To: Members of Congress
From: Knowledge Ecology International
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Re: Measures to cap price increases on prescription drugs and to enhance the transparency of R&D costs.

Knowledge Ecology International (KEI) offers the following comments on H.R.2113 - Prescription Drug STAR Act,[1] as well as H.R. 1093, the Stop Price Gouging Act,[2] and H.R.2296, the FAIR Drug Pricing Act of 2019.[3]

Specifically, our comments concern two issues addressed in various bills: (1) the regulation of price increases for drugs on the market, and (2) the obligations on drug manufacturers to provide disclosures of the factors that are relevant to the price of a drug.

(1) Regulation of price increases for drugs on the market.

In the current version of H.R. 2113, a company is free to increase the price of a prescription drug, so long as the company provides a justification for the increase, when the increase exceeds certain thresholds. The thresholds are a combination of the annual cost of the drug and a high percent increase in the price.

We would prefer a simpler system, similar to that proposed in H.R. 1093 and used in several other countries, which limits the increases in the price to the general rate of inflation. Exceptions to the limits could be permitted, but only with the approval of the Secretary of Health and Human Services (HHS), based upon a compelling and legitimate justification.

These are some international examples of caps on price increases.

[1] https://www.congress.gov/bill/116th-congress/house-bill/2113/text
[2] https://www.congress.gov/bill/116th-congress/house-bill/1093/text
[3] https://www.congress.gov/bill/116th-congress/house-bill/2296//text

- **Australia.** Price increases are not permitted in Australia, annual or otherwise, other than in exceptional circumstances, such as large exchange rate movements. Moreover, prices of patented products undergo statutory reductions at 5 year intervals.[4]
- **Canada.**[5] The price of a patented medicine is not permitted to increase more than the increase in the Consumer Price Index (CPI).
- **Germany.**[6] From the 2018 OECD report on drug pricing: "Legislation also prohibits price increases, in that it requires manufacturers to grant a rebate equalling any price increase versus prices on 1 August 2009. The latter regulation, referred to as 'price moratorium' was extended through 2022, subject to an adjustment for inflation as of 2018, in the 2017 law strengthening the pharmaceutical supply (Gesetz zur Stärkung der Arzneimittelversorgung – AMVSG)."
- **France.** Manufacturers are not allowed to increase prices of medicines whose prices are regulated (e.g. medicines dispensed to outpatients or medicines paid on top of DRG-payments in hospitals) unless they can justify the need to increase prices.
- **United Kingdom.** Price increases are not allowed in the UK post launch unless "modulated" by reductions in prices of other drugs in a company's portfolio that render the change cost neutral. Price increases are allowed but only after a Health Technology Assessment, however no company has used this option to justify a price increase.

It should be noted that the United States is an outlier regarding the freedom to increase prices beyond the general rate of inflation[7].

The international experiences cited above generally extend these controls on price increases to some but not all drugs. The situation in the United States has a number of differences in the way the drug prices are negotiated due to the multitude of

[4] National Health Act 1953, No. 95, 1953, Compilation No. 128, Includes amendments up to: Act No. 64, 2018, This compilation includes commenced amendments made by Act No. 1, 2018. See, for example, see Subdivision D—Other statutory price reductions.
[5] Canada, PMPRB, FAQ: http://www.pmprb-cepmb.gc.ca/about-us/frequently-asked-questions.
[6] Martin Wenzl and Valérie Paris, Pharmaceutical Reimbursement and Pricing in Germany, OECD. June 2018, http://www.oecd.org/els/health-systems/Pharmaceutical-Reimbursement-and-Pricing-in-Germany.pdf
[7] See, for example, Figure 1.9, page 48: OECD (2018), Pharmaceutical Innovation and Access to Medicines, OECD Health Policy Studies, OECD Publishing, Paris. https://doi.org/10.1787/9789264307391-en

buyers/reimbursement entities. The Wholesale Acquisition Cost (WAC) does seem like a manageable and useful metric for prices.

In order to enforce a ceiling on price increases, the government could impose fines on companies (the approach in H.R. 1093), mandate rebates (as in Germany) and/or terminate or shrink the term of patent or regulatory exclusivities (as in H.R.1188/ S.366, bills that would shrink the term of regulatory exclusivities).

One option the Congress should consider is progressive decreases in prices for products or services (like CAR T) if, over time, global revenues exceed benchmarks.

A number of drugs for rare diseases charge very high prices. The high prices are tolerated and accepted, based upon the notion that the small number of patients justifies an extraordinary price and reimbursement. However, when a government-funded drug like Spinraza generates $1.7 billion per year, or Solaris earns $3.6 billion in one year and more than $20 billion since introduction, price reductions are in order. Likewise, when a product for a non-rare disease generates extraordinary revenues, it also places enormous stress on health care budgets, and prices could be lowered in order to curb excessive returns.

By looking at annual and cumulative global sales over time, policy makers could target pricing interventions when returns are excessive, or when extraordinary prices are no longer justified.

If Congress believes that curbing excessive returns or excessive prices will harm innovation, it can address this issue by instituting such measures as increasing the NIH research budget, restoring the 50 percent Orphan Drug Tax Credit for clinical trials, or compensating with cash market entry rewards, all at a lower cost than retaining unfettered pricing. And this is an important point. Measures that lower prices can be combined with measures that progressively de-link R&D financing from prices, protecting both innovation and affordability, while saving money.

(2) Obligations on drug manufacturers to provide disclosures of the factors that are relevant to the price of a drug.

The extensive provisions on transparency in H.R. 2113 (the STAR Act) appear useful, but are flawed for the following reasons: (1) like several other bills, the disclosures are only triggered by price increases, (2) the company is allowed to choose the items to be

disclosed, and (3) it appears as though the company itself provides a summary, which is all that the public will see. This is weak, and merely gives the appearance of transparency, rather than the real thing.

Several other bills, including for example H.R.2296 (the FAIR Drug Pricing Act of 2019), do make reporting mandatory and public, subject to exceptions for confidential commercial information and trade secrets.

KEI, like many others, favors greater transparency. The extensive list of disclosures in several bills (such as H.R. 2296) include items of considerable interest to researchers and policy makers.

We have views on what we think are core items for reporting for any regulated drug, vaccine, or cell- or gene-based therapies, such as CAR T, and the challenge is to anticipate all of the situations where such information would be useful.

Without weighing in on every item in each bill, we can offer what we think would be the most useful disclosures, for any fundamental reform of the pricing and incentive systems.

Revenues. Sales figures for many drugs are public, particularly for the best selling products. Having annual reports on the sales of every single regulated drug, vaccine, cell- or gene-based therapy, would be a useful requirement. While annual sales data are generally available for best selling products, having more complete reporting will permit policy makers and researchers to undertake a number of important analyses. For example, how do revenues change when companies obtain additional FDA indications for existing drugs, or how large a revenue stream is really necessary to motivate a company to conduct clinical trials and seek FDA marketing approval? Knowing what happens for every product or procedure is more useful than only having data on the best selling ones.

Units. Knowing more about the number of units sold is important, and is something that is generally known to large companies that can afford to purchase the expensive reports from IQVIA.[8] This data should be public, and available to everyone.

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[8] https://www.iqvia.com/locations/united-states/commercial-operations/essential-information/sales-information

Geographic segments. At a minimum, data on sales and units should be broken down by the U.S. and the rest of the world, but more detailed disaggregating would be even more useful. If one is concerned about access in developing countries, having sales and unit data for developing countries will reveal a good deal about the vast inequalities of access to many important treatments.

Research and Development Costs. The only reason to grant monopolies and endure high prices is to reward investments in successful research and development. That said, governments do not have useful information on R&D spending by companies. Several bills have been proposed that would require disclosures of R&D outlays relating to specific products.

Clinical trial costs. In our view, the initial focus on disclosure should be on the costs of clinical trials, and in particular, the costs of each trial separately.

Clinical trial costs are the largest element of R&D costs, and they can be directly attributed to specific products or services.

If Congress wanted to only require that some trials be reported, it could limit the disclosure to trials used to obtain regulatory approval. Having all trials reported would be better, and it is hard to know why this is not done already. The key input in a trial is a patient who puts their own health at risk to test a new medical technology. The NIH has a registry for clinical trials, which companies are encouraged to use, that has several different fields, including one identifying who sponsors the trial and another to indicate whether "industry," the NIH or another group funded the trial, but there is no disclosure of the actual costs of the trial.

Having trial costs for each individual trial is quite important. The risks of trials differ considerably by phase. Estimates of capital costs depend upon when trial costs are incurred. The various subsidies such as the Orphan Drug Tax Credit or NIH or BARDA grants are available to some trials but not others. All of these factors explain why breaking out costs by trial is important.

Having costs disaggregated by trial is essential for providing estimates of development costs that can be adjusted for risks and other factors, using data on trial failure/success rates by phase, which is available now, and fairly transparent.[9]

[9] PhRMA claims that overall success rate of drugs entering clinical testing (Phase 1) is about 12 percent, and that number is not particularly controversial. The growing transparency of which trials are undertaken makes it possible to make estimates and reach reasonable consensus on the trial success and failure

Preclinical costs. In contrast to the clinical trial costs, pre-clinical costs are notoriously difficult to assign to specific products or services. The role of the public sector is also considerably more important for preclinical research. Industry studies, such as those by Joseph DiMasi of Tufts University and his colleagues, do not even bother to use project level data for preclinical costs, using instead a hypothetical fixed relationship between clinical and preclinical outlays, based upon aggregate data from PhRMA's annual industry survey, which is proprietary and not transparent.

PhRMA often presents data-free and stylized estimates of the risks associated with private sector investments in preclinical research. In a recent pamphlet on R&D, PhRMA described the preclinical stage of research as something involving "thousands and sometimes millions of compounds that may be screened and assessed early in the R&D process. as well as other activities.[10]

Sometimes overlooked, NIH grants or other federal subsidies for R&D are also risky. A reasonable adjustment for risk can illustrate that a public sector contribution was significant (as opposed to the conceptual error of only comparing the NIH's direct outlays on a specific drug to an estimate of a company's risk-adjusted outlays on preclinical research).

There is considerable public interest in knowing more about the resource flows for pre-clinical research, and it is interesting to have data on the outlays directly related to specific products, but one has to be careful that the legislation does not enable companies to provide arbitrary risk adjustments and allocations among costs, which could give a misleading impression about the costs associated with particular product or services.

Reporting. Companies that sell regulated drugs or medical procedures should provide annual reports on R&D spending. The reports should be in a standardized format that the Secretary of HHS would establish and periodically revise. The periodic revisions will allow the reporting to evolve to address the needs of diverse researchers and policy makers.

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rates, including for specific diseases and for both new molecular entities and for new indications of older drugs.

[10] Biopharmaceutical Research and Development, PhRMA R&D Brocher, 2015. http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf

The R&D spending reports could include the reports on outlays for each clinical trial, plus reporting on non-trial R&D outlays. The design of the reporting would benefit from input from researchers, companies, and policy makers thinking through the ways that such information could be presented, while giving due regard to the challenges of allocating overall R&D expenditures into specific categories. A gradual expansion of the required detail would allow the project to find its footing, and understand the areas where reporting would be most useful.

Public Subsidies. Drug manufacturers should disclose public subsidies in the form of grants, research contracts, low interest loans, tax credits or intellectual property licenses or other concessions from governments that are related to a specific product or service.

As it currently stands, one can piece some information together from public source, but authoritative and accurate reporting would be more useful and more widely used.

The Orphan Drug Tax Credit. In 2017, a U.S. committee proposed making the Orphan Drug Tax Credit transparent. When the Manager's Amendment for the "Tax Cuts and Jobs Act" was posted on the Senate Finance web page, one of the provisions in the tax bill was a proposal (later removed from the bill) to make the Orphan Drug Tax Credit for qualifying clinical trial expenses fully public as to the taxpayer, the amount of the credit, the drug, and the disease or condition.

> SEC. 13401. MODIFICATION OF ORPHAN DRUG CREDIT.
> (b) DISCLOSURE OF CREDITS.—Section 45C is amended by adding at the end the following new subsection:
> '(e) DISCLOSURE OF CREDITS.—The Secretary shall publicly disclose the identity of any taxpayer (in the case of a pass-thru entity, the name of the entity) to whom a credit is allowed under this section, as well as the amount of such credit, the drug with respect to which the qualified clinical testing expenses were taken into account under this section, and the rare disease or condition for which such drug was being tested.''.

The 2017 Senate Finance language was good. It would be even better if the disclosure also identified the specific trial claiming the credit.

Government Funding of Research. In addition to any obligations on industry reporting of R&D, the bill could also ensure that the public expenditures on biomedical R&D for products and services and the licensing and commercialization of U.S.

government-funded R&D is more transparent. The following are measures that could be added to a bill dealing with transparency.

1. Agencies that conduct or fund biomedical clinical trials should annually publish a list of trials funded, including the enrollment and the cost of each trial.

   In recent years, agencies like the NIH and BARDA have been secretive about the costs of trials that the federal government funds.

   In previous years, the National Cancer Institute (NCI) annually published a report on the average costs of trials, by phase, and the average per patient cost, by phase. This was a very useful report, among other things, to evaluate the reporting by DiMasi and other industry consultants. The NIH would also disclose the costs of specific trials on specific drugs.

   There is no reason for policy makers and taxpayers to lack reliable information about the costs of such trials when the federal government is spending billions of dollars to fund trials.

   In one recent case, the NIH solicited public comments on a proposed exclusive license on patents to a new NIH invented CAR T treatment. The NIH invention was already in an NIH sponsored and funded clinical trial involving more than 70 patients. The NIH funded trial was roughly the same size of the trials used to support the FDA registration of Kymriah (tisagenlecleucel) and Yescarta (axicabtagene ciloleucel). Evidence about the cost of the trial would have been highly relevant to an evaluation of the NIH need to grant an exclusive license, and also the number of years of exclusivity in the license. The NIH refused to provide KEI with information on the cost of the trial during the 15 day public comment period on the license, and still refuses to share information on the costs for the several CAR T trials the NIH funds. Meanwhile, Novartis, a giant Swiss pharmaceutical company, claimed to have spent a billion dollars on another NIH funded CAR T technology that Novartis licensed from the University of Pennsylvania. Without better reporting of trial costs, the public can be manipulated and misled on the costs of bring these technologies to practical application.

2. All CRADA agreements involving biomedical research should be published on the agency web page, with either no redactions or limiting redactions to actual trade secrets. Many CRADA agreements are published by the companies

themselves in various SEC disclosures, when material to investors. Taxpayers should have access to the text of such agreements, without having to wait months or years for FOIA requests to be resolved.

3. All licenses to use federally-owned biomedical inventions should be published on the funding agency web page, with no redactions. This should certainly include licenses for patents owned by the federal government, and also, licenses owned by third parties who receive financial support from the federal government, such as the University of California, Cold Spring Harbor Laboratory, or companies like Immunogen, Vertex, or GSK who receive federal grants, contracts or CRADAs.

   Patent licenses are sometimes published by companies in their SEC filings. The NIH and other agencies force the public to file FOIA requests, then delay responding for months, and often ultimately refusing to provide even basic details of the licenses, such as the royalty rate.

4. The royalties for every federally-funded patent license should be public. The Department of the Interior makes royalties from oil leases public.[11] There is no reason why royalties from government-funded patented inventions should be secret, particularly when the licenses are negotiated, sometimes with former NIH employees or friends and colleagues of NIH officials.

When the Bayh-Dole Act was passed in 1980, licenses and later CRADA agreements were considered public documents with few if any redactions. Data on royalty rates and other matters were also public. Drug companies lobbied for changes in the law that have increasingly made these documents and key terms in licenses secret.

Below is the link to a timeline of the amendments to the Bayh-Dole Act that have made licensing information more secret:

- https://www.keionline.org/bayh-dole-confidentiality-timeline

[11] Luis Gil Abinader, Transparency of oil and gas leases on public lands, April 29, 2019. https://www.keionline.org/30565

Concluding Comments

Congress can and should protect the public from price increases on drugs that are already on the market. Capping price increases to changes in the general rate of inflation is a sensible approach, and the policy can be enforced through taxes, fines or losses of exclusivities.

Congress should also give HHS the authority to order price decreases in at least two cases:

1. If global revenues are large for treatments with extraordinary prices (such as prices higher than average incomes), or
2. When cumulative global revenues far exceed the amount reasonably efficient to induce investments (recognizing benefits of robust remuneration to induce investments where risks are significant, but also acknowledging decreasing utility of mega returns as an incentive to invest).

On the issue of transparency, Congress could require the disclosure of some items specifically, and could also require HHS to create standards for reporting while progressively enhancing the detail of reporting over time. Among the areas where disclosures will be most useful is the disclosure of costs for each clinical trial used to support the marketing approval of a product or a procedure. Reporting on preclincial R&D outlays should be deferred until the issues are resolved regarding the standards and context for reporting.

Congress should amend the Bayh-Dole Act in order to make the licensing and R&D costs associated with federally-funded biomedical inventions more transparent, and Congress should require federal agencies that fund clinical trials to publish the costs and enrollment for every trial agencies conduct or subsidize.