Title: Medicare Drug Price Negotiation Program Draft Guidance

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Written comments: Request for Comments Regarding the Medicare Drug Price Negotiation Program Draft Guidance (published 5/6/2024)

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Comments by: Fred Ledley, M.D., Edward Zhou, PharmD., Paula Chaves da Silva, Ph.D. Center for Integration of Science and Industry, Bentley University[1]

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This comment focuses on Section 50.1, provisions 1 & 3 of the draft guidance regarding the negotiation of a "maximum fair price" under the Inflation Reduction Act (IRA), research and development (R&D) costs of the primary manufacturer, and prior federal financial support for novel therapeutic discovery and development. Specifically, we argue that **a negotiated, "maximum fair price" must consider both public sector (federal) and private sector (manufacturer) investments and provide returns to both commensurate with the scale and risk of their investments.** This comment addresses three issues and makes specific recommendations regarding each:

1. **In negotiating a "maximum fair price," both parties may be expected to consider their investment and returns.**
2. **Prior federal financial support for R&D may be estimated from the NIH investment in basic and applied research related to each product.**
3. **The return on federal investment in discovery and development should be estimated as a social return on investment (SROI) based on elements of social value created by new drugs.**

These comments are based on research conducted at the Center for Integration of Science and Industry characterizing the federal investment in the discovery and development of the ten drugs selected for price negotiation in the first year of the IRA as well as the health benefit accruing to the public from the Medicare Part D spending on these drugs (Zhou et al. 2024; Ledley 2024). Those studies followed a series of papers describing (i) methods for characterizing the NIH contribution to the drugs approved 2010-2019 including funding for basic and applied research, clinical development, and patents related to each drug, (ii) the total NIH investment cost accounting for estimated costs of clinical failures and discount rates for public sector investment, (iii) the cost savings to industry from this NIH investment, and (iv) an

[1] Dr. Ledley is Director of the Center for Integration of Science and Industry and Professor in the Departments of Natural & Applied Sciences and Management. Dr. Zhou is a Research Fellow in the Center for Integration of Science and Industry and Adjunct Professor, Department of Natural & Applied Sciences. Dr. Chaves da Silva is a Research Fellow at the Center for Integration of Science and Industry.

accounting-based approach for estimating social and private value creation from selected products.[2]

Contact information: Fred D. Ledley, Center for Integration of Science and Industry, Jennison 143, Bentley University, 175 Forest Street, Waltham, MA; email: fledley@bentley.edu; tel: +1.781.891.2046; website: www.bentley.edu/sciindustry

1. A "fair price" negotiation should consider the investment and returns of both parties.

The IRA identifies specific elements that CMS may consider in negotiating a "maximum fair price" as well as a process of cost analysis. The elements identified by CMS resemble those considered in other federal policies or legal precedents relating to "fair" or "reasonable" prices. While not directly applicable to the IRA, these precedents share the common principle that a "fair" or "reasonable" price cannot be determined purely by cost analysis, but require considerations of markets, competition, investment, risk, and return.

In a free market, a product may be considered to have a "fair market value" that is determined by negotiation between informed and unpressured parties. Legal precedent defines the fair market value as *"price that a prudent businessperson would pay for an item or service under competitive market conditions, given a reasonable knowledge of the marketplace."*[3] The "fair market value" is often considered a reflection of the inherent value of a product.

The concept of a product having a "fair price" is different in that it recognizes that the parties in a "fair price" negotiation may consider not only the intrinsic value of a product, but costs related to the product, market competition, or expectations for return on investments in the product. For example, government procurement requires that contracting officers determine a "fair and reasonable" price. Like the IRA, federal policies regarding "fair and reasonable" price begin with a cost analysis to identify cost elements such as material, labor, and manufacture or acquisition costs as well as competitive market factors, investments, profit, and the cost of capital (i.e., expected return on investment) among other factors.[4] A separate legal precedent

[2] This research is described in a series of papers including Cleary et al. (2018); Cleary et al. (2020); Cleary et al. (2023); Ledley and Cleary, (2023); Zhou et al. (2023); Chaves da Silva et al. (submitted).

[3] From *United States v. Cartwright, 411 US 546* quoted by Legal Information Institute, Cornell Law School fair market value | Wex | US Law | LII / Legal Information Institute (cornell.edu)

[4] For example, Title 48—Federal Acquisition Regulations System CHAPTER 1—FEDERAL ACQUISITION REGULATION SUBCHAPTER C—CONTRACTING METHODS AND CONTRACT TYPES PART 15—CONTRACTING BY NEGOTIATION Subpart 15.4—Contract Pricing 15.404-1 Proposal analysis techniques. "(a) General. The objective of proposal analysis is to ensure that the final agreed-to price is fair and reasonable."; "4) "Cost analysis may also be used to evaluate data other than certified cost or pricing data to determine cost reasonableness or cost realism when a fair and reasonable price cannot be determined through price analysis alone."; " (c) Cost analysis is the review and evaluation of any separate cost elements and profit or fee in an offeror's or contractor's proposal, as needed to determine a fair and reasonable price or to determine cost realism, and the application of judgment to determine how well the proposed costs represent what the cost of the contract should be, assuming reasonable economy and efficiency." https://www.law.cornell.edu/cfr/text/48/15.404-1

for determining a "reasonable price" holds that a reasonable price "*…involves balancing of the investor and consumer interests…*" and should allow companies to achieve returns "*…commensurate with returns on investments in other enterprises having corresponding risks…*"[5] In each of these precedents for "fair" or "reasonable" price, it is expected that both parties will consider their respective investments and returns.

Consistent with these precedents, the IRA explicitly authorizes CMS to consider both "research and development costs of the manufacturer for the drug" and "prior federal financial support for novel therapeutic discovery and development with respect to the drug" in price negotiations. By analogy to models of fair or reasonable pricing, the **"maximum fair price" of a drug under the IRA cannot be solely determined by analysis of the value provided by a pharmaceutical product (i.e., cost-effectiveness thresholds), but must also consider the investments made by both the public and private sectors, the scale and risks of these investments, and the returns** among other factors including market competition.

The draft guidance explicitly recognizes that monetary costs are typically estimated with the cost of capital. For industry costs, the guidance recognizes that (in calculating industry costs) research and development (R&D) costs apply a cost-of-capital adjustment to each company's R&D spending to reflect the "time-value" of the investment. Specifically, the guidance recommends using an 8.1% cost of capital in estimating industry investment costs.[6] Theoretically, public sector spending is not associated with a cost of capital, but the Office of Management and Budget recommends estimating the cost of federal (public) spending with either a 3% discount rate reflecting the historical cost of borrowing or a 7% discount rate (OMB 1992, 2017). In this context, both manufacturer and federal investments should be estimated with appropriate adjustments to assure that both the public and private sector receive at least the minimal expected returns.

Building on these precents and policies, we offer several specific recommendations concerning the draft guidance and how CMS should consider both manufacturer R&D costs and prior federal financial support for discovery and development.

> **Recommendation #1. The draft guidance should explicitly state that the negotiation of the "maximum fair price" shall consider the investment cost of both the**

[5] "…involves a balancing of the investor and consumer interests," which does not, however, 'ensure that the business shall produce net revenues.' ... From the investor or company point of view it is important that there be enough revenue not only for operating expenses but also for the capital costs of the business. These include service on the debt and dividends on the stock... By that standard the return to the equity owner should be commensurate with returns on investments in other enterprises having corresponding risks." Quoted in Congressional research Service op cit and referencing: FPC v. Hope Natural Gas Co., 320 U.S. 591, 603 (1944) (citing Chicago & Grand Trunk Ry. v. Wellman, 143 U.S. 339, 345–46 (1892); and Missouri ex rel. Southwestern Bell Tel. Co. v. Public Serv. Comm'n, 262 U.S. 276, 291 (1923).

[6] We would note that various values for cost of capital have been used in the literature describing industry investment costs, with 10.5% being the most commonly used value (DiMasi, Grabowski, and Hansen 2016; Wouters, McKee, and Luyten 2020; Rennane, Baker, and Mulcahy 2021) and the one used in our comparisons of federal and industry spending on new drug approvals (Cleary et al. 2023b; Zhou et al. 2024).

manufacturer's R&D and federal financial support as well as the returns on both manufacturer and federal investments.

Recommendation #2. The draft guidance should explicitly state that both manufacturer costs and federal funding should be estimated with appropriate adjustments for the time-value of this investment.

2. Federal funding for new drug discovery and development can be estimated from the NIH investments in basic or applied research related to each product.

It is widely recognized that basic and applied biomedical research funded by the federal government makes a substantive contribution to the discovery or development of most, or all, new drugs, with the government contribution focused primarily on basic or applied research and industry responsible for clinical development and commercialization.[7] While most research on the federal contribution to new drug approvals focuses on studies contributing to clinical trials or patents, our work has demonstrated that a mature body of basic research on the drug target is requisite for drug approval. Specifically, our analysis on >500 drugs shows that few targeted therapeutics are approved before basic research matures beyond an analytically described "established" threshold and that clinical development timelines average three years longer when clinical trials are initiated before the "established" threshold is reached (McNamee, Walsh, and Ledley 2017; Cleary, Jackson, and Ledley 2020; Beierlein et al. 2017; McNamee and Ledley 2017). Therefore, we believe that federal funding for both applied research on drugs in development and basic research on their targets constitute "federal financial support for novel therapeutic discovery and development" and elements that CMS needs to consider in negotiating a fair market price.

Much of the research describing federal spending on drug discovery or development, however, is unable to delineate drug-specific costs.[8] We have described a method for estimating NIH funding for basic or applied research contributing to approval of specific drugs. The method identifies NIH-funded projects that supported published research related to the drug target (basic research) prior to approval of a first-in-class product associated with that target or the

[7] There is an extensive research on the public sector contribution to new drug approvals (Comroe Jr and Dripps 1976; Toole 2012; Sampat and Lichtenberg 2011; Chakravarthy et al. 2016; Stevens et al. 2011; Nayak, Avorn, and Kesselheim 2019; Cleary, Jackson, and Ledley 2020; Zhou, Jackson, and Ledley 2023; Cleary et al. 2023a)

[8] Many studies of the NIH contribution to pharmaceutical innovation consider total NIH budget allocations (Sekar 2020; Lazonick and Tulum 2011; Moses et al. 2015) or categories of funding included in the Research, Condition, and Disease Categories (RCDC) and Research Portfolio Online Reporting Tools (RePORT) (Torrey et al. 2020; Sampat, Buterbaugh, and Perl 2013; Ballreich et al. 2021)

approved drug (applied research) prior to first FDA approval[9] (Cleary, Jackson, and Ledley 2020; Cleary et al. 2023b; Cleary et al. 2018; Zhou et al. 2024; Zhou, Jackson, and Ledley 2023). Our studies have identified $187 billion in NIH funding leading to drug approvals from 2010-2019, with 83% of this total representing basic research and 17% representing applied research (Cleary, Jackson, and Ledley 2020; Cleary et al. 2023a). Follow-on studies demonstrated that only 3.3% of total NIH funding involved phased clinical trials leading to first FDA approval (Zhou, Jackson, and Ledley 2023).[10]

We have identified NIH funding totaling $11.7 billion for basic or applied research leading to approval of the drugs selected for price negotiation in year 1 of the IRA (Zhou et al. 2024).[11] Drug specific NIH spending is shown in Table 1. Table 1 also shows drug specific NIH investment costs calculated with estimated cost of failed clinical trials and a 3% discount rate appropriate for public investments (OMB 1992, 2017).

This analysis also estimated the NIH investment cost with spillovers resulting from the application of basic research on each drug target to an average of 2.85 new molecular entities (NMEs) (Santos et al. 2017; Cleary et al. 2023b). This reflects the average NIH investment cost across a broad portfolio of first-in-class and follow-on products (Table 1).

Table 1. Estimated federal (NIH) spending and investment costs leading to first approval of drugs selected for price negotiation in year one of the IRA

Generic Name (Brand Name)	Total NIH Funding[a]	NIH Investment Cost (3%)[b]	Investment Cost with Spillovers (3%)[c]
etanercept (Enbrel)	$2,606.3	$2,799.5	$1,036.2

[9] Briefly, the method involves identifying publications (PMIDs) in the PubMed database related to the drug or the drug target using validated search parameters. Drug searches included 12 years before first drug approval and resulting PMID are designated applied research. Target searches included 12 years before approval of a first-in-class drug associated with that target and resulting PMID are designated basic research. NIH-funded projects (grants) associated with these PMID are then identified in the NIH Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER) database. NIH costs are estimated from one year of project funding corresponding to the publication year, eliminating PMIDs with publication dates before the first year of project funding and accounting for lags of 1-4 years after the end year of project funding. Duplicate project year and NIH funding arising from are eliminated separately for each data point shown. Clinical development costs are estimated from PMID describing phase 1, phase 2, or phase 3 trials or NCT numbers. The method is described in the eMethod section of Cleary et al. (2023) with modifications described by Zhou et al. (2023); Zhou et al. (2024).

[10] This research estimated the average NIH spending for each first-in-class drug approved 2010-2019 to be $1.4 billion/drug, comparable to the $1.5 billion average industry spending reported by DiMasi et al. (2016). The average NIH investment cost was estimated to be $1.7 billion/drug (calculated with estimated costs of failed clinical trials and a 3% annual discount rate on public investments reflecting the cost of government borrowing (OMB 1992, 2017)). This amount is not less than industry spending on drugs reported by (Wouters, McKee, and Luyten 2020) with estimated costs of pre-human research, failed clinical trials, and a 10.5% cost of capital. The estimated cost savings to industry study also estimated the cost savings to industry was $2.9 billion/drug, comparable to average industry costs estimated by Dimasi et al. (2016) and greater than those reported by Wouters et al. (2020).

[11] The analysis did not estimate NIH costs related to insulin aspart, which was considered a follow-on product to recombinant insulin approved in 1982. No NIH funding data is available before 1985.

insulin aspart (Novolog)	N/A	N/A	N/A
sitagliptin (Januvia)	$227.5	$317.5	$163.8
ustekinumab (Stelara)	$6,482.1	$6,951.5	$2,501.8
rivaroxaban (Xarelto)	$763.6	$895.4	$379.0
apixaban (Eliquis)	$790.6	$910.9	$404.8
ibrutinib (Imbruvica)	$566.0	$683.8	$382.5
empagliflozin (Jardiance)	$434.2	$539.6	$249.0
dapagliflozin (Farxiga)	$437.3	$547.9	$257.3
sacubitril[d]/valsartan (Entresto)	$901.1	$1,078.6	$435.4

All values are in millions and inflation-adjusted to 2018. Rows are not additive as NIH funding may contribute to more than one drug. a. NIH funding for basic research and applied research. b. NIH costs with estimated cost of failure and 3% discount rate. c. Spillovers based on allocating basic research costs to 2.85 drug approvals per biological target. d Sacubitril is the NME in this combination product. Table adapted from Zhou et al. 2024.

NIH funding for basic and applied research provides substantial cost-savings to industry. The cost savings to industry may be estimated as the additional industry spending that would have been necessary to establish a body of basic research requisite for successful drug development. Cost savings are estimated from total NIH spending on basic and applied research calculated with an 8.1%, and 10.5% cost of capital expected by industry.[12] The estimated drug-specific cost savings are shown in Table 2.

Table 2. Estimated federal (NIH) investment costs leading to first approval of drugs selected for price negotiation in year one of the IRA with estimated cost savings to industry after cost of capital adjustments used by industry or by CMS price negotiations.

Generic Name (Brand Name)	Total NIH Funding[a]	Savings to Industry (8.1%)[b]	Savings to Industry (10.5%)[c]
etanercept (Enbrel)	$2,606.3	$3,652.7	$4,176.2
insulin aspart (Novolog)[d]	N/A	N/A	N/A
sitagliptin (Januvia)	$227.5	$393.7	$455.8
ustekinumab (Stelara)	$6,482.1	$9,348.5	$10,815.4
rivaroxaban (Xarelto)	$763.6	$1,248.9	$1,485.8
apixaban (Eliquis)	$790.6	$1,260.2	$1,494.1
ibrutinib (Imbruvica)	$566.0	$871.1	$1,001.7
empagliflozin (Jardiance)	$434.2	$704.7	$821.3
dapagliflozin (Farxiga)	$437.3	$714.5	$832.0
sacubitril[e]/valsartan (Entresto)	$901.1	$1,491.6	$1,763.8

Values are in millions and inflation-adjusted to 2018. Rows are not additive as NIH funding may contribute to more than one drug. a. NIH funding for basic and applied research. b. NIH costs (including estimated costs of

[12] This calculation is based on the NIH investment cost for basic research without spillovers, assuming that corporate basic research would be treated as intellectual property and would need to be replicated by other companies developing other products associated with the same target.

clinical failures) calculated with 8.1% discount rate.[13] c. NIH costs (including estimated costs of clinical failures) calculated with a 10.5% discount equivalent to the cost of capital used by DiMasi et al. 2016. d. The first-in-class recombinant insulin was approved in 1982. No data on NIH funding is available before this date. e. Sacubitril is the NME in this combination product. Table adapted from Zhou et al. 2024.

We offer several specific recommendations concerning CMS consideration of "federal financial support for novel therapeutic discovery and development."

Recommendation #3. Since the NIH provides >80% of all federal financial support for life science research (Boroush and Guci 2022), we consider estimates of the NIH investment cost with estimated clinical failures to be an appropriate proxy for federal financial support for discovery and development.[14] We further recommend that federal financial support be estimated with the 3% discount rate suggested by OMB.

Recommendation #4. Consideration of the "federal financial support" should not be limited to the "*extent to which the Primary Manufacturer benefited from federal financial support…*" nor should it be limited to "*…funding for the discovery and development…*" nor should it be limited to any specific time period related to the initiation of research, any action on the part of the primary manufacturer, or to the development or regulatory process. The Act places no limits on the beneficiary of federal funding, explicitly includes "prior" federal financial support, and does not limit the timeframe of this support. **The language in the guidelines should state explicitly that "*CMS shall consider all federal financial support with respect to the selected drug prior to directly contributing to discovery or development through drug approval.*"**

Recommendation #5. There should be no limits on the form of federal financial support considered by CMS. The definition of "federal financial support for novel therapeutic discovery and development" should be restated to explicitly include the "appropriation or licensing of discoveries, research, or development (i.e., regulatory approvals) or utilization of research resources, capabilities, consortia, centers, facilities, or personnel receiving federal financial support and related to the selected drug." We would further recommend that the draft guidance explicitly address federal financial support provided through public private partnerships with government,

[13] This value is explicitly cited in the draft guidance "*The use of 8.1 percent is consistent with assumptions used by the Congressional Budget Office (CBO), see "Research and Development in the Pharmaceutical Industry," CBO (April 2021), available at https://www.cbo.gov/publication/57126."*

[14] It is critical that the methods used to identify federal financial support identify support for both basic and applied research. Case study methods are frequently used to characterize the NIH contributions related to specific patents (Azoulay et al. 2019; Sampat and Lichtenberg 2011) or clinical trials of approved products (Nayak, Avorn, and Kesselheim 2019; Chakravarthy et al. 2016; Zycher, DiMasi, and Milne 2010). These methods, however, implicitly focus on federal contributions to development and do not capture contributions to basic research, which are, by definition, undertaken "without specific applications towards processes or products in mind."(NSF 2018). Broader, analytical methods are required to capture both basic and applied science as well as the broad body of research necessary to replicate, refute, or refine scientific advances, without which applications of federally funded research may not be successfully adopted by industry (Bretz, Maurer, and Xi 2019; NAS 2019).

academia, or non-profit organizations as well as support provided through cancer centers, clinical consortia, Clinical and Translational Science Awards, Program Project Grants, or Collaborative Agreements.[15]

3. The return on federal investment in discovery and development can be estimated as a social return on investment (SROI) based on elements of social value created by new drugs.

Our comments are predicated on the concept that there should be an equitable return on investments made by both the public and private sector.[16] For industry, the return is measured in terms of the value provided to shareholders and contributions to the GDP. For government, we believe return should be measured in terms of the social value created through commercialization of new drugs. Social value has been defined as the "*…benefits or reductions of costs for society … that go beyond the private gains and general benefits of market activity*" (Phills, Deiglmeier, and Miller 2008) or the value accruing to "*…non-investor stakeholders affected by business: individuals, employees, communities, and society*" (Lingane and Olsen 2004).

There is evidence from broad econometric studies that the value provided to society from innovative drugs (i.e., consumer surplus) is often greater than the value provided to producers (i.e., producer surplus) (Lakdawalla et al. 2010; Camejo et al. 2014; Philipson and Jena 2006).These methodologies are unable to distinguish the impacts of individual drugs on society and are not applicable to assessing the social value or returns provided by specific products.

We have described an accounting-based approach, which recognizes that there are multiple elements to the value created by new medicines (Neumann, Garrison, and Willke 2022; Lakdawalla et al. 2018; Stiglitz 2019) ranging from health benefits and pharmaceutical revenues to job creation, scientific advances, increased economic activity, an expanded tax base, and

[15] The Clinical Translational Science Award programs represent the centerpiece of the NIH's efforts to accelerate innovation by "reengineering the clinical research enterprise"(Zerhouni 2005; Zerhouni 2003) but typically provide patient populations, centers for data or laboratory analysis, and training or salaries for clinical investigators rather than direct funding for investigator-initiated clinical or translational research. The initial Broad Agency Announcement (BAA) of funding available from ARPA-H (March 15, 2023) extends this focus, describing strategies for achieving "Health Science Futures" through investments in molecular platforms, biological engineering approaches, foundational advances in degenerative diseases and personalized medicine, AI-enabled models, and "clinical trial readiness" (ARPA-H 2023). Zhou et al. (2023) characterized the NIH project type utilized to support clinical development of drugs approved 2010-2019. The analysis showed that >90% of NIH costs for phased clinical development were provided by "Program Projects and Centers", which typically support core research capabilities, or "Collaborative Agreements", which typically fund government-initiated research programs and includes the Clinical Translational Science Awards (CTSA) program (Liverman et al. 2013).

[16] There is longstanding concern that industry practices fail to balance the value accruing to society with the value accruing to corporations and their shareholders (Mazzucato 2016; Leopold, Chambers, and Wagner 2016; Angelis et al. 2023; Mattingly et al. 2021; GAO 2022). Lazonick and Mazzucato have described a disconnect between those who contribute labor and capital to innovation and those who realize financial rewards (Lazonick and Mazzucato 2013).

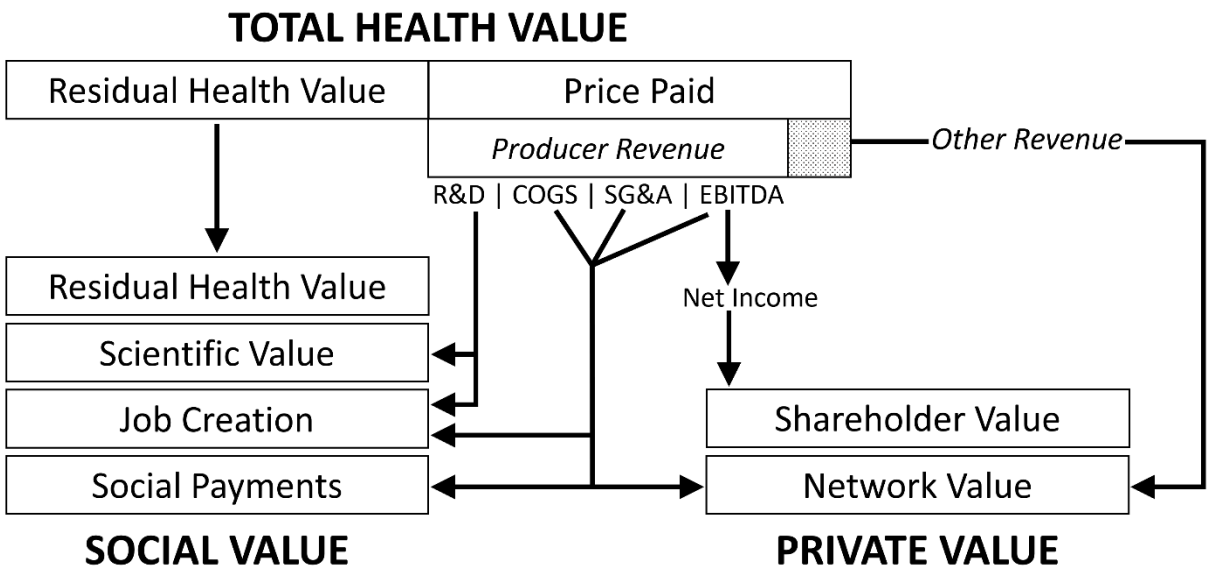
support for public institutions. This approach is based on the concept of estimating "total stakeholder value" as the sum of value accruing to different stakeholders (Mitchell et al. 2015; Lingane and Olsen 2004).

This model posits that the total value created through commercialization of a new pharmaceutical product is the "total health value" accruing to those who use the products.[17] A portion of this value is then distributed among different stakeholders from the price paid for the drug and how this revenue is expensed or invested by the pharmaceutical manufacturer (Chaves da Silva, Conti, and Ledley submitted; Zhou et al. 2024). **In this analysis, the "residual health value," or total health value minus the price paid, represents the most appropriate measure of the value retained by the patient or social sector.**[18] A schematic of this method is shown in Figure 1.

[17] Total health value is estimated from the health benefit (in QALYs) to individual taking a specific product (ICER 2020; Neumann, Cohen, and Weinstein 2014; Weinstein, Torrance, and McGuire 2009; Cohen, Neumann, and Ollendorf 2023) and the number of people to use the product. Health value can then be described in dollars based on individuals' willingness to pay per QALY (WTP/QALY), specifically their WTP/QALY (Martín-Fernández et al. 2014). This use of the QALY metric is distinct from its application in Health Technology Assessment (HTA) or cost-effectiveness studies (ICER 2020; Neumann, Cohen, and Weinstein 2014; Weinstein, Torrance, and McGuire 2009).

[18] Residual Health Value is the health-related, consumer surplus as a measure of the social benefits of drugs relative to the producer surplus as a measure of the value retained by industry (Camejo et al. 2014; Philipson and Jena 2006)). More importantly, this reflects clinical evidence that high drug prices are associated with economic insecurity, poor adherence to treatment regimens, food insecurity, and poor housing, all of which represent social determinants of health that impact health outcomes and can lower the net benefit of being prescribed expensive products (XCENDA 2020; Herman et al. 2015; IQVIA 2020; Berkowitz et al. 2015; Berkowitz, Seligman, and Choudhry 2014; Berkowitz et al. 2018; Blanchard et al. 2013; Afulani et al. 2015; Caouette, Boss, and Lynn 2020). For example, with respect to Medicare Part D. a 2020 report from IQVIA notes: "the cost exposure of Medicare Part D patients represents a potentially significant cost barrier to adherence" (IQVIA 2020). The negative residual health values described in this report are similar to those described by (Woods et al. 2021) which the authors ascribe to the "health opportunity cost" of high drug prices for branded drugs.

Figure 1. Schematic of method for estimating social and private value creation from commercialization of individual drugs or classes of drugs.[19]



Our 2024 working paper (Zhou et al. 2024) describes a preliminary analysis of the total and residual health value created by Medicare Part D spending on the ten drugs selected for price negotiation in the first year of the IRA 2017-2021. Table 3 shows the total Medicare Part D spending on each drug and the number of beneficiaries.

Table 3. Medicare Part D spending and number of beneficiaries treated with drugs selected for price negotiation in first year of the IRA 2017-2021.

Brand name (Generic Name)	Initial indication	Part D spending[a] (millions)	Number of beneficiaries[b]
Enbrel (etanercept)	Rheumatoid arthritis	$9,985	239,511
NovoLog[c] (insulin aspart)	Diabetes mellitus (Type 1, 2)	$11,965	4,292,206
Januvia (sitagliptin)	Diabetes mellitus (Type 2)	$17,066	4,619,191
Stelara (ustekinumab)	plaque psoriasis	$4,306	58,569
Xarelto (rivaroxaban)	prophylaxis of deep vein thrombosis and pulmonary embolism	$19,442	5,579,404
Eliquis (apixaban)	nonvalvular atrial fibrillation	$36,614	10,724,482
Imbruvica (ibrutinib)	mantle cell lymphoma	$11,459	119,019
Jardiance (empagliflozin)	Diabetes mellitus (Type 2)	$8,187	2,252,196
Farxiga (dapagliflozin)	Diabetes mellitus (Type 2)	$3,085	908,804
Entresto (sacubitril/valsartan)	chronic heart failure	$4,271	1,141,574

[19] Schematic of method for estimating social and private value creation from commercialization of individual drugs or classes of drugs. The method is described in detail: Chaves da Silva and Ledley, A Novel Framework to Estimate Social and Private Value Created Through Commercialization of a Pharmaceutical Product (Tech Note 2024-1), https://scholars.bentley.edu/cisi_pubs/4/. Figure adapted from Chaves da Silva et al., submitted.

TOTAL	**$126,381**	**29,934,956**

Part D spending values are inflation-adjusted to 2018. a. Part D spending includes amounts paid by Medicare Part D plan sponsors and beneficiaries but not manufacturers' discounts or rebates. b. Number of beneficiaries = number of Part D beneficiaries utilizing the drug. c. Includes multiple forms/types of the drug. NovoLog includes Fiasp; Fiasp FlexTouch; Fiasp PenFill; NovoLog; NovoLog FlexPen; NovoLog PenFill. Enbrel includes Enbrel Mini and Enbrel Sureclick. Source: CMS (https://data.cms.gov). Table adapted from Zhou et al. 2024.

Table 4 shows the total and residual health value created for beneficiaries by Medicare Part D spending on these drugs. **Excluding Januvia and NovoLog, total Medicare Part D spending was $97.3 billion and the total health value created by these sales is estimated to have been $67.7 billion from 2017-2021. This results in a negative residual health value of -$29.7 billion, analogous to a negative consumer surplus.**[20]

Table 4. Total health value created 2017-2021 by Medicare Part D spending on drugs subject to price negotiation in the first year of the IRA.

Brand Name (Generic Name)	QALYs/year per Beneficiary	Total Health Value		Residual Health Value[b]
		QALYs	$[a]	
Enbrel (etanercept)	0.08	19,161	$1,993	-$7,993
NovoLog (insulin aspart)[c]	N/A	N/A	N/A	NA
Januvia (sitagliptin)[c]	N/A	N/A	N/A	NA
Stelara (ustekinumab)	0.14	8,200	$853	-$3,453
Xarelto (rivaroxaban)	0.03	167,382	$17,408	-$2,034
Eliquis (apixaban)	0.02	214,490	$22,307	-$14,307
Imbruvica (ibrutinib)	0.13	15,472	$1,609	-$9,850
Jardiance (empagliflozin)	0.06	135,132	$14,054	$5,867
Farxiga (dapagliflozin)	0.05	45,440	$4,726	$1,640
Entresto (sacubitril[d]/valsartan)	0.04	45,663	$4,749	$478
TOTAL	**0.55**	**650,940**	**$67,698**	**-$29,652**

Dollar values are in millions and inflation-adjusted to 2018. a. Calculated with WTP/QALY of $104K. b. Total health value minus Medicare Part D spending including amounts paid by Medicare Part D plan sponsors and beneficiaries but not manufacturers' discounts or rebates. c. NovoLog and Januvia are not included in this analysis. d. Sacubitril is the NME in this combination product. Table adapted from Zhou et al. 2024.

This preliminary analysis was based on publicly available data on Medicare Part D spending. A complete analysis of the total and residual health value created through commercialization of these products and the balance between social and private value creation requires data on the number of people utilizing the drug and the price paid in US and global populations. While those data were not available for our research, they will be provided to CMS under the provisions of the IRA. As such CMS will be uniquely positioned to make a complete assessment of the health value, social value, and private value created by these products and the balance

[20] This estimate of the residual health value includes the amounts paid by the Medicare Part D plan sponsors and beneficiaries but does not take into account manufacturer's discounts or rebates. There is no publicly available data on the rebates associated with individual drug products (Feldman et al. 2021; Anderson-Cook, Maeda, and Nelson 2019; Dicken 2023). Using estimated average rebate increasing from 17.5% in 2014 to 25% in 2021, there would be a negative residual health value of -$6.9 billion. (Zhou et al. 2024). A complete analysis would require data on the price paid net discounts and rebates.

between social and private value creation. **We believe that such an assessment should serve as the basis for estimating the total social return on investment as well as more traditional return on investment metrics related to the value created for shareholders or the economy.**

We would emphasize that benchmarking the Medicare Part D price to the health value provided by the product as anticipated in value-based pricing results in zero residual health value. This pricing strategy does not provide a consumer surplus or margin contributing to the social return on federal investments in these product (Tremblay, Poirier, and Monfort 2024; Shafrin et al. 2023). This approach could allow manufacturers to realize most of the return from product sales (Basu et al. 2023). **We argue that the maximum fair price should be a price at which the social value (i.e., residual (net) health value + job creation + science + payments to the public sector) is comparable to the private returns to industry (Laplane and Mazzucato 2020; Lazonick and Mazzucato 2013; Ledley 2024; Zhou et al. 2024).**

We offer the following recommendations:

> **Recommendation #6. CMS should utilize data provided by industry concerning the number of individuals treated with each product and the price paid to estimate the total health value created and the distribution of this value between social value and private value.**
>
> **Recommendation #7. The maximum fair price should be established that provides for both social and private value creation as well as an equitable balance between the social returns on public sector investments and financial returns on producer investment. These returns should be commensurate with the scale and risk of their respective contributions.**

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Endnotes