Patterns of Bioequivalence Recommendations and Trends of Abbreviated New Drug Approval Over Time

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Introduction

Background:

The Office of Generic Drugs (OGD) began publishing bioequivalence (BE) recommendations for specific (complex/non-complex) products in 2007 to support generic drug development and assist sponsors with identifying methodology for drug products submitted under an abbreviated new drug application (ANDA)[1].

Objective:

To describe patterns of BE recommendations published by the OGD and trends of ANDA approvals over time.

Methods

Study Design:

A cross-sectional study of ANDAs approved from 2007-2015 (n= 4,028).

Data Resources:

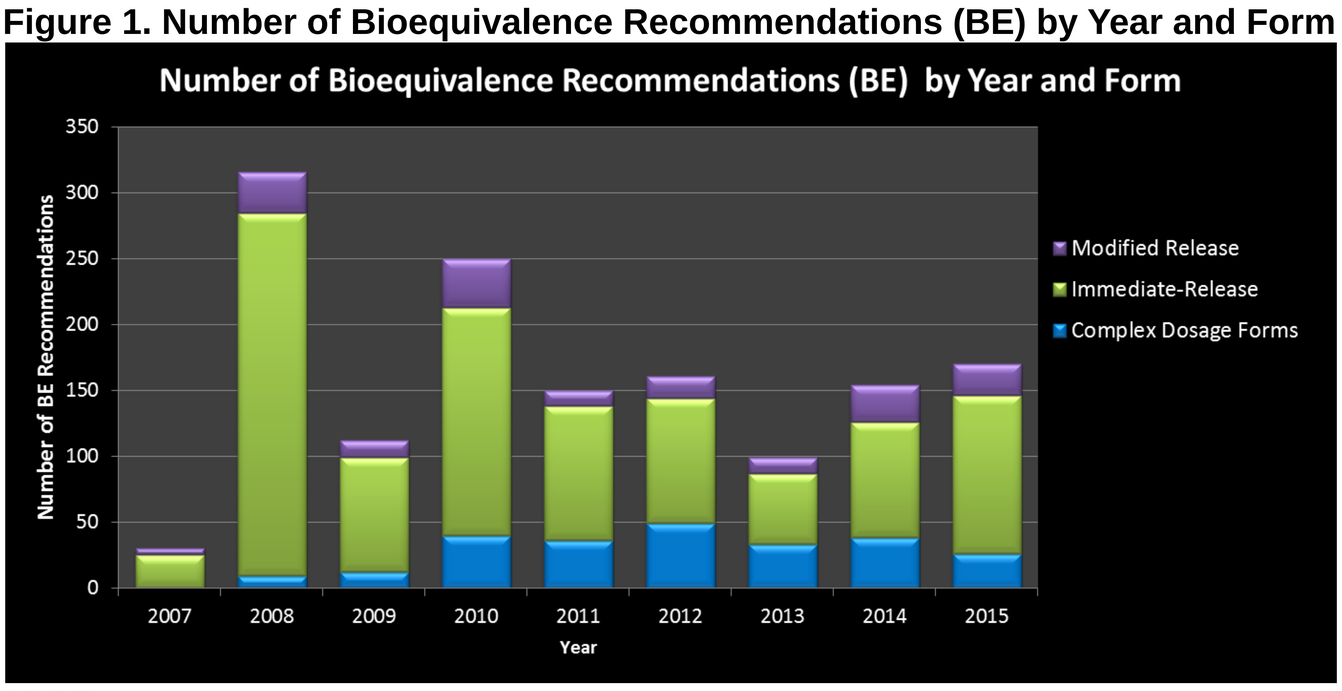
Data were retrieved from the publically available product-specific BE recommendation website[2], Drugs@FDA[3], and National Drug Code (NDC) directory[4] databases.

Analysis:

- Trends over time and the distribution of ANDAs approved that have BE recommendations compared to those ANDAs approved that did not have BE recommendations were examined.
- Patterns of pharmacologic drug class between BE recommendations and ANDAs approved were examined.
- ANDA approval per recommendation in each pharmacologic drug class were evaluated.
- Descriptive statistics and chi-squared tests were used.

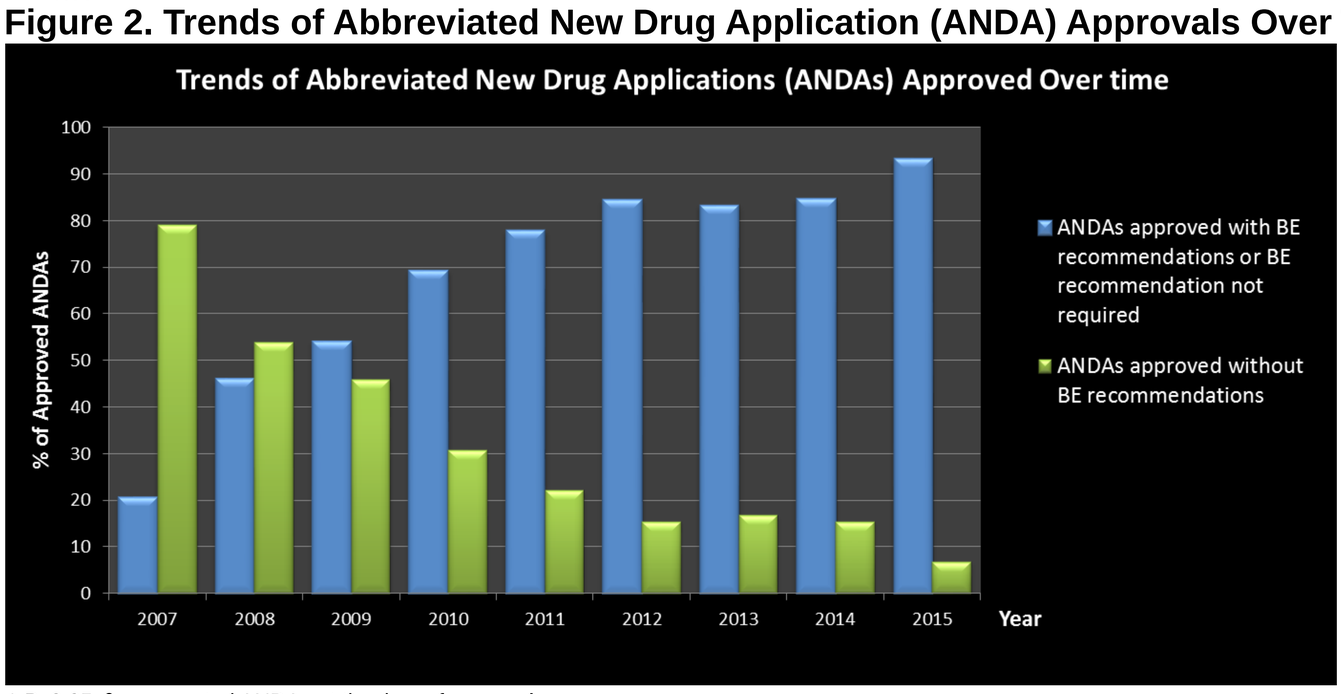
Results

Figure 1. Number of Bioequivalence Recommendations (BE) by Year and Form



* $P<0.05$

Figure 2. Trends of Abbreviated New Drug Application (ANDA) Approvals Over Time[a]



* $P<0.05$; [a] represented ANDAs at the time of approval..

Table1. Proportions of Pharmacologic Drug Class between Bioequivalence Recommendations (BE) and Abbreviated New Drug Applications (ANDAs) Approved[a,b]

BE	Percentage	ANDAs Approved	Percentage	Approval per Recommendation
Pharmacologic Drug Class	(%)	Pharmacologic Drug Class	(%)	(n)
Corticosteroid	3.68	Opioid Agonist	4.31	3.34
Opioid Agonist	3.51	Anti-epileptic Agent	4.24	4.66
Nonsteroidal Anti-inflammatory Drug	3.08	Angiotensin 2 Receptor Blocker	3.43	5.74
Anti-epileptic Agent	2.48	Atypical Antipsychotic	3.33	6.24
Retinoid	2.05	Dihydropyridine Calcium Channel Blocker	2.58	6.31
Azole Antifungal	1.97	Serotonin Reuptake Inhibitor	2.36	5.36
Kinase Inhibitor	1.97	Corticosteroid	2.33	1.72
Angiotensin 2 Receptor Blocker	1.63	Nonsteroidal Anti-inflammatory Drug	2.07	1.83
Atypical Antipsychotic	1.46	Serotonin-3 Receptor Antagonist	2.07	8.25
Lincosamide Antibacterial	1.28	Cholinesterase Inhibitor	2.04	6.50

* $P<0.05$; [a] represented the first 10 highest proportions of pharmacologic drug classes; [b] Average ANDA approval per recommendation in each pharmacologic class

Main Findings

- A total of 1,440 published BE recommendations between 2007-2015 were identified.
- The number of recommendations was highest in 2008 (n=316) resulting from publishing advice already given via letters over the past 10 years whereas the later recommendations were reviews done at the time ($P<0.05$) (Figure1).
- Corticosteroids had the highest proportion of BE recommendations, followed by opioid agonists, and nonsteroidal anti-inflammatory drugs (Table 1).
- Opioid agonists, anti-epileptics, and angiotensin II receptor blockers were pharmacologic classes with a high proportion of approved ANDAs ($P<0.05$) (Table 1).
- Of those approved ANDAs, psychotropic and anti-hypertensive products had a high average number of approved ANDAs per recommendation in each pharmacologic drug class, particularly serotonin-3 receptor antagonist, cholinesterase inhibitor, dihydropyridine calcium channel blocker (Table 1). However, this could be affected by differences in reference listed drug patent expiry.
- Overall, 67.13% of ANDAs approvals had sufficient BE recommendations, either recommendation available or not required at the time of approval (Figure 2).
- The mean number of ANDAs (±SD), excluding solutions/injectables, per recommendation was 2.58 (±4.35).
- An analysis of ANDAs approved over time demonstrated the share of ANDAs approved with recommendations was consistently higher than the share of ANDAs approved without recommendations ($P<0.05$) (Figure 2).

Conclusions

- The number of published BE recommendations varied over time. BE recommendations cover a wide range of pharmacologic classes and the majority of ANDAs were approved for products with BE recommendations.
- Findings support the continuing need for BE recommendations for more complex products that may further facilitate ANDA approvals.

References

1. http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075207.htm
2. http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075207.htm
3. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm
4. http://www.fda.gov/Drugs/InformationOnDrugs/ucm142438.htm

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