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Ensuring Timely Availability and Use of Low-Cost, High-Quality Generic Drugs

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Background

- Rising prescription drug prices
  - 2014-2016: net retail prices increased 10% annually
    -Truveris (2017).
  - Driven primarily by
    - Higher launch prices
    - Markups on existing brand-name drugs
- Long median length of market exclusivity
  - Widely-used drugs: 12.5 years (IQR: 8.5-14.8 years)
  - First-in-class drugs: 14.5 years (IQR: 13.3-15.8 years)
    -Wang, Liu, Kesselheim. JAMA Intern Med (2015).
- Impact on patients
  - 2016 national survey of adults: 20% of 2,001 respondents did not fill a prescription in the past year due to cost
    -Osborn et al. Health Aff (2016).

Restricted Distribution Networks and REMS

- Restricted distribution networks to control drug access
  - Single specialty pharmacy or multiple certified pharmacies
  - Independent or part of REMS
  - FDA (March 2016): ~150 inquiries from generic manufacturers unable to obtain brand-name samples necessary for bioequivalence testing
- Shared REMS with elements to assure safe use (ETASU)
  - Statutory requirement to operate shared ETASU REMS
    - Exceptions: if burden outweighs benefits or if patented
  - Strategies
    - Refusal to engage or purposeful prolongation of discussions
    - ETASU REMS patenting

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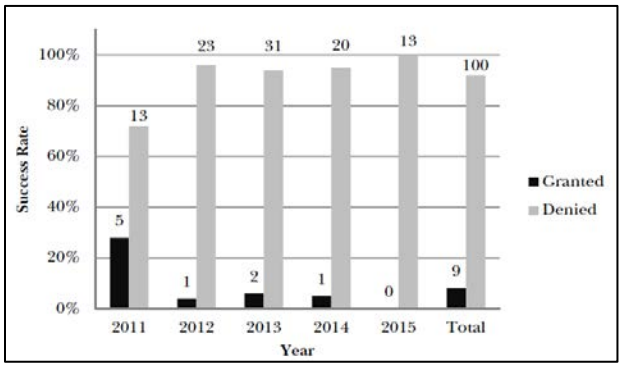
Eleventh Hour Citizen Petitions

- Citizen petitions: allow individuals—including companies—to request that the FDA take or refrain from taking an administrative action

- 2000-2012: 40% of 505(q)(2) petitions filed within year of generic entry
  -Feldman & Wang et al. NEJM (2017).

- 2011-2015
  - 124 505(q)(2) petitions
    - 108 (87%) by brand-name manufacturers
    - Only 8% granted



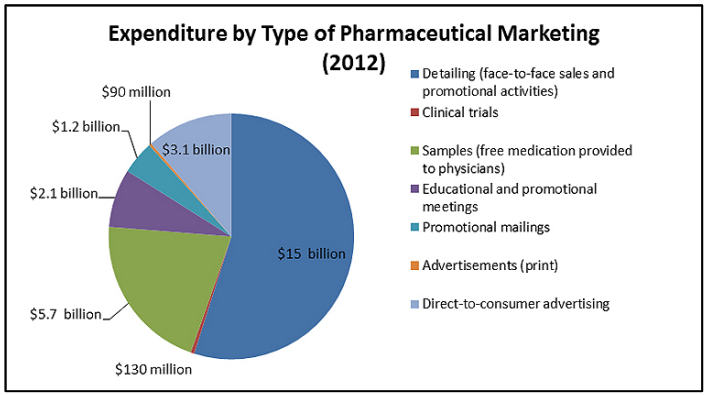
-Carrier & Minniti. Am U Law Rev (2016).

- E.g., ViroPharma: 2006-2012
  - 24 citizen petitions to delay generic vancomycin (Vancocin)

- 2013-2015
  - FDA: citizen petitions delayed 5 drug approvals

Pharmaceutical Promotion and Generic Skepticism

- Pharmaceutical marketing: 2012
  - Physicians: $24 billion
  - Direct-to-Consumer: $3.1 billion



-Pew Charitable Trusts (2013).

- Falling but lingering generic skepticism
  - Belief that generic drugs are not as safe or effective as brand-name drugs or that generic drugs cause more adverse events than brand-name drugs
  - Physicians and patients: ~33% generic skeptics

-Kesselheim et al. JAMA Intern Med (2016); JGIM (2016).

- Suboptimal substitution
  - Bioequivalent: $12 billion in forgone savings (2012 estimate)

-IMS (2013).

  - Therapeutic: $73 billion in forgone savings (2010-2012 estimate).

-Johansen & Richardson. JAMA Intern Med (2016).

Curbing Restricted Distribution and REMS Misuse

- Compel sample deposit as a condition of drug approval
  - Sufficient for bioequivalence testing by 3 generic manufacturers
  - Condition receipt of sample by generic manufacturer on
    - Commitment to market product for a minimum 5-year period
    - Receipt of FDA safety certification for REMS-covered drugs

- Encourage Congress to pass the CREATES Act, which would
  - Authorize generic manufacturers to petition a court to require sale of drug samples if a brand-name manufacturer blocked access
  - Mandate FDA safety certification for REMS-covered drugs
  - Allow FDA to require shared REMS or approve separate REMS

- Request Congress to prohibit REMS patenting

- Request Congress to require government-owned and operated REMS

Deterring Delaying Citizen Petitions

- Provide early guidance on showing bioequivalence for complex drugs
  - Levy user fees to conduct necessary research
  - Permit brand-name manufacturers to voice concerns during guidance development
- Adopt a rebuttable presumption of delay for late-filed petitions
  - Presume that brand-name manufacturer petition pertaining to generic application filed <9 months before the expiry of the primary patent on the brand-name drug is a delaying tactic
  - Require a preliminary finding that the petition will likely be granted based on compelling evidence in order to proceed to a full review

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Promoting Evidence-Based Decision-Making

- Use Sentinel to conduct generic drug safety surveillance
- Support comparative safety and effectiveness research and dissemination
  - Request Congress to levy user fees as part of PDUFA VI
  - Request DOJ to earmark a proportion of settlements
- Address deficiencies in generic labeling
  - Issue annual reports on generic drug safety and label changes
  - Create a central online repository of dynamic labels
- Require generic drugs to have same appearance as brand-name version

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