

Drug: Brand name: Juxtapid; INN lomitapide
Undisclosed Patents: Daniel Rader/University of Pennsylvania

Knowledge Ecology International
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Introduction

Knowledge Ecology International (KEI) asks the Department of Health and Human Services (DHHS) to investigate under-reporting of NIH research funding on six patents granted to Daniel

J. Rader as the sole inventor, and assigned to a single entity, the Trustees of the University of Pennsylvania, and to remedy the non-disclosure of NIH funding for the six inventions.

The six patents all have the same priority date of March 5, 2004 and are six of the eight patents listed in the FDA Orange Book for the drug Juxtapid (INN lomitapide), a treatment for Homozygous Familial Hypercholesterolemia (HoFH).

The Rader patents extend the monopoly on Juxtapid by seven years and six months. The current price of Juxtapid is \$1,380 per day, an increase of 70 percent since 2013. The University of Pennsylvania has played a significant role in the development of this drug, acquiring two of the patents as a donation from Bristol-Myers Squibb (BMS), relicensing the BMS and the Penn patents to Aegerion Pharmaceuticals in 2006, and filing five of its six patents after the Aegerion license and four after Juxtapid was approved by the FDA.

Since 1996, Daniel Rader has been the principal investigator for NIH grants involving \$72 million. The KEI has focused on four grants the were specifically related to BMS-201038, a compound now named lomitapide and sold in the United States under the brand name Juxtapid.

Aegerion has been involved in several controversies, including a 2017 criminal conviction in the United States for violations of FDA laws regarding the marketing and promotion of Juxtapid.

KEI is asking the NIH to take title to the patents, which is a remedy available under the Bayh-Dole Act for non-disclosure of federal funding of patented inventions. At a minimum, the Department of Health and Human Services should require the University of Pennsylvania to correct the failure to disclose the NIH grants and acknowledge the federal government rights in the patent.

Juxtapid (INN lomitapide)

On Dec. 24, 2012 the FDA approved Juxtapid (INN lomitapide), a microsomal triglyceride transfer protein inhibitor, to treat patients with homozygous familial hypercholesterolemia (HoFH). HoFH is a cause of severe and life threatening heart disease in the early teen years and sometimes even in early childhood. The FH Foundation estimates 2,000 people in the U.S. have HoFH.

The generic name for Juxtapid is lomitapide. When in development, the drug was first known as BMS-201038, and then AEGR-733. The trade name in Europe is Lojuxta.

The efficacy and safety of lomitapide in the HoFH population was evaluated in one, single-arm, 78-week, phase 3 trial involving 29 subjects.¹

¹ https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/203858Orig1s000MedR.pdf

The Juxtapid Patents

According to the March 12, 2018 version of the FDA Orange Book, there are 8 patents for Juxtapid. The first two patents were originally assigned to BMS. The last six all identify Daniel J. Rader as the inventor and are assigned to the Trustees of the University of Pennsylvania.

Table 1: Orange Book Patents for Juxtapid

Orange Book Patent	Expiration	Inventor	Original Assignee
5712279	02/21/2020	Biller; Dickson; Lawrence; Magnin; Poss; Robl; Sulsky; Tino	Bristol-Myers Squibb Company
6492365	12/10/2019	Wetterau, II; Sharp; Gregg;	Bristol-Myers Squibb Company
7932268	08/19/2027	Rader; Daniel J.	Trustees of the University of Pennsylvania
8618135	03/07/2025	Rader; Daniel J.	Trustees of the University of Pennsylvania
9265758	03/07/2025	Rader; Daniel J.	Trustees of the University of Pennsylvania
9364470	03/07/2025	Rader; Daniel J.	Trustees of the University of Pennsylvania
9433617	03/07/2025	Rader; Daniel J.	Trustees of the University of Pennsylvania
9861622	03/07/2025	Rader; Daniel J.	Trustees of the University of Pennsylvania

The Six Rader Patents

Daniel J. Rader has held teaching positions at the University of Pennsylvania since 1994, and is currently Chair of the Department of Genetics at the Perelman School of Medicine at the University of Pennsylvania.

KEI has determined the six Rader patents failed to disclose federal funding. The patents in question are listed in Table 2.

Table 2: The 6 Rader Hyperlipidemia and Hypercholesterolemia Patents

Patent No.	Date filed	Date Granted	Priority date	Title
7,932,268	2005-03-07	2011-04-04	2004-03-05	Methods for treating disorders or diseases associated with hyperlipidemia and hypercholesterolemia while minimizing side effects.
8,618,135	2011-03-11	2013-12-31	2004-03-05	Methods for treating disorders or diseases associated

				with hyperlipidemia and hypercholesterolemia while minimizing side effects.
9,265,758	2013-11-08	2016-02-23	2004-03-05	Methods for treating disorders or diseases associated with hyperlipidemia and hypercholesterolemia while minimizing side effects.
9,364,470	2015-12-04	2016-06-14	2004-03-05	Methods for treating disorders or diseases associated with hyperlipidemia and hypercholesterolemia while minimizing side effects.
9,433,617	2016-05-16	2016-09-06	2004-03-05	Methods for treating disorders or diseases associated with hyperlipidemia and hypercholesterolemia while minimizing side effects.
9,861,622	2016-07-25	2018-01-09	2004-03-05	Methods for treating disorders or diseases associated with hyperlipidemia and hypercholesterolemia while minimizing side effects.

Note that all six patents in Table 2 have different filing and grant dates, but the exact same title and the exact same priority date of March 5, 2004.

The Penn Acquisition of BMS Patent Rights and Subsequent License to Aegerion

Daniel Rader filed for his first patent on BMS-201038 on March 7, 2005.

In 2006, the University of Pennsylvania acquired both of the BMS patents and relicensed the BMS and the Rader patents to Aegerion. The Penn agreement with Aegerion is described by Aegerion in a 10-K filing, excerpts of which are attached as Annex 1.

In 2013, the University of Pennsylvania sold a portion of its royalty income for \$55 million to an unnamed party, with MTS Health Partners, LP serving as financial advisor and Covington & Burling, LLP serving as legal advisor to the University.^{2 3}

In 2015, Aegerion applied for and received a year extension on the 5,712,279 patent.⁴

The original BMS patents expire in less than two years. The six Rader patents extend the monopoly by seven years and six months.

² Press Release. University of Pennsylvania Sells a Portion of its Royalty Interest in Juxtapid® for \$55 Million. MTS Health Partners. June 25, 2013.

³ Brenda Wang, [Prescription drug developed by Penn brings millions in revenue: While Penn sold part of its ownership of Juxtapid, the U. still receives royalties from the sale of the drug](#). the Daily Pennsylvanian, October 32, 2013.

⁴ [80 FR 18414](#).

The Related and Undisclosed Research Grants from National Institute of Health

According to the National Institutes of Health RePORTER database, Daniel Rader was the principal investigator for grants to support 89 projects and 83 sub-projects, including 86 projects and 72 projects awarded to the University of Pennsylvania. The total funding received by the University of Pennsylvania was \$68,111,241. Another \$3,967,177 was awarded to other institutions, where Rader also served as the principal investigator.

Rader received funding from one or more NIH agencies every fiscal year from 1996 to 2018, including grants totalling \$12,005,614 for the fiscal years 2000 to 2004.

Of particular interest are four grants whose titles include the compound name BMS-201038. BMS-201038 is also known as AEGR-773, and more recently by the generic name lomitapide, a drug currently marketed under the brand names Juxtapid in the United States and Lojuxta in the European Union.

Table 3: The NIH Grants for BMS-201038

Grant number	Title	PI	Project Start Date	Project End Date	Agency
3 M01 RR000040-41S1	CHRONIC DOSING OF BMS-201038 AND HEPATIC FAT ACCUMULATION, AND REVERSIBILITY	RADER, DANIEL JAMES	12/1/00	11/30/01	NCRR
5 M01 RR000040-42	CHRONIC DOSING OF BMS-201038 AND HEPATIC FAT ACCUMULATION, AND REVERSIBILITY	RADER, DANIEL JAMES	12/1/01	11/30/02	NCRR
5 M01 RR00004-44	BMS-201038 IN PATIENTS WITH HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA	RADER, DANIEL JAMES	12/1/03	11/30/04	NCRR
5 M01 RR000040-45	MICROSOMAL TRIGLYCERIDE TRANSFER PROTEIN (MTP) INHIBITOR BMS-201038	RADER, DANIEL JAMES	12/1/04	11/30/05	NCRR

The grants describe the use of BMS-201038 for the treatment of patients diagnosed with homozygous familial hypercholesterolemia.

Although there are no abstracts available for these grants, the project terms given for the grants are as follows:

Table 4: Project Terms for the BMS-201038 Grants

3 M01 RR000040-41S1: antihypercholesterolemic agent; clinical research; clinical trial phase I; dosage; drug screening /evaluation; human subject; human therapy evaluation; hypercholesterolemia; liver metabolism; magnetic resonance imaging; nuclear magnetic resonance spectroscopy

5 M01 RR000040-42: antihypercholesterolemic agent; clinical research; clinical trial phase I; dosage; drug screening /evaluation; human subject; human therapy evaluation; hypercholesterolemia; liver metabolism; magnetic resonance imaging; nuclear magnetic resonance spectroscopy

5 M01 RR00004-44: antihypercholesterolemic agent; clinical research; clinical trial phase I; dosage; drug screening /evaluation; human subject; human therapy evaluation; hypercholesterolemia; liver metabolism; magnetic resonance imaging; nuclear magnetic resonance spectroscopy

5 M01 RR000040-45: antihypercholesterolemic agent; benzimidazole analog; clinical research; drug screening/evaluation; familial hyperlipoproteinemia type II; human subject; human therapy evaluation; low density lipoprotein; metabolism disorder chemotherapy; patient oriented research.

Note that BMS-201038 is a microsomal triglyceride transport protein (MTP) that reduces concentrations of plasma cholesterol.

All the patents listed above in Table 1 provide several key terms/words that appear to be the subject matter of the grants, including, to mention a few:

- The present invention provides methods and compositions for treating hyperlipidemia and/or **hypercholesterolemia**. (ABSTRACT)
- Administering to the subject an effective amount of an **MTP inhibitor** to inhibit hyperlipidemia and/or **hypercholesterolemia**. (ABSTRACT)
- Capsules containing 1 mg **MTP inhibitor BMS 201,038** and capsules containing 50 mg **BMS 201,038** are produced from the following ingredients. (PAGE 17)
- Claim 1 - A method of treating a subject suffering from hyperlipidemia or hypercholesterolemia, the method comprising orally administering to the subject an effective amount of an MTP inhibitor, wherein said administration comprises three step-wise, increasing dose levels of the MTP inhibitor, wherein each dose level is 50% of the immediately following dose level, wherein the third dose level is about 0.2 to about 0.59 mg/kg/day, and wherein the MTP inhibitor is N-(2,2,2-trifluoroethyl)-9-[4-[4-[[[4'-(trifluoromethyl) [1,1'-biphenyl]-2-yl] carbonyl] amino]-1-piperidinyl] butyl]-9H-fluorene-9-carboxamide, methanesulfonate; wherein each dose level is administered for a period of about 7 to about 35 days; and wherein the

subject suffering from hyperlipidemia or hypercholesterolemia has homozygous familial hypercholesterolemia. (PAGE 20)

Juxtapid Prices

Juxtapid is expensive.

GoodRx says that the average cash price of Juxtapid is \$43,259.10 for 28 capsules, or \$1,544.97 per day, or \$559,900 per year. Goodrx says a “fair price” is \$36,779 for 28 capsules, or \$1,313.52 per day, \$479,440 per year.

Drugs.com provides a discounted price of \$38,628 for 28 capsules (the same price for the 5, 10 and 20 mg capsules). Taken daily, this works out to \$1,380 per day, or just over \$0.5 million per year.

Aegerion has increased the price of Juxtapid several times.

- In 2012, the initial price was \$644 per day.
- In 2013, the price was increased to \$808 per day, an increase of 25 percent.
- In 2016, Truven Health Analytics estimated the cost at \$1,000 per day.
- In 2018, Drugs.com offered the drug (at a discount) for \$1,380 per day.

The high price for Juxtapid/Lojuxta is a significant barrier to access.

In many countries, the drug is not available at all. One country where the drug is available is Colombia. According to the Colombia Observatory of Drug Prices, the cost of 28 20mg capsules was 121,753,411 Colombian pesos, or \$42,613.69, a price that is equal to \$1,521.91 per day, and \$555,500 per year. According to some commentators, it is "the most expensive drug in the country."⁵

In March 2017, the price in the United Kingdom for Lojuxta (lomitapide) 20mg capsules, was £17,765.00, equal to \$24,763.52, or \$884.41 per day, at current exchange rates.

⁵ Alejandro Ramírez Peñ, [Cápsulas de \\$110 millones encabezan lista de drogas más caras del país: Estas son las más costosas. Entre mayo y junio, entrarían nuevos productos a control de precios.](#) 12 de abril 2017; Laura Fernanda Bolaños. [Juxtapid cuesta lo mismo que un Mercedes-Benz](#), La República. 30 de marzo de 2017

Requested Remedies for Non-disclosure

The Bayh-Dole Act and federal regulations and guidelines obligate contractors to disclose government rights in subject inventions, including via: (1) a requirement to disclose within a reasonable time that federal funding contributed to a subject invention; (2) contractual requirements for disclosure; and (3) required language to be inserted in patent applications and the patents, stating the role of federal funding and the government's rights.

After establishing a failure by the patent holder to disclose the federal funding, an agency may choose to require the patent holders to provide a disclosure to iEdison and to submit a Certificate of Correction to the United States Patent and Trademark (USPTO). The agency also has consequential remedies. In particular, a failure to disclose subject inventions pursuant to 35 U.S.C. § 202(c)(1) permits the federal government to "receive title to any subject invention not disclosed to it within such time."

The disclosure itself is an acknowledgement that the federal government has certain rights in the patents, and that the patent holder has certain obligations. When federal funding is involved, the patent owner has an obligation to manufacture the invention substantially within the United States and to make the invention "available to the public on reasonable terms." The federal government obtains a worldwide royalty-free right to use the patent, and may grant a compulsory license to the patent under the Bayh-Dole march-in provisions of 35 U.S.C. § 203(a).

The failure to make a timely disclosure of the federal funding should be seen as an attempt to evade these responsibilities and as a denial of the government's rights in the invention.

KEI recommends that the federal government take title to the invention, since the lesser remedy of requiring late disclosure has not, in the past, provided an adequate incentive for patent holders to comply with the disclosure obligations.

See Annex 4 below for a more detailed discussion of the specific statutory, regulatory and contractual obligations to disclose federal funding in patented inventions, and the remedies when funding is not disclosed (also published as [KEI Briefing Note 2018:1](#)).

Note that the Orphan Drug exclusivity, which is seven years from the FDA approval of the orphan indication, expires on December 21, 2019.

If the NIH takes title to the patents, the monopoly on Juxtapid will end on February 21, 2020. This is the preferred remedy, and one that is entirely appropriate given the clear bad faith in non-disclosure.

By merely requiring disclosure of the NIH grants in the subject inventions, the DHHS will at a very minimum have considerable leverage in negotiating lower prices on the drugs, given the fact that after February 2020, the U.S. government will have both royalty-free rights in the patents, which it can use to acquire generic drugs royalty-free, or march-in rights.

ANNEX 1: Dates of Note

2000, December 1. Start date for grant with title: CHRONIC DOSING OF BMS-201038 AND HEPATIC FAT ACCUMULATION, AND REVERSIBILITY.

2004, March 5. Priority date for all six patents.

2005, March 7. Rader filing date for patent 7,932,268.

2005, November 30. End date for grant with title: MICROSOMAL TRIGLYCERIDE TRANSFER PROTEIN (MTP) INHIBITOR BMS-201038.

2006, May. BMS transfers patents to the University of Pennsylvania (Penn).

2006, May 22. Penn licenses patents to Aegerion Pharmaceuticals.

2006, May 23. Kynamro receives orphan designation for treatment of homozygous familial hypercholesterolemia.

2007, October 23. Juxtapid receives orphan designation for treatment of homozygous familial hypercholesterolemia.

2012, Dec 21. FDA approves Juxtapid for homozygous familial hypercholesterolemia. Initial price is \$295,000 per year.

2013, January 29. FDA approves Kynamro for homozygous familial hypercholesterolemia. Initial price is \$176,000 per year.

2013, June. Penn sells portion of royalty income to undisclosed buyer for \$55 million.

2013, September 12. Repatha (INN Evolocumab) receives orphan designation for homozygous familial hypercholesterolemia.

2015, April 6. Federal Register notice of Aegerion's application for a five year patent extension.

2015, August 27. Amgen's Repatha (INN Evolocumab) approved by the FDA, for homozygous familial hypercholesterolemia.

2017, September 22. Aegerion Pharmaceuticals Inc. agreed to plead guilty in the United States District Court for the District of Massachusetts to two misdemeanor counts of violating the Federal Food, Drug, and Cosmetic Act (FD&C Act) involving the introduction of misbranded Juxtapid (lomitapide) into interstate commerce.

ANNEX 2: The Aegerion License

Excerpts from the Aegerion Pharmaceuticals, Inc. 10-K, for the fiscal year ending December 31, 2013.

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License - University of Pennsylvania

In May 2006, we entered into a license agreement with The Trustees of the University of Pennsylvania, ("UPenn") pursuant to which we obtained an exclusive, worldwide license from UPenn to certain know-how and a range of patent rights applicable to lomitapide. In particular, we obtained a license to certain patents and patent applications owned by UPenn relating to the dosing of MTP-I compounds, including lomitapide, and certain patents and patent applications and know-how covering the composition of matter of lomitapide that were assigned to UPenn by Bristol-Myers Squibb Company ("BMS") for use either as a monotherapy or with other dyslipidemic therapies to treat patients with HoFH. We also have the right to use lomitapide in the field of monotherapy or in combination with other dyslipidemic therapies for treatment of patients with other severe forms of hypercholesterolemia unable to come within 15% of NCEP's LDL-C goal on maximal tolerated oral therapy, as determined by the patient's prescribing physician, or with severe combined hyperlipidemia unable to come within 15% of NCEP's non-HDL-C goal on maximal tolerated oral therapy, as determined by the patient's prescribing physician, or with severe hypertriglyceridemia unable to reduce TG <1,000 on maximal tolerated therapy. We refer to the patents and patent applications assigned by BMS to UPenn and licensed to us by UPenn as the BMS-UPenn assigned patents.

To the extent that rights under the BMS-UPenn assigned patents were not licensed to us under our license agreement with UPenn or were retained by UPenn for non-commercial education and research purposes, those rights, other than with respect to lomitapide, were licensed by UPenn back to BMS on an exclusive basis pursuant to a technology donation agreement between UPenn and BMS. In the technology donation agreement, BMS agreed not to develop or commercialize any compound, including lomitapide, covered by the composition of matter patents included in the BMS-UPenn assigned patents in the field licensed to us exclusively by

UPenn. Through our license with UPenn, as provided in the technology donation agreement, we have the exclusive right with respect to the BMS-UPenn assigned patents regarding their enforcement and prosecution in the field licensed exclusively to us by UPenn.

The license from UPenn covers, among other things, the development and commercialization of lomitapide alone or in combination with other active ingredients in the licensed field. The license is subject to customary non-commercial rights retained by UPenn for non-commercial educational and research purposes. We may grant sublicenses under the license, subject to certain limitations.

We are required to make royalty payments to UPenn at a range of royalty rates in the high single digits on net sales of lomitapide in countries where lomitapide has patent protection, and of any other products covered by the license (subject to a variety of customary reductions), and share with UPenn specified percentages of sublicensing royalties and certain other consideration that we receive under any sublicenses that we may grant. As a result, we paid to UPenn \$0.9 million in royalty payments, and accrued an additional \$1.2 million in royalties, in the year ended December 31, 2013. During 2013, we also paid UPenn \$0.1 million in development milestone payments related to the development of lomitapide for the treatment of HoFH. We will be required to make development milestone payments to UPenn of up to an aggregate of approximately \$2.6 million if we decide to develop lomitapide for indications within the licensed field other than HoFH, and we achieve certain milestones in such development efforts. All such development milestone payments for these other indications are payable only once, no matter how many licensed products for these other indications are developed.

This license agreement with UPenn will remain in effect on a country-by-country basis until the expiration of the last-to-expire licensed patent right covering the product in the applicable country. We have the right to terminate this license agreement for convenience upon 60 days prior written notice to UPenn or for UPenn's uncured material breach of the license agreement. UPenn may terminate this license agreement for our uncured material breach of the license agreement, our uncured failure to make payments to UPenn or if we are the subject of specified bankruptcy or liquidation events.

ANNEX 3: Criminal and Civil Cases brought against Aegerion by US Department of Justice regarding Juxtapid

Excerpts from a September 22, 2017 FDA [Press Announcement](#).

“Today, Aegerion Pharmaceuticals Inc. agreed to plead guilty in the United States District Court for the District of Massachusetts to two misdemeanor counts of violating the Federal Food, Drug, and Cosmetic Act (FD&C Act) involving the introduction of misbranded Juxtapid (lomitapide) into interstate commerce. In connection with this agreement, the criminal information filed today charged that Juxtapid was misbranded because Aegerion failed to

comply with the requirements of the Juxtapid Risk Evaluation and Mitigation Strategy (REMS) program and because the drug's labeling lacked adequate directions for all of Juxtapid's intended uses. . .

“As alleged in court documents filed by the U.S. Department of Justice today, rather than following the REMS requirement to distribute Juxtapid only for the narrow indication for which it was approved, Aegerion instead sought to render the diagnosis of homozygous familial hypercholesterolemia (HoFH), a rare disorder that that causes high cholesterol levels and early cardiovascular disease, as vague and indefinite as possible in order to extend the product use to additional patient populations. As part of the required REMS, Aegerion failed to give health care providers complete and accurate information about HoFH and how to properly diagnose it. Aegerion also filed a misleading REMS assessment report to the FDA in which the company failed to disclose that it was distributing Juxtapid using a definition of HoFH that was inconsistent with Aegerion's pre-approval filings with the FDA and that did not correspond to any peer-reviewed clinical standard for diagnosing HoFH. As such, Aegerion failed to comply with the required elements under the REMS to assure safe use of Juxtapid, in violation of the FD&C Act. In addition, Aegerion management and sales personnel also distributed Juxtapid not only for the treatment of HoFH, but also as a treatment for high cholesterol generally, without adequate directions for such use.”

ANNEX 4: Related News Reports and other Background Materials concerning Juxtapid

[About homozygous familial hypercholesterolemia \(HoFH\)](#). The FH Foundation.

2012. Deborah Mitchell, [Cholesterol Drug Juxtapid Costs \\$200K Plus, Has Serious Effects](#). *Emax Health*. December 25, 2012.

2012. Matthew Herper, [Aegerion Cholesterol Drug Approved. Will It Treat 300 Patients, Or 3,000?](#) *Forbes*. December 24, 2012.

2013. Matthew Herper, [How A Mourning Entrepreneur And A Dogged Doctor Rescued A Rare Disease](#). *Forbes*. April 17, 2013.

2013. Patricia Resende, [Aegerion stock soars on price boost for cholesterol drug, Juxtapid](#). *Boston Business Journal*. May 16, 2013.

2013. Brenda Wang, [Prescription drug developed by Penn brings millions in revenue: While Penn sold part of its ownership of Juxtapid, the U. still receives royalties from the sale of the drug](#). *The Daily Pennsylvanian*. October 23, 2013.

2013. Adam Feuerstein, [FDA Slaps Aegerion CEO For 'Serious' Violations of Drug Promotion Law](#). *TheStreet*. November 11, 2013.

2014. Dan Mangan, ['Fast Money' faux pas: Firm draws FDA warning, DOJ subpoena](#). *CNBC*. January 13, 2014.

2014. Adam Feuerstein, [Aegerion, Seattle Genetics CEOs Accused in Suit of Cocaine Use: Both CEOs deny allegations in an ugly divorce case that they snorted cocaine with a Jefferies & Co. health care investment banker](#). *The Street*. Oct 27, 2014.

2015. Eric Palmer, [Aegerion dumps CEO who got it into FDA trouble for talking too freely](#). *Fierce Biotech*. July 27, 2015.

2015. Alexandre Hisayasu, [Polícia investiga médicos por fraude na Saúde: Profissionais são investigados por suspeita de receitar um remédio que não tem autorização da Agência Nacional de Vigilância Sanitária](#). *O Estado de S. Paulo*. 9 Novembro 2015.

2016. Ben Adams, [More woe for Aegerion as ax swings again; withdraws Juxtapid from EU](#). *Fierce Biotech*. July 21, 2016.

2016. Robert Weisman, [Aegerion Pharmaceuticals to merge with Canadian drug maker](#). *Boston Globe*. June 15, 2016.

2016. Lisa LaMotta, [Better Together? Aegerion and QLT Merge to Solve Problems](#). *Scrip Intelligence*. June 24, 2016.

2016. John Carroll, [New CEO Szela cuts Aegerion staff again, pulls Juxtapid out of the EU](#). *End Points*. July 20, 2016.

2016. James Radke, [HoFH Drug Juxtapid No Longer Available in EU](#), *Rare Disease Report*. July 21, 2016.

2017. Laura Fernanda Bolaños, [Juxtapid cuesta lo mismo que un Mercedes-Benz](#). *La República*. March 30, 2017.

2017. Alejandro Ramírez Peñ, [Cápsulas de \\$110 millones encabezan lista de drogas más caras del país: Estas son las más costosas. Entre mayo y junio, entrarían nuevos productos a control de precios](#). *El Tiempo*. April 12, 2017.

2017. Department of Justice, [Drug Maker Aegerion Agrees to Plead Guilty: Will Pay More Than \\$35 Million to Resolve Criminal Charges and Civil False Claims Allegations Friday](#). *Office of Public Affairs, News Release*. September 22, 2017.

2017. Eric Topor, [Drugmaker Aegerion's Plea Deal Rejected as Too Soft](#). *BNA*. November 21, 2017.

2017. Eric Sagonowsky, [Judge Orders Aegerion's Juxtapid Case to Trial, with some choice of words for corporate please](#). *Fierce Pharma*. November 21, 2017.

2017. Food and Drug Administration, [Criminal and Civil Actions Filed Against Aegerion Pharmaceuticals Inc.](#) *FDA News Release*. September 22, 2017.

2017. Nate Raymond, [Patient assistance charity says U.S. contacted it in probe](#). *Reuters*. September 25, 2017.

2018. Nate Raymond, [U.S. judge sentences Novelion's Aegerion in drug marketing case](#). *Reuters*. January 30, 2018.

2018. Max Stendahl, [Doctor Pleads Guilty as Part of Aegerion Drug Misbranding Probe](#). *Boston Business Journal*. February 28, 2018.

ANNEX 5: Statutory, Regulatory and Contractual Obligations to Disclose Federal Funding in Patented Inventions

The following text is from:

Bayh-Dole Obligations to Disclose Federal Funding in Patented Inventions

KEI Briefing Note: 2018:1. Andrew Goldman. Revised March 16, 2018

Legal, Regulatory, and Contractual Obligations⁶

The Bayh-Dole Act and federal regulations and guidelines make clear several obligations for contractors in the disclosure of government rights in subject inventions, including: (1) a requirement to disclose that federal funding contributed to an invention; (2) contractual requirements for disclosure; and (3) required language to be inserted in patent applications and the patents, stating the role of federal funding and the government's rights.

⁶ See: <https://www.keionline.org/bayh-dole/failure-to-disclose>

First, contractors are required to disclose subject inventions discovered with federal funding in a timely manner and with sufficient detail to describe the invention.

Under 35 U.S.C. § 202(c)(1), any contractor that receives funding from the federal government is required to “disclose each subject invention to the Federal agency within a reasonable time after it becomes known to contractor personnel responsible for the administration of patent matters.”⁷

Under 37 C.F.R. § 401.3(a), each federal funding agreement shall contain the “standard patent rights clause” found at 37 C.F.R. § 401.14(a), barring specific circumstances and exceptions.⁸ Subsection (c)(1) of the patent rights clause outlines the disclosure requirements, including a two month time limit on the disclosure of patents and a requirement that the disclosure have sufficient detail:⁹

37 C.F.R. § 401.14(a)(c)(1)

(c) Invention Disclosure, Election of Title and Filing of Patent Application by *Contractor*

(1) The *contractor* will disclose each subject invention to the *Federal Agency* within two months after the inventor discloses it in writing to *contractor* personnel responsible for patent matters. The disclosure to the *agency* shall be in the form of a written report and shall identify the contract under which the invention was made and the inventor(s). It shall be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or electrical characteristics of the invention. The disclosure shall also identify any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure. In addition, after disclosure to the *agency*, the *Contractor* will promptly notify the *agency* of the acceptance of any manuscript describing the invention for publication or of any on sale or public use planned by the *contractor*.

...

(4) Requests for extension of the time for disclosure, election, and filing under subparagraphs (1), (2), and (3) may, at the discretion of the *agency*, be granted.

⁷ The statute defines a “subject invention” at 35 U.S.C. § 201(e) as “any invention of the contractor conceived or first actually reduced to practice in the performance of work under a funding agreement,” and defines a contractor at 35 U.S.C. § 201(c) as “any person, small business firm, or nonprofit organization that is party to a funding agreement.”

⁸ The exceptions do not contain reference to the disclosure requirements.

⁹ Italics in original.

Second, in implementing this regulation, agencies may require disclosure through documentation and/or via iEdison, an online electronic system for reporting inventions and patents discovered under federal grants, or via other documents to be submitted.¹⁰ iEdison is run by the National Institutes of Health (NIH), but is used by a wide variety of agencies, including:

Agency for Health Care Research and Quality (AHRQ)
Agricultural Research Service (ARS)
Agency for Toxic Substances and Disease Registry (ATSDR)
Air Force Office of Scientific Research (AFOSR)
Air Force Research Laboratory Information Directorate (AFRL/RI)
Air Force Materiel Command Legal Office (AFMCLC/JAZ)
Army Medical Research and Materiel Command (ARMY/MRMC)
Army Natick Soldier Systems Center (ARMY/SSC)
Army Research Laboratory (ARMY/ARL)
Army Research Office (ARMY/ARO)
Army Space and Missile Defense Command (ARMY/SMDC)
Centers for Disease Control and Prevention (CDC)
Defense Advanced Research Projects Agency (DARPA)
Defense Microelectronics Activity (DMEA)
Defense Threat Reduction Agency (DTRA)
Department of Energy (DOE)
Department of Homeland Security
Science and Technology Directorate (DHS/S&T)
Department of Transportation (DOT)
Economic Development Administration (EDA)
Environmental Protection Agency (EPA)
Food and Drug Administration (FDA)
Indian Health Service (IHS)
International Trade Administration (ITA)
National Institute of Food and Agriculture (NIFA)
National Institutes of Health (NIH)
National Institute of Standards and Technology (NIST)
National Oceanic and Atmospheric Administration (NOAA)
National Science Foundation (NSF)
Nuclear Regulatory Commission (NRC)
Office of Naval Research (ONR)
U.S. Agency for International Development (USAID)
United States Forest Service (USFS)

¹⁰ iEdison.gov

iEdison was created in 1995 in the wake of findings by the Office of Inspector General of the Department of Health and Human Services that the NIH was not sufficiently overseeing and monitoring compliance with Bayh-Dole requirements, including disclosure.¹¹

By way of example of how agencies require disclosure, the NIH requires contractors to disclose subject inventions via iEdison, as well as via HHS Form 568, entitled, “Final Invention Statement and Certification (For Grant or Award),” available at: <https://grants.nih.gov/grants/hhs568.pdf>.

The NIH specifies the required information on a FAQ related to the use of iEdison, and also notes that contractors should disclose the subject invention even if they have, in the past, failed to report the invention within the two month period:¹²

5. What information is required to report a subject invention?

The invention disclosure must include the following information:

- Either the EIR Number, Invention Docket Number, or both.
- Invention Title
- Names of all of the inventors and the institutions with which they are associated
- Invention Report Date
- Description of the Invention that must meet the standards set forth per 37 CFR Sec. 401.14 (a)(c)(1):

“. . . be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological or electrical characteristics of the invention.”37 C.F.R. 401.14(a)(c)(1)
- Primary Funding Agency
- All funding agreement numbers and names of the funding agencies
- Any publication, on sale or public use of the invention and whether a manuscript describing the invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure

¹¹ <https://oig.hhs.gov/oei/reports/oei-03-91-00930.pdf>

¹² Available at: https://era.nih.gov/iedison/iedison_faqs.cfm#VIII5 (accessed Jan. 6, 2017).

9. If I upload a patent application, can that patent application satisfy the Invention Disclosure Report requirement?

Yes, so long as the EIR Number or Invention Docket Number is included on the submission, the patent record containing the patent/patent application number has been reported in iEdison, and you upload proof that the patent application was filed with the USPTO, e.g., a USPTO submission receipt.

10. What should a grantee/contractor do if a subject invention hasn't been reported to the awarding agency within the required 2 month period?

Always report the invention, even if it is late. The invention report date should be the date the inventor notified the awardee institution of the subject invention. Provide an explanation in the "Explanatory Notes" section of the invention record.

On February 17, 2016, NIH issued a notice entitled "Reminder: All Subject Inventions Must Be Reported on the HHS 568 - Final Invention Statement and Certification (For Grant or Award) and in iEdison." The notice explained that failure to disclose the subject invention via both iEdison and Form 568 could result in the loss of rights in the invention.¹³

Finally, under 35 U.S.C. § 202(c)(6) and 37 C.F.R. § 1.77(b)(3), contractors are required to state within the patent application that the federal government contributed funding to support the discovery of the invention and that the government retains certain rights:

35 U.S.C. § 202(c)(6)

(c) Each funding agreement with a small business firm or nonprofit organization shall contain appropriate provisions to effectuate the following:

...

(6) An obligation on the part of the contractor, in the event a United States patent application is filed by or on its behalf or by any assignee of the contractor, to include within the specification of such application and any patent issuing thereon, a statement specifying that the invention was made with Government support and that the Government has certain rights in the invention.

35 C.F.R. § 1.77(b)(3)

(b) The specification should include the following sections in order:

¹³ National Institutes of Health, Reminder: All Subject Inventions Must Be Reported on the HHS 568 - Final Invention Statement and Certification (For Grant or Award) and in iEdison, NOT-OD-16-066 (Feb. 17, 2016), NIH Guide Notice, <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-066.html>.

...

(3) Statement regarding federally sponsored research or development.

The Manual of Patent Examining Procedure contains the following recommended language:

“This invention was made with government support under (identify the contract) awarded by (identify the Federal agency). The government has certain rights in the invention.”¹⁴

Remedies for Non-Disclosure

Non-disclosure Permits the Federal Government to Receive Title to the Invention

Failure to disclose subject inventions pursuant to 35 U.S.C. § 202(c)(1) permits the Federal Government to “**receive title to any subject invention not disclosed to it within such time**” (emphasis added).

The patent rights clause at 37 C.F.R. § 401.14(a) specifies this right to claim title in subsection (d):

37 C.F.R. § 401.14(a)

(d) Conditions when the Government May Obtain Title

The contractor will convey to the Federal agency, upon written request, title to any subject invention—

(1) If the contractor fails to disclose or elect title to the subject invention within the times specified in (c), above, or elects not to retain title; provided that the agency may only request title within 60 days after learning of the failure of the contractor to disclose or elect within the specified times.

...

In the past, the Federal Government has utilized its authority to claim title in subject inventions that have not been properly disclosed, as in the case of *Campbell Plastics Engineering & Mfg., Inc. v. Brownlee*, 389 F.3d 1243 (Fed. Cir. 2004) (finding that federal government claim of title in invention was legitimate under federal acquisition regulations and supported by the Bayh Dole Act where disclosure submissions were “piecemeal” and violated the contractual agreement with the government); see also *Central Admixture Pharmacy Services, Inc. v. Advanced Cardiac*

¹⁴ MPEP (9th ed. Rev. 07.2015, Nov. 2015), § 310.

Solutions, P.C., 482 F.3d 1347, 1352-53 (Fed. Cir. 2007) (“Critically, *Campbell Plastics* holds that a Bayh–Dole violation grants the government *discretionary* authority to take title. . . . When a violation occurs, the government can choose to take action; thus, title to the patent may be avoidable.”).

In *Campbell Plastics*, the court found that the contract was clear and unambiguous, but moreover the government’s claim to title was “buttressed by the policy considerations behind the Bayh Dole Act.” *Id.* at 1248. These include, specifically under 35 U.S.C. § 200, the need “to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions.”

Correction of the Patent Will Establish Other Enforceable Rights For the Federal Government

Even if the Government permits the continued use of its invention, forcing a correction to the patent will create enforceable obligations and rights designed to protect the public interest. These rights can be used as leverage to force concessions in pricing.

Local Manufacturing

Under 35 U.S.C. § 204, for example, there is a requirement (waivable in individual cases) that the subject invention be manufactured substantially in the United States.¹⁵

35 U.S.C. § 204

Notwithstanding any other provision of this chapter, no small business firm or nonprofit organization which receives title to any subject invention and no assignee of any such small business firm or nonprofit organization shall grant to any person the exclusive right to use or sell any subject invention in the United States unless such person agrees that any products embodying the subject invention or produced through the use of the subject invention will be manufactured substantially in the United States. However, in individual cases, the requirement for such an agreement may be waived by the Federal agency under whose funding agreement the invention was made upon a showing by the small business firm, nonprofit organization, or assignee that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible.

Practical Application

¹⁵ See also the patents rights clause regarding preference for United States industry at 37 C.F.R. § 401.14(a)(i).

Government rights in a subject invention also implicates the requirement repeated in numerous sections of the Bayh-Dole Act that there be “practical application” of the invention, including once in 35 U.S.C. § 203 on march-in rights, and nine times in 35 U.S.C. § 209 on licensing federally-owned inventions. “Practical application” is defined under 35 U.S.C. § 201(f) to mean “manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized **and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms.**” (Emphasis added.)

The phrase “available to the public on reasonable terms” to is a statutory obligation in the Bayh-Dole Act that only has meaning if the invention is available at a reasonable price, and while the NIH has been loath to enforce this requirement, the Congress is increasingly focused on a practical implementation of such an obligation. For example, in 2017, the Senate Armed Services Committee adopted a directive in a committee report to require enforcement of this obligation when the prices of a medical technology were higher in the United States than the median price charged in seven countries with large economies with at least 50 percent of U.S. per capita income.¹⁶ There is also U.S. and international case law, as well as statutes in the U.K. and South Africa, defining the phrase “reasonable terms” to include the price of a product of service.¹⁷

March-In Rights and the Royalty-Free Right

Under 35 U.S.C. § 203(a), the government may require the grant of a license to a third party, or may grant such a license itself, if any of four conditions are met, including the obligation of practical application:

35 U.S.C. § 203

(a) With respect to any subject invention in which a small business firm or nonprofit organization has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or

¹⁶ 115TH Congress, 1st Session, 2017, Senate Report 115–125. National Defense Authorization Act for Fiscal Year 2018. Report to accompany S. 1519, page 173.

¹⁷ See KEI 10 March 2017 Comments on Army Exclusive License on Zika Virus Vaccine Patents to Sanofi, available at https://www.keionline.org/wp-content/uploads/2017/03/KEI-March_10_2017-3rd-Comments-Zika.pdf.

exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such—

- (1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;
- (2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;
- (3) action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
- (4) action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204.

The government also retains a perpetual non-exclusive royalty-free license in the invention, written into any funding agreement under 35 U.S.C. § 202(c)(4), and again iterated as a required term and condition for any license of a federally-owned invention under § 209(d)(1). The royalty-free right, as opposed to the march-in rights, has no precondition and can be used at any time, for any reason.

35 U.S.C. § 202

...

(c) Each funding agreement with a small business firm or nonprofit organization shall contain appropriate provisions to effectuate the following:

...

(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.

35 U.S.C. § 209

...

(d) Terms and Conditions.—Any licenses granted under section 207(a)(2) shall contain such terms and conditions as the granting agency considers appropriate, and shall include provisions—

(1)
retaining a nontransferable, irrevocable, paid-up license for any Federal agency to practice the invention or have the invention practiced throughout the world by or on behalf of the Government of the United States;
...

Both of these rights provide significant leverage to the United States, as they could be used to allow affordable competition. Even the viable threat of use of either of these rights might be sufficient to prompt price reductions or other concessions increasing access while decreasing price.

In some cases there may be more than one patent in a particular medicine, and not all patents may have government rights. In the event that there is at least one patent with government rights, the government could potentially use the royalty-free right in conjunction with the government use provision of 28 U.S.C. § 1498. While § 1498 has been used many times by the military, interest in using the government use law alone on medical technologies has been complicated by uncertainty as to the extent of compensation owed.¹⁸ Using the royalty-free right and § 1498 together would lessen the amount of compensation owed to the patent holder.

¹⁸ See, e.g. May 12, 2015 letter from Senator Bernard Sanders to Secretary of the US Department of Veterans Affairs, Robert McDonald.
<https://www.keionline.org/wp-content/uploads/2015/05/12may2015-Sanders-McDonald-Veterans-1498.pdf>; and <https://www.keionline.org/22842>.