

**Comments of Knowledge Ecology International (KEI)
on the December 2015 U.S. Senate Finance Committee report: “The Price of Sovaldi and
Its Impact on the U.S. Health Care System”**

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To: Report_Feedback@finance.senate.gov

I. What is the appropriate price for a drug protected by a patent or another exclusive right?

Once a drug is subject to competition, and no longer protected by a patents, patent extensions, pediatric extensions, orphan drug exclusivity, test data exclusivity or other legal barriers to entry by generic or biosimilar products, the private sector and the government have the possibility of using good procurement practices to obtain affordable prices. But during the period when the product is sold as a monopoly, there is no expectation that prices can be described as affordable or reasonable. Companies charge what the market will bear, and do their own math, looking at demand elasticities to maximize profits, normally at prices are above marginal costs.

If governments want to challenge the prices offered by the companies, it would be helpful to have a clear set of objectives.

There is renewed interest in value based pricing. While there are good reasons to think harder about the value of drugs, as measured by health outcomes, other factors are also important, and here is a quick review of some relevant issues.

1. **Measurement is hard.** The challenges of measuring health outcomes are well known, if sometimes under appreciated. That said, measurement of benefits is going to be part of any system involving third party payers, and it does not have to be perfect.¹
2. **Heterogeneous values.** The same drug can have a different value for different patients. For example, for the HCV market, the “value” of treating patients in HCV depend upon an assessment of a patient’s health. A relatively small number of persons who are infected have stage 3 or 4 liver damage, and the value of treating these patients is higher than for patients who may clear HCV without treatment, or for which the disease is progressing so slow it may not impact life expectancy. But all persons infected with HCV would be targets for treatment if prices were not an issue.² New cancer drugs are so expensive it is difficult to obtain authorization from reimbursement authorities for

¹ 2014. Narmeen Haider, Aidan Hollis, James Love. "Delinkage Proposals and the Measurement of Health Benefits." Whittier Law Review, Volume 25, Number 3, Spring 2014.

² "Discussion paper: An economic perspective on delinking the cost of R&D from the price of medicines." UNITAID. February 2016.

off-label use. Some patients respond better (or worse) than others to particular drugs, and the perceived value of the median patient can reduce treatment options for patients who would otherwise benefit.

3. **Size of the market.** Sofosbuvir/Sovaldi illustrates a flaw with an approach that focuses only on health outcomes, but does not address the size of the market. According to the CDC, There are 2.5 million to 4.7 million persons infected with HCV in the United States.³ The Fabry disease gene is carried by perhaps 11 thousand persons. The lives of patients suffering from both diseases are equal in one sense, but the costs and consequences for society of providing drugs to both groups is not the same. We tolerate relatively high prices for drugs for rare diseases on the grounds that as a society, we don't want to only take care of people with the most common diseases. On the other hand, drug companies use the high prices for rare diseases as leverage to argue for higher prices for diseases that have a high incidence. If a small number of patients warrants higher prices, why don't larger numbers of patients (HCV, Herceptin, etc) merit lower prices?
4. **Budget are important.** It's one thing to say that a drug has a value of \$X, and another thing to pay \$X for everyone who need the drug. When the cost of buying drugs strains or exceeds the budget constraint, the consequences can be various forms of rationing, including restrictive formularies, complicated paperwork, delays in access, increased co-payments or no reimbursements. When the Department of Veterans Affairs ran out of money to pay for HCV drugs, they restricted access until they received new spending authority from the Congress. If the "value" of a treatment was arrived in the context of a realistic budget constraint, such restrictions on access can be avoided.⁴
5. **R&D costs are important.** In the discussion above about the size of the market, there is an understanding that we accept higher prices for rare disease because of an implicit model of drug development costs. We assume that the fixed costs of drug development are high, and that prices need to be higher when there are fewer patients to defray the costs. There is also evidence that R&D costs vary considerably between different types of drugs. One element of this evidence concerns the large differences and skewed distribution of the size of clinical trials. In 2010, for example, one drug, Carbaglu, was approved on the basis of evidence from just 30 patients, while the Pradaxa review involved tens of thousands of patients. As a group, oncology drugs were approved using trials that were 27 percent of the size of drugs for other illnesses, according to one analysis.⁵ In some cases, government agencies or tax exempt charities subsidize R&D costs, including, for example the Congressional appropriations to the Army that

³ <http://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#a5>

⁴ For a discussion of a recent Senate proposal to protect veterans, see: <https://www.youtube.com/watch?v=xAY4Ua7B2mQ>

⁵ "The Size of Trials cited in FDA medical reviews for the lead indication of new drugs, 2010 to 2014," *forthcoming*. The 27 percent number is subject to revision pending final reviews of the data.

subsidize prostate cancer trials, the extensive VA CRADAs for HCV drugs, or countless other grant programs in the NIH, other federal agencies, state and local governments, governments outside of the United States, and tax expenditures, such as the U.S. Orphan Drug Tax Credit. The Orphan Drug Tax Credit does not receive enough attention. It is a 50 percent subsidy for qualifying clinical trial costs, and 47 percent of new drug approvals in 2015 qualified for the credit.⁶

Drug prices that advance national objectives.

If the United States was not committed to medical innovation, it would simply push for very low drug prices and eliminate as many legal monopolies as possible. This is clearly not the case. The United States has strong political commitments to stimulate R&D on new drugs, and this includes billions of dollars in research grants, research contracts, and subsidies, tax expenditures such as the Orphan Drug Tax Credit, and a plethora of intellectual property and regulatory policies that create and extend monopolies for new products as a reward for the development of new products. The costs of these programs are high, and particularly high for drugs like sofosbuvir that enjoy legal monopolies. But with an aging population, slow rates of economic growth, exploding drug prices and weakened international competitiveness, it is now time for reforms.

It is useful to think about drug prices on patented drugs as mechanism to pay for R&D, and in particular, for the clinical development of products. High prices play a positive role in stimulating R&D, but a negative role in terms of limiting access, and imposing financial hardships on taxpayers, patients and employers. When resources are limited, prices cannot be unlimited, without having harsh consequences for access.

Drug prices could be set to be as consistent as possible with the following simplified and stylized objectives:

Objectives

1. Prices should be high enough to induce innovation in areas where innovation is desired, including for rare diseases,
2. Prices should not distort medical decisions or restrict access,
3. The cost of buying drugs should not exceed budget constraints,
4. Within a given budget constraint, prices should optimize desired innovation.

⁶ Novel Drugs Summary 2015, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, January 2016..

This list could be expanded, but it can also be the basis of models of drug pricing, including this fairly crude but reasonable one.⁷

Pricing Model

1. For products that have roughly the same value of patients to individuals, have higher prices for products with fewer patients and lower prices for products with larger numbers of patients.
2. Given (continually revised) estimates of the cost functions of drug development for different diseases and conditions, set prices to maximize the expected number of new products, taking into account the expected costs and risks at each stage of development, the premium placed on developing drugs that improve outcomes and address gaps in treatment, or address health care needs that are particularly costly or otherwise deemed important.
3. Eliminate cost-based formularies for treatment, but require rebates from drug manufactures when total system costs exceed target budgets, in order to hold total costs constant, regardless of the product mixes.
4. When drugs earn excessive cumulative returns, such as Herceptin (cumulative \$60+ billion) or Harvoni (\$2b+ per month), lower prices or eliminate monopolies through compulsory licenses or by terminating non-patent exclusive rights. Since the overall revenue is held constant by the rebates, lowering prices for the super-blockbuster drugs frees up resources for the other incentives/rewards to be given to other products).

Ultimately the rewards for R&D are much easier to manage and make optimal when the rewards for successful R&D efforts are fully delinked from product prices, and I am attaching also some citations discussing delinkage alternatives,⁸ as well as four proposals submitted to the UN Secretary General High Level Panel on Access to Medicines on February 28, 2016.

⁷ Following the approach described here: James Love, "Talking Drug Prices, Pt 4 Drug pricing is out of control, what should be done?", PLOS Blogs. October 19, 2015.

⁸ "Discussion paper: An economic perspective on delinking the cost of R&D from the price of medicines." UNITAID. February 2016; Alternatives to the Patent System that are used to Support R&D Efforts, Including both Push and Pull Mechanisms, with a Special Focus on Innovation-Inducement Prizes and Open Source Development Models, World Intellectual Property Organization, CDIP/14/INF/12, September 19.; Narmeen Haider, Aidan Hollis, James Love. "Delinkage Proposals and the Measurement of Health Benefits." Whittier Law Review, Volume 25, Number 3, Spring 2014; Testimony of James Packard Love. "The de-linkage of R&D costs and drug prices through the Prize Fund for HIV/AIDS will cost less, expand access, accelerate and improve innovation, and replace an incentive system that is expensive, inefficient and unsustainable." Hearing before the United States Senate, Committee on Health, Education, Labor and Pensions, Subcommittee on Primary Health and Agency on The High Cost of High Prices for HIV/AIDS Drugs and the Prize Fund Alternative, May 15, 2012, Washington, DC; James Love and Tim Hubbard, "Prizes for Innovation of New Medicines and Vaccines," Annals of Health Law, Vol. 18, No 2, pages 155-186, Summer.

1. "The Need for Global Negotiations on Agreements to Fund R&D within the Context of a Progressive De-linking of R&D Costs from Product Prices". Supported by 12 organizations; 1 individual; 3 Members of European Parliament.
2. "Increasing the Transparency of Markets for Drugs, Vaccines, Diagnostics and other Medical Technologies". Supported by 17 organizations; 2 individuals; 3 Members of European Parliament.
3. "The Role of R&D Subsidies for Clinical Trials in Progressive Delinkage of R&D Costs from Product Prices"
4. "Trade Agreements and the Supply of Public Goods"

(Copies here: <http://www.keionline.org/node/2431>)

II. "What tools exist, or should exist, to address the impact of high cost drugs and corresponding access restrictions, particularly on low-income populations and state Medicaid programs?"

Compulsory licensing

Compulsory licensing of patents and other exclusive rights, including as a threat, is the most important mechanism to provide leverage on drug prices. This is not well implemented in US law at present, although it does exist to some extent for certain government funded drugs.

There is a general government use statute, 28 USC 1498(a), but it suffers from risks associated with the open ended compensation required for non-voluntary use of patents.

The Xtandi petition

We call attention to the petition recently filed by Knowledge Ecology International (KEI) and the Union for Affordable Cancer Treatment (UACT) asking the agencies to use their "march-in rights" authority (35 U.S.C. § 203) or royalty-free rights in patents (35 U.S.C. § 202(c)(4)⁹) for the three Orange Book patents on the prostate cancer drug Xtandi. (See: <http://keionline.org/xtandi>)

Xtandi was developed at UCLA with the support of grants from the NIH and the U.S. Army. UCLA licensed the patents on the drug to Astellas Pharma, a Japanese drug company. The

⁹ "(4) With respect to any invention in which the contractor elects rights, the Federal agency shall have a nonexclusive, nontransferrable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any subject invention throughout the world: Provided, That the funding agreement may provide for such additional rights, including the right to assign or have assigned foreign patent rights in the subject invention, as are determined by the agency as necessary for meeting the obligations of the United States under any treaty, international agreement, arrangement of cooperation, memorandum of understanding, or similar arrangement, including military agreement relating to weapons development and production."

price for Xtandi is \$129,000 per patient per year in the United States, and two to four times higher in the United States than other high-income, high-GDP countries.

Below is a table, from the KEI/UACT petition, that compares the prices of Xtandi in the United States and 13 other high-income, high-GDP countries:

Prices for Xtandi 40mg capsule/tabs, in the United States and 13 high income countries.

Country	Price per unit, national currency		EX Rate (Jan. 6, 2016)	Price per unit, USD	Percent of 2015 AWP	2014, GNI Per Capita, Atlas Method, USD
USA, April 2015 AWP	88.48	USD	1	\$88.48	100%	\$55,200
USA, 2014 Medicare	69.41	USD	1	\$69.41	78%	\$55,200
Australia	33.04	AUD	0.71	\$23.46	27%	\$64,540
Belgium	29.15	EUR	1.08	\$31.48	36%	\$47,260
Canada, Quebec	28.35	CAN	0.71	\$20.12	23%	\$51,630
France	24.75	EUR	1.08	\$26.73	30%	\$42,960
Germany, public insurance	34.19	EUR	1.08	\$36.93	42%	\$47,640
Italy, procurement price	24.08	EUR	1.08	\$26.01	29%	\$34,270
Japan	3,138.80	Yen	0.0084	\$26.37	30%	\$42,000
The Netherlands	29.15	EUR	1.08	\$31.48	36%	\$51,890
Norway	294.78	NOK	0.11	\$32.43	37%	\$103,630
Spain	29.98	EUR	1.08	\$32.38	37%	\$29,440
Sweden	224.705	SEK	.12	\$26.96	30%	\$61,610
Switzerland	35.82	CHF	0.99	\$35.46	40%	\$88,120*
UK	24.42	GBP	1.46	\$35.65	40%	\$43,430

*Only 2013 was available for Switzerland.

Sanders’ proposal for Veterans

Senator Bernie Sanders proposed legislation as an amendment to “Subchapter II of chapter 73 of title 38, United States Code,” on July 22, 2015, that would allow the Secretary of Veterans Affairs to determine that the price of a particular drug or medical technology was excessive, and then set a “reasonable and affordable royalty” on the use of the patents that would be paid as compensation to the patent holder.¹⁰ (Senator Sanders withdrew the amendment shortly

¹⁰ More information available at: <http://keionline.org/node/2290>.

thereafter, pending discussion with other members of the Committee, and a promise of a hearing on the proposal.)

This legislation was proposed in response to the inability of the Department of Veterans Affairs to afford the price of new HCV treatments, and in particular Sovaldi and Harvoni. Senator Sanders proposed the legislation after the VA declined to use its authority under 28 USC 1498 to issue compulsory licenses for “government use” (by or for the federal government) of the patents on Gilead’s HCV drugs, citing concerns over the uncertainty of the compensation that would be required under 28 U.S.C. 1498(a).

Sanders proposed a method for determining compensation, for the Department of Veterans Affairs, when high prices prevented access to medicines.

The proposed legislation would allow the Secretary to “determine that the price of a medical technology is excessive or presents a barrier to care” if:

“(1) the price of the technology is the primary factor prohibiting the Secretary from being able to provide access to the technology to all veterans for whom the technology is considered clinically appropriate; and

(2) there is no comparable and equally efficacious technology available to the Department at a reasonable and affordable price.”

In setting a “reasonable and affordable royalty,” the Secretary would be required to consider the budgetary constraints of the Department of Veterans Affairs, the expected recoupment of R&D costs by the patent holder, and other appropriate factors, such as the health impact of the product on patients:

“(c) REASONABLE AND AFFORDABLE ROYALTY.—In determining a reasonable and affordable royalty under subsection (a), the Secretary shall consider the following:

(1) The impact of paying the royalty on the budget of the Department for providing hospital care and medical services to veterans under chapter 17 of this title.

(2) The extent to which the owner of the patented invention has recovered or is expected to recover, through sales other than under this section, the research and development costs incurred by such owner.

(3) Such other factors as the Secretary considers appropriate, including the impact of the patented invention on improving health outcomes for individuals.”

When some members of the Senate Committee on Veteran's Affairs questioned the constitutionality of the proposal to limit the compensation of patent holders, KEI created an informational video describing the history of U.S. jurisprudence and legislation concerning sovereign immunity and the government's rights to use patented inventions, available here: <http://keionline.org/node/2324>.

III. Transparency

See: "Increasing the Transparency of Markets for Drugs, Vaccines, Diagnostics and other Medical Technologies." February 28, 2016. <http://www.keionline.org/node/2431>

Additional information:

James Love, "Talking Drug Prices, Pt 4 [Drug pricing is out of control, what should be done?](#)", *PLOS Blogs*. October 19, 2015.