

**Potential Savings That Might Be Realized By the Medicare Program
From Enactment Of Legislation Such As
The Access To Life-Saving Medicine Act (H.R. 6257/S. 4016)
That Establishes A New cBLA Pathway For Follow-On Biologics**

**A Report To Pharmaceutical Care Management Association (PCMA)
Based Upon A Preliminary Assessment Of Available Data**

January 2, 2007

EXECUTIVE SUMMARY

With Medicare Part B costs generally, prescription medicines costs as a whole, and biologics costs in particular continuing to escalate disproportionately to Medicare funding, legislation that establishes a pathway to enable comparable follow-on biologics (FOBs) to be licensed by the United States Food and Drug Administration (FDA) can provide a market-based mechanism to help manage Federal budgetary expenditures by maximizing efficiency of the biologics segment with respect to R&D, licensure, manufacturing, and competition. Life-saving and enhancing biologics can cost tens of thousands of dollars a year or more per patient so introducing as much competition as possible is vital to making these treatments more accessible to consumers. When more than one biologic is available in the market (let alone more than two – i.e., more than the innovator and a single FOB), and approval of interchangeable FOBs is enabled, market forces can be expected to increase competition and incentivize reduced costs of goods through more efficient and modernized manufacturing. These competition-based cost reductions should be translated into some level of savings for payors, patients, and the health care system. To date, the potential savings that might be anticipated have not been quantified, due, in no small part, to the unique challenges in evaluating the limited available data.

This report presents the results of a preliminary assessment of freely accessible data from public/published sources. Recognizing the inherent limitations on those data, the report estimates the savings by the nation's largest payor, Medicare, that would be enabled by authorizing FDA to approve comparable, as well as interchangeable, FOBs that reference biologics already licensed under the Public Health Service Act (PHS Act) whose patents have expired. It preliminarily projects that – applying the Congressional Budget Office's (CBO's) projections for Medicare spending to just the subset of PHS Act licensed biologics in the top 200 Medicare Part B reimbursed categories – the estimated cost-savings would be on average \$1.49 billion per year or \$14.9 billion over a standard 10-year “scoring” period from FY2007-FY2016. Similarly, the report projects –applying the SMI Trustees' projections for Medicare expenditures – that the estimated savings would be on average \$1.41 billion per year or approximately \$14.1 billion over the same 10-year period (FY2007-FY2016). Essentially, the projected savings utilizing either the CBO or the SMI figures are comparable. Among the myriad of potential savings that these projected savings do not encompass are those that might be projected for the End Stage Renal Disease (ESRD) program, whose drugs costs were not evaluated in conducting this preliminary assessment.

Recognizing that the magnitude of potential savings from FOBs goes well beyond Federal payors, the preliminary assessment that resulted in this report did not attempt to estimate savings that might be realized by private payors, even though these can be expected to be considerable given the potential for projected Medicare savings. In addition, this preliminary assessment does not consider numerous other factors that could increase Medicare spending and/or the savings that the program might realize, such as any biologics that are not already approved. Consequently, within the bounds and limitations of the available data, this report presents a conservative projected estimate of possible savings that might ultimately be realized over a 10-year “scoring” period following enactment of FOBs legislation. In doing so, it reinforces the emerging consensus that legislation establishing a pathway for interchangeable FOBs and fostering robust, science-based comparability assessments will enhance market efficiencies and could lower overall health-care costs through multiple product approvals and marketplace competition.

Introduction

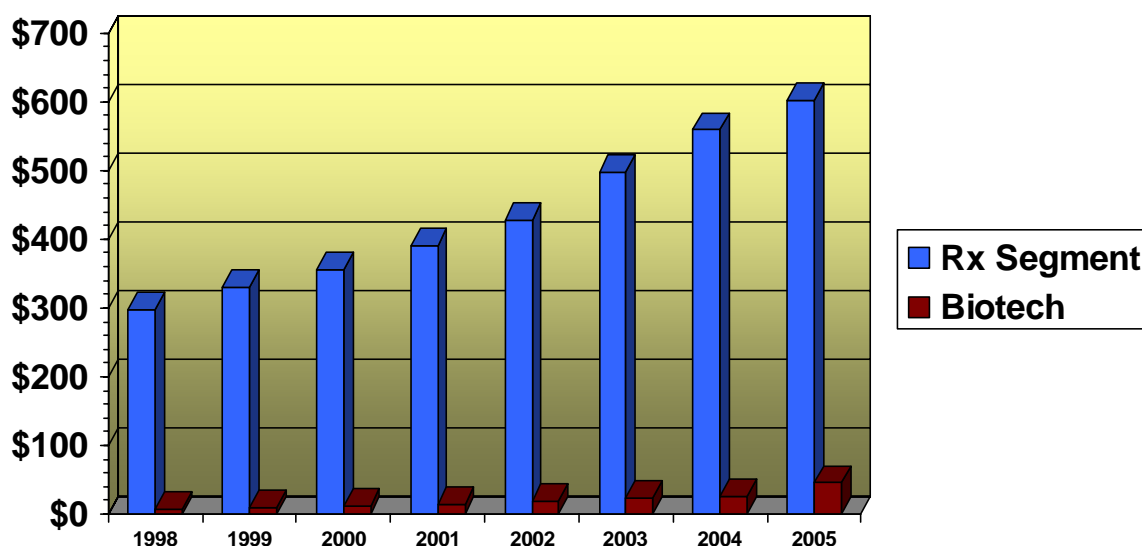
The U.S. Food and Drug Administration (FDA) approved the first recombinant protein product, Eli Lilly's Humulin (recombinant human insulin), in 1982. Nonetheless, the "advent" of the biotech revolution often is traced to the licensure of Genentech's first product, Protropin (recombinant human growth hormone), in 1986 – a year in which FDA also licensed Roche's Roferon-A and Schering-Plough's Intron A, as well as the first recombinant hepatitis B vaccine, Merck's Recombivax. During the 1990s, the biotechnology industry flourished as corporate investments in recombinant therapeutics and associated research and development fueled a long-running pipeline of biologic license application (BLA) submissions under the Public Health Service Act (PHS Act). Before the turn of the century, the biotech industry had several "billion-dollar" products, and its two leading companies (Amgen and Genentech) were among the largest biopharmaceutical companies based on market capitalization. As the industry approaches the quarter-century mark of its first approval, there is a diverse portfolio of biotechnology products in development and over 100 biotechnology-derived products (covering over 150 diseases) approved by FDA. While presenting a tremendous opportunity for the industry and the patients and healthcare providers the industry serves, that increasingly-costly portfolio presents unique access and affordability considerations because so many biotechnology products are covered under the Federal Medicare program. Life-saving and enhancing biologics can cost tens of thousands of dollars a year or more per patient so enabling competition is critical to making these treatments more accessible to consumers.

Over the past five years, the biological product segment in the United States (U.S.) has experienced increased positive growth in the number of products licensed by FDA and subsequently marketed, even though recent trend lines are negative and suggest a slowing of successful R&D output and market entry, with only four (4) recombinant BLA approvals during calendar year 2006. Nonetheless, biological products have experienced a disproportionate share of growth in terms of their market share of the prescription drug segment, which in and of itself has grown as a proportion of healthcare spending. Among the key drivers impacting this trend for biologics, in addition to the evident possibilities for the technology, is the industry's historic ability to command, and exact, high price premiums on biotech products. Some portion of this growth in biologics expenditures also is attributable to the increasing diversity of diseases and conditions being treated with biological products. Early on, biotech products often were developed as "orphan drugs," but some of these same biologics have greatly expanded their indications, and thus the marketing segments for these biologics have evolved (typically broadened) over time to become major contributors to health-care expenditures in terms of the numbers of patients they treat, as well as their individual cost on a per-patient or per-treatment course basis. Indeed, many of the older recombinant products, as well as some of the newer biotech products, fall into maintenance categories and are used for managing chronic diseases, and quite a few are used for the rest of a patient's life. For example, a chronic condition such as rheumatoid arthritis (RA) can be caused by hereditary factors, an error in the immune system, or biological factors, and is currently incurable but eminently treatable. Historically, RA has been treated with a combination of nonsteroidal anti-inflammatory drugs, cyclooxygenase 2 inhibitors, disease-modifying antirheumatic drugs, corticosteroids, along with other drugs. However,

current treatments for RA include biologics such as Enbrel® (etanercept), Remicade® (infliximab), Humira® (adalimumab), and Kineret® (anakinra), which are biologic response modifiers that target tumor necrosis factor-alpha [TNF-a] and interleukin-1 [IL-1].

As the biopharmaceutical industry confronts an overall slowdown in output of FDA-approved and marketed products from R&D pipelines, as well as declines in sales growth (and exponential growth in the number of FDA “approvable” actions), especially for small molecule blockbuster drugs, the biological products segment has been consistently growing and consuming a greater proportion of biopharmaceutical expenditures. Even in those years in which biologics have represented a small fraction of overall prescriptions, their market share has been disproportionate because of their premium pricing and their historic enjoyment of comprehensive reimbursement – both being pivotal economic factors that have created unparalleled revenue streams for biotech manufacturers and increasingly skyrocketing costs for patients and payors. The global pharmaceutical segment, according to IMS Health, accounted in 1999 for about \$331 billion, of which biotech drugs represented less than 3% of sales. Three years later, in 2002, the total segment had grown to about \$427 billion, and biotech drugs had increased to 4.5% of total sales. By 2005, total pharmaceutical sales topped \$602 billion with biotech drug sales approaching 7.6%.¹

Figure 1: Growth In Rx Drug Segment And Biotech Share Of That Segment (US \$ Billions)



These trends are of particular significance in the context of the demographics of the Medicare population, where the use of biologics by the now-aging baby boomer population is expanding, while the population paying into the Medicare Trust Funds is shrinking. Historically, Medicare has consisted of two primary programs: Part A, providing hospital insurance to cover inpatient care for beneficiaries, including medicines provided during hospital stays, as well as limited coverage for nursing home care or hospice services; and Part B, providing supplementary insurance for enrollees who pay monthly premiums to cover charges for office visits and other outpatient services as well as certain categories of physician-administered drugs as part of an office visit, and also most drugs administered as part of hospital outpatient programs,

office-based parenteral oncology, and immunosuppressive agents, specific immunizations, and drugs used for end-stage renal disease (e.g., erythropoiesis-stimulating proteins), including, most importantly, many biologics. (Under Part B, coverage is usually limited to drugs or biologicals administered by infusion or injection by a physician. If the injection is generally self-administered, it is typically not covered under Medicare Part B.) Two additional programs have been added to Medicare during the past decade: Medicare Part C (Medicare Advantage), providing beneficiaries with the option of choosing a managed care version of the traditional benefits package with varying degrees of prescription drug coverage; and Medicare Part D, the new prescription drug benefit, for which the Centers for Medicare and Medicaid Services (CMS) pays for the vast majority of the drug costs with the benefit administered by Medicare health maintenance organizations (HMOs) and preferred provider organizations (PPOs) as well as stand-alone drug benefit plans.

A leading cause of concern for the Medicare population is that both Medicare Part B and Medicare Part D are under the umbrella of the Supplemental Medical Insurance (SMI) Trust Fund, and Part D drug plans will be faced with the increasing challenge of assuring access to these medicines while holding cost-sharing amounts and premiums to affordable levels. As in the case of Part B drugs, the federal government has a large stake in the development and access to drugs covered under Part D. The cost of many biologics are likely to exceed the Part D catastrophic benefit threshold (in 2006, \$3,600 in beneficiary out-of-pocket spending or \$5,100 in total covered drug spending). As a result, there is increasing attention to cost-containment and savings maximization within the Medicare program. One market-based approach being considered as an option to maximize savings without imposing some form of governmental price controls is to enable FDA approval of follow-on biologics (FOBs) – including interchangeable and thus competitive biologics products.

The End-Stage Renal Disease (ESRD) Program

Although not limited to seniors, the total cost of Medicare Part B also includes the end-stage renal disease (ESRD) entitlement program costs. The ESRD program pays for dialysis and associated medication costs for greater than 90% of ESRD patients in the United States. Payments to ESRD facilities are made according to composite rates, which represent bundled payments for certain services, products, and drugs, and payment amounts differ based on the specific drug used as well as the site of care. However, some drugs, such as injectables, are not covered by the composite rate and are billed to Medicare separately for payment. The cost of the ESRD program is considered particularly significant in light of the fact that epoetin therapy is the single largest expenditure for the Medicare drug program.²

Recent Congressional attention on the costs of ESRD has been precipitated by concerns of overuse by dialysis facilities. According to Cotter et al, in 2001, 42% of ESRD dialysis patients were over-treated with epoetin therapy, and their hematocrit range exceeded the FDA-recommended target hematocrit range. Various reasons have been suggested for this overuse, such as the liberal epoetin therapy coverage benefit when ESRD facilities have been faced with minimal payment rate changes, along with high volume epoetin therapy usage to balance out decreased coverage benefit.³ As a result, between 2003 and 2004, the per-patient per-month (PPPM) costs for dialysis fell by 2.1 percent, whereas the costs of epoetin therapy,

intravenous iron, and intravenous vitamin D increased between 11 and 13 percent during this same period.⁴

The exact Medicare Part B expenditure attributable to ESRD epoetin therapy is not readily available. Thus, this preliminary assessment has not attempted to project the potential savings that competition could enable for ESRD over the next ten years. However, the United States Renal Data System does provide total Medicare cost as reported for ESRD patients by claim type, and those data suggest the potentially-significant value that could accrue to Medicare through such competition (see Table 1. below).

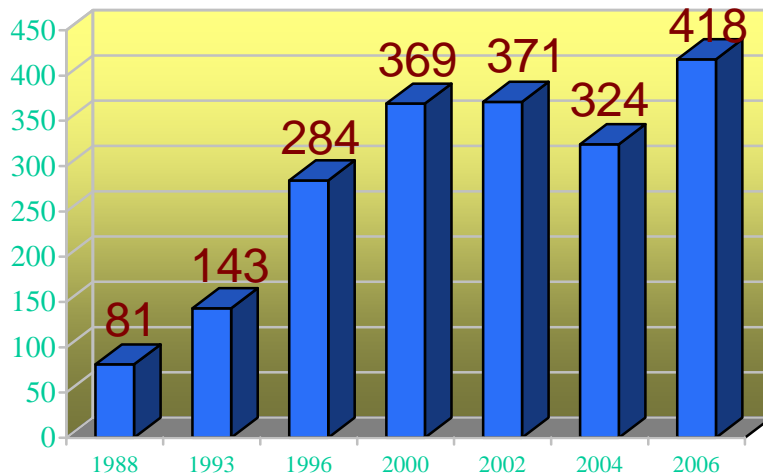
Table 1: Total Medicare Costs (\$) of reported ESRD patients: by claim type			
	2002	2003	2004
Claim Type			
Outpatient ESA*	1,402,748,888	1,558,930,836	1,823,371,054
Physician/Supplier ESA*	3,867,598	11,457,612	10,173,003
Total spent on ESA	1,406,616,486	1,570,388,448	1,833,544,057
Change in Total ESA Cost for Outpatient and Physician/Supplier		163,771,962	263,155,609
Data Source: 2006 Annual Data Report, United States Renal Data System, Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States			
*ESA=Erythropoiesis stimulating agent			

While the calculations in this report do not include any of the epoetin therapy costs which are a part of ESRD spending under Medicare Part B, they do include the cost of epoetin that is administered for other medical purposes as reflected in the top 200 HCPCS for prescription drugs reimbursed under Medicare Part B. Given the significant costs of epoetin therapy in that latter context, it could be anticipated that any discounting of epoetin enabled by competition could significantly affect total spending under the Medicare Part B drug program with such competition producing reductions in both the ESRD and non-ESRD biologics expenditures.

Potential For Achieving Savings Through Establishment Of A FOBs Pathway

In the context of the overall growth of Medicare spending generally and on biologics in particular, it is noteworthy that many more biotechnology medicines are in development than have already been approved (by a factor of approximately three). According to the Pharmaceutical Research and Manufacturers of America (PhRMA), 418 biological products currently are in various stages of clinical trials/development.⁵

Figure 2: Biotechnology Medicines In Development Over Time



* Reference PhRMA

Although none of these, without a new regulatory pathway, could be direct competitors with those already-licensed biologics, insofar as they will not be interchangeable, they can be expected to expand the overall spending on biologics by providing more treatments for more conditions, and perhaps providing better alternatives, or at least greater choices, for conditions that are currently treated but not cured.

Collectively, the top five biologics that already have been licensed by FDA and are marketed in the U.S. account for approximately 30% of Medicare Part B spending:

Table 2: Global Sales for the Top 5 Biotechnology Products

Product	Company	INN	Worldwide Sales (US \$ Billions)
Enbrel	Amgen	Etanercept (fusion protein of antibody-Fc and p75-TNF receptor protein)	3.657
Remicade	J&J	Infliximab, chimeric Mab	3.477
Procrit	J&J *	Erythropoietin Alpha	3.324
Aranesp	Amgen	Darbepoetin Alfa	3.273
Rituxan	Genentech/Roche	Rituximab, humanized Mab	3.154

Source: Info. Service Biotechnology

* Amgen manufactures erythropoietin alpha and markets it in the U.S. under the trade name Epogen for use in kidney failure; the same active ingredient manufactured by Amgen is the active ingredient in the product sold by J&J under the trade name Procrit for use in oncology patients in the U.S. and for all indications ex-U.S. (except China and Japan), and in the product manufactured under license by J&J and sold ex-US only under the trade name Eprex.

Procrit (which Amgen manufactures for J&J, for non-nephrology uses in the U.S., and for all approved uses overseas, but which is indistinguishable from Amgen's own Epogen) and Aranesp account for 17% of Medicare Part B spending alone, Remicade accounts for 5%, and Rituxan consumes 8% of Part B spending.⁶ These percentages can be considered particularly significant on a per patient basis given that the average daily cost of a biologic is over 25 times greater than that of an innovative chemical drug, and the latter is similarly more costly than comparable chemical generic drugs.⁷

In the face of the ever-expanding Federal budgetary expenditures on innovative biotech products, it is noteworthy as Senator Hatch and others have long recognized that there presently is no statutory pathway for follow-on versions of PHS Act biologics (often commonly, but inappropriately, referred to in the vernacular as “biogenerics”). On September 29, 2006, legislation was introduced in the recently-adjourned 109th Congress, H.R. 6257/S. 4016, to establish a new statutory pathway to enable FDA approval of comparable biologic license applications (cBLAs). The legislation establishes science-based criteria to enable data-driven licensing decisions by FDA for follow-on and second-generation biologics. The legislation would achieve this result by allowing FDA to extrapolate from the already-established scientifically-rigorous process (and the Agency's expertise in assessing comparability) to enable approval of such products without the need for repetition of expensive and duplicative clinical trials. The legislation is limited to amending only the Public Health Service (PHS) Act and grants FDA the authority required for the Agency's expert scientific and clinical review staff to review and license cBLAs for biological products that are “comparable” to previously-approved (reference) biological products. In order to be licensed, the bill requires a cBLA sponsor to demonstrate that there are no clinically-meaningful differences between the follow-on and the reference product. The cBLA must also demonstrate that the new product shares the “principal molecular structural features” of the reference product through the newly-defined process of “thorough characterization,” and establish that the products share the same mechanism(s) of action, if known. The bill takes the novel step of adding requirements to the PHS Act in this latter regard, such that a cBLA generally will need to conduct one or more clinical trials (not currently a requirement in the Act) and can be approved on that basis along with the prior finding of safety and effectiveness of the reference product. The legislation would authorize FDA to license a product for *all* conditions of use of the reference product sharing the same mechanism of action for which the cBLA applicant demonstrates comparability for a *single* condition of use, or, in the case of a product with an unknown mechanism of action, for the condition(s) of use for which the data submitted establishes comparability. A cBLA sponsor may elect, but is not required, to establish interchangeability between its follow-on product and the reference product. Interchangeable products can be expected to be the most competitive in the marketplace as a result of enabling automatic substitution at the dispensing level.

II. Actual Baseline Data

This report presents an initial, conservative, and therefore minimal estimate of the potential savings that might be realized by the Medicare program as a result of market-based competition that would flow from adoption of a cBLA pathway such as that proposed in this legislation (which is expected to be reintroduced in the 110th Congress in 2007). In order to calculate a preliminary estimate of those potential savings, historical expenditure data (actual) over the preceding three fiscal years was compiled, and projected expenditures for the Fiscal Year just-completed (FY2006) were calculated based upon governmental projections of estimated spending increases.

For reference and baseline data purposes, Table 3 provides year-by-year actual Medicare Part B, and Top 200 Healthcare Common Procedure Codes (HCPCS) allowed charges for FY2003-FY2005, along with projected estimates for FY2006. This baseline data set has been used to calculate projections of potential savings in Medicare expenditures that might be enabled through marketplace competition by FOBs over the next 10 years.

Table 3: Actual data 2003, 2004, 2005, plus estimated 2006

	FY2003	FY2004	FY2005	FY2006 (estimated)
Total Medicare Expenditure*	\$280,800,000,000	\$308,900,000,000	\$336,400,000,000	\$345,200,000,000
Total Part B Spending	\$126,100,000,000	\$138,300,000,000	\$153,500,000,000	\$161,000,000,000
Total Part B spending on Drugs	\$10,340,000,000	\$10,870,000,000	\$12,900,000,000	\$13,519,200,000
Part B Spending Yearly % Increase (SMI Trustees' Projections)	N/A	9.67%	10.99%	4.8% (estimated and used to calculate the numbers above)
Top 200 HCPCS **	\$22,329,049,436	\$24,550,040,833	\$25,170,131,762	\$26,378,298,086
Biologics in Top 200 (calculated) **	\$3,646,033,737	\$4,475,965,354	\$4,875,303,485	\$5,109,318,052
Biologics as a % \$ Value of Top 200 HCPCS (% by number of products)	16.33% (8.50%)	18.23% (11.00%)	19.37% (12.50%)	19.37% (12.50%)

*2004 Annual Report of the Board of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds, 2005 Annual Report of the Board of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds, and 2006 Annual Report of the Board of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds

**Part B Physician/Supplier Nat'l Data, CY 2003-05 Top 200 Level II Healthcare Common Procedure Coding System (HCPCS/Alpha-Numeric) Codes

III. Data And Tables On Projected Potential Savings

Within the Top 200 HCPCS, covered PHS Act biologics were identified, and, based upon the total dollar value they represent, were calculated as a percentage of the value of the total Top 200 HCPCS, and also were calculated as a percentage of the total number of biologics within the Top 200 HCPCS, for each of the three Fiscal Years (FY2003, FY2004, and FY2005) – the only years for which the data are publicly accessible. Estimated projections were calculated (applying the SMI percentage increases) for FY2006 since the final numbers have yet to be published by CMS.

Data on Medicare projections were available from two different government sources, the SMI Trustees and the Congressional Budget Office (CBO), each of which has generated spending projections applying various conservative economic assumptions that take into account a range of variables that are subject to constant change, *e.g.*, population growth, economic growth, and revenue increases and decreases, to name a few. Because of the availability of both data sets, two sets of calculations were performed to project the minimal estimates of the lower end of the range of potential savings from the cBLA pathway provisions of legislation such as H.R. 6257/S. 4016.

Although much greater savings potentially might be realizable, and indeed are almost inevitable over the long-term, very careful and conservative assumptions were utilized to project the estimate savings forecast based upon this preliminary assessment. Given the myriad of economic and other factors that could impact cBLA development and approval, market entry, and competition, all calculations proceeded from the premise of not overstating the basis of the projected savings in order to ensure the credibility of the resulting estimated projections in this preliminary assessment, such that it could make a useful contribution to the ongoing debate. Thus, multiple factors that reasonably could be expected to substantially increase Medicare costs, and thus potentially inflate the overall savings achieved through cBLA legislation, were excluded. The excluded factors that could reasonably be expected to inflate Medicare costs during the “scored” 10-year projection period and/or to increase Medicare savings during that period, include: FDA licensure of multiple cBLAs and ensuing market entry of multi-source follow-on products competing against the same currently-licensed (reference) biologic; FDA approval of new biologics and CMS coverage of newly-licensed biologics beyond those currently licensed and covered by Medicare; Federal payments for biologics outside of Medicare Part B (under Medicare Part A, Part C, and Part D); and FDA approval of competing next-generation biologics that could displace (at higher or lower costs) biologics currently covered by Medicare. Other legislative provisions, such as the non-patent exclusivity and tax credit provisions of H.R. 6257/S. 4016 also were not factored into the analysis in evaluating potential savings from (or costs of) the legislation. The full set of judicious assumptions underlying these estimates are delineated in the following section.

Table 4a and 4b provide detailed projections of the total potential savings over the course of a standard 10-year scoring projection period estimating savings from FOBs that could be realized by Medicare Part B (only), using both the CBO and SMI projections for increases in Medicare expenditures. The calculations use CBO projections for Medicare spending that take into account

changing Medicare population demographics along with the demographics of those paying Medicare payroll tax and future recessions/economic trends. The estimated impact of cBLA legislation is projected on the basis of anticipated potential biologic drug savings due to competition from a single follow-on product based upon Medicare Part B costs arising from the biologic products that currently are part of the top 200 HCPCS. In order to project the estimated proportion of the currently-approved biologics that could be expected to be off-patent in any given year, given the extraordinarily-limited publicly-accessible information on the critical factor of biologic patent expirations, the patent expiration dates for a standard industry sample of 32 leading biotech products (CuraScript/Pictet) was utilized to calculate the accumulated percentage of off-patent products in that sample annually over the “scored” 10-year period. The resulting annual percentages for that bucket then were applied each year to the entire biologics segment as the only available means by which to gauge the scope of potential off-patent biologics in a given year. Once these percentages of the potentially-off-patent biologics segment were calculated for each year, a conservative, mid-range prospective erosion curve for follow-on penetration developed by Merrill Lynch for epoetin was applied to calculate the estimated projected savings over that same period. The total savings over 10 years was then averaged to calculate an average of the annualized projected amount of savings for each of the 10 years.

Table 4a: Average Savings Projections Using SMI Medicare Expenditure Forecasts

	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	FY2015	FY2016
Total Medicare Expenditure (SMI Trustees' Projections) (Billions)*	\$462.40	\$499.00	\$537.40	\$572.90	\$613.90	\$659.50	\$709.60	\$761.80	\$817.20	n/a
Total Part B Spending ((SMI Trustees' Projections) (Billions)*	\$170.00	\$179.00	\$187.00	\$197.00	\$207.00	\$223.00	\$245.00	\$268.00	n/a	n/a
Part B Spending Yearly % Increase (SMI Trustees' Projections)	5.59%	5.29%	4.46%	5.34%	5.07%	7.72%	9.86%	9.39%	n/a	n/a
% increase in biologics over previous year (using SMI Trustee's projections for all Part B)	5.59%	5.29%	4.46%	5.34%	5.07%	7.72%	9.86%	9.39%	9.39% (assume same as 2014)	9.39% (assume same as 2014)
Estimated cost of biologics in Top 200 HCPCs applying SMI projected % increases (Billions)	\$5.39	\$5.68	\$5.93	\$6.25	\$6.57	\$7.07	\$7.77	\$8.50	\$9.30	\$10.17
% biologics off patent (Using Pictet Biotech Newsletter reported data)**	32%	36%	41%	50%	68%	73%	73%	86%	100%	100%
Value of biologics off-patent (Billions)	\$1.73	\$2.04	\$2.4	\$3.13	\$4.47	\$5.16	\$5.67	\$7.31	\$9.30	\$10.17
% discount of the FOBs (using the Merrill Lynch erosion curve mid-level)***	5%	12%	20%	25%	28%	30%	30%	30%	30%	30%
Estimated Savings to Part B from FOBs (Billions)	\$0.09	\$0.25	\$0.49	\$0.78	\$1.25	\$1.55	\$1.70	\$2.19	\$2.79	\$3.05
Average (over 10 years) per year Savings to Part B from FOBs (Billions)	\$1.41	\$1.41	\$1.41	\$1.41	\$1.41	\$1.41	\$1.41	\$1.41	\$1.41	\$1.41
									Total savings over 10 years (Using SMI estimates) (\$Billions)	\$14.14

Data Sources:

*2004 Annual Report of the Board of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds, 2005 Annual Report of the Board of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds, and 2006 Annual Report of the Board of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds

** CuraScript Specialty Pharmacy Management Guide & Trend Report 2004, citing The Pictet Funds Biotech Newsletter, Pictet Funds, Vol. 3.3, April 2004; CuraScript data

*** Merrill Lynch estimates and Company Data

Table 4b: Average Savings Projections Using CBO Medicare Expenditure Forecasts

	FY2007	FY2008	FY2009	FY2010	FY2011	FY2012	FY2013	FY2014	FY2015	FY2016
Total Part B Spending (CBO Projections) (Billions)*	\$159.40	\$166.60	\$175.90	\$187.70	\$205.90	\$215.90	\$238.70	\$258.90	\$280.60	n/a
Part B Spending Yearly % Increase (CBO Projections)	6.62%	4.51%	5.58%	6.70%	9.69%	4.86%	10.60%	8.46%	8.38%	n/a
% increase in biologics over previous year (using CBO projections for all Part B)	6.62%	4.51%	5.58%	6.70%	9.69%	4.86%	10.60%	8.46%	8.38%	8.38% (assume same as 2015)
Estimated cost of biologics in Top 200 HCPCs applying CBO projected % increases (Billions)	\$5.54	\$5.79	\$6.12	\$6.53	\$7.16	\$7.51	\$8.30	\$9.00	\$9.76	\$10.58
% biologics off patent (Using Pictet Biotech Newsletter reported data)**	32%	36%	41%	50%	68%	73%	73%	86%	100%	100%
Value of biologics off-patent (Billions)	\$1.77	\$2.09	\$2.5	\$3.26	\$4.87	\$5.48	\$6.06	\$7.74	\$9.76	\$10.58
% discount of the FOBs (using the Merrill Lynch erosion curve mid-level)***	5%	12%	20%	25%	28%	30%	30%	30%	30%	30%
Savings to Part B from FOBs (Billions)	\$0.09	\$0.25	\$0.50	\$0.82	\$1.36	\$1.64	\$1.82	\$2.32	\$2.93	\$3.17
Average (over 10 years) per year Savings to Part B from FOBs (Billions)	\$1.49	\$1.49	\$1.49	\$1.49	\$1.49	\$1.49	\$1.49	\$1.49	\$1.49	\$1.49
									Total savings over 10 years (Using CBO estimates) (Billions)	\$14.90

Data Sources:

* CBO's Projections of Medicare Spending for 2005 to 2015

** CuraScript Specialty Pharmacy Management Guide & Trend Report 2004, citing The Pictet Funds Biotech Newsletter, Pictet Funds, Vol. 3.3, April 2004; CuraScript Data.

*** Merrill Lynch estimates and Company Data

A summary of these projections are presented in Table 3, which reflects that the estimated cost-savings applying the CBO’s projections would be on average \$ 1.49 billion per year or \$14.9 billion over the entire 10-year period from FY2007-FY2016, and the estimated savings applying the SMI Trustees’ projection would be on average \$1.41 billion per year or approximately \$14.1 billion over the same 10-year period (FY2007-FY2016). Essentially, as reflected in Table 4a, Table 4b, Table 5, and Figure 3, the projected savings utilizing both the CBO and SMI figures are comparable. As set forth in the introduction to this report, ESRD-related epoetin therapy costs are not included in this preliminary assessment, even though their inclusion could be expected to generate savings greater than the conservative estimations above. Thus, it is anticipated that the estimated potential savings projected in this report do not fully capture the actual savings that could be realized.

Figure 3: Summary of the Projected Cost Savings from FOBs from 2007-2016

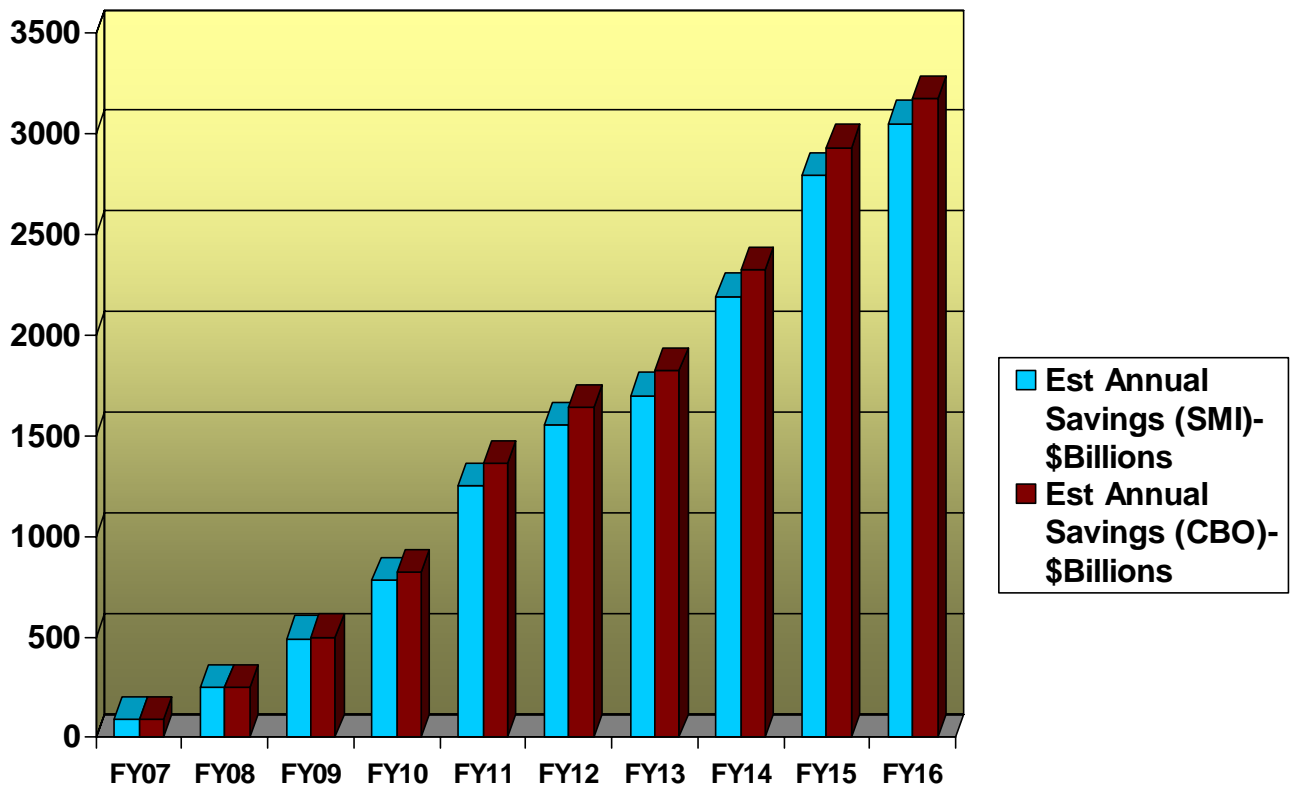


Table 5: Summary Of Total Projected Savings

Projection	Total Projected Savings (US \$ Billions)
Projections Based Upon SMI Trustees’ Spending Estimates	
Total savings over 10 years based on SMI Trustees Projections	\$14.14 Billion
Average Part B per year Savings based on SMI Trustees Projections	\$1.41 Billion/Year
Projections Based Upon CBO’s Spending Estimates	
Total savings over 10 years based on CBO Projections	\$14.90 Billion
Average Part B per year Savings based on CBO Projections	\$1.49 Billion/Year

The following section provides a detailed explanation of the assumptions and methodology used in this preliminary assessment to forecast these conservative estimated ranges of the potential future Medicare Part B savings from cBLA legislation.

IV. Bill Scoring Data Assumptions

All of the data compiled and relied upon in generating this preliminary assessment are publicly accessible through government-issued publications and-or privately-published but accessible data. No data were purchased, no subscription databases were searched, and no third-party contractors were contracted in order to conduct this preliminary assessment. Instead, as an initial step in the process at this stage of the debate, publicly-available data was relied upon in order to roughly gauge the potential for projected savings, recognizing that more elaborate, detailed, and ultimately much more expensive macro- and microeconomic analyses could be conducted for PCMA (and perhaps already are being undertaken for others).

The core of the calculations presented in this preliminary assessment is based upon CMS data for the top 200 HCPCS allowed charges over three years (2003 through 2005) and estimated for 2006 (using the SMI Trustees’ projections). Accordingly, the most commonly-covered biologics, such as Procrit, Aranesp, Remicade, and Rituxin, were captured in the data. Notably, the HCPCS payment lists have not included flu vaccines since 2003. In 2001, flu vaccines constituted 1.2% of Medicare Part B spending;⁸ however, spending on vaccines changes with regards to the cost of the vaccine, which is dependent upon supply and volume of beneficiaries being inoculated, and can be anticipated to have increased in subsequent years but was not available for 2004-2006 (which, if the calculations were adjusted to include flu vaccines, would increase projected expenditures and thus projected savings). Furthermore, as indicated above, calculations were based only on currently-licensed PHS Act biologics marketed in the U.S. and

covered by Medicare as of 2005, and not those products often referred to as biologic drugs approved under the Food Drug and Cosmetic Act (FD&C Act), such as insulin, hyaluronidase, human growth hormone, and enoxaparin. The projections do not attempt to include the anticipated additional expenditures that will be made by Medicare in covering new innovative PHS Act biologics that can be expected to be approved by FDA and covered by CMS between 2006 and 2016. In sum, the potential savings are derived from historical and estimated current payments for only a subset of all the biologics presently covered by Medicare Part B.

For the covered subset of currently-marketed biologics included in the calculations, the projected patent expirations were derived by applying the patent expiration dates reported by the Pictet Funds Biotech Newsletter (April 2004), which were calculated as a percentage of that sample reported to be off-patent in any given year, which percentages were then extrapolated to all biologics (beginning with 32% in 2007). According to those projections using the sample assembled in the Pictet Funds data, 100% of the currently-available biologics would be off-patent by 2015. Due to the inherent challenges in evaluating the often-patent-stacked patent estates claiming biologics, and the resulting patent terms, the calculations have not been adjusted to factor in specific patent expiries for specific products, or to factor in potential at-risk launches that individual follow-on sponsors (from the innovator or generic industries) might elect to pursue or any of the resulting patent-infringement litigation.

As currently-available biological products are going off-patent, some biologics are being replaced by more expensive next-generation biologics and switching/substitution is occurring in the Medicare-covered populations. For example, the introduction of Aranesp has displaced Amgen's first-generation epoetin product, Epogen, which is an anticipatable outcome as Aranesp does offer the advantage of less frequent injections to patients for the same clinical outcome. If FOBs are an option to fill the natural gap following expiration of patents on currently-marketed first-generation products, then an opportunity would be created for market entry and competition for these products, albeit with a follow-on product developmental lag time anticipated to range from 2-5 years. Increased competition for follow-on products to first-generation biologics would be anticipated to create a pressure to reduce the cost of these products, thereby producing a positive cost disparity between the first and subsequent generations of biologic products that does not presently occur, thereby potentially enabling increased savings as well as producing incentives for further innovation. However, any projections on the developmental lag time for FOBs can also reasonably assume that a number of both innovator and generic manufacturers (including contract manufacturers) presently have excess capacity that can be used to produce FOBs and thereby reduce the lag time to market. As production technology advances, manufacturers may increasingly be able to buy intermediate materials for their products instead of having to start with basic raw materials. This may further increase productivity by maximizing production efficiency, which could also lessen the time to market and increase patient access. New generic or follow-on entrants are more likely to, and indeed are expected to, utilize state-of-the-art technology as well as tighter parameters to define their products – the latter of which follow-on sponsors would need to do for regulatory reasons if they were to have the opportunity to seek an FDA designation of interchangeability for their products. Greater production efficiency, gained from technological advances, can be expected to enhance the quality and reduce the cost of goods as a result of lower production costs, which should be passed on to the healthcare system and can be anticipated to become an important part of

negotiations with payors, including CMS. The estimates resulting from this preliminary assessment and presented in this report, however, do not attempt to account for those increased efficiencies or the enhanced competition and savings that are expected to result. Instead, the projections assume a single cBLA and single follow-on competitor over the ten-year period. Thus, again, the numbers projected are conservative in the estimated savings that they anticipate could be realized by the Medicare program.

In the generic chemical drug segment, market entry of generics typically generates savings that can range from 60-90%. However, there are indisputable differences between the chemical and biologics industries, such as average complexity and cost of manufacturing, which in some cases potentially could impact market entry and ensuing marketplace discounting. The only available example for projecting potential savings from a follow-on biologic is Omnitrope, which has been reported as being launched overseas at a discount of 25%. However, most market analysts have projected the range of discounts from FOBs to fall between 25-40%. Given these data points, all calculations were based on estimates of savings to be realized over time from a single follow-on product's entry into the biologics market. The prospect of multiple market entrants, and the savings that could be triggered by multiple competitors triggering "most-favored nation" clauses and comparable discounting mechanisms, have not been calculated, despite the established evidence from the generic drugs segment that savings increase as the number of subsequent competitors increase within a disease/drug category. The erosion curve used in this study is one that was developed by Merrill Lynch (ML) based on an estimated mid-range case "biogeneric" risk rating as applied to company data for Epogen.⁹

Currently, the PHS Act does not authorize FDA approval of interchangeable FOBs. Legislation that creates a cBLA PHS Act pathway can be expected to not only increase competition within the biological product segment, but also can be expected to support FDA's already existing legal authority to increase the number of approvals of substitutable biologic drugs under the FD&C Act, such as insulin, human growth hormone, hyaluronidase, enoxaparin, etc., based upon applications submitted as abbreviated new drug applications (ANDAs) and Section 505(b)(2) NDAs. As a result of those biologic drug approvals – which will result in further competition for other biotech medicines covered by Medicare – enactment of cBLA legislation and development of FOBs can be expected to increase competition across the entire biologics segment. In addition, to the extent cBLA legislation reinforces FDA's application of robust comparability principles, the legislation could reduce regulatory burdens across the breadth of the industry – innovator and follow-on alike – and thereby enable greater product price elasticity in the marketplace. The estimates in this report do not attempt to take into account the potential savings that could result from these factors, but they could be significant for all sponsors of future biologics and for the Medicare programs covering those sponsors' products.

Similarly, potential Medicare savings from cBLA legislation and FOBs could be impacted by Europe's approval of biosimilars – the term the EU applies to FOBs. Europe has an established biosimilar pathway, has approved biosimilar hGH, and is preparing to approve biosimilar versions of insulin, G-CSF, and EPO, which are expected to be going off-patent in Europe much earlier than in the U.S. European data related to production, post-marketing issues, and adverse events can be expected to be used as appropriate by cBLA sponsors in the U.S. to optimize

FOB development and marketing plans, and some of those biosimilars potentially may be exported to the U.S. under the newly-revised DHS/FDA personal importation policies. This is due to the fact that manufacturers of biologics are increasingly global in their marketing and, to do so, have been supporting standardization of regulations across the principle markets. The International Committee on Harmonization (ICH) has led the efforts of both the industry and regulatory authorities in the EU, U.S., and Japan to standardize filing requirements to the best extent possible, thereby removing the disparate and often-superfluous or repetitive requirements that currently inhibit the easy flow of information and products through the approval process of each jurisdiction's regulatory authority, thereby further streamlining the efficiencies for the sponsors of the products in each of these regions. Any efforts to enable the approval of FOBs in any of the other principle markets thus can be expected to have an impact on the product filings, and therefore approvals, in the U.S. Once again, potential competition and savings resulting from these on-going international initiatives have not been factored into the projected estimates captured in this report.

V. Policy Implications:

With Medicare Part B costs generally, prescription medicines costs as a whole, and biologics costs in particular increasingly running disproportionately to Medicare funding, cBLA legislation offers the opportunity for enactment of a market-based mechanism to manage Federal budgetary expenditures by maximizing efficiency of the biologics segment with respect to R&D, licensure, manufacturing, and competition. When more than one biologic is available in the market (let alone more than two – the innovator and a single FOB), and approval of interchangeable FOBs is enabled, market forces will increase competition as well as incentives for reduced costs of goods, and these should be translated into savings across the health-care system. This report presents the results of a preliminary assessment that estimates the potential savings that might be realized by the nation's largest payor, Medicare, without attempting to estimate savings that might be realized by any other segment of the health-care system. Even though the health care market is not perfect and there will always be some aspects of it that are not conducive to regulation, legislation that provides a pathway for interchangeable FOBs and fosters robust, science-based comparability assessments will enhance market efficiency and lower costs through multiple products and marketplace competition.

In addition to such legislation alleviating some of the principle constraints on FDA and the biopharmaceuticals industry that have resulted in the premium pricing of biotechnology medicines by increasing efficiency of regulation, related reforms involving the practice of medicine potentially could enhance those efficiencies further. Through programs such as AHRQ's Evidence Based Practice reports and US Preventive Services Task Force (USPSTF) recommendations/practice guidelines, efficiencies concerning the optimal and appropriate use of biotechnology medicines would add value to their availability for individuals and society as a whole and thereby could foster even greater cumulative savings. However, in considering such reforms, Congress must remain cognizant of the reality that the practice of medicine is dependent on both physician and patient behavior – modification of which would itself present unique challenges (the implications of which are outside the scope of this report).

References

¹ Source: IMS Health Total Market Estimates and Global Pharma Forecasts (includes IMS Audited and Unaudited Markets) (Information Current As of Feb 27, 2006) (available at http://imshealth.com/ims/portal/front/articleC/0,2777,6599_77478579_77478598,00.html); 2004 Year In Review, Trends, Issues and Forecasts, Presented by Doug Long, IMS.

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³ Ibid.

⁴ 2006 Annual Data Report, Atlas of Chronic Kidney Disease & End-Stage Renal Disease in the United States, United States Renal Data System.

⁵ Biotechnology Medicines in Development, 2006 Report, Pharmaceutical Research and Manufacturers of America (PhRMA).

⁶ Herb B. Kuhn, Director, Centers for Medicare and Medicaid Services (CMS), Testimony before the Subcommittee on Health of the House Committee on Ways and Means, July 13, 2006.

⁷ DGA Spring Policy Conference – Medicaid (April 2, 2005), Presentation by Bruce Lott, Senior Director of State Affairs, Generic Pharmaceutical Association.

⁸ MedPac Report to Congress. Chapter 9: Medicare payments for outpatient drugs under part B. Variation and Innovation in Medicare, June 2003.

⁹ Merrill Lynch biogeneric risk estimates and Company Data.