PRE-COMPETITION*

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As the costs of pharmaceutical research and development rise and concerns grow about the pace of innovation, both federal agencies and industry participants have turned to new forms of collaboration to increase the efficiency and effectiveness of biomedical research. Industry participants, many of them competitors, come together to define joint research and development objectives and to share project results in what are widely known as "pre-competitive" collaborations. There is a prevailing understanding among both industry and governmental actors that these pre-competitive endeavors are not only permissible, but encouraged.

While the term "pre-competitive" is prevalent in the pharmaceutical industry, it is missing from the antitrust lexicon. Neither the courts nor the federal agencies charged with enforcing U.S. antitrust laws have ever recognized pre-competitive activity as immune from antitrust challenge. Rather, antitrust regulators have repeatedly emphasized that when competitors collaborate, anticompetitive behavior may arise regardless of the stage at which collaborating occurs.

This Article critically examines the phenomenon of pre-competitive collaboration through an antitrust lens. It analyzes the apparent disconnect between the industry reliance on pre-competition as a way of demarcating procompetitive arrangements among competitors, on the one hand, and the absence of any such distinction in antitrust law or practice, on the other. It then explores the ways that this disconnect may manifest

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itself in the choice and structure of collaborative arrangements and suggests a framework for refocusing attention on collaborations that are procompetitive, irrespective of the stage of development.

INTRODUCTION

Pre-competitive collaboration has become all the rage in some of today's most competitive markets. Industries in which such collective activity has gained traction include semiconductors,[1] advanced materials,[2] nanotechnology,[3] manufacturing,[4] software,[5] automotive,[6] and biotechnology and pharmaceuticals ("biopharma").[7] One recent survey commissioned by the Institute of Medicine ("IOM") identified fifty significant pre-competitive collaborations in the biopharma industry alone,[8] and the topic of pre-competitive collaboration has

1. *See, e.g.*, Elias G. Carayannis & Jeffrey Alexander, *Strategy, Structure, and Performance Issues of Precompetitive R&D Consortia: Insights and Lessons Learned from SEMATECH*, 51 IEEE TRANSACTIONS ON ENGINEERING MGMT. 226, 226 (2004).

2. *See, e.g.*, STEERING COMM. FOR NASA TECH. ROADMAPS & NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., NASA SPACE TECHNOLOGY ROADMAPS AND PRIORITIES: RESTORING NASA'S TECHNOLOGICAL EDGE AND PAVING THE WAY FOR A NEW ERA IN SPACE 82 (2012) (noting that NASA's goals include making "appropriate efforts to develop pre-competitive technology relevant to the needs of the commercial space sector").

3. *See, e.g.*, NAT'L SCI. AND TECH. COUNCIL COMM. ON TECH. & SUBCOMM. ON NANOSCALE SCI., ENG'G, AND TECH., NATIONAL NANOTECHNOLOGY INITIATIVE STRATEGIC PLAN 11 (2011), https://www.whitehouse.gov/sites/default/files/microsites/ostp/nni_strategic_plan_2011.pdf [https://perma.cc/PCU4-TLV8] ("Nanotechnology's enormous potential to address global challenges relating to water, health, and energy renders it an ideal subject for collaboration on pre-competitive and non-competitive research."); *see also* Theodore H. Wegner & Philip E. Jones, *Advancing Cellulose-Based Nanotechnology*, 13 CELLULOSE 115, 116 (2006) (discussing the need for identifying pre-competitive technological needs as part of innovation strategy).

4. *See, e.g.*, Gregory L. Smith & James C. Muller, *PreAmp—A Pre-competitive Project in Intelligent Manufacturing Technology: An Architecture to Demonstrate Concurrent Engineering and Information Sharing*, 2 CONCURRENT ENGINEERING 107, 107 (1994) (describing pre-competitive R&D in the area of design and manufacturing of printed circuit assemblies).

5. STEPHEN WEBER, THE SUCCESS OF OPEN SOURCE 21 (2004) (characterizing pre-competitive collaboration in the software industry as "[c]ompetitors shar[ing] early stages of research that benefit all").

6. *See* Sean Elkins et al., *Four Disruptive Strategies for Removing Drug Discovery Bottlenecks*, 18 DRUG DISCOVERY TODAY 265, 268 (2013).

7. *See infra* Part I.

8. Jill S. Altschuler et al., *Opening Up to Precompetitive Collaboration*, 2 SCI. TRANSLATIONAL MED. 1, 1 (2010).

been the focus of at least two major IOM studies in the last five years.[9]

In this context, the term "pre-competitive" connotes early-stage research and development ("R&D") that is directed to non-product specific research tools or data with the goal of benefitting the entire industry rather than a single firm.[10] In theory, pre-competitive collaboration enables competitors to pool resources, know-how, and intellectual property to advance the emergence of cutting edge technologies, collect and disseminate data, develop common research platforms and standards, and tackle other problems that are common across an industry.[11]

These perceived benefits have attracted the interest of U.S. governmental agencies, and many pre-competitive collaborations have been encouraged by the agencies that regulate or otherwise oversee the industries in which they are formed. The first prominent pre-competitive research consortia were formed in the 1980s in the U.S. computer industry to support a government-backed strategy for meeting global competition.[12] Around the same time, the Department of Defense played an integral role in forming Sematech, a semiconductor industry consortium organized to enhance the

9. For copies of both of these studies, see generally INST. OF MED. OF THE NAT'L ACADS., EXTENDING THE SPECTRUM OF PRECOMPETITIVE COLLABORATION IN ONCOLOGY RESEARCH (2010) [hereinafter IOM 2010 REPORT]; INST. OF MED. OF THE NAT'L ACADS., ESTABLISHING PRECOMPETITIVE COLLABORATIONS TO STIMULATE GENOMICS-DRIVEN PRODUCT DEVELOPMENT (2011) [hereinafter IOM 2011 REPORT].

10. *See* IOM 2010 REPORT, *supra* note 9, at 1 (defining pre-competitive collaboration as "basic and preclinical research on drug targets and the early stages of clinical testing"); Liza S. Vertinsky, *Patents, Partnerships, and the Pre-Competition Collaboration Myth in Pharmaceutical Innovation*, 48 U.C. DAVIS L. REV. 1509, 1516 (2015) (defining pre-competitive collaboration as "early stage research where the knowledge, results, and materials that are shared do not—at least purportedly—confer a competitive advantage by being shared").

11. *See* Altschuler et al., *supra* note 8, at 1. Analogies can be drawn to industry-wide collaborations in the design and adoption of technical interoperability standards such as Wi-Fi, USB, and LTE in which competitors work together to establish common protocols that enable different vendors' products to interoperate in a seamless manner. *See generally* CARL SHAPIRO & HAL R. VARIAN, INFORMATION RULES: A STRATEGIC GUIDE TO THE NETWORK ECONOMY (1999) (discussing the role cooperation and compatibility play in a network economy).

12. *See, e.g.*, NORMAN S. ZIMBEL, COOPERATION MEETS COMPETITION: THE IMPACT OF CONSORTIA FOR PRECOMPETITIVE R&D IN THE COMPUTER INDUSTRY, 1982–92, at v (1992), http://www.pirp.harvard.edu/pubs_pdf/zimbel/zimbel-p92-10.pdf [https://perma.cc/T66X-DWBX] (discussing the study of the evolution of U.S. pre-competitive research consortia for high-performance computing in the 1980s and 90s).

competitiveness of the U.S. semiconductor industry.[13] Since then, a range of governmental agencies including the National Institutes of Health ("NIH"), Food and Drug Administration ("FDA"), National Science Foundation ("NSF"), and National Aeronautics and Space Administration ("NASA") have facilitated the formation of pre-competitive consortia and collaborations seeking to advance R&D in the domains that they oversee.[14] While many of these efforts have focused on basic science and discovery, there has been an increasing emphasis on activities more closely connected with product development. Pressure to move collaborations downstream into areas closer to commercial development has come from both government actors eager to show concrete economic results from public R&D investments and from private firms concerned about filling their product pipelines while controlling cost and risk.[15]

This focus on pre-competitive, product-directed R&D has been particularly pronounced in the biopharma industry, in which productivity challenges are increasingly pushing competitors into collaboration. Joint activity among competitors in this industry is not only tolerated, but encouraged, by governmental agencies that oversee the industry, so long as it occurs in areas deemed to be pre-competitive.[16] The theory, presumably, is that such collective activities benefit the entire industry rather than an individual firm and must therefore avoid antitrust concerns. Consequently, as comfort with pre-competitive collaborations has grown in the biopharma industry, both governmental agencies and private firms increasingly operate as if an antitrust "safe harbor" exists for pre-competitive collaboration.[17]

13. *See generally* Douglas A. Irwin & Peter J. Klenow, *Sematech: Purpose and Performance*, 93 PROC. NAT'L ACAD. SCI. 12,739 (1996) (noting how the U.S. government financially backed the semiconductor industry leading to the formation of Sematech).

14. With respect to the NIH and FDA, *see infra* Part I. NASA has employed pre-competitive collaborations as part of its aeronautics program. *See, e.g.*, LISA PORTER, NASA'S NEW AERONAUTICS RESEARCH PROGRAM 5 (2007), http://www.hq.nasa.gov/office/aero/pdf/armd_overview_reno_4.pdf [https://perma.cc/58JC-532Y]. NSF has supported pre-competitive R&D strategies through programs such as the Industry/University Cooperative Research Centers program. *See Industry/University Cooperative Research Centers Program (I/UCRC)*, NAT'L SCI. FOUND., https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=5501 [https://perma.cc/V3HF-HFLB].

15. *See* Editorial, *Expanding Precompetitive Space*, 10 NATURE REVS. DRUG DISCOVERY 883, 883 (2011); *see also* Altschuler et al., *supra* note 8, at 1 (citing increasing numbers of collaborations "at the product-development end of the R&D value chain").

16. *See* discussion and examples *infra* Section I.A.

17. Though not addressed in any detail, some groups in the biopharma industry have begun to acknowledge a need for antitrust review of certain collaborations among competitors. *See, e.g.*, IOM 2010 REPORT, *supra* note 9, at 33 ("Concerns over privacy, conflict of interest, antitrust law, and the sharing of international data can inhibit pre-

Despite the frequent invocation of the term "pre-competitive" by firms and agencies in the biopharma sector, the term has little, if any, purchase in the literature or doctrine of antitrust law. In fact, as far as determinable, no U.S. antitrust statute, regulation, agency guidance, consent decree, or judicial decision has ever recognized or even sought to define "pre-competition" or "pre-competitive" activity. More importantly, neither the courts nor federal antitrust agencies have designated pre-competitive activity as immune from antitrust challenge.[18] In fact, the Department of Justice ("DOJ") and Federal Trade Commission ("FTC") have expressly identified the potential for anticompetitive R&D arrangements in markets before the emergence of defined products (so-called "innovation markets" or "R&D markets").[19]

competitive collaborations."); INST. OF MED. OF THE NAT'L ACADS., SHARING CLINICAL TRIAL DATA: MAXIMIZING BENEFITS, MINIMIZING RISK 190 (2015) (describing antitrust issues addressed by author Jorge Contreras at IOM panel discussion of clinical trials data sharing).

18. The National Cooperative Research and Production Act (NCRPA), 15 U.S.C. §§ 4301–06 (2012), permits firms that wish to engage in joint research or production to make a public notification listing their names and the scope of their joint activity, whereupon they are granted immunity from certain antitrust remedies, including treble damages under the Sherman Act. *See infra* Part II.B.1.

19. U.S. DEP'T OF JUSTICE & FED. TRADE COMM'N, ANTITRUST GUIDELINES FOR THE LICENSING OF INTELLECTUAL PROPERTY 10–11 (1995) [hereinafter IP LICENSING GUIDELINES]. As part of their analysis of relevant markets within which to assess competition, the DOJ and FTC refer in the IP Licensing Guidelines to three kinds of markets: product markets, technology markets, and innovation markets. *Id.* at 8, 10. A proposed update to the IP Licensing Guidelines was released by the FTC and DOJ for public comment on August 12, 2016. U.S. DEP'T OF JUSTICE & FED. TRADE COMM'N, ANTITRUST GUIDELINES FOR THE LICENSING OF INTELLECTUAL PROPERTY: PROPOSED UPDATE—REDLINE (2016), https://www.ftc.gov/system/files/documents/reports/antitrust-guidelines-licensing-intellectual-property-proposed-update-1995-guidelines-issued-us/ip_guidelines_published_proposed_update.pdf [https://perma.cc/PX66-R6LG] [hereinafter IP LICENSING GUIDELINES PROPOSED UPDATE]. The IP Licensing Guidelines Proposed Update replace the term "innovation markets" with "research and development market[s]." *Id.* at 15–17. This change is not intended to be substantive, but rather a clarification of how these markets have actually been defined in enforcement actions. *See, e.g.*, Press Release, Fed. Trade Comm'n, FTC and DOJ Seek View on Proposed Update of the Antitrust Guidelines for Licensing Intellectual Property (Aug. 12, 2016), https://www.ftc.gov/news-events/press-releases/2016/08/ftc-doj-seek-views-proposed-update-antitrust-guidelines-licensing [https://perma.cc/F4RV-CTR8]. The Antitrust Guidelines for Collaborations Among Competitors issued by the FTC and the DOJ in April 2000 still refer to "innovation markets" through reference to the IP Licensing Guidelines. FED. TRADE COMM'N & U.S. DEP'T OF JUSTICE, ANTITRUST GUIDELINES FOR COLLABORATIONS AMONG COMPETITORS, § 3.32(c), at 17 (2000) [hereinafter COLLABORATION GUIDELINES]. Section 3.32(c), Research and Development: Innovation Markets, refers to section 3.2.3 of the IP Licensing Guidelines. *Id.* In this Article we use the terminology of the IP Licensing Guidelines Proposed Update, referring to "research and development markets" rather than "innovation markets." *See Market Definition in Antitrust: Theory*

This Article critically examines the phenomenon of pre-competitive collaboration through an antitrust lens.[20] The authors observe that while many pre-competitive collaborations may indeed offer procompetitive benefits and thereby avoid antitrust concern, it is not the case that *every* collaboration conducted prior to product release or as part of a common technology platform will be immune from antitrust condemnation. Accordingly, the tendency to focus on pre-competitive collaborations as inherently procompetitive and deserving of some form of antitrust safe harbor is misguided. And far from being benign, this misconception has the potential both to encourage early-stage collaborations that may in fact be anticompetitive, and to discourage later-stage, yet manifestly procompetitive, collaborations. This Article focuses on the biopharma industry because of the prominent role that pre-competitive collaboration has taken in the policy debate over the spiraling costs of drug development and the enthusiasm with which the NIH, the FDA, and private firms have embraced the pre-competitive model.

The Article proceeds in three parts. Part I provides a detailed analysis of pre-competitive collaboration in the biopharma sector. This Part addresses the market pressures that have led competitors to collaborate, as well as the policy goals of agencies in actively promoting such collaborations. It then offers three case studies illustrating the objectives, organizational structure, and collaborative activity of biopharma pre-competitive collaborations at different stages along the product commercialization path: (1) the SNP Consortium, an early-stage basic science collaboration that worked alongside the Human Genome Project to release DNA marker data to the public; (2) the international Serious Adverse Events Consortium, a jointly-funded industry effort to identify genetic markers for adverse reactions to existing therapeutics; and (3) the Accelerating Medicines Partnership, a collaboration among pharmaceutical firms to identify drug targets for four identified disease categories.

Part II outlines the legal framework established by the U.S. courts and antitrust enforcement agencies to analyze horizontal arrangements among competitors, particularly those involving the licensing of intellectual property and the conduct of R&D. It looks

and Case Studies, 2012 A.B.A. SEC. ANTITRUST L. 471, 471 (using the terminology of "innovation markets" as well).

20. While previous authors have analyzed the antitrust implications of specific industry collaborations, their focus has not been on the general practice of pre-competitive collaboration. *See, e.g.*, Irwin & Klenow, *supra* note 13, at 12,740–41.

specifically at the agencies' analyses of R&D markets,[21] much of which has occurred in the context of merger transactions within the pharmaceutical industry. Part II examines the factors that these agencies weighed to determine whether an R&D collaboration may be considered procompetitive or anticompetitive.

Part III applies this established antitrust framework to pre-competitive collaborations at different stages along the product development cycle. It uses hypothetical examples to illustrate the disconnect between current industry understandings and uses of pre-competitive collaborations and the actual analysis conducted by courts and agencies to determine whether R&D collaborations among competitors are procompetitive or anticompetitive. This Part goes on to identify measures that may reduce antitrust concerns in such collaborations.

The Article concludes by urging both industry participants and governmental agencies to evaluate more closely the potential procompetitive and anticompetitive features of any proposed industry collaboration, and not simply to rely on a conclusory characterization of such activities as pre-competitive or to presumptively favor pre-competitive collaborations over collaborations at later stages of product or market development.

I. PRE-COMPETITIVE COLLABORATIONS AS INNOVATION STRATEGIES

Rising costs, shrinking budgets, massive risks of failure at even late stages of drug development, and the complexity of those diseases that are still in need of treatments are forcing pharmaceutical firms to search for new approaches to drug discovery and development.[22] In the past, pharmaceutical companies have worked largely in silos,

21. This Article relies on the IP Licensing Guidelines as a description of the analytical framework that the FTC and DOJ apply in the context of arrangements involving intellectual property licenses. As discussed in note 19, *supra*, a draft update to these guidelines, the IP Licensing Guidelines Proposed Update, has been released for comment. While the IP Licensing Guidelines Proposed Update were, at the time this Article went to press, still in draft form and may change, this Article adopts their updated terminology and refers to R&D markets in place of innovation markets.

22. For a discussion of the challenges facing traditional models of pharmaceutical development and the need for change, see Mark Kessel, *The Problem with Today's Pharmaceutical Business—an Outsider's View*, 29 NATURE BIOTECH. 27, 27–28, 30 (2011); *see also* Janet Woodcock, *Precompetitive Research: A New Prescription for Drug Development?*, 87 CLINICAL PHARMACOLOGY & THERAPEUTICS 521, 522–23 (2010).

pursuing closed, highly secretive drug discovery and development.[23] But the traditional fully integrated business models that large pharmaceutical firms have relied upon for decades are no longer either efficient or sustainable.[24] The decline in the productivity of pharmaceutical R&D is well documented.[25] The number of new FDA approved drugs per billion dollars of R&D spending roughly halved every nine years between 1950 and 2010.[26] Although the total number of new drug approvals by the FDA has increased since 2010, many of the new drug approvals are for orphan drugs that have huge price tags, significant tax incentives and regulatory support, and very small patient populations.[27] Meanwhile, private sector investments in disease areas with the largest public health burdens in the United States, such as certain types of cancer, diabetes, and Alzheimer's disease, remain stagnant at best, and the results of development efforts remain disappointing.[28] Both public sector actors, such as the

23. *See, e.g.*, Barbara Mittleman, Garry Neil & Joel Cutcher-Gershenfeld, *Precompetitive Consortia in Biomedicine—How Are We Doing?*, 31 NATURE BIOTECHNOLOGY 979, 980 (2013).

24. *See, e.g.*, PRICEWATERHOUSECOOPERS, PHARMA 2020: CHALLENGING BUSINESS MODELS 1–4 (2009).

25. *See, e.g.*, Bernard Munos, *Lessons from 60 Years of Pharmaceutical Innovation*, 8 NATURE REVS. DRUG DISCOVERY 959, 959 (2009) (presenting corporate perspective on the problem, suggesting that lack of growth in drug-output ratio may reflect limits of current R&D model); Fabio Pammolli, Laura Magazzini & Massimo Riccaboni, *The Productivity Crisis in Pharmaceutical R&D*, 10 NATURE REVS. DRUG DISCOVERY 428, 428 (2011) (examining the decline in pharmaceutical R&D productivity using a large database of R&D projects); Jack W. Scannell et al., *Diagnosing the Decline in Pharmaceutical R&D Efficiency*, 11 NATURE REVS. DRUG DISCOVERY 191, 191–92 (2012) (surveying literature examining the decline in pharmaceutical R&D productivity). *But see* Iain M. Cockburn, *Is the Pharmaceutical Industry in a Productivity Crisis?*, *in* 7 INNOVATION POLICY AND THE ECONOMY 1, 1–4 (Josh Lerner & Scott Stern eds., 2007) (acknowledging the problem of the rising cost per new drug, but suggesting that trends of decline are exaggerated).

26. *See, e.g.*, Scannell et al., *supra* note 25, at 191 (suggesting that the pharmaceutical industry is following "Eroom's Law" (Moore spelled backwards), when it comes to productivity growth).

27. For a summary of new drug approvals over the past decade, see U.S. FOOD AND DRUG ADMIN. CTR. FOR DRUG EVALUATION AND RESEARCH, NOVEL NEW DRUGS 2014 SUMMARY 1–3 (2015). For a discussion of the shift towards niche market strategies focusing on orphan diseases, see Ashish Kumar Kakkar & Neha Dahiya, *The Evolving Drug Development Landscape: From Blockbusters to Niche Busters in the Orphan Drug Space*, 75 DRUG DEV. RES. 231, 231 (2014). *See also* Elie Dolgin, *Big Pharma Moves from 'Blockbusters' to 'Niche Busters'*, 16 NATURE MED. 837, 837 (2010). For a discussion of the high pricing of orphan drugs, see John-Paul Michaud, Robin Modi & M. Ian Phillips, *Is Orphan Drug Pricing Blowing a Bubble? The Unique Situation of Orphan Drugs and Why High Prices Will Likely Persist*, 1 EXPERT OPINION ON ORPHAN DRUGS 675, 675 (2013).

28. *See, e.g.*, PRESIDENT'S COUNCIL OF ADVISORS ON SCI. & TECH., EXEC. OFFICE OF THE PRESIDENT, REPORT TO THE PRESIDENT ON PROPELLING INNOVATION IN DRUG DISCOVERY, DEVELOPMENT, AND EVALUATION, at vi–ix (2012); SOEREN

NIH and publicly funded institutions such as universities and academic medical centers, are facing their own fiscal woes, limiting their ability to contribute to costly R&D ventures.[29] The decline in productivity, along with the growing disconnect between the size of investment flows and the magnitude of unmet medical needs, have been of immense concern to the NIH, the FDA, and other public sector stakeholders.[30]

The challenges facing the U.S. biopharma industry come at a time when breakthroughs in science and technology should be leading to rapid progress in drug discovery and development.[31] There have been major scientific advances in our understanding of the nature and causes of different diseases, in some cases leading to entirely new disease classifications and strategies for interventions.[32] Tools for biomedical research have become increasingly powerful, enabling advances including the sequencing of the human genome, the mapping of individual genetic variations, the study of genes in new animal models, and the ability to monitor and study proteins and measure cellular responses.[33] Translating these breakthroughs into a new generation of medical therapies has, however, been frustratingly slow.[34]

MATTKE ET AL., RAND CORP., THE NEW NEGLECTED DISEASES? 4 (2013), http://www.rand.org/content/dam/rand/pubs/perspectives/PE100/PE117/RAND_PE117.pdf [https://perma.cc/A9BY-WNGB] (explaining why pharmaceutical companies invest less money in developing drugs for common diseases such as Alzheimer's).

29. *See, e.g.*, Richard Harris & Robert Benincasa, *U.S. Science Suffering from Booms and Busts in Funding*, NPR (Sept. 9, 2014, 3:03 AM), http://www.npr.org/sections/health-shots/2014/09/09/340716091/u-s-science-suffering-from-booms-and-busts-in-funding [https://perma.cc/EVM4-VFXA]; Melissa Korn, *Once Cash Cows, University Hospitals Now Source of Worry for Schools*, WALL ST. J. (Apr. 22, 2015, 4:40 PM), http://www.wsj.com/articles/universities-get-second-opinion-on-their-hospitals-1429725107.

30. *See, e.g.*, Eduardo Porter, *A Dearth in Innovation for Key Drugs*, N.Y. TIMES (July 22, 2014), http://www.nytimes.com/2014/07/23/business/a-dearth-of-investment-in-much-needed-drugs.html [https://perma.cc/G5ZD-6URD] (suggesting that firms are flocking to rare diseases because development is cheaper and profits are higher, leaving behind some of the disease areas with the biggest public health costs); *see also* PRESIDENT'S COUNCIL OF ADVISORS ON SCI. & TECH., *supra* note 28, at vii–viii.

31. *See, e.g.*, Sally Rockey & Francis Collins, *One Nation in Support of Biomedical Research?*, NIH DIRECTOR'S BLOG (Sept. 24, 2013), https://directorsblog.nih.gov/2013/09/24/one-nation-in-support-of-biomedical-research/ [https://perma.cc/GL4Q-W9UG].

32. *See* PRESIDENT'S COUNCIL OF ADVISORS ON SCI. & TECH., *supra* note 28, at vi.

33. *Id.* at 5–6.

34. *See, e.g.*, John Carroll, "*Frustrated" NIH Chief Plots $1B Drug Development Effort*, FIERCEBIOTECH (Jan. 24, 2011, 8:18 AM), http://www.fiercebiotech.com/story/frustrated-nih-chief-plots-1b-drug-development-effort/2011-01-24 [https://perma.cc/WX9J-PSQJ] (discussing Francis Collins's announced frustration with private sector translation efforts and his plan to support translational efforts through the new National Center for Advancing Translational Sciences).

A. Emergence of Pre-Competitive Strategies in Biopharma

Pharmaceutical firms have a long history of collaborating with academic researchers in early stages of R&D, but the recent combination of constrained resources, rising costs, unmet medical needs, and expansive scientific opportunities has fueled an increased interest in collaboration in both the public and private sectors.[35] While some pharmaceutical industry collaborations are simply efforts to expand traditional partnering arrangements between industry and academia, there has been a significant expansion of alternative models of cross-industry collaboration including strategic alliances, open innovation approaches, and—increasingly—what the biopharma industry refers to as pre-competitive collaborations.[36]

Genomics was home to the earliest and largest efforts to collaborate in pre-competitive space. The groundwork for this collaboration was laid by the Human Genome Project ("HGP"), the ambitious, multinational, publicly funded project that raced private sector efforts to sequence the human genome in the late 1990s and early 2000s.[37] As a publicly funded project shaped by principles of open access and knowledge sharing, the HGP insisted that its participating sequencing centers release all human sequence data to the public within twenty-four hours after being generated under a data release protocol known as the Bermuda Principles.[38] Eventually, even the private sector participants in the race to sequence the

35. *See, e.g.*, John A. Wagner, *Open-Minded to Open Innovation and Precompetitive Collaboration*, 87 CLINICAL PHARMACOLOGY & THERAPEUTICS 511, 514 (2010) ("Precompetitive collaboration is increasingly recognized as a driver for enhanced efficiency, while simultaneously increasing our grasp of heightened complexity.").

36. *See, e.g.*, Isa Khanna, *Drug Discovery in Pharmaceutical Industry: Productivity Challenges and Trends*, 17 DRUG DISCOVERY TODAY 1088, 1093–94 tbl.1 (cataloging numerous precompetitive collaborations in the biopharma industry); Mittleman et al., *supra* note 23, at 979–80 (identifying five strategic avenues of industry innovation, including independent operation, mergers and aquisitions, and three cooperative models); Asher Mullard, *Partnering Between Pharma Peers on the Rise*, 10 NATURE REVS. DRUG DISCOVERY 561, 561–62 (2011) (discussing growth in pharma-pharma collaborations, including analysis of an early model provided by the Dundee Kinase Consortium).

37. For general histories of the HGP, see generally JAMES SHREEVE, THE GENOME WAR (2004) and VICTOR K. MCELHENY, DRAWING THE MAP OF LIFE—INSIDE THE HUMAN GENOME PROJECT (2010). Planning for the HGP began in the late 1980s and is generally agreed to have concluded the early 2000s, though work continues to refine the human genomic map. MCELHENY, *supra*, at ix–x.

38. *Summary of Principles Agreed at the First International Strategy Meeting on Human Genome Sequencing*, HUMAN GENOME PROJECT INFO. ARCHIVE, http://www.ornl.gov/sci/techresources/Human_Genome/research/bermuda.shtml [https://perma.cc/NQX4-UDVQ]; *see also* Jorge L. Contreras, *Bermuda's Legacy: Policy, Patents, and the Design of the Genome Commons*, 12 MINN. J.L. SCI. & TECH. 61, 84–85 (2011).

genome were persuaded to deposit their sequence data in the publicly accessible GenBank database.[39]

Much has been written about the scientific advances enabled by the culture of rapid and widespread data sharing fostered by the HGP.[40] This data sharing ethos spread from the government and academic labs first involved in the HGP to select industry research labs, resulting in a series of innovative pre-competitive data sharing initiatives that sought to preserve free and unrestricted access to basic information about the human genome. Public efforts to sequence the human genome were thus accompanied by industry-driven and-funded collaborations designed to gather and make additional genomic data public, often in efforts to preempt the patenting of genetic information by others.[41] One prominent example was the SNP Consortium ("TSC"), an early stage, basic science collaboration that worked alongside the HGP to release DNA marker data to the public.[42]

In these early collaborations, the term "pre-competitive" was used largely to refer to the nature of the genomic data that was being gathered and shared. Genomic data was seen as constituting a base of common scientific knowledge upon which firms could later build competitive product and service offerings. Innovations in the ways that genomics data could be created, gathered, sorted, and shared facilitated the growth of genomics-based cross-industry initiatives.[43]

39. *See* Contreras, *supra* note 38, at 85 n.101.

40. *See, e.g.*, Francis Collins, *Opinion: Has the Revolution Arrived?*, 464 NATURE 674, 675 (referring to the "radical ethic of immediate data deposit adopted by the [HGP]" as the current "norm for other community research projects"); Jane Kaye et al., *Data Sharing in Genomics—Re-shaping Scientific Practice*, 10 NATURE REVS. GENETICS 331, 332 box 1 (2009) ("These policies have created a climate in which data sharing has become the default, and [grant] applicants must demonstrate why their data should be exempt from the requirement that it should be deposited for use by other scientists."); Nikos C. Kyrpides, *Fifteen Years of Microbial Genomics: Meeting the Challenges and Fulfilling the Dream*, 27 NATURE BIOTECHNOLOGY 627, 627 (2009) ("Over time, as the substantial benefits of prepublication release of genome data have been recognized, many funding agencies and most of the large sequencing centers now adhere to the rapid data release policy set forth as the Bermuda Principles in 1996 and renewed in 2003."); Heidi L. Williams, *Intellectual Property Rights and Innovation: Evidence from the Human Genome*, 121 J. POL. ECON., no. 1, 2013, at 1, 1, http://economics.mit.edu/files/8647 [https://perma.cc/WB5J-3YVH].

41. *See* Contreras, *supra* note 38, at 85–86.

42. *See infra* Section I.C.1.

43. For a discussion of some of these data sharing initiatives, see Nicole Szlezak et al., *The Role of Big Data and Advanced Analytics in Drug Discovery, Development and Commercialization*, 95 CLINICAL PHARMACOLOGY & THERAPEUTICS 492, 492 (2014); Robin Robinson, *A New Era of Collaboration: Knowledge Sharing*, PHARMAVOICE (Oct. 2014), http://www.pharmavoice.com/article/knowledge-sharing/ [https://perma.cc/L2GD-3JDP].

These early pre-competitive collaborations informed strategies to create similar open and shared spaces in other areas of biomedical R&D.

Budget constraints and soaring development costs made pre-competitive strategies attractive to pharmaceutical firms in areas beyond genomics because of the strategies' efficiency.[44] Such strategies appeal to firms eager to distribute the costs and risks involved in R&D among multiple industry participants in ways that do not compromise their own competitive advantages.[45]

Pre-competitive collaborations have also been attractive to government policymakers interested in accelerating pharmaceutical innovation in cost effective ways.[46] Dr. Francis Collins, as director of the National Human Genome Research Institute from 1993 to 2008, was an early advocate of pre-competitive collaborations as a mechanism for accelerating biomedical research.[47] As the current director of the NIH, Dr. Collins continues to advocate for pre-competitive collaboration strategies to identify promising therapeutic targets and biomarkers.[48] The Accelerating Medicines Partnership ("AMP"), a collaboration among pharmaceutical firms and the NIH

44. *See, e.g.*, Sally Rockey & Francis Collins, *One Nation in Support of Biomedical Research?*, NAT'L INSTS. OF HEALTH (Sept. 24, 2013), https://nexus.od.nih.gov/all/2013/09/24/one-nation-in-support-of-biomedical-research/ [https://perma.cc/G6P6-VVNS]; *see also* Hamilton Moses et al., *The Anatomy of Medical Research: US and International Comparisons*, 313 JAMA 174, 174, 185 (2015) (examining trends in U.S. and international research funding, showing a decline in growth of U.S. funding and a shift away from early-stage research funding, and suggesting the United States will lose its lead in biomedical innovation without a change in investment trends).

45. *See* IOM 2011 REPORT, *supra* note 9, at 10–19 (examining examples from other industries engaging in pre-competitive collaborations and identifying best practices and a framework for cross-industry sharing of biological resources).

46. *See generally* Jorge L. Contreras, *Leviathan in the Commons: Biomedical Data and the State*, *in* GOVERNING MEDICAL RESEARCH COMMONS (Brett Frischmann, Michael Madison & Katherine Strandburg eds., Oxford Univ. Press, forthcoming 2017) (discussing governmental interventions in biomedical data generation projects in fields including genomics and clinical trials).

47. *See, e.g.*, Francis S. Collins et al., *A Vision for the Future of Genomics Research*, 422 NATURE 835, 839, 844 (2003).

48. *See, e.g.*, *Continuing America's Leadership in Medical Innovation for Patients: Hearing Before the S. Health, Educ., Labor & Pensions Comm.*, 114th Cong. 4 (2015), http://www.nih.gov/about-nih/who-we-are/nih-director/continuing-americas-leadership-medical-innovation-patients [https://perma.cc/HB9H-YD3R] (testimony of Francis S. Collins, Director, National Institutes of Health) (discussing Accelerating Medicines Partnership, a pre-competitive partnership, with the hope that "[t]hrough this truly innovative and collaborative approach, we believe we can learn how to treat and cure disease faster").

to identify drug targets for four identified disease categories, provides one example.[49]

The FDA has also tried to generate private interest in pre-competitive collaboration within the biopharma sector. The Critical Path Initiative ("CPI"), launched by the FDA in 2004, provides a concrete example of the FDA's commitment to fostering pre-competitive collaborations as part of a larger mission of "[t]ransforming the way FDA-regulated products are developed, evaluated and manufactured."[50] The primary goal of the CPI was to encourage industry members to share data, expertise, and resources in order to produce more reliable testing methods.[51] As part of these efforts, the FDA subsequently formed the Critical Path Institute, a nonprofit organization charged with identifying and seeking to overcome barriers to industry collaboration to address what it characterized as "pre-competitive regulatory science issues," "focusing on standards, applied science, and technology that advance the field for all stakeholders and benefit the public."[52]

In line with the goals of the CPI and the efforts of the Critical Path Institute, the FDA has subsequently sought to foster pre-competitive collaboration through both direct funding of partnerships and indirect, but public, support of pharmaceutical industry initiatives.[53] One such initiative is the international Serious Adverse Events Consortium ("iSAEC"), which has sought to identify and release to the public genetic markers associated with serious adverse drug reactions, an area that is central to the FDA's public health and safety mission.[54] In each of these instances, the status of an activity as pre-competitive has played a role in the FDA support. The next

49. *See* Vertinsky, *supra* note 10, at 1549; *see also infra* Section I.C.3.

50. *See Critical Path Initiative*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/ [https://perma.cc/48NL-G6YC] (last updated Oct. 23, 2015).

51. *See, e.g.*, Raymond L. Woosley, Richard T. Myers & Federico Goodsaid, *The Critical Path Institute's Approach to Pre-competitive Sharing and Advancing Regulatory Science*, 87 CLINICAL PHARMACOLOGY & THERAPEUTICS 530, 530–31 (2010).

52. *See, e.g.*, *id.*

53. *See generally, e.g.*, FOOD & DRUG ADMIN., CRITICAL PATH INITIATIVE REPORT ON PROJECTS RECEIVING CRITICAL PATH SUPPORT, FISCAL YEAR 2010 REPORT (2010), http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/CriticalPathInitiative/UCM249262.pdf [https://perma.cc/NMX6-5LXN] (reporting on projects supported by CPI during the 2010 fiscal year).

54. *See infra* Section I.C.2.; *see also* Arthur L. Holden et al., *The International Serious Adverse Events Consortium*, 13 NATURE REVS. DRUG DISCOVERY 795, 795 (2014); Contreras, *supra* note 46, at 18 (discussing the FDA's role in iSAEC).

Section discusses the evolving understanding of the term "pre-competitive" in the biopharma industry.

B. Evolving Uses of the Term "Pre-Competitive"

Although the term "pre-competitive" is used widely in the biopharma literature, it does not have a single, generally accepted definition. A survey of ways in which the biopharma industry is using the term suggests a common industry understanding of pre-competitive as covering activities and results that are generated through a cooperative process by industry stakeholders and which have broad application to the industry as a whole.[55] To illustrate, a sample of definitions of pre-competitive provided by pharmaceutical firms, FDA commentators, and NIH commentators includes: "science participated in collaboratively by those who ordinarily are commercial competitors,"[56] "competitors sharing early stages of research that benefit all,"[57] collaborations involved in "aggregating, accessing, and sharing data that are essential to innovation, but provide little competitive advantage,"[58] and "standards, data, or processes that are common across an industry and where the adoption, use, or prosecution of which provides no competitive advantage relative to peers."[59] In the descriptions provided by industry stakeholders, pre-competitive collaborations are almost always portrayed as complements to market competition,[60] allowing firms to pool costs and risks in areas that offer little individual competitive advantage in order to enhance competition in

55. Our informal survey of the use of the term included a literature search of biopharma industry publications, NIH, FDA, and federal government policy papers, and participation in conference presentations and workshops involving the study and evaluation of some of the existing pre-competitive collaborations.

56. Woodcock, *supra* note 22, at 521 (describing emergence of pre-competitive collaborations in biomedicine and their defining features).

57. *See, e.g.*, John A. Wagner et al., *The Biomarkers Consortium: Practice and Pitfalls of Open-Source Precompetitive Collaboration*, 87 CLINICAL PHARMACOLOGY & THERAPEUTICS 539, 539 (2010) (describing the Biomarkers Consortium as one example of a pre-competitive collaboration that is driving innovation and increasing productivity).

58. *See About the Pistoia Alliance*, PISTOIA ALLIANCE, http://www.pistoiaalliance.org/about/ [https://perma.cc/W8R7-7SLS] (describing the alliance's mission to transform R&D innovation through pre-competitive collaboration).

59. *See* Chris Waller, *Precompetitive Collaborations* 2 (Oct. 26, 2010), http://www.slideshare.net/wallerc/precompetitive-collaborations [https://perma.cc/J8Z4-8QAB].

60. *See, e.g.*, Mittleman et al., *supra* note 23, at 979 ("[D]espite the formation of consortia as a complement to market competition and government regulation in recent years, too few [consortia] exist to mitigate lost opportunities and deliver on other potential mutual gains for public and private stakeholders in the drug development enterprise.").

downstream areas where they can most effectively exploit their competitive advantages.

From this shared starting point, various definitions of pre-competition within the biopharma literature emphasize one or more of the following aspects of the collaboration: (1) the types of activities, data, or research plans that are being shared; (2) the rules governing the protection and sharing of results; and (3) the nature of the participants within the collaboration.

Many definitions of pre-competition, including those offered by pharmaceutical firms when describing their own initiatives, focus on the first category: the nature of the activity or type of data being shared, designating certain activities and types of data as pre-competitive. As noted above, early pre-competitive collaborations in the biopharma industry focused on collecting and sharing data about the human genome, which was considered by many industry stakeholders to be "fundamentally pre-competitive information."[61] Technologies enabling the accumulation of massive amounts of biological data have heralded the growth of "Big Data" opportunities in drug discovery and development, but harnessing the benefits of big data for pharmaceutical R&D requires collaboration in data pooling, data sharing, and the development of tools for effective data use.[62] Some definitions of pre-competition focus on the distinction between pre-competitive tools and resulting products, further distinguishing between technologies that are tied to differentiating strategies and those that are generally enabling with potential wide use across the industry.[63] This effort to differentiate based on the type of technology depends heavily on the perspectives of different stakeholders, however, since many of the tools regarded as generally enabling inputs by pharmaceutical companies are the object of intense competition by those producing the tools.[64]

61. *See, e.g.*, Francis S. Collins, Michael Morgan & Aristides Patrinos, *The Human Genome Project: Lessons from Large-Scale Biology*, 300 SCIENCE 286, 288 (2003).

62. *See, e.g.*, Kara Dolinski & Olga G. Troyanskaya, *Implications of Big Data for Cell Biology*, 26 MOLECULAR BIOLOGY OF THE CELL 2575, 2575–76 (2015) (discussing big data and its implications in biological research); *see also* Peter Tormay, *Big Data in Pharmaceutical R&D: Creating a Sustainable R&D Engine*, 29 PHARMACEUTICAL MED. 87, 87, 91 (2015) (discussing opportunities that "Big Data" offers for improving productivity of pharmaceutical R&D and need for pre-competitive collaboration to utilize these opportunities).

63. *See, e.g.*, Christopher J. Welch, Joel M. Hawkins & Jean Tom, *Precompetitive Collaboration on Enabling Technologies for the Pharmaceutical Industry*, 18 ORGANIC PROCESS RES. DEV. 481, 482 (2014).

64. *See, e.g.*, *id.*

One of the most dominant themes in FDA and NIH descriptions of pre-competitive collaboration is the idea that research data and other results that are publicly shared will broadly benefit the industry. This mindset, with its focus on rules for governing public access, likely finds its roots in the HGP's aggressive data release programs[65] and continues in current NIH policies on genomic data release.[66] Today, an emphasis on public access to research results pervades much of the reasoning offered by U.S. biomedical research agencies regarding pre-competitive collaboration. For example, Dr. Francis Collins describes the AMP as a pre-competitive partnership characterized by combined public and private sector efforts to identify promising therapeutic targets and to openly share these findings with the public.[67] Janet Woodcock, the director of the FDA Center for Drug Evaluation and Research emphasizes the importance of making research results publicly available.[68] She explains, "In contrast to the guarded nature of commercial scientific findings, the results of precompetitive research are meant to be made publicly available, subjected to scientific scrutiny, and contribute to knowledge that improves the prospects for invention-based competition . . . ."[69] She is careful, however, to distinguish between research that provides generally applicable tools and techniques and results that are focused on the development of a specific product.[70]

The nature of the participants also influences the perception of a collaboration as being pre-competitive. Many collaborations described as pre-competitive involve some form of university or governmental involvement.[71] Academic participants in collaborations may harbor different understandings of what pre-competitive means,

65. *See supra* note 38 and accompanying text.

66. *See, e.g.*, Final NIH Genomic Data Sharing Policy, 79 Fed. Reg. 51,345, 51,352 (Aug. 28, 2014) ("[B]asic sequence data and certain related information (e.g., genotypes, haplotypes, *p*-values, allele frequencies) are precompetitive. Such data made available through NIH-designated data repositories, and all conclusions derived directly from them, should remain freely available without any licensing requirements.").

67. *See infra* Section I.C.3; *see also Driving Innovation Through Federal Investments, Hearing Before the S. Appropriations Comm.*, 113th Cong. 7 (2014), http://www.appropriations.senate.gov/imo/media/doc/hearings/NIH%20written%20testimony%20for%204%2029%20SAC%20Hearing%20FINAL.PDF [https://perma.cc/UQ3C-FEAZ] (testimony of Francis S. Collins, Director, National Institutes of Health).

68. *See* Woodcock, *supra* note 22, at 521.

69. *Id.*

70. *See id.* ("Precompetitive research is a subset of translational research that is focused on improving the tools and techniques needed for successful translation, and not on development of a specific product.").

71. *See, e.g.*, IOM 2011 REPORT, *supra* note 9, at 16–17.

but to outsiders much academic research activity would likely be considered pre-competitive.[72]

In addition to variations in characterizing the defining features of pre-competitive collaborations, there has been a trend toward more expansive views of what is considered pre-competitive.[73] As interest in pre-competitive collaborations has grown among both public and private stakeholders, so too has a willingness to conceptualize pre-competition in broader terms, as "pre-competitive spaces" that can be created through collaboration. In the medical device context, such pre-competitive spaces have been referred to by the FDA as "[a]reas of research and development that possess common aspects across an industry segment not tied to a proprietary device."[74] According to one Pfizer executive, "[t]he basic biology, the understanding of disease, biomarkers of prognosis, and even drug responses all can be areas of pre-competitive R&D."[75] He goes on to explain that areas that Pfizer may currently consider to be competitive could eventually become areas of pre-competitive R&D.[76]

This evolution in thinking treats the contours of pre-competition as an industry choice rather than an objective standard. As described by several industry experts, "Consortia offer unique opportunities for stakeholders to redefine the precompetitive space, develop new work streams and jointly produce tools and resources."[77] Others have urged a "reboot" of the pharmaceutical industry by "extending the notion of 'precompetitive' collaboration to encompass later stages of research to allow [public-private partnerships] to flourish."[78] One ambitious initiative called Arch2POCM imagined a world of drug discovery and development in which all R&D work up to and including Phase II clinical trials would be considered pre-competitive.[79] Removing data access and intellectual property restrictions from essential parts of the

72. *See, e.g.*, *id.* Note the chapter title "Requisites for Successful Pre-competitive Collaboration—Requisites from Academia" suggests that the term "pre-competitive" may have a different meaning in academia than it does in industry. *See id.* at 13.

73. *See, e.g.*, *id.* at 3.

74. *See, e.g.*, James Coburn, *Digital Library of Modeling and Simulation: Who, What, When, Where, How* 4 (June 11, 2014), http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM358859.pdf [https://perma.cc/5RXC-84L4].

75. IOM 2011 REPORT, *supra* note 9, at 13–14.

76. *See id.* at 14.

77. Mittleman et al., *supra* note 23, at 980.

78. Elkins et al., *supra* note 6, at 268.

79. *See, e.g.*, Chris Cain, *Making the Case for Precompetitive Clinical Development*, 4 SCIBX 1, 1 (2011).

Arch2POCM plan would create a broad pre-competitive environment for drug discovery and development.[80]

C. Three Examples of Pre-Competitive Collaboration

Early successes with pre-competitive collaborations have fueled efforts to expand the number of pre-competitive collaborations[81] and to expand the boundaries of pre-competitive spaces.[82] New industry-driven pre-competitive initiatives continue to emerge in a wide range of areas, all the way from developing improved mouse models of disease to sharing data about adverse reactions to approved drugs.[83] This Section provides three detailed examples of biopharma pre-competitive collaborations that draw increasingly closer to the product commercialization path: (1) TSC, a collaboration focused on early-stage scientific research; (2) iSAEC, an industry effort to identify genetic markers for serious adverse reactions to approved drugs; and (3) the AMP, a pharmaceutical collaboration to identify drug targets for four identified disease categories. These examples illustrate the ways in which industry participants have thought about and organized pre-competitive activities at different stages along the biopharma R&D life cycle.

1. Early-Stage Scientific Research: The SNP Consortium

The SNP Consortium, or TSC, is one of the earliest examples of the use of pre-competitive collaboration strategies in the biopharma industry. Single nucleotide polymorphisms ("SNPs") are single base pair variations in the human genome that occur on average once every 300–1,000 nucleotides.[84] They are the most common form of human genetic variation, serving as milestones or markers across the human genome.[85] TSC was established in 1999 as a two-year, $45 million initiative funded by a group of leading pharmaceutical and information technology firms and the Wellcome Trust to build a high-

80. *Id.*

81. *See, e.g.*, Mittleman et al., *supra* note 23, at 980 (arguing for the need for more pre-competitive collaborations).

82. *See, e.g.*, Cain, *supra* note 79, at 2.

83. *See, e.g.*, Chris Cain, *A Mind for Precompetitive Collaboration*, 19 SCIBX 1, 1 (2012) (examining increase in pre-competitive consortia backed by industry).

84. *See, e.g.*, NAT'L INSTS. OF HEALTH, HELP ME UNDERSTAND GENETICS 208 (2016); *see also* Arthur L. Holden, *The SNP Consortium: Summary of a Private Consortium Effort to Develop an Applied Map of the Human Genome*, 32 BIOTECHNIQUES (SUPP.) S22, S22 (2002).

85. *See, e.g.*, NAT'L INSTS. OF HEALTH, *supra* note 84, at 208.

density map of SNPs along the human genome.[86] The project was motivated by the hope that these SNPs could later be used to help identify genetic differences associated with disease and individual variations in treatment.[87]

TSC built upon and complemented the work being done by the HGP. Its initial goal was to identify up to 300,000 SNPs throughout the human genome and to map at least half of these.[88] An unexpectedly large influx of genomic data from the HGP enabled TSC to exceed its original goals, and by 2001 researchers had cataloged the locations of 1.4 million SNPs along the human genome.[89] As SNPs were identified, they were validated, mapped, and deposited in publicly available databases maintained by the consortium and NIH's National Center for Biotechnology Information.[90] TSC made the data publicly available with no early access by participating firms.[91]

In contrast to the HGP, which was largely government funded and government driven, TSC was a private sector initiative. Its backers were comprised of ten of the world's largest pharmaceutical firms, two large information technology firms, and the Wellcome Trust, one of the world's largest medical research charities.[92] It was financed through member contributions, with each member required to provide financial support and contribute to the collaborative management of the project.[93] Membership was open, but interested parties were required to provide the required financial and non-

86. John Hodgson, *Analysts, Firms Pour Cold Water on SNP Consortium*, 17 NATURE BIOTECHNOLOGY 526, 526 (1999).

87. *See Human Genome Project and SNP Consortium Announce Collaboration to Identify New Genetic Markers for Disease*, NAT'L HUMAN GENOME RES. INST. (July 2000), http://www.genome.gov/10001456 [https://perma.cc/SFE7-5KU2].

88. *See, e.g.*, Gudmundur A. Thorisson & Lincoln D. Stein, *The SNP Consortium Website: Past, Present and Future*, 31 NUCLEIC ACIDS RES. 124, 124 (2003).

89. *Ten Vignettes: Stories of Genetic Discovery*, NAT'L HUMAN GENOME RES. INST. (Mar. 9, 2012), http://www.genome.gov/10003809#al-10 [https://perma.cc/BU6Q-TH2F].

90. *See* Stephen T. Sherry et al., *dbSNP: The NCBI Database of Genetic Variation*, 29 NUCLEIC ACIDS RES. 308, 308 (2001).

91. *See* Holden, *supra* note 84, at S23.

92. *See* Contreras, *supra* note 38, at 96 n.146 ("The SNP Consortium Ltd. was incorporated in March 1999 with the following sponsoring (i.e., dues-paying) members: The Wellcome Trust Limited, Pfizer Inc., Glaxo Wellcome Inc., Hoechst Marion Roussel, Zeneca Inc., Hoffman-La Roche Inc., Novartis Pharmaceuticals Corporation, Bristol-Myers Squibb Company, SmithKline Beecham Corporation, Bayer Corporation and Monsanto Corporation. Technology giants Motorola, Inc. and International Business Machines Corporation joined as sponsoring members in November 1999 and Amersham Pharmacia Biotech Inc. became a sponsoring member in 2001.").

93. *See, e.g.*, Hodgson, *supra* note 86, at 526.

financial resources in order to become members.[94] The ten pharmaceutical companies who were part of the founding group were each reported to have contributed $3 million to TSC's budget.[95] TSC was overseen by a board of directors comprised of one member from each dues-paying member organization.[96] The CEO and chairman of TSC was independent of any member organization and the sole employee of the consortium.[97]

The founders' underlying motivation behind TSC was to accelerate the discovery and publication of SNP data in order to ensure that it remained accessible to researchers and the industry free from patent encumbrances.[98] TSC adopted a multi-prong approach to ensure that the SNP data it discovered would not be patented.[99] First, it contractually prohibited the academic researchers performing SNP discovery and mapping activity from seeking patent protection on their discoveries.[100] Second, it released all SNP data it discovered to public databases, thus creating voluminous prior art.[101] Finally, it adopted a novel "protective" patenting strategy in which it filed patent applications disclosing all newly identified and mapped SNPs with the U.S. Patent and Trademark Office ("PTO") in order to enter this data into the PTO prior art database and to establish clear priority dates to defeat later patent applications.[102] These patent applications were later converted into Statutory Invention

94. *Id.*

95. *Id.*

96. *SNP Consortium Announced*, BIOPROCESS ONLINE (Apr. 19, 1999), http://www.bioprocessonline.com/doc/snp-consortium-announced-0001 [https://perma.cc/59SN-J8LK].

97. *See id.* ("The SNP Consortium is a non profit entity . . . with an independent chairman.").

98. *See, e.g.*, Holden, *supra* note 84, at S26 ("The overall IP objective is to maximize the number of SNPs that (*i*) enter the public domain at the earliest possible date, and, (*ii*) are free of third-party encumbrances such that the map can be used by all without financial or other IP obligations.").

99. TSC's patent deterrence strategies are described in detail in Contreras, *supra* note 38, at 96–97. Contreras served as TSC's legal counsel responsible for developing and overseeing the implementation of these strategies. TSC's defensive patenting strategy has also been favorably cited in Robert Merges, *A New Dynamism in the Public Domain*, 71 U. CHI. L. REV. 183, 189–91 (2004), and Rebecca S. Eisenberg, *The Promise and Perils of Strategic Publication to Create Prior Art: A Response to Professor Parchomovsky*, 98 MICH. L. REV. 2358, 2368–69 (2000).

100. *See* Contreras, *supra* note 38, at 121–22.

101. *Id.* at 96–97.

102. *See id.* Although any genomic data released to the public (*e.g.*, through NIH's GenBank database) can act as prior art defeating a later patent application, it is often inconvenient for patent examiners to search databases external to the PTO. Moreover, it is often difficult to establish the precise date that data was uploaded to a particular public database. For these reasons, TSC elected to submit its SNP data directly to the PTO by means of provisional patent applications. *See id.* at 97.

Registrations ("SIRs") or, following the 1999 Patent Act amendments providing for the publication of patent applications after eighteen months,[103] abandoned.[104] None of the TSC applications were prosecuted to issuance, but instead TSC utilized the PTO publication system to deter independent patenting of the discovered SNPs.[105]

Despite this program of patent deterrence with respect to the basic SNP data and map generated by TSC, the consortium made it clear that TSC participants were free to pursue patents based on discoveries made using SNPs.[106] Thus, the SNP map created by TSC was intended to act as a public research tool, but not to prevent patenting of downstream diagnostics or therapeutics developed by TSC participants or by others.

Given the participation of private firms representing a large share of the worldwide pharmaceutical market, TSC was careful from the outset to implement policies and practices designed to reduce the risk of antitrust liability. It filed public notices of its membership under the National Cooperative Research and Production Act of 1984 ("NCRPA") with the attorney general and the FTC, entitling it to certain immunities from enhanced antitrust damages.[107] It also adopted an antitrust compliance policy prohibiting its members from exchanging competitive information in connection with any TSC activity and otherwise from engaging in anticompetitive or collusive behavior under the auspices of TSC.[108]

While taking these natural steps to preempt antitrust concern about a consortium of competitors sharing information, TSC also relied on its characterization as a pre-competitive collaboration to ameliorate antitrust concerns.[109] Consortium members that were

103. American Inventors Protection Act of 1999, Pub. L. No. 106-113, Appendix I § 4502, 113 Stat. 1501, 1501A-561 to -563 (1999) (codified as amended at 35 U.S.C. § 122 (2012)).

104. *See* Contreras, *supra* note 38, at 97 n.151 (explaining how abandonment of published patent applications following the 1999 amendments accomplished largely the same disclosure goals as filing of a statutory invention registration prior to the amendments which provided for the publication of U.S. applications).

105. *See id.* at 97 & n.151.

106. *See, e.g.*, *National Advisory Council for Human Genome Research Summary of Meeting*, NAT'L HUMAN GENOME RESEARCH INST. (May 17–18, 1999), http://www.genome.gov/10001364 [https://perma.cc/W5A4-A4MJ] (summarizing a presentation by TSC Chairman and CEO, Arthur Holden, to advisory council on the formation and structure of TSC).

107. *See infra* Section II.B.1.

108. The SNP Consortium Ltd., Compliance Guidelines (1999) (on file with the North Carolina Law Review).

109. *See, e.g.*, *National Advisory Council for Human Genome Research Summary of Meeting*, *supra* note 106.

industry competitors treated the SNP map as a pre-competitive research tool, with open access to the data produced guaranteed from the outset.[110]

TSC has been cited as a leading example of early-stage pre-competitive collaboration directed at the development of basic research tools and scientific data.[111] It also provided a model for subsequent pre-competitive collaborations, such as iSAEC, to build upon.[112]

2. Taking the Model Downstream: The International Serious Adverse Events Consortium

Between 1976 and 2007 twenty-eight drugs were withdrawn from the U.S. market for safety reasons, including the occurrence of serious adverse events ("SAEs") that were not fully appreciated during clinical trials.[113] SAEs of some pharmaceutical products have included birth defects, liver damage, serious skin rash, kidney and renal injury, cardiac irregularity, and psychological effects. While some SAEs may be predictable based on the properties of a drug, many may instead be idiosyncratic, with predisposing genotypes.[114] Identifying genetic risk factors for SAEs would therefore have significant benefits for patient care, pharmaceutical developers, and drug safety regulators.[115] For these reasons, drug safety has become a high priority for the FDA.[116]

Nevertheless, historically it has been difficult to study SAEs in the field. Cases are relatively rare, occur sporadically around the world, are often undiagnosed or misdiagnosed by clinicians to whom symptoms are presented, are not classified or reported in a uniform

110. Minna Allarakhia, *Open Source Biopharmaceutical Innovation—A Mode of Entry for Firms in Emerging Markets*, 6 J. BUS. CHEMISTRY 11, 17 (2009).

111. *Whitehead Human Genome Project and SNP Consortium Announce Collaboration to Identify New Genetic Markers for Disease and Enhance Utility of Human Genome "Working Draft"*, WHITEHEAD INST. (July 11, 2000), http://wi.mit.edu/news/archive/2012/whitehead-human-genome-project-and-snp-consortium-announce-collaboration-identify [https://perma.cc/M43E-T8LQ] (quoting Chairman and CEO of TSC Arthur Holden).

112. Contreras, *supra* note 38, at 102–04.

113. *See, e.g.*, Russell A. Wilke et al., *Identifying Genetic Risk Factors for Serious Adverse Drug Reactions: Current Progress and Challenges*, 6 NATURE REVS. DRUG DISCOVERY 904, 905 (2007).

114. *Id.* at 904.

115. *Id.*

116. *See, e.g.*, Janet Woodcock, Director, Center for Drug Evaluation and Research, FDA, Statement before Senate Committee on Health, Education, Labor and Pensions, (Feb. 1, 2000), http://www.fda.gov/NewsEvents/Testimony/ucm115007.htm [https://perma.cc/U2ES-2ME9].

manner, and may be caused by a number of different but chemically related pharmaceutical products.[117] Collecting adequate numbers of cases and DNA samples from affected patients, and analyzing and determining the genetic factors that may underlie SAEs, requires a level of cross-industry collaboration hitherto unseen in the biopharma industry.[118]

The impetus for the international Serious Adverse Events Consortium, or iSAEC, arose from recognition by the FDA and industry that collaboration was essential to determine whether a genetic basis existed for certain drug-induced SAEs.[119] Drug safety assessment was seen by industry stakeholders as "a major area of pre-competitive research . . . since the development of new approaches to predict potential side effects is of paramount importance to reduce late-stage drug failures, a shared concern for patients, industry and regulatory authorities alike."[120]

iSAEC is a non-profit corporation formed in 2007 with the goal of identifying genetic variants useful in understanding the risk of drug-related SAEs.[121] iSAEC was launched with the financial and scientific support of six pharmaceutical firms.[122] Three more pharmaceutical firms and the Wellcome Trust were added after the consortium concluded a preliminary research program.[123] Three associate but non-dues-paying and non-voting members also joined following this initial research phase.[124] The FDA is actively involved in the consortium as an observer, advisor, and collaborator but does not have formal membership status.[125] iSAEC membership now includes nine of the largest U.S., European, and Japanese pharmaceutical firms; two large information technology providers; a U.S. hospital network; and the Wellcome Trust.[126] It remains privately funded by its members, who are either voting or non-voting

117. Wilke et al., *supra* note 113, at 904.

118. *Id.* at 905, 912.

119. *See* Holden et al., *supra* note 54, at 795.

120. Michael Goldman, Carolyn Compton & Barbara B. Mittleman, *Public-Private Partnerships as Driving Forces in the Quest for Innovative Medicines*, 2 CLINICAL & TRANSLATIONAL MED. 2, 2 (2013).

121. *See* Holden et al., *supra* note 54, at 795. At the time this article went to print, Jorge Contreras served as legal counsel to iSAEC. *Id.*

122. *Id.*

123. *Id.*

124. *Id.*

125. *Id.*

126. *Collaborators*, INT'L SAE CONSORTIUM, http://www.saeconsortium.org/index.php?q=node/3 [https://perma.cc/N8VA-ZP99].

depending on the nature of their contributions.[127] The board of directors includes one representative from each voting member, plus an independent chairman and CEO.[128]

Like TSC, iSAEC has made antitrust filings under the NCRPA and has adopted an antitrust compliance policy prohibiting the exchange of competitive information by its members and implementing other measures to reduce the risk and appearance of improper collusion.[129] All board meetings are conducted with the involvement of legal counsel.[130]

iSAEC commits to making its research results available to the public and free of any patent encumbrances using a defensive patenting strategy based on that of TSC.[131] Both members and collaborators are contractually prohibited from patenting the genetic associations and related discoveries made with iSAEC support, although they are not prevented from patenting downstream discoveries enabled by these findings.[132] To ensure that its results remain in the public domain, iSAEC files U.S. patent applications on DNA markers identified in its studies with the intention of abandoning them after publication.[133] Users of iSAEC data "must agree not to seek patents claiming any DNA markers or [genetic] associations disclosed in, or derived from, the iSAEC data" or any patents that "would otherwise block access to, or use of, [this] data."[134] This agreement to preserve the public nature of the results produced by iSAEC is seen as important in alleviating antitrust concerns that might otherwise arise from coordination among a group of competitors.[135]

Like TSC, iSAEC has helped to develop and refine a model of pre-competitive collaboration that entails open use research practices and standards and accompanying limitations on intellectual property restrictions. These data sharing and patent limitation requirements

127. *See* Holden et al., *supra* note 54, at 795.

128. *Id.*

129. Int'l Severe Adverse Events Consortium, Antitrust Policy (amended Feb. 28, 2008) (on file with the North Carolina Law Review).

130. Author Jorge Contreras serves as legal counsel for iSAEC.

131. *See supra* Section I.C.1.

132. *See* Jorge L. Contreras, Aris Floratos & Arthur L. Holden, *The International Serious Adverse Events Consortium's Data Sharing Model*, 31 NATURE BIOTECH. 17, 18 (2013) (discussing IP strategy and policies of iSAEC).

133. *Id.*

134. *Id.*

135. *See id.* at 17–18 ("This public commitment of IP serves as a cornerstone of iSAEC's charitable tax-exempt status and also alleviates concerns regarding potential antitrust challenges to this coordinated research activity.").

emphasize the "public goods" focus of the collaborations. The consortium is proposed as a useful reference point for other public-private consortia "seeking to facilitate pre-competitive research."[136]

3. Expanding the Boundaries of Pre-Competition: The Accelerating Medicines Partnership

The creation of the Accelerating Medicines Partnership, or AMP, marked an ambitious effort by the NIH, the FDA, and some of the world's largest pharmaceutical firms to push collaborative efforts downstream into areas of drug discovery and development that were formerly highly secretive and competitive.[137] When AMP was first launched it was heralded as "the first national cross-sector partnership of its size and scale" and "the latest initiative in the drug development market to embrace open data exchange, encouraging collaboration over competition as pathways for promoting innovation."[138]

AMP was formed in February 2014 as a public-private partnership among the NIH, the FDA, ten biopharma firms, and multiple disease advocacy groups and disease research foundations.[139] The mission of AMP, and the hope of its NIH advocates, is to provide a new model for drug discovery and development that involves collaborating in the identification and validation of promising biological targets of disease.[140] It is promoted as a "precompetitive collaboration [that] harnesses collective capabilities, scale, and resources across multiple sectors to improve the therapeutic

136. *Id.* at 17.

137. *See, e.g.*, Monica Langley & Jonathan D. Rockoff, *Drug Companies Join NIH in Study of Alzheimer's, Diabetes, Rheumatoid Arthritis, Lupus*, WALL ST. J. (Feb. 3, 2014, 11:00 PM), http://www.wsj.com/articles/SB10001424052702303519404579353442155924498 ("Ten big drug companies that have spent billions racing one another to find breakthroughs on diseases like Alzheimer's have formed an unusual pack to cooperate on a government-backed effort to accelerate the discovery of new medicines.").

138. *See, e.g.*, Aaron Kesselheim & Yongtian Tan, *Accelerating Medicines Partnership: A New Public-Private Collaboration for Drug Discovery*, HEALTH AFF. BLOG (Apr. 8, 2014), http://healthaffairs.org/blog/2014/04/08/accelerating-medicines-partnership-a-new-public-private-collaboration-for-drug-discovery/ [https://perma.cc/KT3N-BZ45].

139. For a list of memberships and a description of AMP, see *Accelerating Medicines Partnership*, NAT'L INSTS. OF HEALTH, https://www.nih.gov/research-training/accelerating-medicines-partnership-amp [https://perma.cc/W3BF-75MG]. Current industry members of AMP include: AbbVie, Biogen, Bristol-Myers Squibb, GlaxoSmithKline, Johnson & Johnson, Lilly, Merck, Pfizer, Sanofi, and Takeda. *Id.*

140. *Id.*

development efforts for complex, heterogeneous diseases."[141] AMP is focusing initially on three disease areas that share attributes of complexity, high risk, high cost, significant amounts of data, a track record of failed industry efforts, and significant public need for therapies.[142] These characteristics create fertile ground for new collaborative models.

AMP takes the form of a five-year agreement among ten large pharmaceutical firms, the NIH, and a number of disease-based foundations to collaborate in identifying promising drug and diagnostic targets to treat four diseases—Alzheimer's, type 2 diabetes, rheumatoid arthritis, and lupus.[143] The collaboration is managed by the Foundation for the NIH, an independent tax-exempt organization.[144] Funding for the initiative is shared fairly equally between public and private participants, with the NIH providing $121.5 million over five years, the ten pharmaceutical firms providing $110.6 million and patient advocacy groups providing $1.6 million.[145] Participants are expected to pool not just funds, but also expertise, data, and other resources.[146] AMP is structured as an umbrella partnership for the three initial programs focusing on separate disease areas.[147] Each program has its own budget, its own steering committee comprised of representatives from the NIH, the FDA, participating industry members and patient advocacy organizations, and its own set of milestones.[148] The steering committees are governed by the AMP executive committee, which again includes representatives from the NIH, the FDA, participating industry members, and patient advocacy organizations.[149]

The AMP arrangement took more than two years of intense negotiations to conclude, and it ultimately focuses on areas that are both of significant public health concern and in which pharmaceutical firms have struggled in their individual discovery and development

141. *What Is AMP?*, NAT'L INST. ON AGING, https://www.nia.nih.gov/alzheimers/amp-ad?utm_source=20150305_AMP&utm_medium=email&utm_campaign=ealert [https://perma.cc/93JW-DMNX].

142. *Id.*

143. *See, e.g.*, Langley & Rockoff, *supra* note 138.

144. *See Accelerating Medicines Partnership*, *supra* note 139.

145. *Id.*

146. *Id.*

147. *Id.*

148. *Id.*

149. *Id.*

efforts.[150] Each disease area has its own pilot program lasting between three and five years, complete with a research plan and set of milestones designed to characterize biomarkers of disease and disease progression and to identify biological targets most likely to respond to new therapies.[151] The pilot project for Alzheimer's disease received the bulk of the AMP funding.[152] This project involves searching for new biomarkers for disease progression through four NIH-funded clinical trials designed to test ways to delay or prevent disease onset.[153] The project also includes analysis of shared brain tissue samples from Alzheimer's patients to validate jointly identified biological targets, develop new models of late-onset Alzheimer's disease, and screen compounds provided by collaborators against novel disease targets.[154]

The type 2 diabetes project will collect and pool genetic and clinical data on patients provided by collaborators or developed through project studies with the goal of finding and validating promising molecules and pathways as targets for therapeutic development.[155] The NIH National Institute of Diabetes and Digestive and Kidney Diseases ("NIDDK") will provide "a website that will function as a 'smart PubMed', gathering all of the genetic and patient data from ongoing and completed trials."[156] The third pilot, focusing on rheumatoid arthritis and lupus, will analyze single cells from newly collected tissue and blood samples to better understand the diseases and aid in the search for new drug targets.[157]

150. *Industry and Non-Profits Join Forces to Speed Validation of Disease Targets*, NAT'L INSTS. OF HEALTH (Feb. 4, 2014), http://www.nih.gov/news/health/feb2014/od-04.htm [https://perma.cc/5PD5-N3SP].

151. *See* Jocelyn Kaiser, *NIH, 10 Drug Companies Partner to Study Four Diseases*, SCIENCE (Feb. 4, 2014, 3:45 PM), http://www.sciencemag.org/news/2014/02/nih-10-drug-companies-partner-study-four-diseases [https://perma.cc/ZDM8-AYBL].

152. *Id.*

153. *Id.*

154. *Id.*

155. *See Accelerating Medicines Partnership: Type 2 Diabetes*, NAT'L INSTS. OF HEALTH, http://www.nih.gov/research-training/accelerating-medicines-partnership-amp/type-2-diabetes#approach [https://perma.cc/J2ZP-HUM6].

156. *See, e.g.*, Sara Reardon, *Pharma Firms Join NIH on Drug Development*, NATURE (Feb. 4, 2014) http://www.nature.com/news/pharma-firms-join-nih-on-drug-development-1.14672 [https://perma.cc/3WBU-F394].

157. *See Accelerating Medicines Partnership: Autoimmune Diseases of Rheumatoid Arthritis and Lupus*, NAT'L INSTS. OF HEALTH, http://www.nih.gov/research-training/accelerating-medicines-partnership-amp/autoimmune-diseases-rheumatoid-arthritis-lupus [https://perma.cc/CG95-LYVM] ("The partnership will integrate several new or developing technologies to analyze single cells and groups of cells involved in autoimmunity in new ways; collect tissue samples, including synovium (the tissue that lines joints) from people with RA and lupus for molecular analysis; develop computational

All of these projects include agreements among the collaborators to contribute financial support and scientists who are experts on the relevant disease, share research data and tissue and blood samples with each other and with the public.[158] The goal of the project is for the collaborators to gain a better understanding of how each disease works through their collaborative efforts and data sharing, to use this knowledge to identify biological targets that can be attacked with potential drugs, and to measure how diseases progress and respond to treatments.[159]

AMP has been characterized as pre-competitive both by reference to the type of data that is being shared and by the public nature of its results. The NIH has promoted AMP as an arrangement that should not face antitrust concerns because it involves early, pre-competitive research and the results will be made freely available.[160] Participants are pooling large quantities of data and engaging in joint analysis of this data to identify useful biological markers and drug targets.[161] The data that is being shared is described as data that does not, on its own, convey any competitive advantage for the participating firms.[162] Instead, the parties must work together to identify useful targets from within this aggregation of data, thus increasing the odds that they are all picking the right drug targets to pursue in subsequent private drug development projects.[163]

The AMP participants are contractually obligated to make all of the data and methods from the early-stage clinical trials that are conducted jointly by collaborators in AMP freely available. Only after the information is published are participants permitted to use the information in their own proprietary drug programs. As the projects progress, it is anticipated that participants will shift into product development activities that are more competitive. The details of AMP agreements are confidential, but reports suggest that

tools to integrate different data types to characterize molecular pathways; and make the data available to the broad research community for further analysis.").

158. *See, e.g.*, Langley & Rockoff, *supra* note138.

159. *See id.*

160. *See id.* ("The project shouldn't face any antitrust concerns, the NIH says, because it involves early, 'pre-competitive' research and will make all results freely available."); *cf.* Vertinsky, *supra* note 10, at 1549–51.

161. *See* Vertinsky, *supra* note 10, at 1549–51.

162. *Id.* at 1550.

163. *See* Reardon, *supra* note 157; *see also BioCentury This Week Episode 180: NIH's Collins, PhRMA's Chin Explain Accelerating Medicines Partnership* (BCTV television broadcast Mar. 2, 2014), http://www.biocentury.com/bctvthisweek/all/2014-03-02/nihs-collins-phrmas-chin-explain-accelerating-medicines-partnership-bctv [https://perma.cc/64K7-6DQC].

participants may obtain proprietary rights over drug candidates and otherwise stake out proprietary positions in downstream areas of interest.[164]

AMP provides an important example of a prominent pharmaceutical industry collaboration that has stretched the definition of "pre-competitive" activity far beyond early conceptions of basic scientific research. As NIH Director Dr. Francis Collins describes it, "We're going to increase the odds of picking the right [drug and diagnostic targets] at the very beginning and avoid wasting time and money chasing duds," but once the information from the early-stage trials is published, "the full competitive power of [the] pharmaceutical industry can kick in."[165] Inherent in this approach is the idea that participants can redefine the innovation process to broaden the areas in which the process is cooperative and narrow the areas in which the process is competitive. AMP is portrayed as complementary to the competitive drug development process, facilitating competition in those areas where it will be most meaningful.

These examples illustrate the progression of pre-competitive collaborations in the biopharma industry. While various private and public policy rationales have been offered in support of pre-competitive collaborations, what remains unclear is the degree to which antitrust law has been taken into account in pre-competitive collaborations' structuring and implementation—at least beyond efforts to characterize the collaborations as pre-competitive.

II. THE ANTITRUST FRAMEWORK FOR ANALYZING INDUSTRY COLLABORATIONS

As the analysis above suggests, there appears to be a prevailing intuition among governmental agencies and private sector participants that pre-competitive collaborations are, by their nature, procompetitive. While it may indeed be true that many pre-competitive collaborations in the biopharma sector offer substantial procompetitive benefits, it is not necessarily the case that all do. Rather, each such pre-competitive collaboration must be analyzed under the existing antitrust law framework that has been established by statute, case law, and guidance from enforcement agencies. Part II summarizes the antitrust framework for analyzing collaborations among competitors. It begins with the general antitrust framework as

164. *See* Reardon, *supra* note 156.
165. *Id.*

applied to agreements in restraint of trade and then focuses on the more specialized guidelines and approaches that have been developed by antitrust authorities to deal with the unique challenges posed by R&D collaborations and R&D markets.

A. Standard Framework Governing Agreements in Restraint of Trade: Sherman Act Section 1

Section 1 of the Sherman Act prohibits any "contract, combination . . . or conspiracy, in restraint of trade."[166] Key to the existence of a violation of section 1 is the existence of concerted action among two or more firms: an "agreement" in restraint of trade.[167] In addition, in order to be condemned, such an agreement must be "unreasonably restrictive of competitive conditions."[168] Finally, as with most antitrust offenses, the parties to such an agreement must possess sufficient power to distort competitive processes in one or more markets, otherwise known as "market power."[169] The prohibition against anticompetitive agreements under section 1 applies both to agreements among firms at the same level in the supply chain (i.e., agreements among competitors, or "horizontal" agreements) as well as to agreements among firms at different levels of the supply chain (i.e., agreements among suppliers and distributors, or "vertical" agreements).[170]

Any agreement having potentially anticompetitive effects would be analyzed under section 1 using a framework developed by the courts over the last century. This framework is also employed by the principal antitrust enforcement agencies, the DOJ Antitrust Division and the FTC, in assessing whether or not to bring an antitrust enforcement action in a particular case.

The first step in the antitrust analysis of any agreement is determining whether it should be deemed illegal per se, or whether it should be analyzed under the so-called "rule of reason." Illegality per

166. 15 U.S.C. § 1 (2012).

167. *See* 6 PHILLIP E. AREEDA & HERBERT HOVENKAMP, ANTITRUST LAW: AN ANALYSIS OF ANTITRUST PRINCIPLES AND THEIR APPLICATION, ¶ 1400, at 3 (3d ed. 2010).

168. Standard Oil Co. v. United States, 221 U.S. 1, 58 (1911).

169. *See* 2B PHILLIP E. AREEDA, HERBERT HOVENKAMP & JOHN L. SOLOW, ANTITRUST LAW: AN ANALYSIS OF ANTITRUST PRINCIPLES AND THEIR APPLICATION, ¶ 500, at 107 (4th ed. 2014); LAWRENCE A. SULLIVAN & WARREN S. GRIMES, THE LAW OF ANTITRUST: AN INTEGRATED HANDBOOK 187 (2d ed. 2006) (acknowledging "[p]ower and the potential for or actual abuse of that power is the common thread running through the fabric of antitrust law").

170. *See* AREEDA & HOVENKAMP, *supra* note 167, ¶ 1402, at 11–20.

se is generally reserved for agreements "whose nature and necessary effect are so plainly anticompetitive that no elaborate study of the industry is needed to establish their illegality."[171] Agreements of a type that "always or almost always tend to raise prices or reduce output" are generally deemed to be illegal per se.[172] Traditionally, such agreements have been directed to price fixing, reducing output, allocating markets, group boycotts, and tying arrangements.[173] While these activities are still viewed with suspicion, the analysis of illegality per se has, in recent years, become less mechanistic, and courts have proven increasingly willing to consider the potential ameliorating effects of arrangements that might otherwise have been condemned as per se violations.[174]

Agreements that are not deemed to be illegal per se are evaluated under the more flexible rule of reason approach. The rule of reason is applied to agreements "whose competitive effect can only be evaluated by analyzing the facts peculiar to the business, the history of the restraint, and the reasons why it was imposed."[175] Under the rule of reason, if a challenged arrangement is found, after all of the circumstances have been weighed, to "impos[e] an unreasonable restraint on competition," it will be deemed illegal.[176]

As formulated by the Supreme Court and U.S. enforcement agencies, the central question in a rule of reason analysis is "whether the relevant agreement likely harms competition by increasing the ability or incentive profitably to raise price above or reduce output, quality, service, or innovation below what likely would prevail in the absence of the relevant agreement."[177] Factors that are considered in assessing whether or not an agreement imposes an unreasonable restraint on competition include "specific information about the relevant business, its condition before and after the restraint was imposed, and the restraint's history, nature, and effect."[178] This

171. Nat'l Soc'y of Prof'l Eng'rs v. United States, 435 U.S. 679, 692 (1978).

172. COLLABORATION GUIDELINES, *supra* note 19, § 3.2, at 8 (2000).

173. N. Pac. Ry. v. United States, 356 U.S. 1, 5 (1958).

174. *See, e.g.*, Nat'l Collegiate Athletic Ass'n v. Bd. of Regents of Univ. of Oklahoma, 468 U.S. 85, 100–01 (1984) (holding that a collective agreement to limit output (number of collegiate athletic events broadcast on television) should be analyzed under the rule of reason because the agreement was arguably necessary for any product to be available at all); *see also* 7 AREEDA & HOVENKAMP, *supra* note 167, ¶ 1509, at 441; SULLIVAN & GRIMES, *supra* note 169, at 243–60.

175. *See Nat'l Soc'y of Prof'l Eng'rs*, 435 U.S. at 692.

176. *See, e.g.*, Leegin Creative Leather Prods., Inc. v. PSKS, Inc., 551 U.S. 877, 885–86 (2007); Cont'l T.V., Inc. v. GTE Sylvania Inc., 433 U.S. 36, 49 (1977).

177. COLLABORATION GUIDELINES, *supra* note 19, § 3.1, at 7.

178. State Oil Co. v. Khan, 522 U.S. 3, 10 (1997).

analysis, as conducted by the agencies with respect to horizontal agreements, often includes one or more of several considerations: (a) intent of the parties, (b) limitations on independence and competition, (c) exchange of information, (d) duration, (e) markets and market power, and (f) offsetting procompetitive benefits.

While anticompetitive intent alone does not constitute a violation of the antitrust laws, the intent of the parties in entering into an agreement is relevant in assessing its likely competitive effects.[179] Thus, if evidence of a manifestly anticompetitive intent exists with regard to the formation of an arrangement among competitors, it is more likely than not that anticompetitive effects will follow.[180] But, by the same token, evidence of procompetitive intentions will not necessarily negate the anticompetitive impact of an arrangement among competitors.[181]

A second factor is the extent to which agreements impose limitations on independence and competition among the parties. Agreements that limit the parties' independent decision making or combine control over their production, pricing, assets, or other competitive factors tend to reduce their incentive or ability to compete independently, and may thus harm competition.[182] Some agreements expressly or implicitly limit the parties' ability to compete in certain markets.[183] The degree to which independent competition is eliminated through an agreement has a direct bearing on its anticompetitive effect.

The nature and extent of information exchange is a third factor. The exchange of information is often necessary to achieve the legitimate purposes of a collaborative business arrangement. However, when competitively sensitive information such as pricing, output, customers, and business plans is shared by competitors, collusion may be facilitated, prices fixed, and competition reduced.[184] As noted by the agencies, "The competitive concern depends on the

179. *See* Bd. of Trade of Chi. v. United States, 246 U.S. 231, 238 (1918); *see also* COLLABORATION GUIDELINES, *supra* note 19, § 3.31, at 12.

180. *See* Richard S. Wirtz, *Purpose and Effect in Sherman Act Conspiracies*, 57 WASH. L. REV. 1, 24 (1981) (noting "[p]urpose is arguably the only reliable guide to the agreement's effects. When the record shows that the parties sought to injure competition . . . it is right to shift the burden of proof to the party who denies that such effects will follow").

181. *Bd. of Trade of Chi.*, 246 U.S. at 238.

182. COLLABORATION GUIDELINES, *supra* note 19, § 3.31, at 12.

183. *Id.* § 3.34(a), at 19.

184. *Id.* § 3.31(b), at 15; *see also* SULLIVAN & GRIMES, *supra* note 169, at 260–70 (outlining historical development of information exchange cases).

nature of the information shared."[185] Often, structural features of an arrangement will offer clues regarding the likelihood that competitive information will be exchanged among the parties, and safeguards can be implemented to reduce the likelihood of such exchanges. For example, if the parties agree not to assign marketing personnel to participate on committees in an R&D collaboration, then competitive information is less likely to be exchanged.[186] Likewise, competitive information from the parties can be consolidated by independent third parties who will then utilize it to advance the collaboration's goals.[187]

Fourth, the duration of an agreement among competitors will have a bearing on its anticompetitive effect. On balance, short-term agreements are more likely than long-term agreements to result in the parties' competition, both within and outside the field of collaboration.[188] When the duration of a horizontal agreement exceeds ten years, the agencies are likely to treat the arrangement as a merger.[189]

The fifth factor, market power, plays an important role in the analysis. In order for an agreement to be condemned under the antitrust laws, the parties must possess sufficient power to distort competitive processes in one or more markets, otherwise known as "market power."[190] Market power is often measured by "the ability to raise price profitably by restricting output."[191] For an agreement to be condemned under the rule of reason, the parties must be shown both to have restrained competition in a defined product and geographic market, and to have played a "significant role in that market."[192]

185. COLLABORATION GUIDELINES, *supra* note 19, § 3.31(b), at 15–16 (noting current information is more concerning than historical information, company-specific information is more concerning than aggregated information).

186. *See id.* § 3.34(e), at 21.

187. *Id.*

188. *Id.* § 3.34(f), at 21.

189. *Id.* § 1.3, at 4–5 & n.10. Under the agencies' joint Guidelines for Horizontal Mergers, the central question for analysis is whether or not a merger between actual or potential competitors may substantially lessen competition. *See* FED. TRADE COMM'N & U.S. DEP'T OF JUSTICE, GUIDELINES FOR HORIZONTAL MERGERS 1–2 (2010). This assessment is made under the assumption that "mergers should not be permitted to create, enhance, or entrench market power or to facilitate its exercise." *Id.* at 2.

190. *See* AREEDA ET AL., *supra* note 169, ¶ 500, at 107. Note that market definition and the concept of market power are relevant not only to section 1 concerted conduct claims, but also to claims of monopolization under section 2 of the Sherman Act, 15 U.S.C. § 2 (2012), and to mergers under section 7 of the Clayton Act, 15 U.S.C. § 18 (2012). Much of the literature and analysis concerning market definition arises in the merger context.

191. AREEDA ET AL., *supra* note 169, ¶ 501, at 109.

192. 7 AREEDA & HOVENKAMP, *supra* note 167, ¶ 1503, at 397.

The definition of product and geographic markets is complex, fact-intensive, and draws heavily on economic analysis.[193] Some of the principal factors evaluated when defining a product market are the degree to which different products can function as substitutes for one another, the degree of price elasticity among different products, and the degree to which producers can easily shift from production of one product to another.[194] Geographic markets are defined based on the ability of suppliers to sell beyond their immediate locations, taking into account factors such as transportation costs, buyer convenience, and customer preferences.[195] This being said, a full-scale economic analysis of relevant markets is not necessarily required if proof of actual anticompetitive harm can be shown.[196]

Once the relevant markets affected by an agreement are defined, the rule of reason analysis turns to the share of these markets controlled by the parties and whether the parties possess sufficient power to adversely affect competition in those markets.[197] The determination of market power involves a fact-specific economic analysis that considers factors such as: (1) the share of the market enjoyed by each party and the parties collectively; (2) concentration of the market; (3) the parties' ability to extract high profit margins; (4) barriers to market entry; (5) control over intellectual property; and (6) behavioral indicators.[198] If the collective market shares of the parties to a horizontal arrangement are sufficiently small, then it may be presumed that their arrangement, regardless of its other features, is unlikely to harm competition in the market.[199]

With these factors in mind, the balancing analysis focuses on any offsetting procompetitive benefits from the arrangements. In the rule of reason analysis, the above considerations are analyzed to determine whether an agreement has, or is likely to have, anticompetitive effects. If so, then these must be weighed against the

193. *See generally* AREEDA ET AL., *supra* note 169, pt. 2, ch. 5, at 107–472 (discussing market structure issues, specifically market power and market definition).

194. *See id.* ¶¶ 561–63, at 378–418.

195. *See id.* ¶¶ 552–53, at 344–65.

196. *See* FTC v. Ind. Fed'n of Dentists, 476 U.S. 447, 460–61 (1986).

197. *See, e.g.*, E. Food Servs., Inv. v. Pontifical Catholic Univ. Servs. Ass'n, 357 F.3d 1, 5 (1st Cir. 2004).

198. *See generally* AREEDA ET AL., *supra* note 169, pt. 2, ch. 5, at 107–234 (discussing defining market power and alternative non-market-based proofs of market power). *See also* SULLIVAN & GRIMES, *supra* note 169, at 62–74.

199. Absent price fixing or other illegal per se activity, the agencies generally will not challenge a competitor collaboration if the collective market shares of the participants are below twenty percent of the relevant market. COLLABORATION GUIDELINES, *supra* note 19, § 4.2, at 26.

agreement's likely procompetitive benefits. Procompetitive benefits exist when an arrangement is likely to benefit consumers through lower prices, higher quality, or more rapid product introductions.[200] If the procompetitive benefits of an agreement outweigh its anticompetitive harm, then the agreement will survive rule of reason review.

B. Antitrust Analysis of R&D Collaborations

As discussed in Section II.A above, agreements in restraint of trade are prohibited under section 1 of the Sherman Act. This Section applies the general antitrust analysis under section 1 specifically to R&D collaborations. Collaborative research agreements,[201] which often involve concerted action by competitors (e.g., different pharmaceutical producers) and parties at different levels of the supply chain (e.g., universities, pharmaceutical producers, biotechnology firms, and healthcare providers), can involve both horizontal and vertical restraints that can give rise to antitrust concern. Some collaborations may serve as "little more than fronts for cartels" with no lawful purpose, and others may integrate the participants' businesses so completely that they are effectively mergers requiring enhanced antitrust scrutiny.[202]

However, legitimate collaborative R&D agreements have long been recognized by courts and antitrust enforcement agencies as offering significant procompetitive benefits. These agreements have the potential to spread the financial burden of costly research, to combine technical skill and knowledge to promote greater innovation, to accelerate the development of new products, and to lower research and production costs through economies of scale, thereby increasing overall social welfare.[203] Collaborations that set out to achieve such goals "often are not only benign but procompetitive."[204] Accordingly, collaborative agreements are typically reviewed under the rule of reason.[205]

200. *See id.* § 2.1, at 6.

201. Collaborative arrangements are also often referred to in the literature as "joint ventures."

202. 7 AREEDA & HOVENKAMP, *supra* note 167, ¶ 1478a, at 341–42.

203. *See* 13 AREEDA & HOVENKAMP, *supra* note 167, ¶ 2115a, at 111–12; COLLABORATION GUIDELINES, *supra* note 19, pmbl., at 1.

204. COLLABORATION GUIDELINES, *supra* note 19, pmbl., at 1.

205. *See* Christine A. Varney, Assistant Att'y Gen., Antitrust Div., U.S. Dep't of Justice, Antitrust Immunities, Remarks Prepared for the American Antitrust Institute's 11th Annual Conference: Public and Private: Are the Boundaries in Transition? 5 (June

1. Joint Ventures and the National Cooperative Research and Production Act

In response to industry concerns during the early 1980s that aggressive antitrust enforcement could chill productive joint research ventures,[206] Congress enacted the National Cooperative Research and Production Act, or the NCRPA.[207] The NCRPA limits potential antitrust liability for horizontal arrangements among competitors that qualify as "joint ventures."[208] It also establishes that such collaborations "shall not be deemed illegal, per se," but will be assessed using a "reasonableness" standard.[209]

For purposes of the NCRPA, a "joint venture" constitutes any group of activities undertaken by two or more parties for the purpose of

> (A) theoretical analysis, experimentation, or systematic study of phenomena or observable facts, (B) the development or testing of basic engineering techniques, (C) the extension of investigative findings or theory of a scientific or technical nature into practical application for experimental and demonstration purposes, including the experimental production

24, 2010), https://www.justice.gov/atr/speech/antitrust-immunities [https://perma.cc/KVV2-FUSS].

206. *See* SULLIVAN & GRIMES, *supra* note 169, at 272. *See generally* Christopher O.B. Wright, *The National Cooperative Research Act of 1984: A New Antitrust Regime for Joint Research and Development Ventures*, 1 HIGH TECH. L.J. 133 (1986) (discussing the adoption of the NCRPA and the conditions that lead to its adoption). This period in American history was characterized by excessive concern over the competitiveness of American industry in the face of increasing foreign (particularly Japanese) competition. *Id.* at 139. In addition to the NCRPA, it gave rise to the Patent and Trademark Law Amendments Act, more commonly known as the Bayh-Dole Act, Pub. L. 96-517, 94 Stat. 3015 (1980) (codified as amended at 35 U.S.C. §§ 200 to 211 (2012)), which enabled universities and other federally-funded researchers to obtain patent protection for their discoveries. *See supra* note 13 (describing collaborations such as Sematech as a response to similar concerns).

207. National Cooperative Production Amendments of 1993, Pub. L. No. 103-42, 107 Stat. 119 (1993) (codified as amended at 15 U.S.C. §§ 4301–4306 (2012)) (amending the 1984 act to add production to the list of protected activities and yielding the commonly-used acronym "NCRPA"). The Act was further amended in 2004 to add "standards development activity" to the activities covered by the Act. Development Organization Advancement Act of 2004, Pub. L. 108-237, sec. 103(1), § 4301(a)(7), 118 Stat. 661, 663 (2004) (codified at 15 U.S.C. § 4301(a)(7) (2012)).

208. 15 U.S.C. §§ 4303, 4305 (2012) (conveying that if a horizontal agreement qualifies as a joint venture under the NCRPA, the venturers may provide notice to the attorney general and the FTC informing them of the joint venture and its membership, and thereafter, any antitrust suit brought against the joint venture will be limited to recovery of actual damages and attorney's fees, rather than the treble damages otherwise available under section 15 of the Sherman Act, 15 U.S.C. § 15 (2012)).

209. *Id.* § 4302.

> and testing of models, prototypes, equipment, materials, and processes, (D) the production of a product, process, or service, (E) the testing in connection with the production of a product, process, or service by such venture, (F) the collection, exchange, and analysis of research or production information, or (G) any combination of the purposes specified in subparagraphs (A), (B), (C), (D), (E), and (F), and may include the establishment and operation of facilities for the conducting of such venture, the conducting of such venture on a protected and proprietary basis, and the prosecuting of applications for patents and the granting of licenses for the results of such venture.[210]

As noted above, the NCRPA ensures that the collaborative activities of joint ventures will be analyzed under the rule of reason. In some instances, even behavior that would normally be condemned as illegal per se may be permissible when conducted by a joint venture. Thus, under the NCRPA, activities including the following may be permitted if they are found to be "reasonably required to carry out the purpose" of a joint venture: exchanging information relating to costs, sales, profitability, prices, marketing, or distribution of any product, process, or service; restricting or requiring the sale, licensing, or sharing of inventions, developments, products, processes, or services not developed through, or produced by, the venture; restricting or requiring participation by any party to the venture in other R&D activities; allocating markets; or restricting, requiring, or otherwise affecting the production of a product, process, or service.[211]

2. Rule of Reason Analysis for Collaborative R&D Arrangements

Collaborative R&D agreements, both under the Sherman Act and the NCRPA, are subject to rule of reason analysis in which potential anticompetitive harms are weighed against procompetitive benefits. While the analysis of these arrangements falls within the general contours of the antitrust rule of reason analysis set forth in Section II.A above, there are a number of special considerations that arise specifically in the context of collaborative R&D agreements. It is the rule of reason, as informed by the special considerations discussed below, which provides the foundation for the framework that we discuss in Part III.

210. *Id.* § 4301(a)(6).
211. *Id.* § 4301(b)(1), (b)(3)(A)–(B), (b)(5)–(8).

a. Consolidation of Research Operations

Collaborative R&D arrangements, by their nature, enable multiple parties to combine or forgo individual R&D activities in the areas addressed by the collaboration. While such consolidation may achieve efficiencies of scale, combine technical skill to foster increased innovation, and eliminate barriers imposed by blocking intellectual property, the combination of formerly competitive R&D programs may also pose risks of anticompetitive harm.

Combining the R&D activities of several competitors, for example, is likely to reduce the number of independent lines of inquiry pursued by the members of the group.[212] While such a reduction may eliminate inefficient or unpromising lines of research, it is also possible that one of the eliminated lines may have yielded the best results. Such combinations may thus lead to lower overall levels of innovation and new product development. Eliminating R&D competition among collaborators may also reduce incentives to improve product quality, to get new and improved products to market quickly, and to offer superior customer service.

These risks are endemic to R&D collaborations, even those with the best intentions. The risks are higher when there is a possibility that participants in an R&D collaboration may intentionally collude to reduce competition. Participants in a collaboration may, for example, agree not to innovate in ways that threaten one another's markets or products.[213]

From the agencies' perspectives, one central question in evaluating an R&D collaboration is whether it is likely to reduce the parties' incentive or ability to engage in independent R&D, presumably in competition with, or complementary to, that of the collaboration.[214] Anticompetitive effects are more likely to be found when a collaborative R&D activity has the potential to reduce the parties' profits in other lines of business (e.g., by rendering an existing product line obsolete), "or when a regulatory approval process limits the ability of late-comers to catch up with competitors already engaged in the R&D."[215]

212. COLLABORATION GUIDELINES, *supra* note 19, § 3.31(a), at 15.
213. 13 AREEDA & HOVENKAMP, *supra* note 167, ¶ 2100e, at 14.
214. COLLABORATION GUIDELINES, *supra* note 19, § 3.31(a), at 15.
215. *See id.*

b. Exchange of Competitive Information

As noted in Section II.A, the exchange of information among competitors can lead to collusion and generally gives rise to antitrust concerns. In R&D collaborations, of course, the exchange of information is often essential to achieve the benefits of the collaboration.[216] The agencies have recognized that sharing of information regarding technology, know how, best practices, and intellectual property by the parties to an R&D collaboration may be necessary to implement the collaborative research program and may thus be procompetitive.[217] Nevertheless, if the shared information includes information related to marketing, product plans, or pricing, collusion and other anticompetitive effects may be found.[218]

c. Overall Competitive Effect and Procompetitive Benefits

If a collaboration agreement is likely to have anticompetitive effects, the next step in the rule of reason analysis is to determine the overall competitive effect of the agreement. This inquiry focuses on whether any identifiable efficiency gains stemming from the agreement would be enough to offset the agreement's anticompetitive effects.[219]

As noted above, numerous procompetitive benefits may arise from collaboration agreements. These include spreading the financial burden of costly research, combining technical skill and knowledge to achieve synergies and promote innovation, enabling the parties to engage in research that they might not have been able to conduct individually, combining intellectual property to avoid blocking positions, accelerating the development of new products, and lowering research and production costs through economies of scale.[220] As noted by one agency official, in some cases collaboration may even result in "product and service offerings that would be completely unavailable without coordination among otherwise competitive firms."[221] Thus, even when anticompetitive effects are theoretically possible, or even likely, the significant procompetitive

216. *See id.* § 3.31(b), at 15.
217. *Id.*
218. *Id.*
219. *Id.* § 3.37, at 24–25.
220. *See* 13 AREEDA & HOVENKAMP, *supra* note 167, ¶ 2115a, at 111–12; COLLABORATION GUIDELINES, *supra* note 19, § 3.31(a), at 14; SULLIVAN & GRIMES, *supra* note 169, at 729.
221. Varney, *supra* note 205, at 5.

benefits that may arise from R&D collaborations could outweigh the harms under a rule of reason analysis.

3. The Challenges of Market Definition in R&D Collaborations

As with other potentially anticompetitive agreements, R&D collaborations must be analyzed with respect to their impact on defined markets.[222] There are two types of markets that must be evaluated in connection with R&D collaborations: (1) the market for the parties' and the collaboration's products and services and (2) the market for relevant R&D.[223] In terms of the pharmaceutical industry, this distinction has been characterized as competition in the development of new drugs and competition in the sale of drugs.[224] Below, we discuss the definition of both product and R&D markets in the pharmaceutical industry.

a. Product Markets

Just as with other agreements among competitors, collaborative R&D agreements may have an effect on the product or service markets in which the parties compete. Products relevant to an R&D collaboration include both the products that the parties to the collaboration produce and sell individually, and those that the collaboration will produce and sell.[225] For example, Firm A is a producer of pliable synthetic materials, and Firm B is a producer of industrial helium. These two firms form a joint venture to develop and produce high-altitude weather balloons. Both the product markets for pliable synthetic materials and helium, as well as the product market for weather balloons, are implicated in the venture.

b. R&D Markets

Cooperative research agreements may affect not only markets for products sold by the parties and the collaboration, but the conduct of R&D itself. This is a so-called "R&D" or "innovation" market. The existence of a "market" in R&D has been recognized both by the U.S. antitrust enforcement agencies and in the NCRPA, which

222. *See supra* Section II.A.

223. COLLABORATION GUIDELINES, *supra* note 19, § 3.32, at 16–17. *See supra* notes 19 and 21 (regarding use of "research and development markets" in place of "innovation markets").

224. M. Howard Morse, *Product Market Definition in the Pharmaceutical Industry*, 71 ANTITRUST L.J. 633, 637 (2003) ("Competition in the pharmaceutical industry occurs on two levels: the development of new drugs, and the sale of drugs.").

225. COLLABORATION GUIDELINES, *supra* note 19, § 3.32, at 16.

requires that the competitive effects of a cooperative research arrangement be evaluated "in properly defined, relevant research, development, product, process and service markets."[226]

As explained by the agencies, an R&D market comprises "the research and development directed to particular new or improved goods or processes, and the close substitutes for that research and development."[227] Thus, if a collaboration is likely to impair R&D relating to future products in a particular field, an R&D market will be implicated.[228]

Gilbert and Sunshine highlight the potential economic harms that may flow from reductions in innovation and the impairment of R&D markets with respect to the parties to a potential merger:

> A reduction in innovation may delay improvements in production processes that would lower the production costs of each of the merging firms, or it may reduce the magnitude of such improvements. In addition, a reduction in innovation may reduce the likelihood of discovery or delay the introduction by each firm of new or improved products. The loss of production improvements would result in higher costs, and possibly higher prices, even in markets where only one of the merging firms is a participant. Similarly, the loss of new or improved products would deny consumers the benefits of these improvements in every market where the firm is a supplier, including markets where only one of the firms is a participant.[229]

226. 15 U.S.C. § 4302 (2012). *See* J. Thomas Rosch, Comm'r, Fed. Trade Comm'n, Antitrust Regulation of Innovation Markets, Remarks at ABA Antitrust Intellectual Property Conference 4–9 (Feb. 5, 2009), https://www.ftc.gov/sites/default/files/documents/public_statements/antitrust-regulation-innovation-markets/090205innovationspeech.pdf [https://perma.cc/7M5P-NQEZ] (offering a brief history of FTC regulation of competition in innovation markets, beginning with a challenge to a proposed Xerox Corporation merger in 1974).

227. IP LICENSING GUIDELINES, *supra* note 19, § 3.2.3, at 11. The IP Licensing Guidelines Proposed Update define R&D markets as consisting of "the assets comprising research and development related to the identification of a commercializable product, or directed to particular new or improved goods or processes, and the close substitutes for that research and development." IP LICENSING GUIDELINES PROPOSED UPDATE, *supra* note 19, § 3.2.3, at 16.

228. *See* COLLABORATION GUIDELINES, *supra* note 19, § 3.32(c), at 17 (noting "if a competitor collaboration may have competitive effects on innovation that cannot be adequately addressed through the analysis of goods or technology markets, the Agencies may define and analyze an innovation market").

229. Richard J. Gilbert & Steven C. Sunshine, *Incorporating Dynamic Efficiency Concerns in Merger Analysis: The Use of Innovation Markets*, 63 ANTITRUST L.J. 569, 570 (1995).

Notwithstanding the theoretical existence of R&D markets, identifying and defining these markets in practice has proven challenging.[230] This is an evolving area of law, with disagreement even among antitrust regulators about the appropriate role of antitrust laws in regulating R&D markets[231] and divergent views regarding the market conditions that best foster innovation.[232] A recent update to the IP Licensing Guidelines attempts to clarify the definition of R&D markets, but ultimately does little more than change the terminology and provide for more flexibility in analyzing intellectual property arrangements that impact R&D markets.[233]

As with product markets, agencies seek to define R&D markets by reference to "close substitutes."[234] That is, an R&D market will include all R&D efforts of similar nature, scope, and magnitude, with access to financial resources, necessary intellectual property, and skilled personnel, and which have the ability to successfully commercialize innovations.[235]

To date, most of the controversies involving the definition of R&D (or innovation) markets have arisen in the context of proposed mergers challenged by the agencies. For example, in 1993, the DOJ challenged the proposed acquisition of General Motors' transmission division by ZF Friedrichshafen, a German transmission manufacturer.[236] Though the transmission businesses of GM and ZF overlapped in only a few specific vehicle markets, the DOJ expressed concern that ZF would reduce its overall transmission R&D efforts after the acquisition, thereby dampening "worldwide technological innovation in the design, development, and production of . . . automatic transmissions" for a range of vehicles.[237]

230. *See* SULLIVAN & GRIMES, *supra* note 169, at 729 ("Both the market definition and the harm-benefit issues [with innovation markets] may be imponderable.").

231. *See* Rosch, *supra* note 226, at 2–3.

232. *See generally* Michael A. Carrier, *Two Puzzles Resolved: Of the Schumpeter-Arrow Stalemate and Pharmaceutical Innovation Markets*, 93 IOWA L. REV. 393 (2008) (discussing various "factors that determine the ideal market structure for innovation in specific industries").

233. *See, e.g.*, Frederick R. Juckniess, *Four Key Changes to Antitrust Guidelines for Licensing of Intellectual Property—DOJ, FTC Invite Comment*, NAT'L L. REV. (Sept. 9, 2016), http://www.natlawreview.com/article/four-key-changes-to-antitrust-guidelines-licensing-intellectual-property-doj-ftc [https://perma.cc/E2GX-YC28].

234. COLLABORATION GUIDELINES, *supra* note 19, § 4.3, at 27.

235. *Id.*

236. Complaint, United States v. Gen. Motors Corp., No. 93-530, 1993 WL 13610315, at *1 (D. Del. Nov. 16, 1993).

237. *Id.* The acquisition was abandoned by the parties following the DOJ's challenge. *See* Rosch, *supra* note 226, at 6–7.

Once an R&D market is defined, as in the analysis of product and geographic markets, the competitive impact of the proposed agreement on that market must be determined.[238] If the parties to the agreement collectively control only a small share of the R&D market, then anticompetitive harm will be deemed to be unlikely.[239] In general, the agencies will not challenge a competitor collaboration in an R&D market if there are at least three or more independent entities outside the collaboration with the incentive or ability to engage in R&D that is the same or a close substitute.[240] On the other hand, if the parties control a large share of the market or hold blocking intellectual property positions, then anticompetitive harm is likely to be found.[241]

4. Exclusion

As noted in Section II.A, group boycotts are generally deemed to be illegal per se under section 1 of the Sherman Act. A group boycott constitutes a concerted refusal by a group of competitors to deal with one or more firms for the purpose of suppressing or restricting competition.[242] These arrangements frequently cut off the boycotted firms' access to a supply, facility, or market necessary for it to compete.[243]

As with other horizontal arrangements, boycott and exclusion issues can arise in the context of collaborative research agreements and joint ventures. These issues can arise both with respect to the refusal to admit a new member to a venture and the expulsion of an existing member from the venture.[244] Of course, the goal of commercial research is, by definition, to benefit the parties conducting the research and disadvantage their competitors.

238. Note that while the IP Licensing Guidelines and the Collaboration Guidelines focus first on defining an R&D (or innovation) market and then on how competition in that market is impacted, the IP Licensing Guidelines Proposed Update adopts a more flexible approach in which the general focus is on anticompetitive effects in R&D and related technology and goods markets. *Compare* IP LICENSING GUIDELINES, *supra* note 19, at 14–15, *with* IP LICENSING GUIDELINES PROPOSED UPDATE, *supra* note 19, at 14–15.

239. *See* COLLABORATION GUIDELINES, *supra* note 19, § 4.2, at 26 ("Agencies do not challenge a competitor collaboration when the market shares of the collaboration and its participants collectively account for no more than twenty percent of each relevant market in which competition may be affected.").

240. *Id.* § 4.3, at 26–27.

241. *See id.*

242. *See, e.g.*, Klor's, Inc. v. Broadway-Hale Stores, Inc., 359 U.S. 207, 211–13 (1959).

243. Nw. Wholesale Stationers, Inc. v. Pac. Stationery and Printing Co., 472 U.S. 284, 294 (1985).

244. *See* 13 AREEDA & HOVENKAMP, *supra* note 167, ¶ 2214, at 340–44.

Nevertheless, antitrust issues can arise if the collaborating firms possess market power and systematically exclude smaller rivals from both participating in the collaboration and accessing its output.[245] This is particularly true if the output of the collaboration is likely to be of significant competitive value (e.g., reducing production costs or improving product quality).[246]

In many cases, however, the parties to an R&D collaboration have no obligation to admit others to their venture, and their refusal to do so does not violate the antitrust laws. For example, there are numerous legitimate reasons for limiting membership in a joint venture to a defined number of participants: the purpose of the venture, the ability to govern and administer it in a rational manner, the complementarity of skills and experience possessed by the existing members, and the expectation that members will contribute necessary assets or intellectual property to the venture.[247] In general, if a refusal to deal is ancillary to a venture's legitimate goals (e.g., reducing costs, improving product quality, or expanding markets), it will not raise antitrust concerns under an application of the rule of reason.[248] Nevertheless, exclusion or expulsion of a party from a venture for reasons that are designed to facilitate price fixing, market allocation, or other illegal activities will likely be considered illegal.[249]

Out of the detailed analysis of the antitrust framework provided above we can extract a more specific framework pertinent to pre-competitive collaborations. Biopharma pre-competitive collaborations will, unless they are simply fronts for covert illegal activity, are analyzed under a rule of reason framework that includes the analysis of factors such as consolidation of research operations and exchange of competitive information and pays attention to both markets for products and services and markets for relevant R&D. Antitrust authorities have responded to concerns about R&D

245. *See* SULLIVAN & GRIMES, *supra* note 169, at 275.

246. *See id.*

247. *See* 13 AREEDA & HOVENKAMP, *supra* note 167, ¶ 2214, at 336–44 (citing examples of joint ventures not violating antitrust laws, including GM and Toyota operating a single manufacturing plant in California and being able to refuse to admit others to their arrangement as well as professional sports leagues such as the NFL having the right to limit league membership and to expel teams for various reasons); *id.* ¶ 2214c, at 340 (discussing application of rule of reason to both exclusion and expulsion cases).

248. *Id.* ¶ 2210b, at 311–13.

249. *See id.* ¶ 2210b, at 312. In addition, collaborative arrangements that are, by their terms, designed to have "open" membership policies may risk greater antitrust liability when excluding or expelling members. *See id.* ¶ 2220, at 361. These arrangements often arise in the context of technical standard setting, but are not common in the realm of biopharma R&D collaborations.

markets primarily in the context of mergers,[250] with less attention to the impact of R&D collaborations on innovation. Part III discusses adapting the existing framework for collaborations among competitors to pre-competitive collaborations and extending analysis of R&D markets beyond the merger context. We then provide hypotheticals that demonstrate its application and from this generate some suggested antitrust guidelines for pre-competitive collaborations.

III. APPLICATION OF THE ANTITRUST FRAMEWORK TO BIOPHARMA PRE-COMPETITIVE COLLABORATIONS

This Part adapts the antitrust analysis discussed in Part II to pre-competitive collaborations in the biopharma industry. It then applies this analysis to hypothetical examples of pre-competitive collaborations, illustrating the potential disconnect between industry understandings and uses of pre-competitive to signal procompetitive collaborations and the actual analysis conducted by courts and agencies to determine whether collaborations among competitors are procompetitive or anticompetitive. This Part goes on to identify measures that may reduce antitrust concerns in such collaborations, including active engagement by governmental agencies, public dissemination of data, and the limitation of intellectual property encumbrances on resulting innovations. It concludes with suggestions for a refocusing of strategies away from efforts to characterize collaborations as pre-competitive and towards a reasoned analysis of where and how collaborations among competitors can satisfy both innovation and competition policy goals.

A. Analytical Framework for Pre-Competitive Collaborations

A violation of section 1 of the Sherman Act, which prohibits any "contract, combination . . . or conspiracy, in restraint of trade" requires the existence of concerted action among two or more firms that is unreasonably restrictive of competitive conditions and the presence of market power on the part of the actors.[251] The act covers both horizontal and vertical arrangements. Pre-competitive collaborations in the biopharma industry encompass both horizontal arrangements (e.g., among groups of pharmaceutical manufacturers)

250. For a detailed discussion of the ways in which antitrust authorities have evaluated R&D, or innovation, markets in the pharmaceutical industry, see generally Carrier, *supra* note 232.

251. 15 U.S.C. § 1 (2012). *See supra* Section II.A.

and vertical arrangements (e.g., among research institutions, biotechnology firms, and pharmaceutical manufacturers), making an analysis of both horizontal and vertical agreements necessary. The antitrust inquiry for these arrangements will turn upon both the impact on competitive conditions and assessments of market power.

The first step in the antitrust analysis of a pre-competitive collaboration is determining whether the arrangement should be deemed illegal per se or examined under a rule of reason analysis. The types of collaborative R&D arrangements that would be considered in the biopharma industry to be pre-competitive are unlikely to trigger concerns of illegality per se and will almost certainly be analyzed under the rule of reason.[252] The DOJ's antitrust guidelines for collaborations among competitors explicitly recognize that many such collaborations "are not only benign but procompetitive"[253] and should generally be analyzed under the rule of reason.[254] These guidelines speak particularly favorably of R&D collaborations, observing that "[m]ost such agreements are procompetitive."[255] Antitrust authorities have been tolerant of collaborations among competitors in a variety of contexts, including collaborative standard setting and the formation of patent pools, suggesting a willingness to look carefully at the efficiency gains that such arrangements among competitors may provide.[256] Moreover, most biopharma pre-competitive collaborations should satisfy the requirements of the NCRPA, as discussed in Section II.B.1, enabling them to avail themselves of certain protections to ensure that the activities of the collaboration will be subject to a rule of reason approach.

The next step is to apply a rule of reason analysis that is informed both by the special considerations used by agencies to evaluate R&D collaborations among competitors and by factors that

252. These collaborative R&D arrangements can be contrasted with reverse payment agreements between pioneer firms and possible generic entrants. But even with these agreements, which have a direct bearing on price and entry, concerns about innovation and market structure make the analysis more complex than a illegal per se approach would allow. For a discussion of antitrust concerns in reverse payment agreements, see Michael Carrier, *Unsettling Drug Patent Settlements: A Framework for Presumptive Illegality*, 108 MICH. L. REV. 37, 40, 67 (2009) (discussing the importance in antitrust analysis of a regulatory regime that addresses the challenged activity and argues for treating reverse-payment agreements as presumptively illegal as a way of supporting competition goals in the applicable regulatory regime).

253. COLLABORATION GUIDELINES, *supra* note 19, at 1.

254. *See id.* § 1.2, at 3.

255. *Id.* § 3.31(a), at 14.

256. *See* Rosch, *supra* note 226, at 10.

are specific to biopharma R&D. While the standard factors guiding a rule of reason analysis—including intent of the parties, limitations on independence and competition, nature and extent of exchange of information, duration, markets and market power, and offsetting procompetitive benefits—are applicable, antitrust authorities recognize the special nature and needs of R&D intensive markets and will tailor their analysis accordingly.[257] After determining the relevant market(s), the analysis should focus on the effects of the collaboration on consolidation of research operations in the relevant market(s), the likelihood of exchange of competitive information, and the balancing of anticompetitive effects and procompetitive benefits of the proposed arrangement.[258] The inevitable consolidation of at least some R&D activities and the widespread sharing of information that takes place within most pre-competitive collaborations should be evaluated in terms of its impact on competition, taking potential entrants and the magnitude of offsetting efficiency benefits into account.

In determining whether a pre-competitive collaboration is procompetitive, courts will consider both the market for the parties' and the collaboration's products and services, and the impact on the market for relevant R&D. In the pharmaceutical industry this distinction has been characterized as competition in the development of new drugs and competition in the sale of drugs.[259]

Product markets relevant to an R&D collaboration include both the products that the parties to the collaboration produce and sell individually, and those that the collaboration will produce and sell collectively. Thus, if parties A and B form a collaboration to develop a new type of influenza vaccine, and A agrees as part of the collaboration to limit sales of an existing prescription analgesic, which competes with B's over-the-counter analgesic, then both the influenza vaccine market (the collaboration's product) as well as the analgesic market (the parties' independent products) would be implicated.

Product markets in the pharmaceutical industry have been defined according to a variety of criteria, both by courts and agencies. According to one 2003 survey, the FTC has defined pharmaceutical markets in merger and other cases based on some combination of the following factors:

257. *See id.*
258. *See supra* Section II.B.2.
259. Morse, *supra* note 224, at 637.

> (1) whether drugs treat the same disease, condition, or indication;[260] (2) whether drugs treat a disease by interacting with the body in the same manner (i.e., whether they have the same "mechanism of action"); (3) whether drugs have the same specific chemical compounds; (4) whether drugs have the same dosage form such as injectable, liquid, capsule, tablets, or topical; (5) whether drugs have the same frequency of dosage, such as once-a-day or extended release; (6) whether drugs have the same strength of dosage, distinguishing, for example, 30mg and 60mg tablets; (7) whether drugs are branded or generic; (8) whether drugs require a prescription or are sold over-the-counter; and (9) whether drugs are currently marketed or are in development.[261]

The biggest, although not the only, antitrust concern for most pre-competitive collaborations will be their likely impact on R&D markets. R&D markets are particularly important in the pharmaceutical industry. As one commentator recently observed,

> [P]harmaceuticals is an industry that doesn't lend itself to traditional market analysis. Because the bulk of profits in the industry come from temporary monopolies—the government-granted patents—the current marketplace is not where the important competition takes place. Rather, the real rivalry takes place "upstream," as companies compete to innovate, either by developing medicines in their labs or by buying up promising patents and biotech start-ups.[262]

Consistent with this observation, almost all recent agency challenges raising concerns about effects on R&D markets have arisen in the biopharma sector.[263] One such challenge, and a good example of potential antitrust concern arising from arguably pre-competitive activity, was the FTC's 1996 intervention in the proposed merger of Ciba-Geigy and Sandoz.[264] At the time of the merger, each of the parties held U.S. patents critical to the development of then-

260. This criterion is often referred to as "therapeutic class," a 5-digit Uniform System of Classification ("USC") for pharmaceutical products utilized widely throughout North America. *The Uniform System of Classification (USC)*, IMS HEALTH, https://www.imshealth.com/files/web/IMSH%20Institute/USC_Classiification_Process_2011.pdf [https://perma.cc/H23J-B4MR]. For examples of market definition using therapeutic class, see *Market Definition in Antitrust*, *supra* note 19, at 316–17.

261. Morse, *supra* note 224, at 643–44.

262. Steven Perlstein, *Not What the Doctor Ordered*, WASH. POST (Jan. 28, 2009), http://www.washingtonpost.com/wp-dyn/content/story/2009/01/27/ST2009012703641.html [http://perma.cc/W3SG-E424].

263. *See Market Definition in Antitrust*, *supra* note 19, at 487.

264. *In re* Ciba-Giegy Ltd., 123 F.T.C. 842 (1997).

nascent gene therapy technology.[265] Since the FDA had not yet approved any gene therapy products, no market existed for gene therapy products.[266] Prior to the proposed merger, Ciba-Geigy and Sandoz competed to innovate in this emerging field.[267] Notwithstanding the pre-competitive state of the gene therapy field, the FTC was concerned that the combined firm, Novartis, might refuse to license its foundational gene therapy patents to others; the result would have constrained competition in the gene therapy R&D market and limited the future market for gene therapy products.[268] In response to these concerns, the parties entered into a consent decree with the FTC, settling the dispute.[269] Under the decree Novartis agreed to license its gene therapy patents to Rhone Poulenc, one of its principal competitors, thereby preserving at least some competition in the market for gene therapy innovation.[270]

Once an R&D market is defined, the competitive impact of the proposed agreement on that market must be determined. If the parties to the agreement collectively control only a small share of the R&D market, then anticompetitive harm will be deemed unlikely.[271] In general, the agencies will not challenge a competitor collaboration in an R&D market if there are three or more independent entities outside the collaboration with the incentive or ability to engage in R&D that is the same or a close substitute.[272] On the other hand, if the parties control a large share of the market or hold blocking intellectual property positions, as they did in the Ciba-Geigy merger, then anticompetitive harm is likely to be found.[273] Given the high level of concentration in the industry and the specialized nature of drug discovery and development, many of the pre-competitive collaborations will involve collaboration among most, if not all, of the firms with the ability and incentive to pursue a particular drug. This safe harbor-based approach is therefore unlikely to have much effect when evaluating pre-competitive collaborations in the biopharma industry.

265. *Id.* at 846–47.
266. *Id.* at 845.
267. *Id.* at 851.
268. *In re* Ciba-Geigy Ltd., F.T.C. Docket No. C-3725, Analysis of Proposed Consent Order to Aid Public Comment at 6 (Dec. 17, 1996).
269. *Ciba-Geigy*, 123 F.T.C. at 853.
270. *Id.* at 873–77.
271. *See* COLLABORATION GUIDELINES, *supra* note 19, § 4.2, at 26.
272. *Id.* § 4.3, at 26–27.
273. *Id.*; *Ciba-Geigy*, 123 F.T.C. at 873–77.

Pre-competitive collaborations in this industry create some unique challenges for a rule of reason analysis. Many of the collaborations will involve consolidation of some aspects of the R&D process, including shared clinical trials and shared information about possible targets for drug development. Indeed, they are sometimes designed specifically to consolidate R&D capabilities of leading competitors in order to reduce the cost of maintaining competing drug programs. Given the high costs, risks, and uncertainty in drug discovery and development, it may sometimes be efficient to allow combined research efforts to replace competitive individual efforts. But this assessment is difficult to make and requires guessing about the best way to achieve pharmaceutical innovation.

The collaborations will also likely involve the exchange of information that may once have been treated by industry members as proprietary, although the information is now characterized as pre-competitive. The boundary between information that is, or is not, product specific or competitive in nature and information becomes difficult to draw. Moreover, the exchange of information that impacts product decisions may be essential to achieve a collaboration's hoped-for benefits. While most pre-competitive collaborations currently involve sharing of technology, know how, intellectual property, and best practices, there is pressure to expand the realm of data sharing into areas which are more closely linked to downstream product development choices. While antitrust concerns would be raised where the shared information related to drug product plans or pricing, it is unclear how the boundary between general information about a disease and potential pathways for addressing the disease and specific information about a potential drug should be drawn in practice.

Finally, the highly regulated nature of the industry adds to the complexity of analyzing how pre-competitive collaborations will impact competition. The determination of market power may become complicated by the fact that the market works to some degree by allowing for limited periods of market power, via patent rights and data exclusivity, as mechanisms for encouraging the extensive investment needed to develop and sell medical therapies. The market thus relies to some extent on the creation of market power as an innovation strategy.

B. Hypothetical Examples and Application of Framework

The following hypothetical examples illustrate pre-competitive collaborations at various stages during the drug discovery and development cycle. Each example highlights different aspects of the

disconnect between assumptions about pre-competitive collaborations and antitrust concerns regarding whether collaborations are procompetitive or anticompetitive. The first example applies the framework that the agencies would use to evaluate whether a collaboration raises antitrust concerns.[274] The subsequent examples illustrate some of the different concerns that may arise in alternative types of collaborative arrangements.

Example 1: Pre-Competitive Does Not Always Mean Procompetitive

Six pharmaceutical firms that collectively account for more than ninety percent of private U.S. R&D spending on Parkinson's disease enter into a ten-year collaboration agreement. There are no effective treatments for Parkinson's disease on the market. Before the collaboration, each member pursued independent and proprietary research designed to identify and validate biomarkers useful in measuring the progression of Parkinson's disease and the effects of experimental treatments on the progression of the disease. During the collaboration they will pursue joint research studies and clinical trials to identify and validate biomarkers for Parkinson's disease. They form a separate organization that they will jointly control in order to collect and manage tissue samples and data generated by their jointly conducted studies and clinical trials. They will share the results of their joint studies and clinical trials with the public on a no-cost basis through a project portal they collectively fund and control.

Discussion: In this example, the collaboration involves sharing information and capabilities relating to the design of new drugs to diagnose and treat Parkinson's disease. Although there is no current product market, the relevant antitrust inquiry involves a determination of the nature and likely impact on an R&D market.[275] In conducting this analysis, the first step considers the relevant R&D market, then identifies which entities are actual or likely potential competitors of the collaboration. As discussed in Part II, an R&D market "consists of the research and development directed to particular new or improved goods or processes, and the close substitutes for that research and development."[276] Thus, the R&D market in question could be broadly defined as the market for

274. *See* IP LICENSING GUIDELINES, *supra* note 19, § 3.2.3, at 10–11.

275. For a discussion of the FTC's investigation of the proposed Ciba-Geigy merger with Sandoz, involving the nascent market for gene therapy products, see *supra* notes 264–70 and accompanying text.

276. IP LICENSING GUIDELINES, *supra* note 19, § 3.2.3, at 11.

developing new diagnostics and drugs for Parkinson's disease or, even more broadly, for Parkinson's disease and other related neuromotor disorders.

Once the relevant R&D market is defined, the analysis requires assessing whether the collaboration is likely to have anticompetitive effects in the defined market. In undertaking this analysis, attention must be given both to the potential effects on competition between the collaboration and non-participants and competition among the participants. Relevant factors in both of these areas are the degree of concentration in the market, the market share of the collaboration participants, and the presence of independent entities with comparable capabilities and incentives to engage in comparable R&D.

When considering competition between the collaboration and others, market concentration must be assessed. Where there are at least four independent entities with comparable capabilities and incentives to conduct R&D efforts that are close substitutes for the R&D to be conducted by the collaboration, the collaboration will ordinarily be found not to adversely impact competition in the specified market. In this example, most of the firms currently engaged in Parkinson's research will be part of the collaboration, arguably limiting independent competition in this research area. However, the analysis must also consider the likelihood that other pharmaceutical firms will enter this R&D market to compete with the collaboration. The likelihood of independent market entry will depend on factors including the ability of the collaboration to block independent entry by using patents or other intellectual property barriers. In this example, if the collaborators possess key patents relating to the treatment of Parkinson's disease, then antitrust concerns may arise, as they did in *In re Ciba-Geigy Limited*.[277]

Attention must also be paid to the potential effect of the collaboration on the independent R&D efforts of the collaborators, and whether the collaboration is likely to incentivize the participants to reduce investment in or diminish the speed or scope of their independent R&D efforts. Given that the likely goals of the collaboration are to eliminate duplicative R&D activity, achieve economies of scale, and consolidate all Parkinson's-related R&D in the collaboration, participants will likely reduce their independent R&D efforts.

277. *See supra* notes 264–70 and accompanying text.

Given these potential competition-reducing effects, the collaboration will likely be found to create a significant risk of anticompetitive harm in the defined R&D market. In applying rule of reason analysis, these risks must then be weighed against the potential procompetitive benefits arising from the collaboration. Examples of such benefits might include the potential for combining complementary assets and resources to produce an innovation outcome faster, at lower cost, and/or to increase the likelihood of a successful outcome. In this example the collaboration is being formed to share costs and risks at early stages of product development in order to improve the likelihood of success of each individual participant in its own product development activities at later stages of product development.

While these procompetitive benefits may result in the collaboration passing antitrust muster, this result is not guaranteed. Thus, careful attention must be paid to the terms of the collaboration agreement, and measures should be taken to ensure that the agreement's procompetitive benefits outweigh its potential anticompetitive harm. For example, the collaborators may consider offering to license blocking patents on Parkinson's research to other market participants.[278] The most important lesson from this example is that even early-stage collaborations directed toward R&D in pre-competitive markets may result in anticompetitive effects. Ultimately the fact that a collaboration is *pre-competitive* does not ensure that it will be deemed to be *procompetitive*.

Example 2: Early Stage Does Not Always Mean Pre-Competitive

Three leading biotechnology firms, together accounting for seventy-five percent of the current industry spending on investment in developing a biologic treatment for a rare but deadly form of lung cancer, enter into a collaboration agreement. They agree to share all research data that they have previously acquired from their own clinical trials conducted using drug candidates that were ultimately not approved due to poor efficacy.[279] They also commit to sharing samples and conducting joint studies to narrow the most promising

278. *See supra* notes 268–73 and accompanying text.

279. Though the public disclosure of summary clinical trials data on NIH's ClinicalTrials.gov website is required by law, the vast majority of clinical trials data remains private. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 801, 121 Stat. 823, 904–22 (2007) (codified as amended at 42 U.S.C. § 282(j) (2012)). *See generally* INST. OF MED. OF THE NAT'L ACADS., *supra* note 17 (outlining guiding principles and a framework for the responsible sharing of clinical trial data).

approach to find treatments for the disease. They will not make the results of their collaboration public. There are two other smaller firms in the industry pursuing R&D programs for the same rare form of lung cancer. These firms have not been included in the collaboration. There are currently no approved drugs on the market to treat this form of lung cancer and none of the participating firms have active clinical trials, but they all have potential drug candidates that they are in the early stages of researching.

Discussion: In this example, as in the previous one, the collaboration involves sharing information and capabilities that relate to the design of new, currently non-existent, products, and the relevant inquiry will focus on determining the nature and likely impact on an R&D market. Here, the products are biological treatments for a particular form of lung cancer. There are four important differences between this example and the prior one, however: (1) the exclusion of competitors from the collaboration; (2) the failure to share the collaboration data and results with competitors or more broadly with the public; (3) the focus on achieving cost savings by sharing proprietary data and limiting research paths rather than on collaborating to produce new results; and (4) the absence of a separate governance structure to separate collaborative and competitive activities. These differences create strong antitrust concerns that are not meaningfully mitigated by the pre-competitive nature of the collaboration.

As in the previous example, the antitrust analysis will focus on the nature and likely impact of the agreement on an R&D market, which could be broadly defined as the market for developing new treatments for this specific form of lung cancer or for this and a related class of cancers. The next step is to determine whether the collaboration is likely to have anticompetitive effects in the defined market, including any impact on competition among the participants and competition with non-participants. This collaboration raises concerns about both types of competition. First, it may reduce the number of R&D paths being pursued by the participants—indeed, this is one of the intended goals. Participants are sharing proprietary clinical trial data with each other and are committing to joint studies to narrow the development paths that they will pursue. Second, the collaboration may have negative effects on competition with non-participants. The collaboration includes the three largest firms and excludes two smaller competitors. Although the presence of these two competitors may reduce competition concerns by preserving independent R&D paths, the concentration of resources caused by

this collaboration may leave the existing competitors at a disadvantage. If the collaboration negatively impacts these competitors, they may have difficulty staying in the market, and potential entry may be deterred.

Third, the nature of the arrangement seems to be primarily focused on achieving cost savings from consolidating research efforts and avoiding duplicate clinical trials rather than on encouraging more and faster innovation. The collaborators are sharing previously generated data with each other rather than focusing on future jointly generated data, and they are committing to joint studies that may limit the number of R&D paths that they pursue. Private cost savings are not regarded as sufficient procompetitive justification for an otherwise anticompetitive arrangement.

Finally, the structure of the collaboration does not include protections that might limit the sharing of competitive information across firms. There is no independent governance structure for the collaboration that could serve to separate the joint R&D efforts from competitive product development activities.

In this example the collaboration is justified largely on efficiency grounds. It eliminates duplication and waste, may make developing a drug more cost effective and may accelerate discovery of an effective treatment. But rather than pooling efforts to generate new ideas, this hypothetical involves sharing proprietary information to reduce the number of paths being pursued. This may well increase efficiency, but is this collaboration the least restrictive way of achieving these efficiency benefits? Are the restrictions imposed on entry and data sharing reasonably necessary to achieve these benefits? This collaboration would likely cause antitrust concern.

Even more than the previous example, this example shows that early-stage collaborations directed toward R&D in pre-competitive markets may result in anticompetitive effects.

Example 3: Late Stage Collaborations May Not Be Pre-Competitive, But May Nonetheless Be Procompetitive

Two of the pharmaceutical industry's largest firms, A and B, have approved therapies on the market to treat a new and widespread strain of influenza (strain HxNy), representing fifty-five percent of the total market. Comparable products are marketed by three other firms. The market leader, Firm C, has the only influenza drug approved for use in children and also accounts for thirty-five percent of the adult market. A and B wish to form a collaboration to combine

their influenza HxNy R&D efforts to develop a safe and effective treatment for influenza HxNy in children. In the past, A and B have each individually approached C regarding the cross-licensing of patents and data that C holds relating to its influenza HxNy products, but C is not willing to entertain licensing discussions.

The collaboration will be conducted through a new joint venture entity ("JV") in which A and B will each hold a fifty percent share. JV will own all intellectual property arising from the collaboration and will manufacture and market any new product that is developed. As part of the collaboration, A and B will share research data that they formerly treated as confidential and will exclusively license their influenza-related patents to JV. A and B each agree that they will not admit any other pharmaceutical manufacturer into JV or share data or results with any other firm unless both parties and JV agree to do so.

Discussion: This example involves current product markets. Though A and B collectively control fifty-five percent of the total influenza HxNy therapy market, their collaboration will focus on juvenile influenza treatments. In the market for juvenile influenza HxNy treatments, Firm C controls one hundred percent of the market, and both A and B have zero percent. They wish to combine resources in order to compete more effectively with C, which currently enjoys a natural monopoly in this area and has proven unwilling to assist market entry through patent licensing. As such, the collaboration of A and B is unlikely to have adverse effects on competition and instead is likely to result in new products that increase competition in this market and thereby improve consumer choice, reduce prices, and improve quality. Moreover, due to the low market share currently held by A and B in the affected market, the agencies are unlikely to investigate or challenge the collaboration absent some evidence of other illegal activity.[280] Given the substantial outlays that A and B are likely to make with respect to this collaboration, it is not unreasonable for them to close their venture to newcomers who have not invested in the project from the outset.[281]

This example illustrates that a collaboration between competitors may be procompetitive even if it relates to activity that is beyond the pre-competitive stage and, more importantly, that

280. *See supra* note 199 and accompanying text (noting agencies are unlikely to challenge a collaboration controlling less than twenty percent of the relevant market).

281. *See supra* notes 247–49 and accompanying text (discussing exclusion from collaborations).

beneficial collaborations should not be avoided simply because they are perceived not to be pre-competitive.

Example 4: Rules Requiring Immediate Data Disclosure and Limiting the Ability to Patent May Not Always Be Procompetitive

Six of the pharmaceutical industry's largest firms, accounting for sixty-five percent of the private sector R&D efforts to develop treatments for Alzheimer's disease, create a collaboration that is open to all industry stakeholders. Four of these six firms have existing treatments for Alzheimer's disease on the market, but these treatments only reduce the symptoms and or delay the onset of the disease; they do not prevent or cure it. To make joining the collaboration attractive, the six firms agree to share all of the data that they have gathered from past clinical trials on failed Alzheimer's drug candidates with other members of the collaboration. They also agree to share all of the information they have or acquire during the term of the collaboration that is useful in identifying and validating novel biomarkers for Alzheimer's disease. In order to join the collaboration, participants must agree to a data sharing policy that includes requirements (a) to share all research results that fall within the scope of the collaboration with collaboration members and (b) to grant the other collaborators a royalty-free license to intellectual property that may encompass the activities of the collaboration. The results of the collaboration will be shared only with members of the collaboration that have agreed to these terms. The collaboration has no specified end date, and may be dissolved only upon an affirmative vote of all members.

Discussion: The analysis will focus on the effects of this collaboration on the market for R&D relating to treatments for Alzheimer's disease and, perhaps, related dementias. The firms that have formed the collaboration do not account for all of the market, but the goal of the collaboration is to encourage entry by all actual and potential competitors in the R&D market for Alzheimer's drugs. This example primarily involves R&D markets, although it may have product market effects due to the existence of related products owned by participants. The analysis will turn on a comparison of the procompetitive and anticompetitive effects of the proposed arrangement.

This collaboration involves a pooling of resources but may not result in a consolidation of R&D paths. Indeed, the hope might be that by sharing some basic inputs needed to identify possible

products, the result will be to increase the number of R&D paths. At first glance this would seem like a procompetitive arrangement, focusing on enlarging the public domain of knowledge in a complex disease area. The focus is on identifying and validating biomarkers that will be useful to different firms pursuing different competitive products. Entry is not restricted, and data and intellectual property relevant to the collaboration is shared freely with anyone who wants to join.

But there are also more subtle competition concerns. The collaboration requires a substantial amount of information sharing that may include competitive information about project design and selection. It also involves broad intellectual property sharing agreements, which is limited to collaboration members. These requirements could lead to an increase in the concentration of competitively significant assets among participants. The agreement may also reflect a plan of strategically forfeiting rights to preempt competitor intellectual property positions. The requirement will have a distinct impact on different industry members by making certain kinds of biological data freely available within the group while preserving rights over other kinds of data. The presence of this type of arrangement could limit entry into the market because small firms cannot get access to the data they need without giving up their own competitive advantage in the form of proprietary data and intellectual property rights.

This example illustrates that open participation and a focus on freely sharing early stage research results, hallmarks of many pre-competitive collaborations, do not guarantee that the collaboration will be procompetitive.

C. Recommended Practices for Pre-Competitive Research Collaborations

The above analyses demonstrate that R&D collaborations in the biopharma industry need to be structured with antitrust concerns in mind. In this final Section we suggest guidelines for mitigating antitrust concerns for industry participants seeking to form new R&D collaborations or to improve existing collaborations. The following suggestions are derived from the antitrust framework applicable to such collaborations and reflect areas where competitive concerns might arise.

1. Nature and Scope of the Collaboration

Antitrust concerns can arise from both the consolidation of actual or potentially competitive research operations and the potential impact of the collaboration on the markets of the participants in the collaboration.[282] The nature and scope of the collaboration should be designed with both concerns in mind.

Antitrust concerns with the consolidation of R&D capabilities will be greatest when the collaboration involves a combination of formerly competitive R&D programs or a merging of the specialized R&D resources of those firms most likely to engage in developing a particular product. Whenever possible, collaborations should be limited to areas in which the participants are not actively competing. Efforts should be made to compartmentalize the R&D process into areas in which cooperation is essential to solve a common roadblock or provide a particular input to the development process at a reasonable cost. These efforts should not affect areas in which competition in the R&D process will remain.

One central question in evaluating an R&D collaboration is whether it is likely to reduce the parties' incentive or ability to engage in independent R&D, presumably in competition with or complementary to that of the collaboration. Care should be taken not to limit competitive activity outside of the sphere of agreed cooperation. While cooperation may occur in later stages of product development, it should not extend into areas where parties are competing. Rather collaboration should relate to areas that are not product-specific.

Anticompetitive effects are more likely to be found when a collaborative R&D activity has the potential to reduce the parties' profits in other lines of business. For example, when firms are already selling a drug to treat a disease but seek to discover and develop a new and better drug, they may not have strong enough incentives to invest in the potential new drug. Indeed, they may have incentives to delay the development of new drugs. To alleviate concerns, collaborations could be limited to areas where pooling of resources and expertise is necessary to solve a problem or produce results that are too difficult, risky, and expensive for individual firms to reach alone; ensuring that these benefits are made widely available to existing firms and potential entrants may also reduce these concerns. But collaborations that are targeted in areas that are unlikely to

282. *See supra* Section II.B.2 (discussing rule of reason analysis for R&D collaborations).

cannibalize the markets of existing participants will create fewer antitrust concerns.

It is critical to preserve meaningful independent decision making authority over product development choices. Limitations on independent decision making within the collaboration should be minimal and should be confined to those areas of decision making that involve the sharing and use of pooled resources.

When considering the scope of the collaboration, it is important to consider not only the activities covered but also the likely duration of the collaboration. Unless there is a compelling reason not to, collaborations should have a limited duration that is justified in terms of a reasonable timeline for achieving defined goals. Many early pre-competitive collaborations were defined around discrete projects with a time horizon of five years or less.[283] Collaborations of ten years or more might be considered to be mergers, depending on the nature of the collaboration.[284] One of the challenges in evaluating new forms of collaboration is uncertainty about their impact on innovation. Limiting the duration of arrangements and encouraging experimentation with alternative forms will provide important information about the benefits and costs of these arrangements before anticompetitive harm develops. Overall, shorter duration is likely to be regarded more favorably from an antitrust standpoint.

2. Organization and Governance

Pre-competitive collaborations will inevitably involve some consolidation of R&D programs and product-specific assets. The risks of this kind of consolidation are higher when there is a possibility that participants may intentionally collude to reduce competition. The collaboration should thus be structured and governed with an emphasis, whenever possible, on openness (both in terms of participation and in terms of access to results), transparency, and independence from individual competitive concerns.

283. Based upon a review of the websites of many of the biopharma pre-competitive collaborations, most are organized into projects or phases with a term of no more than five years. This includes TSC, one of the earliest examples, as well as the AMP, one of the most recent examples. *See, e.g.*, Thorisson & Stein, *supra* note 88, at 124; *Accelerating Medicines Partnership*, *supra* note 139. For a summary of some pre-competitive collaborations in this space, see ERIC GASTFRIEND & BRYAN LEE, PRECOMPETITIVE COLLABORATIONS IN PHARMA: AN OVERVIEW STUDY (2015), http://futureoflife.org/data/documents/PreCompetitiveCollaborationInPharmaIndustry.pdf [https://perma.cc/8FYZ-6GNP] (summarizing some of the early and current pre-competitive collaborations with links to project sites).

284. *See supra* note 189 and accompanying text.

Entry and Exit: Unless there are strong reasons for limiting participation, a collaboration should be open to any industry member with the relevant expertise and interest. Exclusion of actual or potential competitors from the collaboration could impair competition, and any limitation on participation should be justifiable on efficiency or other legitimate grounds. Anticompetitive effects are more likely to be found when a regulatory approval process limits the ability of non-participants or late-comers to catch up with competitors already engaged in the R&D process, making it even more important to allow open entry when possible. Sharing the results with the public quickly and without restriction may offset some of the concerns of limited entry. Similarly, barriers to exit should be avoided to reduce the risk that potential competitors are prevented from pursuing their own projects if and when they deem the collaboration no longer to be desirable.

Public Sector Participants: Participation in a collaboration by governmental agencies and other public sector actors may be viewed favorably from an antitrust perspective. If government actors are actively engaged in the organization and have some ability to participate in, or at least review, the decisions that are made by the leadership of the organization, they will have the ability to monitor the behavior of competitors. They will also have a greater ability to ensure that the activities of the collaboration are designed with the broader public interest in mind.

Independent Leadership: The organization should ideally have independent leadership and counsel independent of any of the participants, as well as a clear and transparent system of governance. There should be a balanced representation of interests on the governing board to avoid allegations of capture and abuse of voting processes.[285]

Legal Documentation: The collaboration should have clear rules governing the sharing and use of resources and results and should have an antitrust compliance policy in place.

3. Sharing (and Not Sharing) Information and Results

Rules governing what information and results are to be shared, as well as rules governing what kinds of information cannot be shared, are both critical to the collaboration. Antitrust issues can arise

285. *Cf.* Allied Tube & Conduit Corp. v. Indian Head, Inc., 486 U.S. 492, 511 (1988) (condemning petitioner who packed standards-setting group with voting members who "shar[ed] their economic interest in restraining competition").

when there is an exchange of competitive information among participants in a collaboration. If the shared information includes information related to marketing, product plans, or pricing, collusion and other anticompetitive effects may be found. The collaboration should thus have strict policies prohibiting the exchange of this kind of competitive information. This process may require limiting company personnel who are involved in proprietary activities from also engaging in areas of shared R&D.

Moving to rules governing what is shared, there are clear benefits from an antitrust perspective in making the data and intellectual property generated by a collaboration freely and publicly available without undue delay. This practice keeps both members and non-members of the collaboration on an equal footing when they are competing in product and R&D markets. Collaborations should consider requiring the public release of data and rules limiting intellectual property protection for broad research platform and research tools, possibly after an exclusive member period if needed to allow for the opportunity to publish first on research results. To the extent that rules limiting participants' ability to obtain intellectual property protection are not feasible, collaborations should consider rules that require licensing relevant intellectual property broadly and non-exclusively if it is critical to R&D markets. An analogy could be drawn to the fair and reasonable non-discriminatory royalty requirements that have emerged in standard setting organizations.[286]

4. Require More Careful Delineation of Procompetitive Benefits

Pre-competitive collaborations are justified most often in terms of the efficiency gains stemming from the collaboration. But these justifications are often made without a careful analysis and comparison of identifiable efficiencies with the actual and potential costs arising from limitations on competition. The measures discussed above, including limited scope and duration, broad participation that includes public and private actors, and the public release and sharing of data and intellectual property, may serve to limit the potential negative effects on innovation. Requiring collaborations to be specific about the economic and scientific benefits of the collaborative activities that they propose may impose needed discipline on those seeking to form collaborations, as well as provide antitrust authorities

286. *See, e.g.*, Jorge L. Contreras, *Technical Standards and Bioinformatics*, *in* BIOINFORMATICS LAW: LEGAL ISSUES FOR COMPUTATIONAL BIOLOGY IN THE POST-GENOME ERA 113, 123 (Jorge L. Contreras & A. James Cuticchia eds., 2013).

with useful data as they evaluate the collaboration. Requiring collaborations to limit activities to those areas where the desired results are unlikely to be reached through individual efforts and/or will not be reached within a reasonable time or at a reasonable cost will further increase the likelihood that the collaborations will be viewed as procompetitive.

CONCLUSION

Both federal agencies and industry participants have turned to new forms of collaboration to increase the efficiency and effectiveness of biomedical research. Industry participants, many of them competitors, come together to define joint R&D objectives and share project results in what are widely known as pre-competitive collaborations. Their actions suggest a prevailing belief that these pre-competitive endeavors are not only permissible but encouraged. In contrast, neither the courts nor the federal agencies charged with enforcing U.S. antitrust laws have recognized pre-competitive activity as immune from antitrust challenge. Rather, the DOJ and FTC, in the guidance that they have provided regarding collaborations among competitors, have repeatedly emphasized that anticompetitive behavior may arise at many stages, from early R&D to final product marketing and sales. Thus, while many pre-competitive collaborations may offer significant procompetitive benefits and thereby avoid antitrust concern, it is not the case that every collaboration conducted prior to product release or as part of a common technology platform will be immune from antitrust liability. Accordingly, the prevailing intuition within the biopharma and other industries that pre-competitive collaborations enjoy some form of antitrust safe harbor is misguided. Far from being benign, this misconception has the potential both to encourage early-stage collaborations that may in fact be anticompetitive and discourage later-stage, yet manifestly procompetitive, collaborations.

This Article shows that pre-competitive collaborations may not always result in significant procompetitive benefits and, conversely, that collaborations conducted at later stages of the product development life cycle, though not pre-competitive, may actually yield substantial procompetitive benefits. Thus, in the critical search for more effective and rapid forms of collaboration in the biopharma and other industries, we urge policymakers and industry leaders to shed any undue reliance on the notion of pre-competition as a salve for antitrust concern and instead to analyze potential collaborations using the rule of reason framework long recognized by antitrust law

and policy. The infusion of traditional antitrust analysis into current debates regarding the desirability of various forms of industry collaboration will improve resulting collaborative structures and enhance the potential for innovation in evolving product and technology markets.