Statement of Chairman Timothy J. Muris

in the matter of

Genzyme Corporation / Novazyme Pharmaceuticals, Inc.

After an extensive inquiry, the Commission has voted to close its investigation of Genzyme Corporation's September 2001 acquisition of Novazyme Pharmaceuticals Inc.

[1] The Commission's investigation of this matter was initiated shortly after the merger was consummated in the fall of 2001. Commission staff reviewed hundreds of documents, interviewed numerous witnesses, and compiled an exhaustive file upon which the Commission's decision to close is based.

[2] Consistent with confidentiality restrictions on nonpublic submissions, this statement cites publicly available sources. The evidence collected during this investigation is consistent with the cited public information, and, I believe, would only reinforce the facts and positions taken in this statement.

[3] *See, e.g., Amgen Inc. and Immunex Corp.*, Docket No. C-4053 (consent order issued Sept. 3, 2002) (R&D for cytokines that promote the inflammation of human tissues);

causal relationship between innovation and competition."[4] Indeed, the most that could be said was that "no witness maintained that a merger of the only two firms developing a totally new product could *never* have any anticompetitive effects on innovation."[5]

In light of the lack of any clear theoretical or empirical link between increased concentration and reduced innovation, the Global Marketplace Report concluded by "advocat[ing] a conservative approach to the use of innovation market analysis."[6] In doing so, the Report made two recommendations, both of which I support, which characterize subsequent Commission decisions. First, the Report stated that it "seem[s] appropriate to limit the situations that the agencies examine to ones that involve very small numbers of innovation competitors."[7] Accordingly, except under "extraordinary circumstances," innovation market analysis should not even be considered unless the number of competitors is very small.[8]

Second, assuming that an innovation market analysis is appropriate, the Global Marketplace Report concluded that a "careful, intense factual investigation is necessary" to "distinguish between procompetitive and anticompetitive combinations of innovation efforts."[9]

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4 FTC Staff Report, *Anticipating the 21st Century: Competition Policy in the New High-Tech, Global Marketplace*, Vol. I, ch. 7, at 16 (May 1996) (hereafter "Global Marketplace Report").

5 *Id.* at 16 n.51 (emphasis in original).

6 *Id.* at 33.

7 *Id.*

8 *Id.*

9 *Id.* at 18, 20. *See also* Council of Economic Advisers, *Economic Report of the President*, Ch. 5, at 176 (1999).

To the extent there is consensus, it is that neither the presence of many

competitors nor pure monopoly correlates systematically with optimal levels of innovation. But even in such polar cases, predictions about R&D activity are hard

critical gene therapy proprietary portfolios, including patents, patent applications, and know-how" (Complaint ¶ ¶ 14, 15); "GTI's [Sandoz wholly owned subsidiary] U.S. clinical development is being closely coordinated with trials that Sandoz is conducting in Europe" (Separate Statement of Chairman Pitofsky, et al.); "Viagene continues to maintain a leadership position in the development of gene transfer technology products for human therapy, having initiated eight phase I clinical trials, and, in late 1994, begun the first phase II clinical study in the field of gene therapy." (Viagene December 1994 10-K, at p. 3.) Viagene was subsequently acquired by Chiron.); *Baxter Int'l and Immuno Int'l* Docket No. C-3726 (Complaint, Mar. 24, 1997) (Baxter and Immuno are two of only a few firms "seeking FDA approval" for fibrin sealants) (Complaint ¶ 10).

[12] The Dissent states that there has been "more recent thinking" since the 1996 Global Marketplace Report on the proper approach to innovation markets, citing, inter alia, the 2000 Antitrust Guidelines for Collaborations Among Competitors ("Joint Venture Guidelines").

research supports an inference regarding the merger's likely effect on innovation (and hence patient welfare) based simply on observing how the merger changed the number of independent R&D programs. Rather, one must examine whether the merged firm was likely to have a reduced incentive to invest in R&D,[13] and also whether it was likely to have the ability to conduct R&D more successfully.

B. Background on Pompe Therapy Research Programs

Several thousand individuals, mostly infants and children, suffer from Pompe disease, a genetic disorder that is often fatal, particularly for the young.[14] Because there is not yet an effective treatment for Pompe disease, any measure that accelerates the introduction of the first effective therapy, even by a matter of months, would save lives and reduce suffering. For Pompe patients, the paramount goal is the earliest possible introduction of an effective treatment, in quantities sufficient to treat them.

Over the past several years, four research programs for enzyme replacement therapies for Pompe disease have obtained at least preliminary positive results in some animal experiments. Two programs, initiated by Pharming and Synpac, were abandoned after the commencement of

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[13] Mere reductions in dollar outlays on R&D following a merger should not be presumptively considered a reduction in competition or in innovation efforts. Such reductions may reflect efficiencies in consolidation of R&D functions. In addition, although not a consideration in this case, analyzing the welfare effects of shifts in R&D expenditures among potential pharmaceutical products for life-threatening diseases raises very difficult issues.

[14] Pompe Disease is a rare and fatal genetic disorder caused by a deficiency of the enzyme acid alpha glucoside. Without this enzyme, glycogen accumulates in the lysosome of cells and rapidly destroys muscle fibers. Patients with Pompe disease experience severe muscle weakness, difficulty breathing and cardic insufficieny. Ulimately, patients require wheel chair assistance and mechanical ventilation and succumb to cardiopulmonary failure.

[15] Genzyme 2001 10-K, p. 7, states that both the Pharming and Synpac products were in phase II trials as of March 1, 2002. Nevertheless, Genzyme's Paul Kaufman stated on Aug. 22, 2001, that Genzyme had previously announced that it planned to switch from developing the Pharming product to developing a CHO [Chinese Hamster Ovary] enzyme product "based on manufacturing considerations." www.worldpompe.org/newspatient.html; see also Genzyme 2001 10-K, p. 11. The Synpac program involved a CHO enzyme. In an April 17, 2002, press release, Genzyme announced that it would not proceed with development of the Synpac product because that product could not be produced on a commercial scale. Genzyme stated that "Genzyme's internally developed CHO product, when compared with the Synpac enzyme, provided a similarly robust response profile in terms of glycogen clearance. Due to the significantly greater production yields of the Genzyme CHO enzyme, it offers the clearest and most efficient pathway to commercialization based on both clinical and manufacturing considerations." www.amda-pompe.org/Genzyme.htm. Moreover, in an April 17, 2002, joint statement with the International Pompe Association, Genzyme stated that "Genzyme's decision to shift further development from the Synpac CHO product to its own internally produced CHO derived enzyme . . . will allow Genzyme not only to gain better control of production but is also expected to yield more mature enzyme in a shorter period of time. Shifting to the Genzyme produced CHO should ultimately lead to an increased supply of the drug." "IPA/Genzyme Meeting April 16-17 [2002]-Joint Statement," www.worldpompe.org/ipagen.html.

[16] Genzyme 10-Q for quarter ending March 31, 2002, p. 55 ("During the first quarter of 2002, to accelerate the progression to regulatory approval, we concluded a comparison of all of our enzyme programs for the treatment of Pompe disease. The enzyme programs included: [i] the internally produced CHO enzyme program that began in 1999; [ii] the CHO enzyme licensed from Synpac (North Carolina), Inc. in 2000; and [iii] the enzyme obtained in the Novazyme acquisition in 2001.") Genzyme Press Release, April 17, 2002, refers to "the internally produced CHO enzyme that it [Genzyme] began developing last year." See generally Genzyme: Pompe Patient Program, Development History, www.genzyme.com/pompe/pompe_history.asp.

[17] Company information available at www.bioscorpio.com/novazyme_pharmaceuticals_inc.htm.

[18] Genzyme 2001 10-K, p. 33, data for Dec. 31, 2001.

[19] Genzyme Press Release, March 5, 2003. Genzyme was the first company to offer a safe and effective treatment for a lysosomal storage disorder, and it and Transkaryotic Therapies Inc. remain the only two companies that have brought to market an effective therapy for a lysosomal storage disorder. Genzyme now markets therapies for two lysosomal storage diseases, Gauche and Fabry.

[20] Novazyme Interview, May 21, 2001,

merger it became apparent that the obstacles were greater than was understood at the time of the merger, with the result that the program remains in the preclinical stage even today.[23]

Genzyme, meanwhile, previously had entered into joint ventures with Pharming (1998) and Synpac (2000) to develop treatments for Pompe disease.[24] These joint ventures preceded any significant internal development effort at Genzyme.[25] By the time of the Novazyme merger, commercialization of the Pharming product had been abandoned; the Synpac enzyme had shown more promise and was in clinical trials, but manufacturing problems were preventing production on a scale sufficient for commercialization. (Early in 2002, Genzyme announced the suspension of the Synpac program for this reason.[26]) As a result of these scalability problems, Genzyme had begun to ramp up its own internal research program shortly before the Novazyme merger.[27] At the time of the merger, this Genzyme internal effort was still in early preclinical testing. Indeed,

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[23] Genzyme's 2001 Form 10-K, p. GG-24, states with respect to Novazyme's technology: "We currently estimate that it will take approximately three years and an investment of approximately $75 million to $100 million to complete the development of, obtain approval for and commercialize the first product based on this technology platform." A year later, Genzyme's 2002 Form 10-K, p. GG-28, revised this estimate: "As of December 31, 2002, we estimate that it will take approximately six to eight years and an investment of approximately $100 million to $125 million to complete the development of, obtain approval for and commercialize the first product based on this technology platform." From these two statements, one can infer that during 2002 Genzyme learned that an unexpected additional three to five years of preclinical research and $25 million would be required for the Novazyme technology.

[24] Genyme 10-Q, March 31, 2002, pp.55, 59. As the 1996 Global Marketplace Report notes, in biotechnology, "most of the R&D is performed by very small firms that market their output to larger companies with the capabilities to commercialize it." 1996 Global Marketplace Report at 18.

[25] *Supra* nn.15, 16.

[26] *Id*.

[27] *Id*.

of drugs that reach this stage still do not obtain FDA approval. Relevant studies indicate that failure rates are at least 25 percent.[31]

C. Anticompetitive Theories and Evidence of Likelihood of Anticompetitive Harm

In analyzing the potential anticompetitive effects of the Genzyme/Novazyme merger, one must consider the nature and extent of the competition between Genzyme and Novazyme that would have existed absent the merger. Because of the relatively limited number of Pompe patients, therapies for Pompe disease fall under the Orphan Drug Act (ODA). The first Pompe therapy to gain FDA approval will obtain seven years of market exclusivity under the ODA. A second therapy may break that exclusivity only by establishing superiority over the first therapy.

One potential anticompetitive harm arising from the merger relates to whether Genzyme and Novazyme would have engaged in a "race to market" absent the merger.[32] In order for Genzyme and Novazyme to have been in a race to market absent the merger, at least one of them would have had to believe that altering its expenditures on R&D would significantly change its probability of beating the other company to the market with a therapy for Pompe.

The investigation did not reveal evidence that either company believed that it was in such circumstances. The evidence points to the anticipated superiority of Novazyme's

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[31] A number of studies report failure rates of 25 percent or higher for Phase III drugs, e.g., 21.5-27.1 percent (DiMasi, *supra* n.29, at 303); 43.3 percent (R. M. Abrantes-Metz et al., *supra* n.29 at 32); 62 percent for all drugs and 47 percent for biologicals (Adams and Brantner, *supra* n.29).

[32] *General Dynamics* teaches us that it is the competitive influence a firm will likely provide in the present and the future absent the merger that is the relevant yardstick, and not to rely merely on inferences based on past performance. *United States v. General Dynamics Corporation,* 415 U.S. 486 (1974).

program,[33] not to a likelihood that it could be brought to market first. Shortly after the merger, Genzyme stated that comparative testing showed that its internal Pompe enzyme could be developed and commercialized most quickly. Genzyme also stated that the promise of the Novazyme technology was to provide a basis for an improved second-generation therapy.[34]

Under these circumstances, the competition between Genzyme and Novazyme would not have had a substantial effect on the amount or timing of Genzyme's or Novazyme's R&D spending on Pompe, or on when the first Pompe therapy would reach the market. Regardless of Novazyme's program, Genzyme's incentive was to get a Pompe therapy to market sooner rather than later to earn profits on sales of its enzyme.[35] Changes in Novazyme's program would not likely have caused significant changes in Genzyme's program. Similarly, regardless of Genzyme's program, Novazyme's incentive was to get a superior Pompe therapy to market

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[33] A Novazyme Press Release, June 6, 2000, stated: "Dr. Kornfeld, a professor at Washington University School of Medicine in St. Louis, discoverer of the trafficking pathway for lysosomal enzymes and a board director at Novazyme, commented, 'I believe that the ability to target enzyme to the mannose 6-phosphate receptors has the potential to greatly enhance the clinical efficacy of replacement therapy. Novazyme is the only company at present with the technological ability to target these receptors, and I am excited to be involved as Novazyme works towards developing these novel biotherapies.'"

[34] Genzyme Press Release, Aug. 7, 2001, stated: "Novazyme has developed a series of novel protein engineering technologies that have been shown in preclinical studies to greatly enhance the targeting and uptake of replacement enzymes. Genzyme believes that these technologies could potentially lead to improved, second-generation versions of its marketed products and optimal first-generation products for the treatment of various lysosomal storage disorders."

[35] In principle, the pre-merger threat that Novazyme would soon follow with a superior product might have induced Genzyme to abandon its internal program. This did not happen, however, which is not surprising, given the relatively low probability that Novazyme would succeed.

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initial seven years of market exclusivity in order to obtain a total of 14 years of exclusivity under the ODA.

In weighing the anticompetitive harm that might arise from concerns about the potential effects of cannibalization and acts to extend ODA exclusivity, I note at the outset that these harms are relevant only if the Genzyme internal program succeeds. The potential anticompetitive effect is a delay in the second Pompe therapy, not the first.

Moreover, given the regulatory structure of the ODA, Genzyme might not have an incentive to delay a second therapy because of fears of cannibalization or a desire to extend ODA exclusivity. Absent the merger, if Genzyme obtained ODA market exclusivity for its internal Pompe product, then Novazyme could not have brought a Pompe product to market unless that product was sufficiently superior

Novazyme technology to develop therapies for lysosomal storage disorders besides Pompe.[38] Development of a Pompe therapy that incorporates Novazyme's technology therefore might well have spillover benefits for Genzyme programs to develop therapies for other lysosomal storage disorders.

In short, an analysis of Genzyme's incentives in this case does not clearly indicate whether Genzyme would have an incentive to delay the second Pompe product in the event that the first proved successful. Additional evidence is at hand, however, regarding the parties' own assessment of their incentives. In particular, the terms of the Genzyme/Novazyme merger agreement strongly suggest that Genzyme was *not* planning to delay the Novazyme program when it acquired Novazyme. Novazyme's President and CEO, John F. Crowley, two of whose children suffer from Pompe disease, was placed in charge of the merged company's Pompe

[38] Genzyme Press Release, Aug. 7, 2001, stated: "Novazyme has developed a series of novel protein engineering technologies that have been shown in preclinical studies to greatly enhance the targeting and uptake of replacement enzymes. Genzyme believes that these technologies could potentially lead to improved, second-generation versions of its marketed products and optimal first-generation products for the treatment of various lysosomal storage disorders." On Aug. 22, 2001, Genzyme spokesman Paul Kaufman stated: "As we develop therapies for Pompe disease and other lysosomal storage diseases, we will continue to invest in technologies that will improve on our existing products and products in development. Therefore, Genzyme is making continuous investments in enzyme replacement technology, and hence, our investment in Novazyme, with its specific technology." Following meetings with Genzyme on April 16-17, 2002, the International Pompe Association, a patient organization, stated: "Genzyme's development of the Novazyme NZ-1001 product, as a potential next-generation therapy for Pompe's disease, is proceeding and continues to be in pre-clinical development. It is intended that Novazyme's science, which focuses on targeting and uptake of enzyme, will continue to serve as a central component in the efforts to develop improved second-generation versions of the Pompe ERT, improve upon some of their current marketed products, as well as help to develop new therapies for the treatment of additional lysosomal storage disorders."

[42] Genzyme Press Release, April 17, 2002, describes the “comprehensive, blinded pre-

achieved absent the merger – for example, in the case at hand, if Novazyme had entered into a joint venture with a biotechnology company that did not already have a Pompe program. Unlike a proposed merger, which would involve uncertainty regarding both the proposed merger and an alternative joint venture, in this case only the results of a possible joint venture are uncertain. There is no reason to weigh equally the merger's actual benefits with the potential benefits of a joint venture that never occurred. Any number of factors – the possibility that the joint venture would not have occurred, that it would have failed before achieving any benefits, or that the benefits would have taken longer to achieve – render the benefits in the hypothesized "but for" world more conjectural. These speculative gains cannot offset concrete gains that will translate into immense benefits for patients if the Genzyme internal Pompe program fails and the Novazyme program succeeds. Many lives would be saved and much suffering prevented.

E. Weighing the Effects of the Merger

To reiterate, because there is currently no treatment for Pompe disease, the most important goal for patients is to get one effective treatment for Pompe disease on the market as soon as possible, in quantities sufficient to treat the patient population. Accelerating the first effective treatment by even a few months would greatly benefit patients. Patient welfare would also be increased by having a second effective Pompe treatment arrive on the market sooner, although the regulatory constraints of the ODA may hinder the ability to deliver a second product. Some patients who do not respond to the first therapy may respond to the second, while others may simply respond better to the second than to the first. Further, entry of a second therapy would likely cause a reduction in prices. These are significant considerations.

Nevertheless, for a fatal disease without any effective therapy, acceleration of the first effective treatment remains of paramount importance.

The evidence does not suggest that the merger has had a significant effect on the likelihood that Genzyme's internal program will succeed or, if it does succeed, on the date at which a therapy would be available. Consequently, an assessment of the merger must be based on comparing two alternative states of the world.

In the first, Genzyme's internal program fails. It is impossible to assign a precise probability to this event. In any case, the probability would depend on whether one looks at the issue when the parties merged or at present. Based on the rate of failure of such programs, it seems appropriate to estimate about a 25 percent chance that the Genzyme internal program will fail.[44] If the Genzyme internal program fails, then Genzyme will clearly want to pursue the Novazyme program. In this case, the merger is likely to have large patient benefits, because it appears that the merger has accelerated the Novazyme program.

In the alternative state of the world, Genzyme's internal program succeeds. For purposes of this analysis, this state appears to have a probability of around 75 percent. In this alternative state, as discussed previously, it would be anticompetitive for Genzyme to move forward with the Novazyme program more slowly than an independent company would have done, whether out of concerns over possible cannibalization or to extend its market exclusivity period. As also discussed previously, however, Genzyme had offsetting incentives not to delay the Novazyme program at all. There is no basis in the record for concluding that the circumstances that would give Genzyme an incentive to delay – concerns about cannibalization of sales of its internal

[44] *Supra* n.31.

product without sufficient offsetting expansion in demand, reduction in costs, or extension in product line – amount to anything more than a bare theoretical possibility. Indeed, the observable facts regarding Genzyme's behavior, such as the terms of its agreement with Novazyme and the structure of its Pompe program, strongly suggest Genzyme viewed the possibility of delay as so remote that it made no allowance for it in its plans.

In short, from the Commission's investigation, there are strong reasons to believe that the merger will benefit patients in the first state of the world, without a basis for concluding that the merger is likely to result in net harm to patients in the alternative state of the world. On balance, the merger is likely to be procompetitive, and thus patients' lives are more likely to be saved by this merger than to be put at risk.

One final consideration that warrants discussion is the effect of a complaint and eventual order in this case. Neither litigation nor a remedial order would likely benefit Pompe patients. To the contrary, litigation could adversely affect Genzyme's incentives to spend on R&D, and could disrupt the Novazyme research program. To an extent not typically seen in pharmaceutical cases, the Novazyme research effort appears to depend heavily on the efforts of one man – Dr. William Canfield, Novazyme's founder, chairman, and head of its research team. Dr. Canfield's testimony would be central to establishing numerous facts in the case, including, among others, any merger-specific efficiencies related to the Novazyme technology, as well as any claims of merger-related delays. Time that Dr. Canfield spends in the courtroom rather than the laboratory seems likely to delay the Novazyme research effort – precisely the harm that litigation in this matter would be brought to avoid.

[45] For example, on page 4, the Dissent states that "[B]etween 1998 and 2001, Genzyme acquired control over the three other Pompe ERT [enzyme replacement therapy] R&D efforts in the world through joint venture or acquisition." Genzyme did acquire three Pompe R&D programs (Pharming in 1998, Synpac in 2000, and Novazyme in 2001). Nevertheless, the wording of the Dissent might cause a reader to conclude that there was a time when Genzyme, Pharming, Synpac, and Novazyme were all doing independent R&D on Pompe. In fact, when Genzyme formed a joint venture with Pharming in 1998, Genzyme did not have a Pompe program of its own. See *supra* n.14. When Genzyme acquired the Novazyme program in September 2001, the Pharming and Synpac programs had encountered serious obstacles, and

require further discussion. First, some of the statements, which I find to be without support in the record, may cause unwarranted anxiety in the Pompe patient community. Second, the Dissent's proposed approach to innovation analysis, although undertaken for the purpose of safeguarding innovation, in fact would often have the opposite effect.

A. Factual Assertions Regarding Competitive Effects

Several of the Dissent's statements suggest that the Commission has found evidence that the merger already has caused, or is likely to cause, anticompetitive effects. I strongly disagree. For example, the Dissenting Statement expresses the view (at 4-5) that absent the merger Genzyme and Novazyme would have been involved in a "race to market" for Pompe therapies, and that this would likely have accelerated their R&D programs. It later states (at 9): "The evidence collected in this investigation showed that pre-merger competition did in fact bring an additional incentive to race in this particular innovation market." These assertions lack evidentiary support; instead, the evidence indicates that absent the merger, Genzyme's and Novazyme's R&D would not have been influenced substantially by efforts to increase their probabilities of being the first to market.[46]

Genzyme was able to manufacture. Genzyme Press Release, Sept. 10, 2003.

[46] The Dissent also makes some generalizations (nn.9, 21) about competitive behavior relating to innovation in products that fall under the ODA. The Dissent states (at n.9) that "[i]nnovator rivals in other Orphan Drug Act markets race to market to gain exclusivity, thus confirming that innovation competition in Orphan Drug Act markets is just as important as in any other innovation market." The merger investigation identified only one case in which there was a race to market – between Genzyme and Transkaryotic Therapies Inc. to obtain FDA approval for a therapy for Fabry disease. Genzyme 2002 10-K, p. 22. The existence of that one race hardly implies that there is a race every time two companies conduct R&D to find a therapy covered by the ODA.

The same flaw underlies the negative inference that the Dissenting Statement proposes to draw about the merger because of its effect on what Genzyme could do. It states (at 5) that Genzyme "has acquired the power to decide unilaterally and at any time whether to postpone or terminate its own research efforts or Novzyme's R&D project." The Dissent also claims (at 7) that "the Novazyme acquisition . . . extinguishes any chance for competition to push innovation that could possibly bring the first or second Pompe ERT product to the actual goods market sooner." Anticompetitive behavior, however, depends on incentives as well as ability. There is no evidence that the merger significantly changed Genzyme's incentive to bring its first product to market. As discussed above, one cannot make a prediction about the effect of the merger on the Novazyme program without considering Genzyme's incentives. When those incentives are evaluated, the specific facts of this case do not indicate any likely effect on Genzyme's effort to bring a second Pompe therapy to market.

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The Dissent argues (at 14) that closing this investigation could call into question the Commission's continuing commitm clohry]ya(r[(br.yctnsseiiP)4(o)1(rce.8(itm)8.8poe ai isspar ular li8.5(ne or)

[47] In addressing the application of antitrust to innovation issues, the 1999 Annual Report of the President's Council of Economic Advisors states:

proposed that the Commission reject its previous fact-specific approach in favor of legal presumptions, despite the lack of any economic consensus supporting that approach. The adoption of presumptions without economic foundation would constitute a major step backward in antitrust law. Because such a presumption, if adopted, would frequently make the Commission itself an impediment to consumer welfare, I have written this public statement.

> When the overall level and the future path of innovation are at issue, case-by-case analysis of the economic facts is likely to be even more vital than in conventional antitrust investigations.

Council of Economic Advisers, *Economic Report of the President*, Ch. 5, at 177 (1999).