



Division of  
**Pharmacoepidemiology & Pharmacoeconomics**



Department of Medicine, Brigham & Women's Hospital, Harvard Medical School

# **March-In Rights: Prospects and Alternatives**

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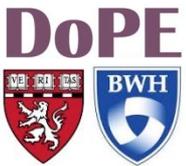
# What is PORTAL?

- Core faculty with expertise in medicine, business, law, epidemiology, ethics; post-docs and numerous students
- Research on interactions among the regulatory, legal, economic, and clinical components of the pharmaceutical marketplace
- No one in our Division has personal financial relationships with any pharmaceutical company
- Current research funding from Greenwall Faculty Scholars Foundation in Bioethics, FDA Office of Generic Drugs, Harvard Program in Therapeutic Science, Laura and John Arnold Foundation, Commonwealth Fund
  - Past research funding from FDA CDRH, Harvard Clinical and Translational Science Center, AHRQ, Robert Wood Johnson Foundation, CVS Caremark



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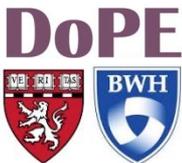
# Bayh-Dole Act

- Goal: encourage investment in R&D and bring the fruits to market
  - US small businesses and non-profits organizations allowed to retain control of patent rights in inventions from research performed under a government funding agreement
    - Extended to large corporations in 1983 memo
  - Can offer exclusive licenses to private firms
  - “March-in rights”
  - Government receives non-exclusive, non-transferable license to practice invention on behalf



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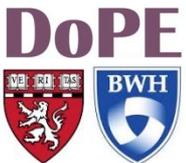
# March-In Rights

- 35 USC 203(a): “...right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor...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 exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that...” one of four conditions are met



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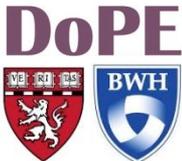
# March-In Right (cont'd)

- 4 circumstances:
  1. Licensee has not taken effective steps to achieve *practical application* of invention
  2. Health and safety needs exist that are not reasonably satisfied by licensee
  3. A government-funded invention is required for a public use specified in the federal regulations and such requirement is not reasonably satisfied by the licensee
  4. A sub-licensee violated its agreement to substantially manufacture the product in the US
- “Practical application”: the invention being used *and* made available to the public on “reasonable terms”

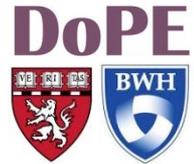


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<b>Statute section</b>	<b>Rationale for Invoking March-In Rights</b>	<b>Petitions Invoking This Rationale</b>
Clause 1	The licensee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the invention	Ceprate, Ritonavir, Latanoprost, Agalsidase, Enzalutamide
Clause 2	Health or safety needs exist that are not reasonably satisfied by the licensee	Ceprate, Ritonavir, Latanoprost, Agalsidase, Enzalutamide
Clause 3	A government-funded invention is required for a public use specified in the federal regulations and such requirement is not reasonably satisfied by the licensee	Ritonavir (2012 petition only)
Clause 4	A sub-licensee violated its agreement to substantially manufacture the product in the US	None



# Conclusion #1

- The legislative history of the Bayh-Dole Act and the plain language of the statute establish that the “reasonable terms” should take price into account, particularly if it is blatantly unreasonable and a key factor in limiting access to the product
  - Maybe not explicit because statute originally limited to small businesses and non-profits
  - Arno PS, Davis MH. Why don't we enforce existing drug price controls? The unrecognized and unenforced reasonable pricing requirements imposed upon patents deriving in whole or in part from federally funded research. *Tulane Law Rev.* 2001;75:631-693.



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Treasure, Avorn, Kesselheim, MQ 2015



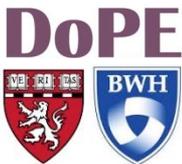
# Arno and Davis' review of legislative history

- *The Senate committee overseeing the Bayh-Dole Act wrote in its Report, “The agencies will have the power to exercise march-in-rights to insure that no adverse effects result from retention of patent rights by these contractors. . . . Although there is no evidence of ‘windfall profits’ . . . the existence of the pay back provision reassures the public . . . .”*
- *The ‘march-in’ rights were developed to address issues of windfall, suppression and detrimental effects . . .*
- *An industry spokesperson . . . stated, “[I]f [a contractor] fails to supply the market adequately at a fair price, then there is reason for requiring it to license both the background patents and the patents stemming from the contract work.”*



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# Conclusion #2

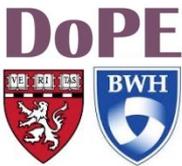
- Not relevant in many circumstances in which government play important role in drug discovery
  - Majority of most transformative drugs in past 25 years have substantial links to government-funded science in academic settings and government labs
  - Require government interest in all listed patents
  - Require another manufacturer interested/able to make the product with FDA approval (agalsidase)



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Kesselheim et al., Health Affairs 2015;  
Stevens et al., NEJM 2011; others



# Conclusion #3

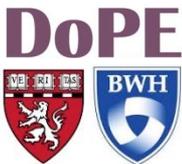
- March-in rights may actually be working
  - No product “left on the shelf”
  - Minor concessions (Abbott and CellPro cases)
  - Getting products out there, even if they are costly



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Treasure, Avorn, Kesselheim, MQ 2015



# Conclusion #4

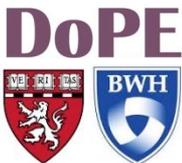
- Little prospect that march-in rights will be invoked in this regulatory and political climate to regulate pricing of a health care product developed from federal funding
  - Difficult to envision more compelling scenarios, outside a price so exorbitant that a majority of patients and payers could simply not afford it (a still hypothetical situation)
  - NIH ill-equipped to invoke a march-in petition, wary of the potentially negative ramifications that the enactment of march-in rights under Bayh-Dole could have on future commercialization



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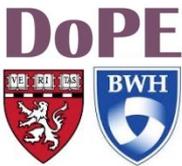
# Important caveat re: CRADA anecdote

- CRADA/reasonable pricing clause experience from 1989-1995 **of questionable current relevance** because manufacturers have reduced their investment in internal drug discovery research and become increasingly dependent on licensing ideas emerging from public funding
- Federally subsidized technology is now a highly cost-effective resource that often forms the basis for therapeutic development
- In modern era, judicious exercise of march-in rights unlikely to chill private-sector interest in commercializing the best ideas arising from university-based settings



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# Section 202: Slightly better alternative?

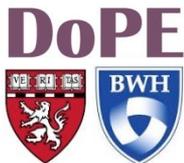
- Requires research grantees that obtain patents claiming federally-funded inventions to confer a nonexclusive, royalty-free license back to the US government, which permits the government to practice the invention or to have it practiced on the government's behalf
  - License allows govt to “use for itself and the public good inventions arising out of research that the Federal Government helps to support” – Sen Bayh
- Generic manufacturer could sell product based on certification that the patents will not be infringed because approval is being sought for the sole purpose of producing for sale to the government



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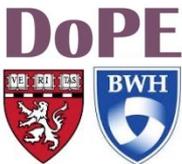
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Engelberg & Kesselheim, Nature Medicine 2016



# Section 202 license implementation

- Advantages
  - No need for NIH to act
  - Does not interfere with private US marketplace
  - Can act as early as 4 years after approval for small molecule drugs
- Disadvantages
  - Applies only to public programs
  - Require government interest in all IP



# Other alternatives

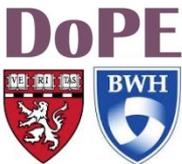
- Section 1498
- Better university stewardship of patents
- Formal NIH “payback” (Wyden, Collins)
- Direct legislative options to address drug pricing (state or federal level)



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Kapczynski & Kesselheim, Health Aff 2016



# Thank you!

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