

### Background

Advertising and promotion of pharmaceuticals is tightly regulated in the United States by the Food and Drug Administration's Office of Prescription Drug Promotion (OPDP). Prescription drug advertising and promotion is primarily regulated by the Federal Food, Drug and Cosmetic Act, the Code of Federal Regulations (CFR) and guidance issued by OPDP. CFR 21:312.7 prohibits manufacturer's from presenting claims of efficacy and/or safety of investigational new drugs (INDs) in a promotional context prior to FDA approval. A recent increase in enforcement actions by the Office of Prescription Drug Promotion citing pre-approval promotion as well as a draft guidance document surrounding communications of INDs to payors may indicate a renewed focus on abating pre-approval promotion.

### Objective

To collect and analyze enforcement actions for pre-approval promotion of investigational new drugs and new uses of approved products in order to identify trends and key takeaways related to the number of enforcement actions, therapeutic areas, and promotional material type.

### Methods

- No Investigational Review Board approval was sought, as OPDP's enforcement actions are public domain available through [fda.gov](http://fda.gov)
- Currently listed and archived enforcement actions were identified by screening enforcement letters from January 1998 through October 2017 for reference to "pre-approval promotion" and "investigational new drugs"
- Letters were classified and stratified by trade name, established name, investigational name, therapeutic area, company, letter type, media type, violations cited, examples of claims made and date of enforcement. Therapeutic areas were categorized based on OPDP's review divisions.

### Results

- 798 enforcement letters from OPDP were identified
- 61 letters citing pre-approval promotion of an investigational new drug or an unapproved use of an approved drug were identified
  - This represents 7.6% of total letters during the 19 year period.
  - One of the 61 letters was a warning letter
- Figure 1** represents the pre-approval letters and total letters by year along with a trend line that illustrates the percentage of pre-approval enforcement letters in each year. The initial five year period included an average 9.3% followed by a five year stretch of no pre-approval letters. From 2008 to 2015 pre-approval letters held an average of 5% of total letters while 2016 had 4 letters from a total of 11 enforcement (36.4%)

### Results (continued)

Figure 1

Number of Total and Pre-approval Enforcement Letters vs. Percentage of IND Enforcement Letters 1998-2017

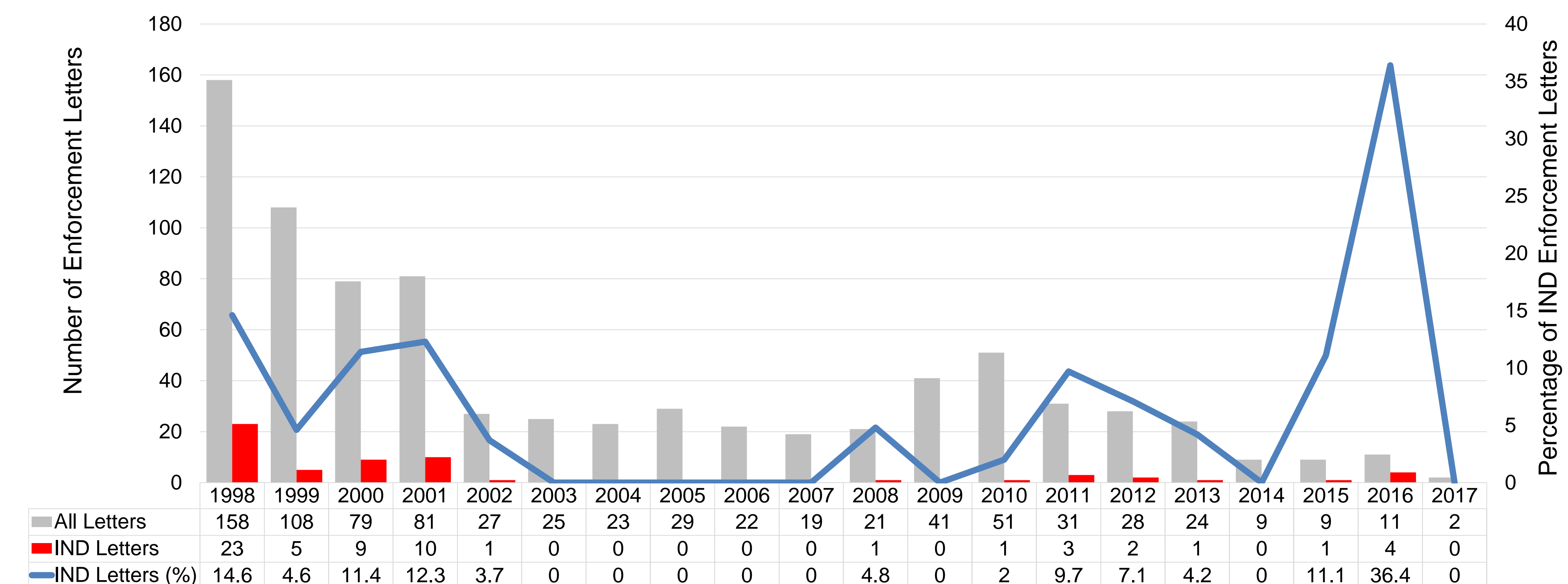


Figure 2

OPDP Pre-Approval Promotion Enforcement Actions on Print, Digital and Conference Materials By Year

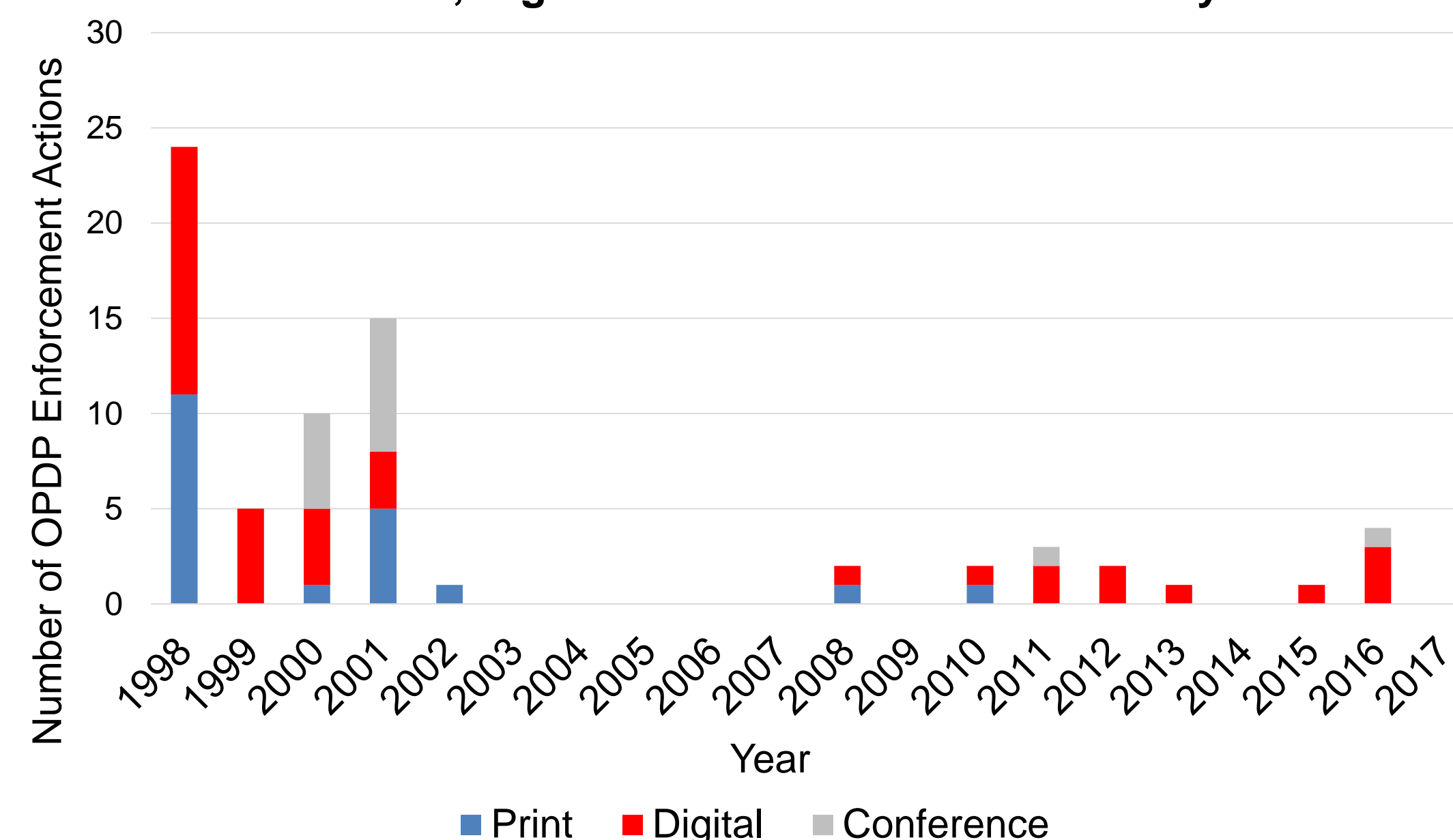
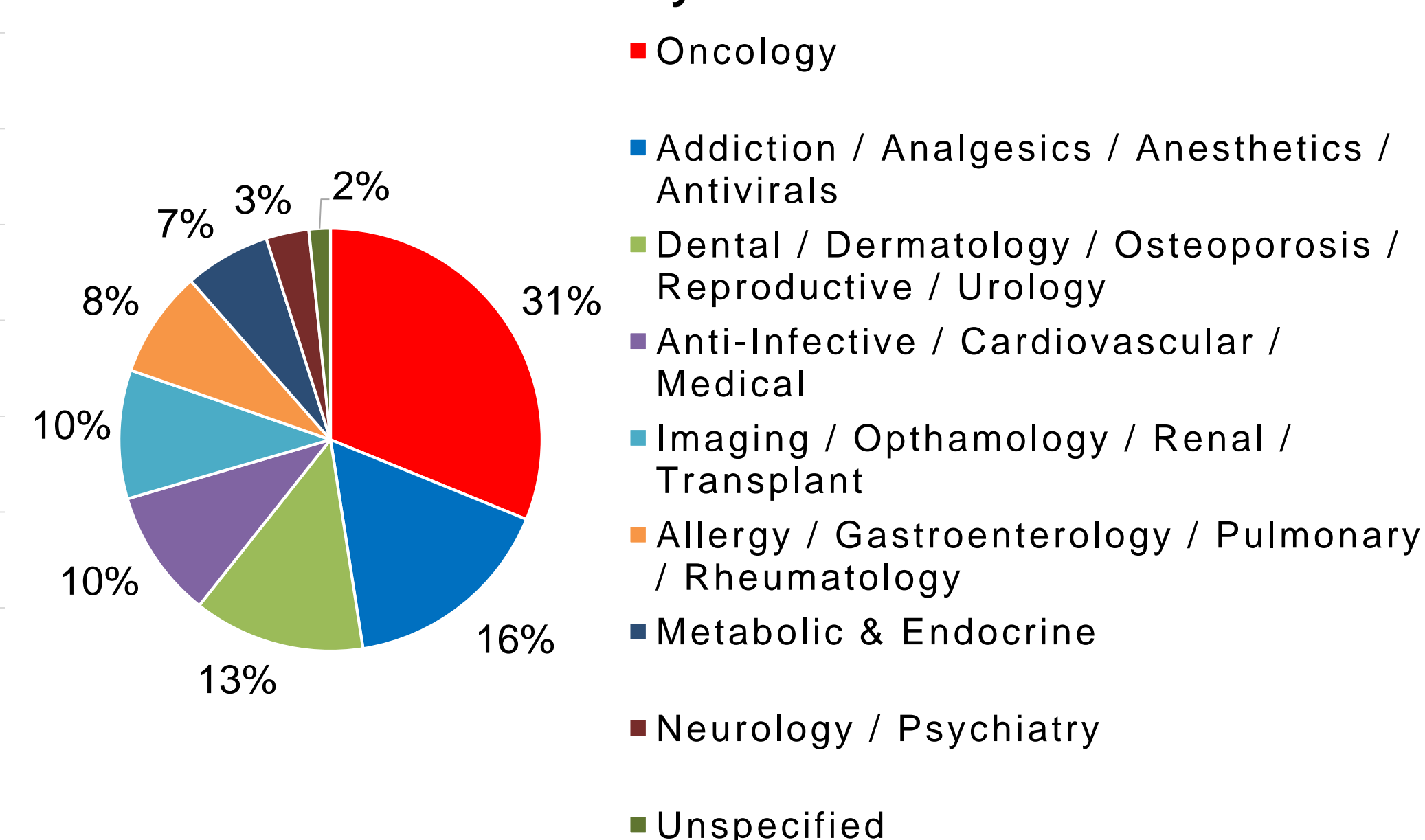


Figure 3

Total OPDP Pre-Approval Promotion Enforcement Actions by OPDP Division



### Results (continued)

- Figure 2.** represents pre-approval enforcement actions issued by year and type of promotional material cited. Of the total letters, 36% cited digital materials, 20% cited print materials, and 14% cited conference materials.
- Figure 3.** represents the percent of the total letters issued by therapeutic area divisions within OPDP. 31% (N=19) of the enforcement actions cited oncology products and 16% (N=10) cited Addiction / Analgesics / Anesthetics / Antivirals products, making up 47% of the total enforcement actions. One letter cited multiple products but did not specify the specific product or therapeutic areas.

### Limitations

- Data collection and trends analysis conducted were prone to human error
- Data collection was limited to publicly available resources via [fda.gov](http://fda.gov)
- OPDP has yet to issue any pre-approval enforcement actions this year

### Conclusions

- Our analysis found that there has been a decline in the total number of enforcement actions issued in the past 19 years. While a similar trend can be seen in the number of pre-approval promotion enforcements, 2015 and 2016 exhibited a spike in the percentage of pre-approval enforcements.
- It is evident that there has consistently been a focus from the FDA on enforcement regarding digital materials, potentially because digital materials reach a larger audience than print or conference materials. Conference materials were enforced upon at a higher rate in 1999-2000 than from 2007-2016.
- Oncology represents an area of risk with nearly a third of all pre-approval enforcements citing an IND for cancer treatment. This may be due to shortened approval timelines and a competitive landscape
- While pre-approval promotion only represents a small portion of total enforcement actions, our analysis depicts OPDP's renewed focus on INDs. It is important for regulatory professionals to be aware of CFR 21:312.7 and its implications in prescription drug advertising and promotion.

### Disclosures

Matthew Bermudez and Dana Huettenmoser are paid employees of Rutgers University participating in Post-Doctoral Fellowships in Promotional Compliance with Johnson & Johnson. Michael Toscani has nothing to disclose.

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