
10.0x	1	0.7x	1/1/2010	(16,500)	32%
7.5x	1	0.5X	1/1/2011	(16,500)	
5.0x	2	0.7x	1/1/2012	(16,500)	
3.0x	2	0.4x	1/1/2013	21,725	
2.0x	2	0.3x	1/1/2014	43,450	
1.0x	2	0.1x	1/1/2015	43,450	
0.0x	5	0.0x	1/1/2016	21,725	
	15	2.6x			

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