



Impact REPORT

ANALYSIS AND INSIGHT INTO CRITICAL DRUG DEVELOPMENT ISSUES

New or modified indications for existing drugs have steadily increased in U.S.

Tufts CSDD study offers comprehensive look at supplemental indication trends

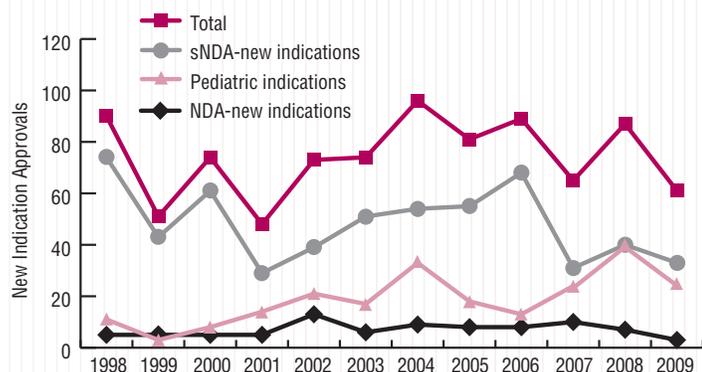
- New or modified indication approvals in the U.S. increased 17% from 1998-03 to 2004-09.
- Antiinfective and CNS drugs each accounted for at least one-fifth of all new or modified indication approvals from 1998 to 2009.
- During 1998-09 the number of new or modified indications per drug ranged from 1 to 20.
- Mean time from approval of a new drug to approval of a new or modified indication averaged approximately 9 years, with a median time of approximately 8 years.
- Mean regulatory approval phase time for new or modified indications declined by 21% from 1998-03 to 2004-09 (from 13.6 months to 10.8 months).
- Mean regulatory approval phase times for new or modified indications during 1998-09 ranged from 8.7 months for antineoplastic drugs to 13.6 months for CNS drugs.

Drug developers seeking new revenue streams have stepped up their efforts to seek regulatory approval for new or modified indications for existing drugs. Those efforts, summarized in this *Tufts CSDD Impact Report*, underscore the enormous pressure on drug firms to expand their markets and bolster sales in the United States.

While new indication approvals can translate into revenue growth, exactly how much growth depends on the indication and the number of competitor products, and therefore can vary widely. Similarly, clinical trials to support new indications can take less time than was required for the original indication since developers often don't have to conduct Phase I studies to determine the pharmacokinetic and pharmacodynamic actions of the drug. However, time savings is not a given. All that said, many drug companies are working to find the right balance between investing precious R&D resources in finding new indications for existing drugs and developing novel compounds.

New or modified indication approvals in the U.S. increased during 1998-09

Trends in the Number of U.S. New Indication Approvals



Source: Tufts Center for the Study of Drug Development

- Aggregate U.S. new (i.e., subsequent to original drug approval) or modified indication approvals increased 17% from 1998-03 to 2004-09.
- 65% of U.S. approvals for new or modified indications during 1998-09 were granted for supplemental NDAs (sNDAs); 9% through original NDAs; and 26% for use in pediatric populations.
- Pediatric indications drove approvals: from 1998-03 to 2004-09, sNDA new indication approvals declined 5%; original NDA new indication approvals increased 15%, but pediatric indication approvals grew by 107%.

Two therapeutic categories accounted for 41% of modified indication approvals in 1998-09

New Indication Approvals by Therapeutic Class and Period of New Indication Approval

Therapeutic Class	1998-2003 (N=374)	2004-2009 (N=449)	1998-2009 (N=823)
Analgesic/Anesthetic	8.3%	9.1%	8.7%
Antiinfective	23.8%	19.2%	21.3%
Antineoplastic	11.2%	15.1%	13.4%
Cardiovascular	18.2%	12.9%	15.3%
CNS	15.5%	23.8%	20.0%
Endocrine	7.8%	8.2%	8.0%
Gastrointestinal	4.3%	4.9%	4.6%
Immunologic	2.7%	2.7%	2.7%
Respiratory	7.5%	3.6%	5.3%

NOTE: New indications approved 1998-09; original approvals 1963-09; grouped by therapeutic category of the original approval

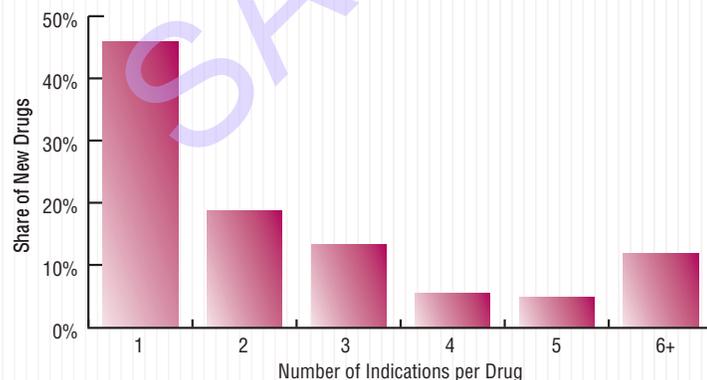
CNS = Central nervous system

Source: Tufts Center for the Study of Drug Development

- Antiinfective and CNS drugs each accounted for at least one-fifth of all new or modified indication approvals from 1998 to 2009.
- Immunologic, gastrointestinal, and respiratory drugs were categories with relatively small shares of new or modified indications.
- Compared to the distribution of original drug approvals by therapeutic category for new drugs with new or modified indications approved in 1998-09, CNS drugs stand out in terms of the number of indications per drug: while only 12% of the original drug approvals were for CNS drugs, those drugs captured 20% of the new or modified indication approvals.

The number of new or modified indications per drug varied widely during 1998-09

Number of New Indications per Drug for Drugs with New Indications Approved 1998-2009



NOTE: New drugs originally approved 1963-09

Source: Tufts Center for the Study of Drug Development

- The number of new or modified indications per drug (originally approved 1963-2009) ranged from 1 to 20 during 1998-09.
- More than half of the drugs with new or modified indications approved during this period had more than one new or modified indication approved.
- Approximately one in eight new drugs with new or modified indications approved from 1998 to 2009 had at least six approved new or modified indications.

The time from original approval to new indication approval varied by indication type

Average Time from Original Regulatory Approval to New Indication Approval (Years)

New Indication Type	1998-2003		2004-2009		1998-2009	
	Mean	Median	Mean	Median	Mean	Median
sNDA – new indication	8.2	6.8	9.0	7.4	8.6	7.3
NDA – new indication	8.0	6.5	6.6	4.5	7.3	5.1
Pediatric indication	11.3	10.4	11.5	10.7	11.5	10.7
All new indications	8.8	7.3	9.6	7.7	9.2	7.6

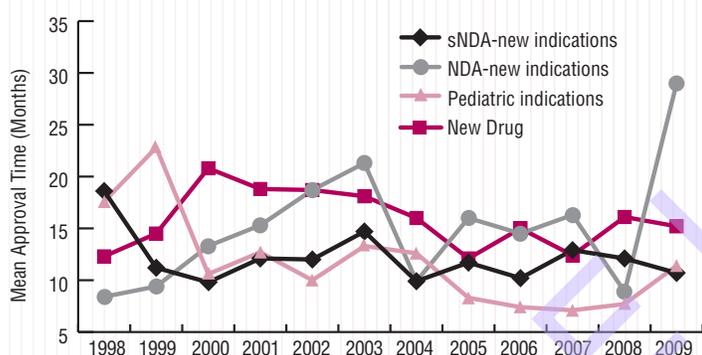
NOTE: New indications approved 1998-09; only therapeutic drugs included

Source: Tufts Center for the Study of Drug Development

- During 1998-09 mean time from approval of a new drug to approval of a new or modified indication averaged approximately 9 years, with a median time of approximately 8 years.
- The average time from original approval to new or modified indication approval increased by less than a year from 1998-03 to 2004-09.
- The average time from original to new indication approval for pediatric indication approvals was 2.9 years longer than for sNDA new indication approvals, and 4.2 years longer than for NDA new indication approvals.

Approval phase times for new or modified indications declined during 1998-09

Annual U.S. New Indication and New Drug Approval Times



Source: Tufts Center for the Study of Drug Development

- Mean regulatory approval phase time for new or modified indications declined by 21% from 1998-03 to 2004-09 (from 13.6 months to 10.8 months).
- Over the same periods, original therapeutic new drug approval phase times declined by 14% (17.0 months to 14.7 months).
- The decline in regulatory approval phase times for new or modified indications was particularly large for pediatric indications (28%; 13.0 months to 9.3 months).

Approval phase times for new or modified indications varied by therapeutic class

Average Regulatory Approval Times for New Indications (Months)

Therapeutic Class	1998-2003		2004-2009		1998-2009	
	Mean	Median	Mean	Median	Mean	Median
Analgesic/Anesthetic	13.9	10.0	12.0	9.9	12.8	10.0
Antiinfective	12.3	10.0	8.3	7.8	10.4	9.7
Antineoplastic	9.7	9.9	8.1	6.0	8.7	7.2
Cardiovascular	11.9	10.1	12.2	9.9	12.0	10.0
CNS	15.7	12.1	12.4	9.9	13.6	10.0
Endocrine	11.9	10.0	14.0	10.1	13.1	10.1
Gastrointestinal	11.3	10.0	8.6	9.7	9.7	9.9
Immunologic	9.1	6.9	11.1	10.0	10.2	9.9
Respiratory	11.0	10.3	12.7	9.9	11.6	10.0

NOTE: New indications approved 1998-09; original approvals 1963-09; grouped by therapeutic category of the original approval

CNS = Central nervous system

Source: Tufts Center for the Study of Drug Development

- Mean regulatory approval phase times for new or modified indications during 1998-09 varied from 8.7 months for antineoplastic drugs to 13.6 months for CNS drugs (56% difference).
- From 1998-03 to 2004-09, mean regulatory approval phase times increased for cardiovascular, endocrine, immunologic, and respiratory drugs, and decreased for anesthetic/analgesic, antiinfective, antineoplastic, CNS, and gastrointestinal drugs.
- The largest increase in mean regulatory approval phase times was seen for immunologic drugs (22%), while the largest decrease was for antiinfective drugs (33%).

About this study

The findings in this report were based on data obtained from the U.S. Food and Drug Administration (FDA) and the Tufts CSDD Approved Drug Database. Data on efficacy supplements approved by the agency from 1998 through 2009 were collected from the FDA's website. Information on the original approvals for drugs that had new indications approved from 1998 through 2009 was obtained from the Tufts CSDD database. Data on original approvals are for NMEs and biologics with BLAs approved by the FDA's Center for Drug Evaluation and Research. The data on efficacy supplements include submission and approval dates, generic name, the sponsor company, application type, the length of the application's approval phase, and the indication for which the drug is used.

The full data set of efficacy supplements contains information on 1,538 approvals. However, the focus of this report is on new or modified indication approvals. The subset taken for analysis for this study consisted of data on 889 approvals. The majority of the approvals were obtained through the FDA's sNDA process, although a relatively small percentage of the new indication approvals were obtained through original NDAs, and a somewhat larger percentage of the approvals are designated for pediatric populations. The pediatric new indications were approved under sNDAs. In the current report, "sNDA new indication approvals" refers to new or modified indications approved through an sNDA other than new pediatric indications.

Joseph A. DiMasi, Ph.D., Director of Economic Analysis at the Tufts Center for the Study of Drug Development, is the principal investigator for the study. Additional results and discussion will be included in a future publication.

Definition of terms

BLA — Biologics license application. An application to the FDA for a license to market a new biological product.

NDA — New drug application. An application to the FDA for a license to market a new drug.

sNDA — Supplemental new drug application. An application to the FDA for a new use, a new dosage strength, or a new way to manufacture an already-approved drug.

NME — New molecular entity. A newly developed compound, whose active ingredient has not been previously approved in the U.S. The term was coined by the FDA for use in its published statistical reports.

Pediatric indication — Use of a drug in pediatric populations for indications already approved for adults.

About the Tufts Center for the Study of Drug Development

The Tufts Center for the Study of Drug Development at Tufts University provides strategic information to help drug developers, regulators, and policy makers improve the quality and efficiency of pharmaceutical development, review, and utilization. Tufts CSDD conducts a wide range of in-depth analyses on pharmaceutical issues and hosts symposia, workshops, and public forums.

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