



Review of Patient Reported Outcome (PRO) Measures for Novel Drug Approvals (NDA) in the United States: 2016-2021

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BACKGROUND

- Patient Reported Outcomes (PROs) are any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else. PROs can be used to measure the effectiveness of a medical intervention.
- PROs are being used to support labeling claims about the products' effects on patients' functional status, experience of care, symptoms and symptom burden, and health related quality of life.
- Since 2006, multiple guidelines have been released by US Food and Drug Administration (FDA) regarding PROs. All guidance documents on PROs indicated that FDA values the patient's voice in clinical trials.
- As the result, PROs are becoming a bigger part of the drug approval process and, more and more new drugs being approved include PROs.
- Previous studies have looked at PRO trends from 2006-to-2011, 2011-to-2015, and 2006-to-2015 but there have been no comprehensive updates in last six years.

PURPOSE

To systematically evaluate PRO information in FDA approved labels for Novel Drug Approvals (NDA) between January 2016-to-December 2021, and to compare the findings with those reported between 2006 and 2015.

OBJECTIVES

- To review PRO information reported in labels for New Molecular Entities (NMEs) approved from January 2016-to-December 2021.
- To review disease categories for which PRO claims were made in FDA labels of Novel Drug Approvals (NDA) between January 2016-to-December 2021
- To compare findings to previously published results from between 2006-to-2015

METHODS

Data Source

- The FDA website (www.accessdata.fda.gov) for "Novel drug Approvals" was accessed to determine the number of New Molecular Entities approved between January 2016 - December 2021.
- Drug labels for new drug approvals (NDAs) approved between January 2016-December 2021, were reviewed
- Biologics License Applications (BLAs) and non-New Molecular Entity were excluded from the review. Similarly, NDAs that included PRO measures in the drug approval package but not in the prescribing information approved by FDA.

Data Collection Form

- A data collection form was created based on past published research on PRO and NDA and, the 2009 Patient-Reported Outcome Measures (PROM) guidance document published by the FDA.
- All included New Drug Applications were then analyzed for the following:
 - Brand name and Year
 - Disease category (ICD-10): Drugs were classified as PRO dependent or non-PRO dependent depending on the ICD-10 code and endpoint evaluation
 - Type of PRO outcome: HRQoL, functional status, symptoms, health behaviors, and patient experience with care.
 - Type of PRO measure: General surveys vs Disease Specific Surveys
 - Primary/secondary endpoint
 - Who answered/responded to the PROM
 - Method of Administration
 - Psychometric properties

Data Analysis

- Data were collected independently by TV and BB. Data analysis was conducted by TP. Conflicts between the two researchers (TV and BB) were resolved by the JM or TP. All analysis was conducted in Microsoft Excel.

RESULTS

Disease Categories (ICD-10)	Table -- PRO labeling of novel drugs approved during the periods 2016-2021 compared with 2006-2015																			
	2006-2010					2011-2015					2006-2015					2016-2021				
	New Drugs Approved		PRO labeling			New Drugs Approved		PRO labeling			New Drugs Approved		PRO labeling			New Drugs Approved		PRO labeling		
PRO-dependent	n	%	n	%	% (total)	n	%	n	%	% (total)	n	%	n	%	% (total)	n	%	n	%	% (total)
Blood and blood-forming organs	6	5.20	2	33.30	7.14	4	2.20	2	50.00	6.67	10	3.36	4	40.00	6.90	8	3.96	2	25.00	5.12
Mental, behavioral, and neurodevelopmental disorders	7	6.00	1	14.30	3.57	6	3.30	1	16.70	3.33	13	4.36	2	15.38	3.45	9	4.46	4	44.44	10.26
Diseases of the nervous system	12	10.30	8	66.70	28.57	11	6.00	5	45.50	16.67	23	7.72	13	56.52	22.41	26	12.87	13	50.00	33.33
Diseases of the eye and adnexa	5	4.30	3	60.00	10.71	3	1.60	0	0.00	0.00	8	2.68	3	37.50	1.01	2	0.49	1	50.00	2.56
Diseases of the ear and mastoid process	0	0.00	0	---	0.00	1	0.50	1	100	3.33	1	0.34	1	100.00	1.72	0	0.00	0	---	0.00
Diseases of the respiratory system	1	0.90	1	100.00	3.57	9	4.90	3	33.30	10.00	10	3.36	4	40.00	6.90	5	2.48	1	20.00	2.56
Diseases of the digestive system	3	2.60	1	33.30	3.57	7	3.80	4	57.10	13.33	10	3.36	5	50.00	8.62	11	5.45	5	45.45	12.82
Diseases of the skin and subcutaneous system	3	2.60	1	33.30	3.57	2	1.10	1	50.00	3.33	5	1.68	2	40.00	3.45	9	4.46	1	11.11	2.56
Diseases of the musculoskeletal system and connective tissue	10	8.60	4	40.00	14.29	3	1.60	2	66.70	6.67	13	4.36	6	46.15	10.34	4	1.98	2	50.00	5.12
Diseases of the genitourinary system	2	1.70	2	100.00	7.14	4	2.20	4	100.00	13.33	6	2.01	6	100.00	10.34	7	3.46	1	14.29	2.56
Total PRO-dependent NMEs	49	42.20	23	46.90	82.14	50	27.50	23	46.00	76.67	99	33.22	46	46.46	79.31	81	40.10	30	38.27	76.92
Non-PRO-dependent																				
Neoplasms	18	15.50	0	0.00	0.00	51	28.00	0	0.00	0.00	69	23.15	0	---	0.00	48	23.76	1	2.08	2.56
Infection and parasitic diseases	14	12.10	0	0.00	0.00	27	14.80	1	3.70	3.33	41	13.76	1	2.44	1.72	26	12.87	0	0.00	0.00
Endocrine, nutritional, and metabolic diseases	13	11.20	1	7.70	3.57	28	15.40	3	10.70	10.00	41	13.76	4	9.76	6.90	23	11.38	7	30.43	17.95
Diseases of the circulatory system	9	7.80	2	22.20	7.14	13	7.10	1	7.70	3.33	22	7.38	3	13.64	5.17	3	1.49	0	0.00	0.00
Pregnancy, childbirth, and the puerperium	0	0.00	0	---	0.00	0	0.00	0	---	---	0	0.00	0	---	---	0	0.00	0	---	0.00
Congenital Malformities, Deformations and Chromosomal Abnormalities	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	3	1.49	0	0.00	0.00
Symptoms not classified elsewhere	0	0.00	0	---	0.00	3	1.60	2	66.70	6.67	3	1.01	2	66.67	3.45	4	1.98	1	25.00	2.56
External causes of morbidity	0	0.00	0	---	0.00	0	0.00	0	---	---	0	0.00	0	---	---	0	0.00	0	---	0.00
Health status and contact with health services	5	4.30	1	20.00	3.57	1	0.50	0	0.00	0.00	6	2.01	1	16.67	1.72	1	0.49	0	0.00	0.00
Injury, poisoning, etc.	2	1.70	1	50.00	3.57	0	0.00	0	---	---	2	0.67	1	50.00	1.72	0	0.00	0	---	0.00
Unclassified	6	5.20	0	0.00	0.00	9	4.90	0	0.00	0.00	15	5.03	0	---	0.00	13	6.44	0	0.00	0.00
Total non-PRO-dependent NMEs	67	57.80	5	7.50	17.86	132	2.50	7	5.30	23.33	199	66.78	12	6.03	20.69	121	59.90	9	7.44	23.08
All diseases – Total NDA	116	100.00	28	24.10	100.00	182	100.00	30	16.50	100.00	298	100.00	58	19.46	100.00	202	100.00	39	19.31	100.00

DISCUSSION & CONCLUSION

- The percentage of total NDAs approved between 2016-2021 with PRO measures included in the labels was similar to the percentage of NDAs, approved between 2016-2021 with PRO measures included in the labels (19.3 vs 19.4, respectively).
- More number of NDAs from 2016-2021 in the PRO dependent category had PRO labeling (30) compared to the data from 2006-2010 (23) and 2011-2015 (23). From the PRO-dependent disease category, 46.46% of drugs included PRO measure in 2006-to-2015, and 38% in 2016-to-2021
- Amongst the ICD-10 disease categories, the diseases of the nervous system had the most PRO claims. This was consistent with the data from 2006-2015.
- There was a slight increase in the non-PRO dependent disease categories i.e., 6.03% of drugs included PRO measures in 2006-2015, compared to 7.37% in 2016-to-2021
- While reviewing the literature and labels for NDAs, the researchers observed that PROs are becoming an important part of drug development.

REFERENCES

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DISCLOSURE

"Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation"