

Supplemental Online Content

Gupta R, Morten CJ, Zhu AY, Ramachandran R, Shah ND, Ross JS. Approvals and timing of new formulations of novel drugs approved by the US Food and Drug Administration between 1995 and 2010 and followed through 2021. *JAMA Health Forum*. 2022;3(5):e221096. doi:10.1001/jamahealthforum.2022.1096

eFigure 1. Drug Sample Selection

eTable 1. Novel Drug Therapeutic Area Classification

eFigure 2. Proportion of Novel Tablets and Capsules Approved by the US FDA From 1995 to 2010 with New Formulation Approvals, Overall and According to Blockbuster Status, Accelerated Approval, WHO Essential Medicine, Orphan Drug Status, Innovation Status, Clinical Usefulness, Therapeutic Area, and Approval Year

eTable 2. Measures of Therapeutic Value of Novel Tablets and Capsules Approved by the US FDA From 1995 to 2010, Including Accelerated Approval, WHO Essential Medicine, Innovation Status, and Clinical Usefulness

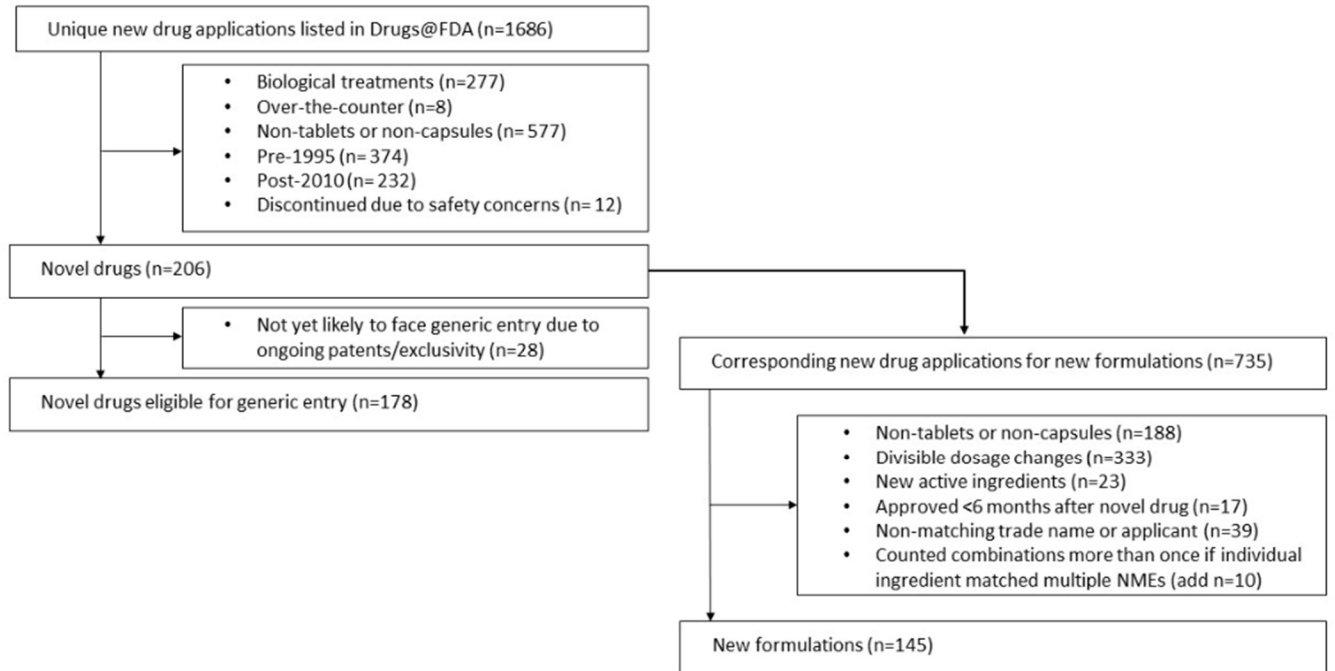
eMethods. Additional New Formulation Approval Timing Analysis With Time Windows Relative to Novel Drug's First Generic Approval

eTable 3. Correlation Between Blockbuster Status and Measures of Therapeutic Value of Novel Tablets and Capsules Approved by the US FDA From 1995 to 2010, Including Accelerated Approval, WHO Essential Medicine, Innovation Status, and Clinical Usefulness

eTable 4. Correlation Between Measures of Therapeutic Value of Novel Tablets and Capsules Approved by the US FDA From 1995 to 2010, Including Accelerated Approval, WHO Essential Medicine, Innovation Status, and Clinical Usefulness

This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure 1. Drug Sample Selection

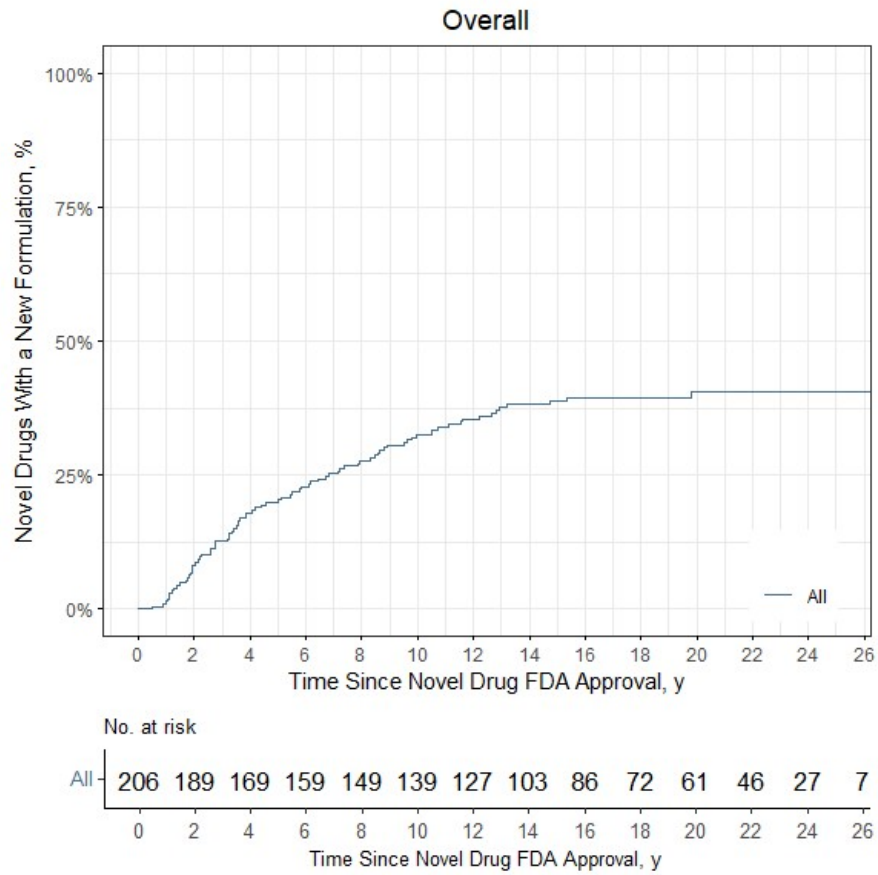


eTable 1. Novel Drug Therapeutic Area Classification

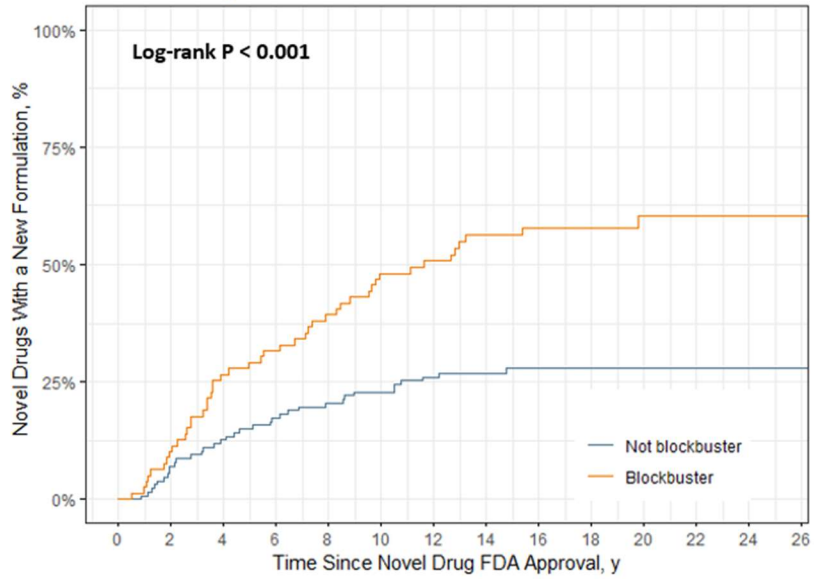
WHO Anatomic Therapeutic Chemical Classification	Final Category
Alimentary tract and metabolism	Gastrointestinal
Blood and blood forming organs	Other
Cardiovascular system	CV, diabetes, & HLD
Dermatologicals	Other
Genitourinary system and sex hormones	Genitourinary system and sex hormones
Systemic hormonal preparations, excluding sex hormones and insulins	Other
Antiinfective for systemic use	Infectious disease
Antineoplastic and immunomodulating agents	Cancer
Musculo-skeletal system	Autoimmune and musculoskeletal
Nervous system	Neurology ^a
Antiparasitic products, insecticides, and repellants	Infectious disease
Respiratory system	Other
Sensory organs	Other
Various	Other

^aThis category were subcategorized into neurology and psychiatry using WHO Anatomic Therapeutic Chemical sublevels.

eFigure 2. Proportion of Novel Tablets and Capsules Approved by the US FDA From 1995 to 2010 with New Formulation Approvals, Overall and According to Blockbuster Status, Accelerated Approval, WHO Essential Medicine, Orphan Drug Status, Innovation Status, Clinical Usefulness, Therapeutic Area, and Approval Year



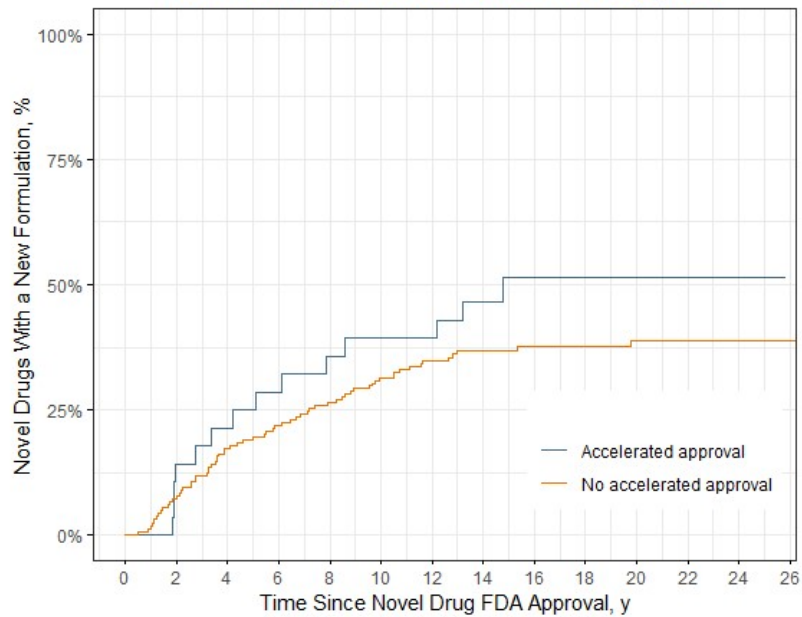
Drug blockbuster status vs no blockbuster status



No. at risk by blockbuster status

Not blockbuster	127	118	111	105	101	98	90	72	62	55	46	36	23	6
Blockbuster	79	71	58	54	48	41	37	31	24	17	15	10	4	1
	0	2	4	6	8	10	12	14	16	18	20	22	24	26

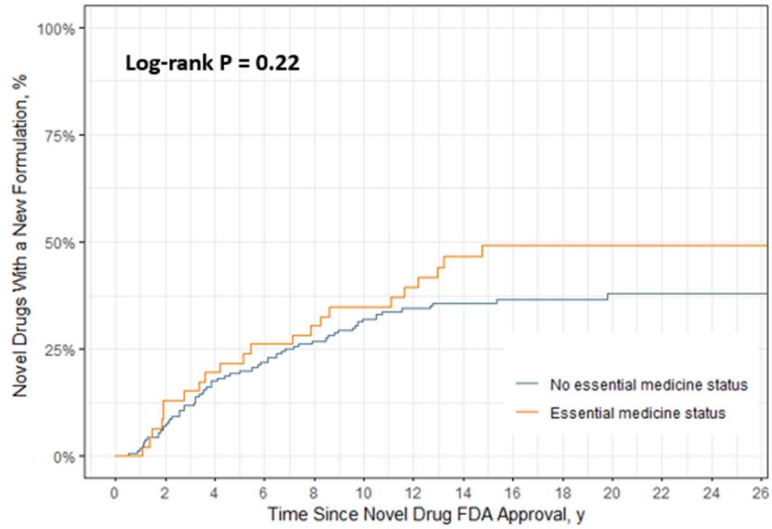
Accelerated approval vs no accelerated approval



No. at risk by accelerated approval status

Accelerated approval	28	24	22	20	18	17	17	13	8	7	7	7	3	0
No accelerated approval	178	165	147	139	131	122	110	90	78	65	54	39	24	7
	0	2	4	6	8	10	12	14	16	18	20	22	24	26

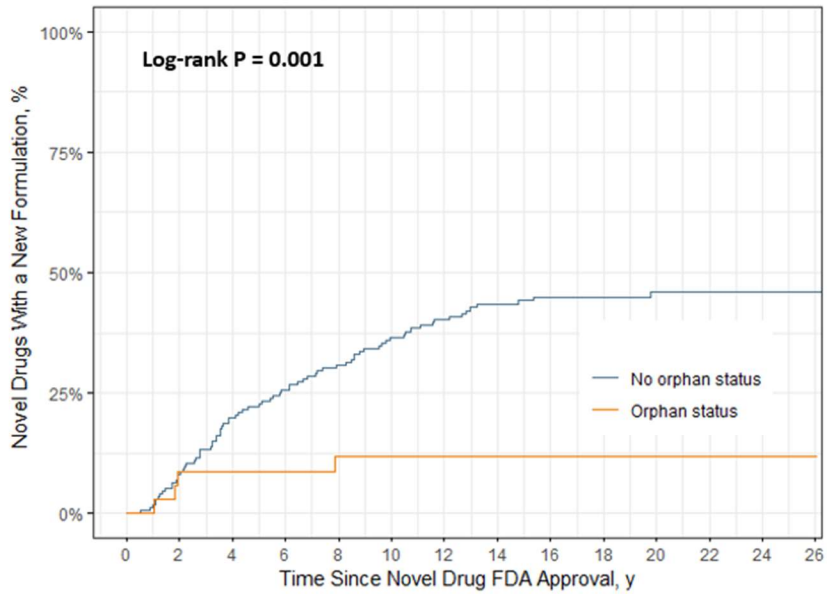
WHO essential medicine status



No. at risk by WHO essential medicine status

No essential medicine status	160	149	132	125	117	109	101	81	69	59	50	36	21	6
Essential medicine status	46	40	37	34	32	30	26	22	17	13	11	10	6	1
	0	2	4	6	8	10	12	14	16	18	20	22	24	26

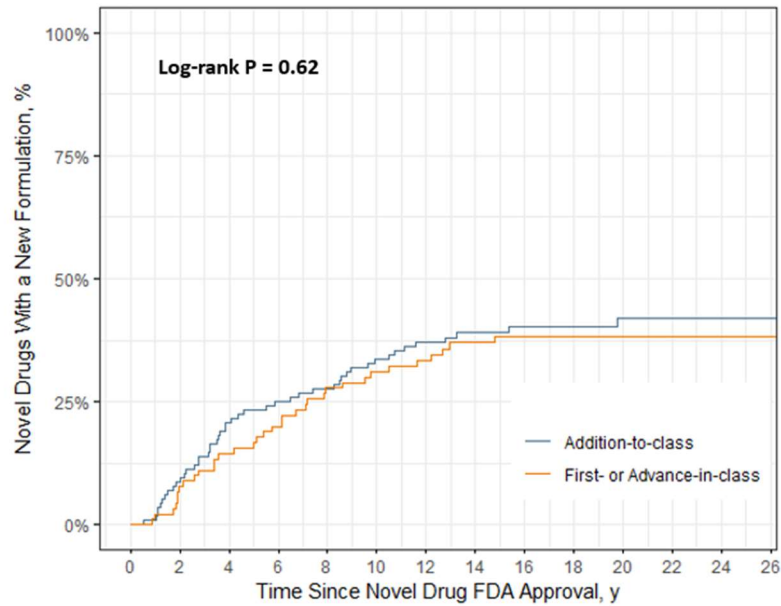
Drug orphan status vs no orphan status



No. at risk by drug orphan status

No orphan status	172	158	138	128	119	109	98	79	67	57	49	35	21	6
Orphan status	34	31	31	31	30	30	29	24	19	15	12	11	6	1
	0	2	4	6	8	10	12	14	16	18	20	22	24	26

Innovation Status

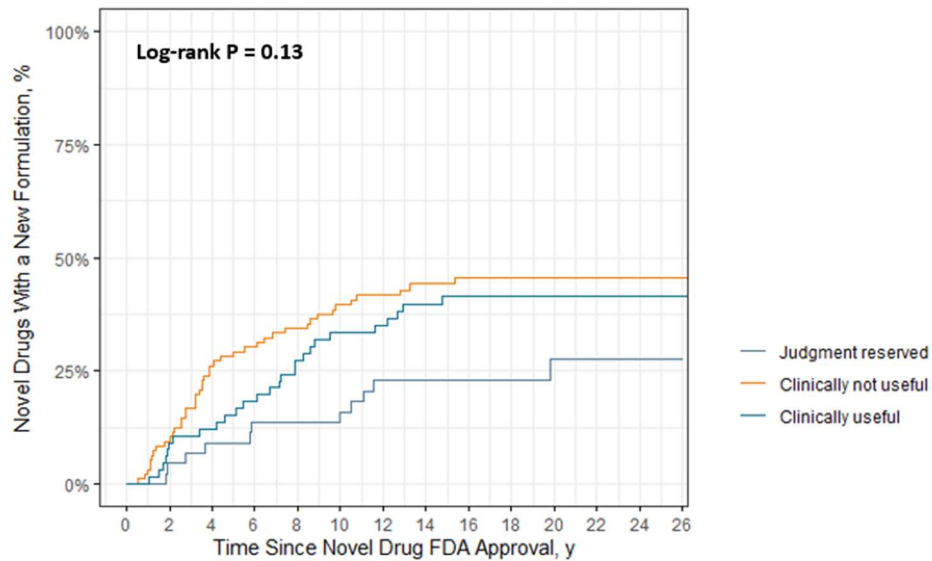


No. at risk by innovation status

	0	2	4	6	8	10	12	14	16	18	20	22	24	26
Addition-to-class	116	106	92	87	84	77	70	55	47	40	35	24	15	4
First- or Advance-in-class	90	83	77	72	65	62	57	48	39	32	26	22	12	3

Time Since Novel Drug FDA Approval, y

Clinical Usefulness

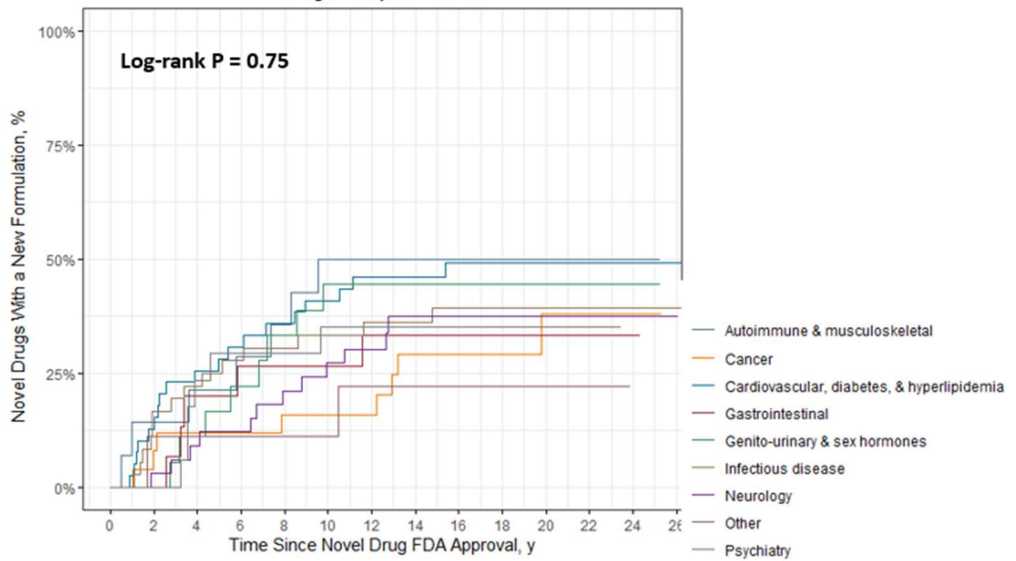


No. at risk

	0	2	4	6	8	10	12	14	16	18	20	22	24	26
Judgment reserved	44	42	40	38	38	37	32	26	22	17	15	13	7	1
Clinically not useful	96	87	71	67	63	58	53	42	34	30	26	18	8	3
Clinically useful	66	60	58	54	48	44	42	35	30	25	20	15	12	3

Time Since Novel Drug FDA Approval, y

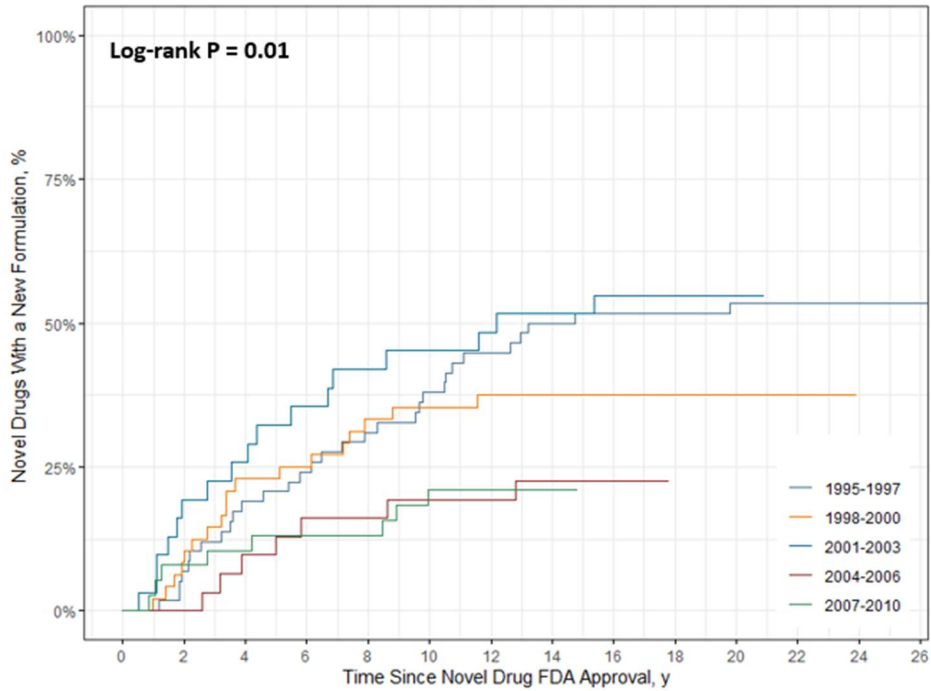
Drug therapeutic area



No. at risk by drug therapeutic area

Autoimmune & musculoskeletal	14	12	11	10	9	7	7	6	6	6	4	3	2	0
Cancer	25	23	22	22	21	21	20	16	11	8	7	7	3	0
Cardiovascular, diabetes, & hyperlipidemia	39	34	29	27	25	23	21	18	15	15	14	11	9	4
Gastrointestinal	15	15	12	11	11	11	10	9	7	7	4	2	1	0
Genito-urinary & sex hormones	18	18	16	14	12	10	8	6	6	4	4	3	3	0
Infectious disease	36	30	28	26	25	24	23	21	17	13	12	10	7	2
Neurology	33	32	30	29	26	24	21	13	11	11	10	5	2	1
Other	9	8	8	8	8	8	6	5	5	3	2	2	0	0
Psychiatry	17	17	13	12	12	11	11	9	8	5	4	3	0	0
	0	2	4	6	8	10	12	14	16	18	20	22	24	26
	Time Since Novel Drug FDA Approval, y													

Drug approval year



No. at risk by drug approval year

1995-1997	58	54	47	44	40	36	32	29	28	28	27	27	27	7
1998-2000	48	44	37	36	32	31	30	30	30	30	30	19	0	0
2001-2003	31	25	23	20	18	17	16	15	14	14	4	0	0	0
2004-2006	31	31	28	26	26	25	25	24	14	0	0	0	0	0
2007-2010	38	35	34	33	33	30	24	5	0	0	0	0	0	0
	0	2	4	6	8	10	12	14	16	18	20	22	24	26
	Time Since Novel Drug FDA Approval, y													

eTable 2. Measures of Therapeutic Value of Novel Tablets and Capsules Approved by the US FDA From 1995 to 2010, Including Accelerated Approval, WHO Essential Medicine, Innovation Status, and Clinical Usefulness

Drug	Accelerated Approval	WHO Essential Medicine Listing	Innovation Status	Clinical Usefulness Based on Prescribe Rating
Abacavir Sulfate (Ziagen)	AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Acamprosate Calcium (Campral)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Acarbose (Precose)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Adefovir Dipivoxil (Hepsera)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Albendazole (Albenza)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Alendronate Sodium (Fosamax)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Alfuzosin Hydrochloride (Uroxatral)	Not AA	No	Addition-to-class	Therapeutically Helpful
Aliskiren Hemifumarate (Tekturna)	Not AA	No	First- or Advance-in-class	Not helpful
Almotriptan Malate (Axert)	Not AA	No	Addition-to-class	Not helpful
Alosetron Hydrochloride (Lotronex)	Not AA	No	First- or Advance-in-class	Not helpful
Alvimopan (Entereg)	Not AA	No	Addition-to-class	Judgment Reserved
Ambrisentan (Letairis)	Not AA	No	Addition-to-class	Not helpful
Amprenavir (Agenerase)	AA	No	Addition-to-class	Not helpful
Anagrelide Hydrochloride (Agrylin)	Not AA	No	First- or Advance-in-class	Judgment Reserved
Anastrozole (Arimidex)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Aprepitant (Emend)	Not AA	Yes	First- or Advance-in-class	Not helpful
Aripiprazole (Abilify)	Not AA	No	First- or Advance-in-class	Not helpful
Artemether; Lumefantrine (Coartem)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Asenapine Maleate (Saphris)	Not AA	No	Addition-to-class	Not helpful
Atazanavir Sulfate (Reyataz)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Atomoxetine Hydrochloride (Strattera)	Not AA	No	First- or Advance-in-class	Not helpful
Atorvastatin Calcium (Lipitor)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Balsalazide Disodium (Colazal)	Not AA	No	Addition-to-class	Judgment Reserved
Bexarotene (Targretin)	Not AA	No	First- or Advance-in-class	Not helpful
Bicalutamide (Casodex)	AA	Yes	Addition-to-class	Not helpful

Bismuth Subcitrate Potassium; Metronidazole; Tetracycline Hydrochloride (Pylera)	Not AA	No	Addition-to-class	Not helpful
Bosentan (Tracleer)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Cabergoline (Dostinex)	Not AA	No	Addition-to-class	Therapeutically Helpful
Candesartan Cilexetil (Atacand)	Not AA	No	Addition-to-class	Not helpful
Capecitabine (Xeloda)	AA	Yes	First- or Advance-in-class	Not helpful
Carvedilol (Coreg)	Not AA	Yes	Addition-to-class	Judgment Reserved
Cefdinir (Omnicef)	Not AA	No	Addition-to-class	Judgment Reserved
Ceftibuten Dihydrate (Cedax)	Not AA	No	Addition-to-class	Judgment Reserved
Celecoxib (Celebrex)	Not AA	No	First- or Advance-in-class	Not helpful
Cetirizine Hydrochloride (Zyrtec Allergy)	Not AA	Yes	Addition-to-class	Therapeutically Helpful
Cevimeline Hydrochloride (Evoxac)	Not AA	No	Addition-to-class	Judgment Reserved
Cilostazol (Pletal)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Cinacalcet Hydrochloride (Sensipar)	Not AA	No	First- or Advance-in-class	Judgment Reserved
Citalopram Hydrobromide (Celexa)	Not AA	Yes	Addition-to-class	Not helpful
Clopidogrel Bisulfate (Plavix)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Colesevelam Hydrochloride (Welchol)	Not AA	No	Addition-to-class	Not helpful
Dabigatran Etxilate Mesylate (Pradaxa)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Dalfampridine (Ampyra)	Not AA	No	First- or Advance-in-class	Judgment Reserved
Darifenacin Hydrobromide (Enablex)	Not AA	No	Addition-to-class	Judgment Reserved
Darunavir (Prezista)	AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Dasatinib (Sprycel)	AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Delavirdine Mesylate (Rescriptor)	AA	No	First- or Advance-in-class	Judgment Reserved
Desloratadine (Clarinex)	Not AA	No	Addition-to-class	Not helpful
Desvenlafaxine Succinate (Pristiq)	Not AA	No	Addition-to-class	Not helpful
Dienogest; Estradiol Valerate (Natazia)	Not AA	No	Addition-to-class	Not helpful
Dirithromycin (Dynabac)	Not AA	No	Addition-to-class	Not helpful
Dofetilide (Tikosyn)	Not AA	No	Addition-to-class	Judgment Reserved
Dolasetron Mesylate (Anzemet)	Not AA	Yes	Addition-to-class	Judgment Reserved
Donepezil Hydrochloride (Aricept)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Doxercalciferol (Hectorol)	Not AA	No	Addition-to-class	Judgment Reserved

Dronedaronone Hydrochloride (Multaq)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Drospirenone; Ethinyl Estradiol (Yasmin)	Not AA	No	Addition-to-class	Not helpful
Duloxetine Hydrochloride (Cymbalta)	Not AA	No	Addition-to-class	Not helpful
Dutasteride (Avodart)	Not AA	No	Addition-to-class	Not helpful
Efavirenz (Sustiva)	AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Eletriptan Hydrobromide (Relpax)	Not AA	No	Addition-to-class	Not helpful
Eltrombopag Olamine (Promacta)	AA	No	First- or Advance-in-class	Judgment Reserved
Emtricitabine (Emtriva)	Not AA	No	Addition-to-class	Not helpful
Entacapone (Comtan)	Not AA	No	Addition-to-class	Judgment Reserved
Entecavir (Baraclude)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Eplerenone (Inspra)	Not AA	No	Addition-to-class	Therapeutically Helpful
Eprosartan Mesylate (Teveten)	Not AA	No	Addition-to-class	Not helpful
Erlotinib Hydrochloride (Tarceva)	Not AA	Yes	First- or Advance-in-class	Not helpful
Eszopiclone (Lunesta)	Not AA	No	Addition-to-class	Judgment Reserved
Etravirine (Intelence)	AA	No	First- or Advance-in-class	Therapeutically Helpful
Everolimus (Afinitor)	Not AA	Yes	Addition-to-class	Therapeutically Helpful
Exemestane (Aromasin)	Not AA	No	Addition-to-class	Not helpful
Ezetimibe (Zetia)	Not AA	No	First- or Advance-in-class	Not helpful
Febuxostat (Uloric)	Not AA	No	Addition-to-class	Not helpful
Ferric Hexacyanoferrate(II) (Radiogardase (Prussian Blue))	Not AA	Yes	First- or Advance-in-class	Judgment Reserved
Fesoterodine Fumarate (Toviaz)	Not AA	No	Addition-to-class	Judgment Reserved
Fexofenadine Hydrochloride (Allegra)	Not AA	Yes	Addition-to-class	Not helpful
Fingolimod Hydrochloride (Gilenya)	Not AA	No	First- or Advance-in-class	Not helpful
Frovatriptan Succinate (Frova)	Not AA	No	Addition-to-class	Not helpful
Galantamine Hydrobromide (Razadyne)	Not AA	No	Addition-to-class	Not helpful
Gefitinib (Iressa)	AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Glimepiride (Amaryl)	Not AA	No	Addition-to-class	Not helpful
Ibandronate Sodium (Boniva)	Not AA	No	Addition-to-class	Not helpful
Iloperidone (Fanapt)	Not AA	No	Addition-to-class	Judgment Reserved
Imatinib Mesylate (Gleevec)	AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Indinavir Sulfate (Crixivan)	AA	No	First- or Advance-in-class	Therapeutically Helpful
Irbesartan (Avapro)	Not AA	No	Addition-to-class	Therapeutically Helpful

Ivermectin (Stromectol)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Lacosamide (Vimpat)	Not AA	No	Addition-to-class	Not helpful
Lamivudine (Epivir)	AA	Yes	First- or Advance-in-class	Judgment Reserved
Lansoprazole (Prevacid)	Not AA	No	Addition-to-class	Not helpful
Lanthanum Carbonate (Fosrenol)	Not AA	No	Addition-to-class	Not helpful
Lapatinib Ditosylate (Tykerb)	Not AA	No	Addition-to-class	Therapeutically Helpful
Leflunomide (Arava)	Not AA	No	First- or Advance-in-class	Not helpful
Lenalidomide (Revlimid)	Not AA	Yes	First- or Advance-in-class	Judgment Reserved
Letrozole (Femara)	Not AA	No	Addition-to-class	Judgment Reserved
Levetiracetam (Keppra)	Not AA	No	Addition-to-class	Therapeutically Helpful
Linezolid (Zyvox)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Lisdexamfetamine Dimesylate (Vyvanse)	Not AA	No	Addition-to-class	Judgment Reserved
Lopinavir; Ritonavir (Kaletra)	AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Losartan Potassium (Cozaar)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Lubiprostone (Amitiza)	Not AA	No	First- or Advance-in-class	Judgment Reserved
Lurasidone Hydrochloride (Latuda)	Not AA	No	Addition-to-class	Judgment Reserved
Maraviroc (Selzentry)	AA	No	First- or Advance-in-class	Judgment Reserved
Meloxicam (Mobic)	Not AA	No	Addition-to-class	Not helpful
Memantine Hydrochloride (Namenda)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Metformin Hydrochloride (Glucophage)	Not AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Midodrine Hydrochloride (Proamatine)	AA	No	First- or Advance-in-class	Therapeutically Helpful
Mifepristone (Mifeprex)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Miglitol (Glyset)	Not AA	No	Addition-to-class	Therapeutically Helpful
Miglustat (Zavesca)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Milnacipran Hydrochloride (Savella)	Not AA	No	Addition-to-class	Not helpful
Mirtazapine (Remeron)	Not AA	No	Addition-to-class	Therapeutically Helpful
Modafinil (Provigil)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Moexipril Hydrochloride (Univasc)	Not AA	No	Addition-to-class	Not helpful
Montelukast Sodium (Singulair)	Not AA	No	Addition-to-class	Judgment Reserved
Moxifloxacin Hydrochloride (Avelox)	Not AA	Yes	Addition-to-class	Not helpful

Mycophenolate Mofetil (Cellcept)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Naratriptan Hydrochloride (Amerge)	Not AA	No	Addition-to-class	Therapeutically Helpful
Nateglinide (Starlix)	Not AA	No	Addition-to-class	Not helpful
Nebivolol Hydrochloride (Bystolic)	Not AA	No	Addition-to-class	Not helpful
Nelfinavir Mesylate (Viracept)	AA	No	First- or Advance-in-class	Therapeutically Helpful
Nevirapine (Viramune)	AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Nilotinib Hydrochloride (Tasigna)	AA	Yes	Addition-to-class	Judgment Reserved
Nilutamide (Nilandron)	Not AA	Yes	Addition-to-class	Not helpful
Nisoldipine (Sular)	Not AA	No	Addition-to-class	Not helpful
Nitisinone (Orfadin)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Olanzapine (Zyprexa)	Not AA	No	Addition-to-class	Not helpful
Olmesartan Medoxomil (Benicar)	Not AA	No	Addition-to-class	Not helpful
Omega-3-Acid Ethyl Esters (Lovaza)	Not AA	No	First- or Advance-in-class	Not helpful
Orlistat (Xenical)	Not AA	No	First- or Advance-in-class	Not helpful
Oseltamivir Phosphate (Tamiflu)	Not AA	Yes	First- or Advance-in-class	Not helpful
Oxcarbazepine (Trileptal)	Not AA	No	Addition-to-class	Therapeutically Helpful
Paliperidone (Invega)	Not AA	Yes	Addition-to-class	Not helpful
Pantoprazole Sodium (Protonix)	Not AA	No	Addition-to-class	Therapeutically Helpful
Pazopanib Hydrochloride (Votrient)	Not AA	No	Addition-to-class	Not helpful
Pentosan Polysulfate Sodium (Elmiron)	Not AA	No	First- or Advance-in-class	Not helpful
Pioglitazone Hydrochloride (Actos)	Not AA	No	First- or Advance-in-class	Not helpful
Pitavastatin Calcium (Livalo)	Not AA	No	Addition-to-class	Not helpful
Pramipexole Dihydrochloride (Mirapex)	Not AA	No	First- or Advance-in-class	Therapeutically Helpful
Prasugrel Hydrochloride (Effient)	Not AA	No	First- or Advance-in-class	Not helpful
Pregabalin (Lyrica)	Not AA	No	Addition-to-class	Not helpful
Quetiapine Fumarate (Seroquel)	Not AA	No	Addition-to-class	Not helpful
Rabeprazole Sodium (Aciphex)	Not AA	No	Addition-to-class	Not helpful
Raloxifene Hydrochloride (Evista)	Not AA	No	First- or Advance-in-class	Not helpful
Raltegravir Potassium (Isentress)	AA	Yes	First- or Advance-in-class	Therapeutically Helpful
Ramelteon (Rozerem)	Not AA	No	First- or Advance-in-class	Not helpful
Ranolazine (Ranexa)	Not AA	No	First- or Advance-in-class	Not helpful
Rasagiline Mesylate (Azilect)	Not AA	No	Addition-to-class	Not helpful

Tiagabine Hydrochloride (Gabitril)	Not AA	No	Addition-to-class	Therapeutically Helpful
Tiludronate Disodium (Skelid)	Not AA	No	Addition-to-class	Judgment Reserved
Tinidazole (Tindamax)	Not AA	Yes	Addition-to-class	Therapeutically Helpful
Tipranavir (Aptivus)	AA	No	Addition-to-class	Therapeutically Helpful
Tizanidine Hydrochloride (Zanaflex)	Not AA	No	First- or Advance-in-class	Judgment Reserved
Tolcapone (Tasmar)	Not AA	No	First- or Advance-in-class	Not helpful
Tolterodine Tartrate (Detrol)	Not AA	No	Addition-to-class	Not helpful
Tolvaptan (Samsca)	Not AA	No	Addition-to-class	Not helpful
Topiramate (Topamax)	Not AA	No	Addition-to-class	Therapeutically Helpful
Toremifene Citrate (Fareston)	Not AA	No	Addition-to-class	Not helpful
Tramadol Hydrochloride (Ultram)	Not AA	No	Addition-to-class	Not helpful
Trandolapril (Mavik)	Not AA	No	Addition-to-class	Not helpful
Trospium Chloride (Sanctura)	Not AA	No	Addition-to-class	Not helpful
Ulipristal Acetate (Ella)	Not AA	Yes	Addition-to-class	Not helpful
Valsartan (Diovan)	Not AA	No	Addition-to-class	Not helpful
Vardenafil Hydrochloride (Levitra)	Not AA	No	Addition-to-class	Not helpful
Varenicline Tartrate (Chantix)	Not AA	Yes	First- or Advance-in-class	Not helpful
Vigabatrin (Sabril)	Not AA	No	Addition-to-class	Therapeutically Helpful
Voriconazole (Vfend)	Not AA	Yes	Addition-to-class	Therapeutically Helpful
Vorinostat (Zolinza)	Not AA	No	First- or Advance-in-class	Judgment Reserved
Zafirlukast (Accolate)	Not AA	No	First- or Advance-in-class	Judgment Reserved
Zaleplon (Sonata)	Not AA	No	Addition-to-class	Judgment Reserved
Zileuton (Zyflo)	Not AA	No	Addition-to-class	Judgment Reserved
Ziprasidone Hydrochloride (Geodon)	Not AA	No	Addition-to-class	Judgment Reserved
Zolmitriptan (Zomig)	Not AA	No	Addition-to-class	Not helpful
Zonisamide (Zonegran)	Not AA	No	Addition-to-class	Not helpful

^a Categorization was based on Prescrire ratings. Drugs that were categorized by Prescrire as “Possibly Helpful,” “Offers an Advantage,” “A Real Advance,” or “Bravo,” were grouped together as “Clinically Useful.” Drugs that were categorized as “Nothing New” and “Not Acceptable” were grouped together as “Clinically Not Useful.” The remaining drugs were categorized as “Judgment Reserved.”

eMethods. Additional New Formulation Approval Timing Analysis With Time Windows Relative to Novel Drug's First Generic Approval

We conducted an additional timing analysis to account for regulatory delays in approval by examining the likelihood of a new formulation in 4 time windows: greater than 6 years before, 2 to 6 years before, 2 years before and after, and greater than 2 years after the novel drug's first generic approval. For the time window around the generic approval, the 2-year period prior to generic approval accounts for the potential time from a generic manufacturer's application submission to FDA approval; the 2-year period after the generic's approval accounts for the possibility of regulatory delays in new formulation approvals, particularly if the company unsuccessfully attempted to time the new formulation approval with the first generic approval. We then performed multinomial logistic regression analysis with presence of the first new formulation in each of the 4 time periods relative to the novel drug's first generic version's approval timing.

Results:

Among the 65 novel drugs with both at least 1 new formulation and a generic, 32 (49%) new formulations were approved more than 6 years before the novel drugs' first generic approval, 14 (22%) were approved 2 to 6 years before generic approval, 15 (23%) were approved 2 years before and after generic approval, and 4 (6%) were approved more than 2 years after generic approval. First new formulations were less likely to be approved in the time period 2 to 6 years before the novel drug's first generic approval (RRR=0.44, 95% CI, 0.23-0.82; $P=0.01$) and 2 years before and after generic approval (RRR=0.47, 95% CI, 0.25-0.87; $P=0.015$), as compared to more than 6 years prior to first generic approval. First new formulations were significantly less likely to be approved more than 2 years after the first generic approval (RRR=0.13, 95% CI, 0.04-0.35; $P<0.001$).

eTable 3. Correlation Between Blockbuster Status and Measures of Therapeutic Value of Novel Tablets and Capsules Approved by the US FDA From 1995 to 2010, Including Accelerated Approval, WHO Essential Medicine, Innovation Status, and Clinical Usefulness

Measure of Therapeutic Value	Blockbuster status	P value
Accelerated approval	0.10	0.76
WHO essential medicine	8.27	0.004
Innovation status	1.68	0.20
Clinical Usefulness Based on Prescribe Rating	4.27	0.12

Pearson- χ^2

eTable 4. Correlation Between Measures of Therapeutic Value of Novel Tablets and Capsules Approved by the US FDA From 1995 to 2010, Including Accelerated Approval, WHO Essential Medicine, Innovation Status, and Clinical Usefulness

	WHO Essential Medicine Listing	P value	Innovation Status	P value	Clinical Usefulness Based on Prescribe Rating	P value
Accelerated approval	22.64	<0.001	23.26	<0.001	12.32	0.002
WHO essential medicine	-	-	16.12	<0.001	16.40	<0.001
Innovation status	-	-	-	-	27.34	<0.001

Pearson- χ^2