2022

Demographic profiles of clinical research participants in FDA-approved NMEs

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Demographic Profiles of Clinical Research Participants in FDA-Approved NMEs

by

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Thesis

Submitted to the School of Health Sciences

Eastern Michigan University

in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

in

Clinical Research Administration

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May 3, 2022

Ypsilanti, Michigan

Acknowledgments

I would like to acknowledge Professor Michael Switzer and Professor Jean Rowan for their support during the process of my thesis, I am grateful.

Abstract

Drug development is a rigorous and expensive process that takes between 10 and15 years. Recruitment and retention of human subjects in clinical trials is challenging. This study collected the demographics of trial participant in trials for New Molecular Entities (NMEs) approved by the U.S. Food Drug Administration (FDA) for 2010 and 2020 to compare demographic representation. Demographic representation of trial participants for 61 FDA-approved NMEs for 2010 and 2020 were gathered; 21 NMEs were excluded from analysis. The trends in demographic representation in trials for the 40 FDA-approved NMEs in 2010 and 2020 were similar, and White participant representation was higher than racial/ethnic minorities. This study was limited by inconsistent reporting of demographic categories such as age and ethnic groups. Recruitment of racial/ethnic minorities remains persistently low, which affects the diversity of drug development programs. There is a compelling need for further research.

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Introduction

Drug development is a rigorous, lengthy, and costly process that takes between 10 to 15 years from the preclinical (bench) to Phase IV (bedside), when the drug gets to the market after obtaining approval from the relevant regulatory authorities; the cost of this process is about $2 billion. The recruitment of the actual calculated sample size for clinical trials in a specified time has been a barrier in the drug development process (Chaudhari et al., 2020). This delay leads to the inability of meeting the clinical trial's deadline, which leads to the rise in the cost and an increase in the time, which affects other aspects of the clinical trials.

According to a report analysing global data of clinical trials that were stopped in the clinical database, 55% of the clinical trials were discontinued because of a substantially lower rate of human subjects completing the clinical trials (Desai, 2020). The efficiency of the average recruitment of human subjects is reported to be < 40% for Phase III and Phase IV of clinical trials. More than 80% of clinical trials worldwide fail to recruit human subjects within the specified time, leading to prolongation of the clinical study time and/or requiring more clinical study sites (Desai, 2020). Inadequate retention of human subjects to the clinical study closeout is a problem because there may be an inadequate number of research participants that will be able to answer the research questions properly. The low statistical power for clinical trials affects the validity of the result, and this has economic, ethical effects and also leads to delays in the clinical trials (Desai, 2020; Ross et al., 1999).

Statement of the Problem

There are several barriers that the pharmaceutical/biotechnology industries, clinical research organizations (CROs), and research professionals encounter during the recruitment of human subjects and their retention in clinical trials. The lack of adequate and diverse clinical trial participants in clinical trials has contributed to many failed trials, loss of funds, loss of time, and lack of validity of the research. Inadequate knowledge of clinical trials by the clinical trial participants and lack of awareness have been a challenge. Also, the inadequate recruitment of women and racial/ethnic minorities is a barrier to clinical trial recruitment and retention. Understanding the demographic profiles of research subjects is crucial to the success of the recruitment and retention of human subjects in clinical trials, and this contributes immensely to the success of clinical trials during the drug development program, which helps to develop novel therapeutics for patients.

Purpose of the Study

The purpose of my research is to further assess the demographic profiles of the population in my environment to understand the demographics of the population that have participated in clinical research, and the reason why people may like to participate. Several factors affect the human subjects in participating in clinical trials such as ethnicity, their level of education, the level of exposure to clinical trials, socioeconomic status, distance to clinical trial sites, and the association between their social status and their participation in clinical trials. This research gathered the demographic data-age; gender; race: White, Black/African American, Asian/Asian American, or mixed race/multiple races; and ethnicity (Hispanic, Latino, non-Hispanic) of clinical trial participants from the reported clinical trials (Phase II, Phase III, and

Pivotal trials) that were conducted for the 61 New Molecular Entities (NMEs) approved by the United States Food and Drug Administration (FDA) for 2010 and 2020. The demographic data gathered will help us to understand the recruitment and retention of clinical trial participants in clinical trials during drug development programs. This will provide more information on the demographic profile of the trial participants' representations, which can help to further develop more strategies to improve the inclusion of a more diverse population in clinical trials and to develop more strategies to improve the retention of clinical trial participants in clinical trials during the drug development programs.

Significance of the Study

The demographic variable data (age, gender, race, and ethnicity) of the clinical trial participants were gathered from the clinical trials conducted for the 61 FDA-approved NMEs for 2010 and 2020. This information will allow the research professionals, pharmaceutical/ biotechnology industries, clinical research organizations, and other interested organizations to gain deeper knowledge on the recruitment and retention of the trial participants, especially the racial/ethnic minorities' clinical trial participants. This information is crucial because it will help research professionals, pharmaceutical/biotechnology industries, and other relevant organizations to develop more strategies to improve the recruitment and retention of trial participants, especially the racial/ethnic minority participants in clinical trials during the drug development programs. It is important to have a more diverse population in the clinical trials, which will help us to gain more knowledge on the safety and efficacy of the novel drugs and to increase the application of the drugs to a more diverse population.

Review of Literature

About 30% of the duration of the drug development program is taken up by the recruitment of human subjects; this costs around 1.2 billion USD (Pateria & Singh, 2015). There are obstacles in recruiting human subjects for clinical trials which range from one to six months delay in most clinical trials; some other pharmaceutical industries and clinical research organizations, encounter longer delays in recruiting human subjects, and these delays cost pharmaceutical industries to lose between $600,000 and $8 million each day of the delay (Ray & Tosti, 2017). About 11% of the clinical study sites failed to recruit one clinical human subject, and 37% of the clinical research sites are under-recruiting research subjects. This has led to inefficiency and reduction in the productive capacity, loss of funds, and time which affects the sponsors and other relevant partners in the drug development program (Ray & Tosti, 2017). Human subjects' recruitment and retention in clinical trials are the main obstacles in clinical trials, and these are very important because of the financial implications and validity of the study.

Appropriate strategies for recruitment and retention of human subjects in clinical trials and effective communication with relevant partners during the drug development program will help to prevent unnecessary delays in the drug development program, which will help create an efficient and organized process, allowing the pharmaceutical industries to make the new products available at the scheduled time at a cheaper price. Appropriate recognition of the possible problems and evaluation of the plans for both the recruitment and retention of human subjects in clinical trials can help to increase the recruitment and retention of clinical trial participants in drug development programs (Chaudhari et al., 2020).

Furthermore, there are strategies to improve the recruitment of the human subjects in clinical trials such as having a good knowledge of the patients' experiences and addressing them in the clinical study plans, by conducting a focus group discussions and surveys, interviewing the patients and medical personnel (physicians) and integrating their responses when designing the protocols and developing the study tool to reduce amendment of protocols, and increasing both patients and investigators commitment. Planning the protocol well in advance and having a well-planned enrollment method will facilitate the identification, assessment, and control of the threats associated with the human subjects' recruitment (Ray & Tosti, 2020).

Recruitment of human subjects should be done appropriately in an ethical manner. The investigators should actively identify the human subjects that are suitable for enrollment in the clinical trial, the human subject should be selected in line with the trial protocol and all human subjects recruited into the study must meet the protocol requirements. The recruitment and the recruitment advertisement materials must be approved by the institutional review board (IRB) or independent ethics committee (ICH GCP 3.1.2), and the potential benefits, risks and other options of the intervention of the study should be presented to the potential research participants before the enrollment to determine their interest and agreement to participate (Shah et al., 2022); this is regarded by the federal regulations and IRB as the beginning of Informed Consent process.

According to the good clinical practice (GCP), the two major elements of recruitment are defining a population of suitable research participants to respond to the research questions and ethically recruiting suitable human subjects. The research subjects should be recruited in line with the *1979 Belmont Report,* which is based on the three fundamental principles that are

focused on the present system of human research protection; respect for persons, beneficence, and justice (Sims, 2010).

Retention of human subjects in clinical trials is an ongoing process. The clinical trial staff must ensure that they do their best to retain the clinical trial participants through to the end of the clinical trial (study closeout) and that they are compliant throughout the study period. These are the activities done by the clinical trial team to motivate and support the human subjects to stay enrolled and be involved in the clinical trial. According to GCP, retention of research participants implies ensuring human subjects submit to the research procedures at the scheduled time, respond to the sets of questions or the interviewers' questions, are involved in any other tasks that the trial protocol requires, and attend follow-up visits as required. The GCP further outlines elements of a successful retention plan, such as making sure they treat human subjects with respect, being mindful of the clinical trial participants' time, recognizing and conquering the obstacles to retention, including the retention plans in the budget and recognizing, and dealing with the difficulties promptly (Chaudhari et al., 2020).

Place of residence, race/ethnicity/culture/language, occupation, gender, religion, education, socioeconomic status, and social capital (PROGRESS) play a crucial role in the recruitment and retention process in clinical trials (Chaudhari et al., 2020). This research further outlined frequent explanations that research subjects give for not getting involved in clinical trials, which are the complexity of the research protocol, sociocultural issues, negativism by the media, unfavorable clinical trial plans, geographical distance, anxiety regarding the placebo, benefits of the investigational products, inadequate knowledge of clinical trials, anxiety

regarding the adverse events, and how some human subjects are been treated may discourage them from participating in clinical trials (Ross et al., 1999; Chaudhari et al., 2020).

Furthermore, some other difficulties affect the recruitment of human subjects into clinical trials. There are reports that some women of childbearing age find it difficult to abstain from sex or use the right type of contraceptives during the period of the clinical trials (Chaudhari et al., 2020). Other issues include the following: the research participants might like to participate in clinical trials because of the free medical check-up, the small money that the researchers or sponsors will offer them for participating in the clinical trials, less educated people may need more time to understand the process of the clinical trial, and people that are on daily wages are reported to refuse participation and staying in the hospital for the trials because of loss of wages. Religious beliefs can be a hindrance; it is noted that clinical trial participants' recruitment during the fasting period for Muslims can be slow because of their religious beliefs, but this is more common in the regions that are largely Muslims. Hospital environments such as the intensive care unit environment can make some people afraid of participating in Phase I clinical trials, delayed Data and Safety Monitoring Board (DSMB) reports, and also delayed funds from the sponsors/clinical research organizations can delay human subjects' recruitment (Chaudhari et al., 2020).

The significance of the involvement of racial and ethnic minorities in clinical research is well recognized, and it contributes to the generalizable knowledge of clinical research. This ensures that the result of the research can be applied to a heterogeneous population (Yankey et al., 2006). It allows for justice and fairness in health care delivery and reliability in ethnicity analyses. It is also reported that there is disproportionately low representation of the racial and

ethnic minorities in clinical research (George et al., 2014). Over 30% of the population in the United States are of racial/ethnic minorities' origin. The National Cancer Institute's recruitment of minority subjects was lower than 18% for its publicly funded cancer clinical trials (phase I-III treatment studies, January 1, 2003 to June 30, 2005), and 17% of the FDA human subjects were of racial and ethnic minorities in the 185 studies of new molecular entities for a period of five years (George et al., 2014).

A retrospective review of FDA medical officers' reviews of clinical trial protocols and product labeling for 185 new molecular entities (NMEs) approved by the United States FDA between January 1, 1995, and December 31, 1999, revealed that 17% of the FDA clinical study human subjects were racial/ethnic minorities (Evelyn et al., 2001). George et al. revealed several obstacles in recruiting racial and ethnic minorities into clinical research for both the human subjects and the researchers. Regarding the researchers, a lack of adequate knowledge about cultural diversity in ethnic minorities can lead to ineffective communication during clinical trials. Previously, White human subjects have been the "gold standard" for human subjects' recruitment for clinical trials, but this cannot be generalizable to the general population including ethnic minorities (George et al., 2014). The health inequalities that affect the racial and ethnic minorities across the United States regarding their access to health care and undesirable health outcomes and the Tuskegee Study are known to be part of the obstacles that affect the involvement of racial and ethnic minorities in clinical research (George et al., 2014; Shavers et al., 2002).

In line with the national priority to ensure there is diversity in human subjects' participation in clinical trials, FDA offered *New Guidance on Enhancing the Diversity of*

Clinical Trial Populations- Eligibility Criteria, Enrolment Practices, and Trial Designs Guidance for Industry (U.S. Food and Drug Administration [FDA], 2020a). The guidelines were set forth by congressional legislation in the early 1990s. These guidelines were established to include women and promote the recruitment of racial and ethnic minority groups in federally funded human participant research (Robinson et al., 2017). The FDA endorsed recruitment practices for clinical trials that reflect the population that will most probably use the drug when approved, mainly by expanding the eligibility criteria for human subjects' enrolment. This guidance takes into consideration the demographic characteristics of the populations to be studied (e.g., ethnicity, age, sex, race, location of residency) and non-demographic features of the populations (e.g., comorbid conditions, disabilities, patient with organ dysfunction, those at the extremes of the weight range, and populations with diseases or conditions with low prevalence).

The FDA- recommended sponsors consider the following when enrolling human subjects along with other relevant FDA recommendations: (a) During the development of the clinical study protocol, they should make sure that the eligibility criteria of the trial are indicative of the sample of the population that the drugs that is been developed is meant for, and it should scrutinize the exclusion criteria to establish the need to ensure the safety of human subjects and to achieve the trial objectives. (b) They should take into consideration the exclusion criteria from Phase II trials, which can be very selective and are frequently, moved to Phase III protocols. This can be stopped or adapted for Phase III trials because Phase III trials' objectives are different from the Phase II trials to avert the needless limitations on the study population. (c) The sponsors are meant to enroll human subjects that are reflective of the features of clinically appropriate populations in terms of sex, ethnicity, age, and race (Robinson et al., 2017).

Baquet et al. further revealed that 32% of Americans would like to participate in clinical trials if offered and 38% of Americans would consider participating in clinical trials if asked, but they will have some reservations (Baquet et al., 2006). Other reasons that were reported to affect participation in clinical trials are racial minority group; older age; lack of suitable clinical trials; disqualification of patients; lower socioeconomic status; ineffective doctor-patient communications in regard to clinical trials; apprehension of academic institutions, research, and the medical system; apprehension of the negative effects of the trials; inadequate knowledge of the benefits of clinical trials by the community and the physicians; inadequate training of the researchers in the culturally acceptable communication approaches; patients' fears regarding the trials; inadequate access to care; inadequate details regarding the clinical trials; and inadequate support for the community outreach (Baquet et al., 2006).

Demographic profiles of human subjects in clinical trials are very important for the analysis of the safety and efficacy of a novel drug. The FDA is in charge of the approval of new drugs or therapeutics by assessing the clinical trials. The purpose of clinical trials is to make sure the new drugs or therapeutics are safe and effective in the desired populations that are meant to use the drugs or therapeutics. The human subjects in the clinical study should be representative of the patient population the drug or therapeutic is meant for (Sacristán et al., 2016).

Despite the efforts of the FDA, there are reports that racial and ethnic minorities, women, and older adults are inadequately represented in drug development programs (Chen et al., 2018). A recent cross-sectional study done on human subjects in the United States vaccine clinical trials revealed that the older adults and racial/ethnic minority groups had lower representation compared to the women who were overrepresented in the trials (Flores et al., 2021); there is an

urgent need to address this inadequate representation in the drug development programs. FDA evaluates the demographics of human subjects in clinical trials and also does the subgroup analyses at the time of the regulatory evaluation of new drug and biologic product marketing applications.

Furthermore, the reports from these clinical studies are utilized to assist the regulatory decisions for the drug applications, the approved drugs can be used in a substantial and more diverse population above the population that the novel drug was exposed to during the clinical trials of the drug development (Chen et al., 2018). The United States FDA has been increasing its priority on improving the demographic representation in clinical trials, FDA introduced an "action plan" to enhance the demographic subgroup analysis in the assessment of new drugs/ therapeutics, with definite guidelines to strengthen the quality of demographic data gathered in post-marketing surveillance systems (FDA, 2020a; FDA, 2014).

Research Questions

- What is the demographic profile of clinical participants in drug (NME, new drug application [NDA]) studies, especially with respect to racial/ethnic minorities?
- Has the demographic profile of clinical trial participants in drug development (NME, NDA) studies changed from 2010 to 2020, especially with respect to racial/ethnic minorities?
- Are racial/ethnic minorities underrepresented in clinical trials?
- Are women/females underrepresented in clinical trials?

Methods

Sample Selection

This research was based on summary demographic data gathered from the reported data from the United States Food and Drug Administration (FDA) website, under "FDA-Approved Drugs," which can be found on the FDA website: Drugs@FDA-Approved Drugs (FDA, 2010; FDA, 2020). All the data were from clinical trials (Phase II/Phase III), including the Pivotal studies conducted for FDA-approved New Molecular Entities (NMEs) in 2010 and 2020. The demographic data were collated from the accessible reported clinical trials. The demographic variables were age groups, gender/sex (males and females), race (White, Black, Asian, mixed/multiple races, and others), and ethnicity (Hispanic/Latino, Non-Hispanic/Latino, and others).

Research Design

An exploration of the FDA-approved NMEs for 2010 and 2020 was done on the FDA website. Inclusion and exclusion criteria were utilized to choose the FDA-approved NMEs in 2010 and the FDA-approved NMEs in 2020.

Inclusion criteria included the following:

- All the FDA-approved NMEs in 2010 and 2020 that have adequate published demographic data from the clinical trials conducted for the FDA-approved NMEs and that were used for the New Drug Application (NDA) submission for the approval of the drugs.

- Each of the FDA-approved NMEs in 2010 and 2020 should have demographic profiles such as age range; sex: male/female; race: White, Black, Asian, mixed/ multiple races, and others; and ethnicity: Hispanic/Latino, Non-Hispanic/Latino, and others.
- All FDA approved NMEs in 2010 and 2020 that are meant for pediatric and adult patients.

Exclusion criteria:

- FDA-approved NMEs in 2010 and 2020 that were only for one single gender/sex either males or females.
- FDA-approved NMEs in 2010 and 2020 that are for pediatric patients only.

Data Collection

All the demographic data were gathered from the clinical trials conducted for the FDA-approved NMEs in 2010 and 2020. All the available demographic data, such as age, sex, race, and ethnicity, were gathered from the clinical trials that were conducted for the FDA-approved NMEs in 2010 and 2020. Some of the data for the FDA-approved NMEs in 2010 and 2020 were excluded because a few of the FDA-approved NMEs were repeated on the FDA website. In this instance, only one of each FDA-approved NME that was repeated was used for the results and analysis.

All the FDA approved NMEs from 2010 and 2020 were identified on the FDA website: Drugs@FDA: FDA-Approved Drugs (FDA, 2020; FDA, 2010). For each of the FDA-approved NMEs in 2010, the demographic data were accessed from the Drugs@FDA: FDA-Approved Drugs (FDA, 2010) on the website in the section of the "Original Approvals or Tentative Approvals," which includes link to the review section that links to the Drug Approval Package

section. The Drug Approval Package section has several links to access the clinical trials that were conducted and used for New Drug Application (NDA) submission for each of the FDA-approved NMEs in 2010. The clinical trial summary data for the FDA-approved NMEs can be found in the Statistical reviews, Medical reviews, and other reviews.

The percentages for each demographic variable (e.g., race, White) that were pertinent to this study were gathered for the results and analysis. The percentages of each of the demographic variables for each NDA study were added together, and the average percentages were calculated for each FDA-approved NME in 2010 for the results and analysis.

The FDA-approved NMEs in 2020 were identified from the Drugs@FDA: FDA-Approved Drugs. The demographic data that were utilized for the NDA submission were accessed from the Drug Trials Snapshots website (FDA, 2021; FDA, 2020). At the end of the page of the website, there is a section for more information on all the demographic data collated from the clinical trials conducted for the FDA-approved NME. The average total percentages of each demographic variable (e.g., race, White) that are relevant to this study were gathered for the results and analysis. The percentages of each of the demographic variables for each NDA study were added together, and the average percentages were calculated for each FDA-approved NME in 2020 for results and analysis.

All the FDA-approved NMEs in 2010 and 2020 were identified and documented; all the indications and age ranges of the FDA-approved NMEs can be found in Appendix B, Appendix D and Appendix E. Most of the drugs have different indications, but some of the FDA-approved NMEs were repeated on the FDA website; the repeated NMEs had similar data, and only one of each of the FDA-approved NME was used for the result and analysis. The FDA-approved NMEs

that did not have reported data and the FDA-approved NMEs without adequate data on race and ethnicities were excluded from the results and analysis.

The published demographic data in the clinical trials conducted for the approval of the FDA NMEs were identified and were collated in Microsoft Excel spreadsheets and Microsoft Word. They were all reported in percentages, and the average percentages for each demographic variable for each year were calculated to get the final results. For this study, there was a comparison of the findings for 2010 and 2020.

Results

All the demographic data for this thesis were from the FDA website. The demographic data were accessed from the published data of the clinical trials/pivotal studies that were conducted for the 61 FDA-approved NMEs in 2010 and 2020.

Table1 shows the FDA approved NMEs in 2010 and 2020, and the number of the NDA/NMEs that contributed data to the analysis, and the number that were excluded.

Table 1

Identification and Selection of NDAs and NMEs

Number of NDAs/NMEs selected by year.	Year 2010	Year 2020
Total number of FDA approved NDAs/NMEs.	16	45
The number that did not have required data	2	1
The number that did not meet the inclusion and exclusion criteria by reason (single sex, pediatric)	4	7
The number that were excluded for other reasons*	3	4
Number of NDA/NMEs that contributed data to the analysis	7	33

*The number of the FDA-approved NDA/NMEs that were repeated on the FDA website, and only one of each of the repeated FDA-approved NMEs was used for data gathering and contributed to the analysis of the final result.

From the Table 1, the number of the FDA NDAs/NMEs that contributed to the data analysis was seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020, making a total number of 40 FDA-approved NMEs in both 2010 and 2020.

All the 61 FDA-approved NMEs in 2010 and 2020; the NMEs indications, age ranges, and sex (male/female) can be found on the FDA website, the label section of the Drugs@FDA: FDA-approved Drugs (FDA, 2020; FDA, 2010), and they are documented in Appendix D and Appendix E. A list of the 61 FDA-approved NMEs and their generic names can be found in Appendix B.

Table 2 lists the FDA-approved NMEs that contributed data to the analysis and the ones that were excluded in 2010.

Table 2

Trade and Generic Names of Included and Excluded FDA-Approved NMEs in 2010

FDA Approved NMEs in 2010 (Included)	FDA Approved NMEs in 2010 (Excluded)
1. Ampyra (dalfapridine)	1. Asclera (polidocanol)
2. Gilenya (fingolimod hydrochloride)	2. Carbaglu (carglumic acid)
3. Laftacaft (alcaftadine)*	3. Ella (ulipristal acetate)
4. Latuda (lurasidone hydrochloride)	4. Halaven (eribulin mesylate)
5. Pradaxa (dabigatran etexilate mesylate)*	5. Jevtana Kit (carbazitaxel)
6. Teflaro (ceftaroline fosamil)*	6. Natazia (estradiol valerate; dienoget)
7. Victoza (liraglutide recombinant)	

*Three FDA-approved NMEs in 2010 were repeated twice on the FDA website; only one of each of the NMEs was used for data gathering and results.

Table 3 lists the FDA-approved NMEs in 2020 that contributed to the data for analysis and the ones that were excluded.

Table 3

Trade and Generic Names of Included and Excluded NMEs in 2020

FDA approved NMEs in 2020 (Included)	FDA approved NMEs in 2020 (Excluded)
1. Ayvakit (avapritinib)	1. Artesunate (artesunate)*
2. Barhemysys (amisulpride)	2. Cetrianna (fluoroestradiol-f-18)
3. Byfavo (remimazolam besylate)	3. Gallium Ga 68 PSMA-11(gallium ga 68 psma-11)*
4. Detectnet (copper dotatate cu-64)	4. Koselugo (selumetinib sulfate)
5. Dojolvi (triheptanoin)	5. Lampit(nifurtimox)
6. Evrysdi (cisdiplam)	6. Orgovyx (relugolix)
7. Gavreto (pralsetinib)*	7. Viltepso (viltolarsen)
8. Gemtesa (vibegron)	8. Zokinvy (lonafarnib)
9. Imcivree (setmelanotide acetate)	
10. Inqovi (cedazuridine; decitabine)	
11. Isturisa (osilodrostat Phosphate)	
12. Klisyri (tirbanibulin)	
13. Nextletol (bempedoic acid)	
14. Nexlizet (bempedoic acid; ezetimibe)	
15. Nurtec ODT(remegepant sulfate)	
16. Olinvyx (oliceridine)	
17. Orladeyo (berotralstat hydrochloride)	
18. Ongentys (opicapone)	
19.Oxlumo (lumasiran sodium)	
20.Pemazyre (pemigatinib)	
21.Pizensy (lactitol)	
22.Qinlock (ripretinib)	
23.Retevmo (selpercatinib)	
24.Rukobia (fostemsavir tromethamine)	
25.Tabrecta (captatimib hydrochloride)	
26.Tauvid (flortaucipir f-18)	
27.Tazverik (tazemetostat)	
28.Tukysa (tucatinib)	
29.Veklury (remdesivir)	
30.Winlevi (clascoterone)	

31.Xeglyze (abametapir)*	
32.Zeposia (ozanimod hydrochloride)	
33.Zepleca (lurbinectedin)	

*Four FDA-approved NMEs were repeated twice on the FDA website; only one of each NME was used for the data gathering and results.

The list of the FDA-approved NMEs in 2010 and 2020, that contributed data to the results and analysis in this study can be found in Appendix C.

Demographic Variables

Table 4 shows the demographic variables used for data gathering.

Table 4

Selected Demographic Variables

Sex	Race	Ethnicity	Age
Male	White	Hispanic/ Latino	<65 years
Female	Black	Non-Hispanic/ Latino	≥65 years
	Asian	Not Reported	
	Other	Unknown	
	Mixed/ Multiple races		
	Native Hawaiian		
	American Indian		
	Asian Pacific		
	Unknown		

There were variations in the reported age categories in all the published data for the clinical trials conducted for the 40 FDA-approved NMEs in 2010 and 2020. The 40 FDA-approved NMEs did not have specific reported age categories. There were variations in the published data for the age categories in the clinical trials for the 40 FDA-approved NMEs because of the indications of the drugs and the age categories of the population that the drugs

were indicated for. Only some of the 40 FDA-approved NMEs specifically reported on the age categories of < 65 years and ≥ 65 years in the demographic profiles of the clinical trials that were conducted for the FDA-approved NMEs, and there were variations in the published data.

Most of the clinical trials conducted for the 61 FDA-approved NMEs were multicenter randomized controlled trials in the United States and other countries. A total of 40 FDA-approved NMEs in 2010 and 2020 contributed to the data analysis and the list can be found in Appendix C.

Table 5 shows the average percentages of demographic data representations for age, sex, race and ethnicity of clinical trials participants in the clinical trials conducted for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020.

Table 5

FDA-Approved NMEs Demographic Profiles: 2010 and 2020

Demographic Profile	Year: 2010 (%)	Year: 2020 (%)
Age		
<65 years	57.3%	65.3%
≥ 65 years	42.7%	34.3%
Sex/ Gender		
Male	47.6%	45.1%
Female	52.5%	54.9%
Race		
White	77%	77%
Black	9.7%	7.3%
Asian	4.3%	7.7%
Other	7.7%	2.9%
Multiple/Mixed Races	0%	0.1%
Native Hawaiian	0.0%	0.2%
American Indian	0.2%	0.4%
Asian Pacific	1.6%	0%
Unknown	0.1%	3.9%
Ethnicity		
Hispanic/Latino	5.7%	14.8%
Non-Hispanic/Latino	41.5%	72.1%
Not reported	0.6%	7.2%
Unknown	0%	4%

Age

There were variations in the reported age categories across the whole spectrum in the clinical trials conducted for seven FDA-approved NMEs in 2010 and the 33 FDA-approved NMEs in 2020. The variations of the age categories depend on the indications of the drugs and the age categories of the population that the drugs were developed for. Some of the FDA-approved NMEs were for both pediatric and adult patients, and some of the FDA approved-NMEs were for adult patients. The variations in the age categories occurred in the 40 FDA-approved NMEs in 2010 and 2020.

The specific age categories of < 65 years and ≥ 65 years were not reported in all the clinical trials conducted for the FDA-approved NMEs in 2010 and 2020; there were variations in the published demographic variables (age categories) in the clinical trials conducted for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020. For the seven FDA-approved NMEs in 2010, the average percentage of representation for < 65 years was 57.3% and for ≥ 65 years was 42.7%, while for the 33 FDA-approved NMEs the average percentage of representations for < 65 years was 65.3% and for ≥ 65 years was 34.3%. There were variations in the reported data for the < 65 years and ≥ 65 years old in the trials conducted for the 40 FDA-approved NMEs. The indications and the age categories of the FDA-approved NMEs in 2010 and 2020 are documented in Appendix D and Appendix E.

Four FDA-approved NMEs were excluded from the seven FDA-approved NMEs in 2010 for age calculations for < 65 years and ≥ 65 years because of the published data in 2010. Nineteen FDA-approved NMEs were excluded from the 33 FDA-approved NMEs in 2020 for the age calculations for < 65 years and ≥ 65 years because some of the NMEs did not have

published data and some did not have the data for both < 65 years and ≥ 65 years in the clinical trials conducted for the 40 FDA-approved NMEs in 2020.

Sex

The sex categories in this study consist of males and females. The males and females had representation in the published demographic data from the clinical trials that were conducted for seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020. From Table 5, males had (47.6%) representation in the reported clinical trials that were conducted for the seven FDA-approved NMEs, and females had (52.5%) representation in the reported clinical trials conducted for the seven FDA-approved NMEs in 2010. The female representation was higher (52.5%) than the male representation (47.6%) in the clinical trials conducted for the seven FDA-approved NMEs in 2010.

From Table 5, in 2020, male representation was (45.1%) while the female representation was (54.9%) in the clinical trials that were conducted for the 33 FDA-approved NMEs. The female representation was (54.9%) than the male representation (45.1%) in the clinical trials conducted for the 33 FDA-approved NMEs in 2020.

Comparing the representations of the sex (males and females) in the clinical trials conducted for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020, the researcher found that female representations (52.5% and 54.9%) were both higher than the male representations (47.6% and 45.1%).

Race

There were variations in the race representation in all the clinical trials conducted for the 40 FDA-approved NMEs in 2010 and 2020. The reported race representations for the 40 FDA-approved NMEs were White, Black, Asian, mixed race/multiple races, Native Hawaiian, Asian Pacific, American Indian, others, and unknown. From Table 5, the White clinical trial participants had higher representation in the reported clinical trials conducted for the 40 FDA-approved NMEs in 2010 and 2020. In 2010, the White clinical trial participants had 77% representation which was higher than the Black with 9.7%, Asian with 4.3%, others with 7.7%, Native Hawaiian with 0.0%, Asian Pacific with 1.6%, American Indian with 0.2%, and unknown race with 0.1% representation in the clinical trials that were conducted for the seven FDA-approved NMEs in 2010.

From the analysis of the results, from the demographic data that were collated from the clinical trials that were conducted for the seven FDA-approved NMEs, the White trial participants had higher representation in the clinical trials that were conducted for the seven FDA- approved NMEs compared to Black clinical trial participants representation (9.7%), Asian representation (4.3%), American Indians (0.2%) and other races (7.7%).

In 2020, the White clinical trial participants had higher representation (77%) than the Black (7.3%), Asian (7.7%), others (2.9%), multiple races (0.1%), Native Hawaiian (0.2%), American Indian (0.4%), and unknown races (3.9%) representation in the reported clinical trials that were conducted for the 33 FDA-approved NMEs.

The demographic data that were collated from the clinical trials that were conducted for the 33 FDA-approved NMEs; White clinical trial participants had higher representation (77%)

than Black representation (7.3%), Asian representation (7.7%), American Indians (0.4%) and other races (2.9%) representations in the clinical trials that were conducted for the 33 FDA-approved NMEs in 2020.

In addition, comparing the clinical trial participants' representation in 2010 and 2020, the White clinical trial participants had similar representation (77% and 77%) and were higher than the rest of the racial and ethnic minorities in the clinical trials conducted for the seven FDA-approved NMEs and 33 FDA-approved NMEs in 2010 and 2020, respectively.

Ethnicity

There were variations in the reported data for the ethnic groups in the clinical trials conducted for both the seven FDA approved NMEs in 2010 and 33 FDA-approved NMEs in 2020; this can account for variations in the average percentages of representations. The ethnic groups consist of the Hispanic/Latino, non-Hispanic/Latinos, unknown, and "not reported ethnicity" in some of the clinical trials that were conducted for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020. From Table 5, the Hispanic/Latino had 5.7% representation while the non-Hispanic/Latino had 41.5% representation in the clinical trials that were conducted for the seven FDA-approved NMEs in 2010; in the same year, the unreported ethnic group was 0.6%. Some of the FDA-approved NMEs in 2010 and 2020 did not have published data on the ethnic groups of the clinical trial participants, some of them had missing data, and there were inconsistencies in the published data for the ethnic groups.

In 2020, the Hispanic/Latino clinical trial participant representation was 14.8%, non-Hispanic/Latinos' representation was 72.1% in the clinical trials that were conducted for the 33 FDA-approved NMEs, the unreported ethnic minorities' participant representation was 7.2%,

and unknown ethnic group representation was 4% in the clinical trials that were conducted for the 33 FDA-approved NMEs.

The ethnic minorities' representation in clinical trials conducted for both the seven FDA-approved NMEs and 33 FDA-approved NMEs were lower than the White participants' representation in both years (2010 and 2020). Regarding the research question "Are racial/ethnic minorities underrepresented in clinical trials?" from the results of this study, the White participants had higher representation than the racial/ethnic minorities.

Discussion

There were variations in the way the demographic data was reported for the clinical trial participants in the clinical trials that were conducted for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020. The demographic data of the clinical trial participants in the clinical trials were collated separately from the FDA website for each year and analyzed separately. From the result, the White clinical trial participant representation was higher than the racial and ethnic minorities, and the female clinical trial participants had higher representation than the male trial participants in the clinical trial conducted for the 40 FDA-approved NMEs.

Comparing the demographic data that were collated from the clinical trials that were conducted for the seven FDA-approved NMEs in 2010 and for the 33 FDA-approved NMEs in 2020, the researcher found that there were variations in the percentages of representation, and indications of the FDA-approved NMEs are not the same. All the FDA-approved NMEs that were used in this study are completely different from each other and they have different indications and they can be found in Appendix D and Appendix E. There were variations in the age categories in the reported clinical trials that were conducted for the seven FDA-approved NMEs in 2010 and for the 33 FDA-approved NMEs; the age categories are dependent on the groups of people that the drugs were developed for. Some of the age categories were < 65 years, and ≥ 65 years were not reported in all the clinical trials conducted for both the seven FDA-approved NMEs in 2010 and the 33 FDA-approved NMEs in 2020 and there were variations.

In this study, the female representations were 52.5% and 54.9% in the collated data from the reported clinical trials conducted for the seven FDA-approved NMEs and 33 FDA-approved NMEs in 2010 and 2020, respectively. The female representation (52.5% and 54.9%) in the

clinical trials conducted for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020 were both higher than male representation (47.6% and 45.1%) in the clinical trials conducted for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020, respectively. The male representation was 47.6% in the clinical trials that were conducted for the seven FDA-approved NMEs in 2010, and the male representation was 45.1% in the clinical trials that were conducted for the 33 FDA-approved NMEs in 2020.

Moreover, from the results, there was a difference between the male representation and female representation. The female representation was higher than the male representation in both FDA-approved NMEs for both years (2010 and 2020). In this study, the analysis of the collated results from the clinical trials conducted for the seven FDA-approved NMEs in 2010 and the 33 FDA-approved NMEs in 2020 with respect to the research question "Are women/females underrepresented in clinical trials?" from the results of this study, the female representation was higher than the male representation.

Furthermore, there were variations in the racial representation in the clinical trials conducted for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020. The White participants representation was higher (77% and 77%) in the clinical trials that were conducted for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020, respectively, when compared to Blacks (9.7% and 7.3%), Asians (4.3% and 7.7%), American Indians (0.2% and 0.4%), Native Hawaiian (0.0% and 0.2%), and other races (7.7% and 2.9%) representation in the clinical trials for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020, respectively. There were variations in the racial representations. With respect to racial/ethnic minorities participation in the clinical trials in the FDA- approved NMEs in 2010 and 2020, their representation was similar when compared to the White representation.

In this study, the number of White clinical trial participants was higher than the racial/ethnic minorities in this study. The racial/ethnic minorities are underrepresented in their participation in the clinical trial during the drug development programs; these similar findings have been reported in many articles, and the FDA recognizes this issue. The FDA has made attempts to resolve this issue to increase and improve the participation of the racial and ethnic minorities in clinical trials (George et al., 2014; Flores et al., 2021; Michos et al., 2021).

Furthermore, from the result of this study, the ethnic minorities, the Hispanics/Latino (5.71% and 14.8%) and non-Hispanics/Latinos (41.5% and 72.1%) representations in the clinical trials that were conducted for the seven FDA-approved NMEs in 2010 and 33 FDA-approved NMEs in 2020 respectively were lower than the White clinical trials participants. Regarding the research question "Has the demographic profile of clinical trial participants in drug development (NME, NDA) studies changed from 2010 to 2020, especially with respect to racial/ethnic minorities?" from the result of this study, the White trial participants had higher representation than the racial/ethnic minorities, and this is the same trend for the FDA-approved NMEs in 2010 and 2020. The demographic profile of the clinical trial participants in drug (NME/NDA) studies especially with respect to racial/ethnic minorities has been explained in the results section and the published data of the representation of racial/ethnic minorities were lower when compared to the White participants representation in the clinical trials conducted for the 40 FDA-approved NMEs in 2010 and 2020. The low participation of the ethnic minorities has been reported in several articles. The FDA is also aware of it and has tried to address the issue (George et al., 2014; Flores et al., 2021; Michos et al., 2021).

Besides, it is critical to involve and increase the number of racial and ethnic minorities participation in the clinical trials during the drug development programs because it will improve

the diversity in the representations of diverse populations, which will help us to gain more knowledge on the safety and efficacy of the drugs that are been developed, and it will also help to improve the application of the drugs to a more heterogeneous population (George et al., 2014; Flores et al., 2021; Michos et al., 2021).

Conclusion

Clinical trials are a reliable source of quality information and scientific evidence that provides high-quality solutions to scientific questions. This grants the relevant regulatory bodies to evaluate the safety and efficacy of the novel drugs, and it also provides important information to the medical professionals on how to utilize the new drugs which help the medical professionals in the management of their patients. There are huge benefits in allowing more diverse people to participate in trials, especially increasing the racial/ethnic minorities' participants in trials, and it will enhance the knowledge regarding the diverse population in drug development programs and will help to advance treatment choices. In the final analysis, this study was done on 40 FDA-approved NMEs in 2010 and 2020; 21 FDA-approved NMEs were excluded from analysis. The results from this study, the White trial participants had higher representation than racial/ethnic minorities. Regarding the research question "Are racial/ethnic minorities underrepresented in clinical trials?" from the results of this study, the White trial participants' representation was higher than the racial and ethnic minorities, and there is similarity between the reported demographic profile of trial participants in the FDA-approved NMEs in 2010 and 2020. This has been reported in several articles, and the FDA has also made considerable efforts to address this issue (George et al., 2014; Flores et al., 2021; Michos et al., 2021). Regarding the research question "Are women/females underrepresented in clinical trials?" from the result of this study, the female representation was higher than the male representation in this study.

Moreover, increasing and improving the recruitment and retention of racial/ethnic minorities in clinical trials participation during the drug development program provides more robust evidence regarding the pharmacokinetics, pharmacodynamics, safety, and efficacy of the

new molecular entities across the whole spectrum of the demographic population. It is really important to improve the recruitment and retention of all participants, particularly the racial/ ethnic minorities in the clinical trials during the drug development programs. This will also help us to address the health disparities that affect the racial and ethnic minorities (Camidge, 2021). The challenges of low recruitment and retention of racial/ethnic minorities in clinical trials can be due to communication issues between the trial participants and research staff, transportation issues (George et al., 2014), and the issue of mistrust between the trial participants and the research staff (Corbie-Smith, 2002; George et al., 2014), etc. The ways to address these issues is for research staff to modify their communication strategies to a culturally acceptable form for the participants; this will increase clinical trial participation (George et al., 2014; Yankey et al., 2006). Researchers can also provide some transportation or subsidize the costs of participants' transportation for them to participate in the trials.

The limitations of this study include the limited number of FDA-approved NMEs that were collated; some of the FDA-approved NMEs did not have adequate reported data on all the required demographics; and some of the FDA-approved NMEs in 2010 and 2020 demographic variables, such as age categories of trial participants, were not uniform and some were not available.

Recommendations

Finally, there is a compelling need for further research on the demographic profiles of clinical trial participants to further understand the heterogeneous population and increase the sponsors' and researchers' knowledge of the reason why the clinical trial participants might be interested in participating in clinical trials and also the reason why they may not be interested in

participating in clinical trials. Having a more equitable, robust, and diverse population in clinical trials will further enhance the sponsors' and researchers' knowledge of the safety and efficacy of novel therapeutics, and this will support the use of the novel drugs in a more diverse population.

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APPENDICES

Appendix A: Demographic Variables and Categories

Age category

- < 65
- ≥ 65

Sex

- Female
- Male

Race

- White
- Black or African- American
- Asian
- American Indian or Alaska Native
- Native Hawaiian or other Pacific islander
- Multiple races
- Asian Pacific
- Other races
- Unknown

Ethnicity

- Hispanic/Latino
- Latino
- Non-Hispanic
- Others
- Unknown
- Not Reported

Appendix B: FDA-Approved NMEs 2010 and 2020

FDA-approved NMEs in 2010

Number & Year: 2010.	**FDA NME: Name of the Drug**	**Active Ingredients/ Generic Name**
1.	Ampyra	dalfampridine
2.	Asclera	polidocanol
3.	Carbaglu	carbaglumic acid
4.	Ella	ulipristal acetate
5.	Gilenya	fingolimod hydrochloride
6.	Halaven	eribulin mesylate
7.	Jevtana kit	cabazitazel
8.	Lastacaft*	alcaftadine
9.	Lastacaft*	alcaftadine
10.	Latuda	lurasidone hydrochloride
11.	Natazia	estradiol valerate; dienogest
12.	Pradaxa*	dabigatran etexilate mesylate*
13.	Pradaxa*	dabigatran etexilate mesylate*
14.	Teflaro*	ceftaroline fosamil*
15.	Teflaro*	ceftaroline fosamil*
16.	Victoza	liraglutide recombinant

*FDA approved NMEs that were repeated on the FDA website.

FDA-approved NMEs in 2020

Number & Year: 2020	**FDA NME: Name of the Drug**	**Active Ingredients/Generic Name**
1.	Artesunate*	artesunate*
2.	Artesunate*	artesunate*
3.	Ayvakit	avapritinib
4.	Barhemsys	amisulpride
5.	Byfavo	remimazolam besylate
6.	Cerianna	fluoroesteadiol f-18
7.	Detectnet	64copper dotatate cu-64
8.	Dojolvi	triheptanoin
9.	Evrysdi	risdiplam
10.	Gallium GA-68 psma-11*	gallium ga-68 psma-11*
11.	Gallium GA-68 psma-11*	gallium ga-68 psma-11*
12.	Gavreto*	pralsetinib*
13.	Gavreto*	pralsetinib*
14.	Gemtesa	vibegron
15.	Imcivree	setmelanotide acetate
16.	Inqovi	cedarudine; decitabine
17.	Isturisa	osilodrostat phosphate
18.	Klisyri	tirbanibulin
19.	Koselugo	selumetinib sulfate
20.	Lampit	nifurtimox
21.	Nexletol	bempedoic acid
22.	Nexlizet	bempedoic acid; ezetimibe
23.	Nurtec ODT	rimegepant sulfate
24.	Olinvyk	oliceridine
25.	Orgovyx	relugolix
26.	Orladeyo	berotralstat hydrochloride
27.	Ongentys	opicapone
28.	Oxlumo	lumasiran sodium
29.	Pemazyre	pemigatinib
30.	Pizensy	lactitol
31.	Qinlock	ripretinib
32.	Retevmo	selpercatinib

33.	Rukobia	fostemsavir tromethamine
34.	Tabrecta	capmatinib hydrochloride
35.	Tauvid	flortaucipir- f-18
36.	Tazverik	tametostat hydrochloride
37.	Tukysa	tucatinib
38.	Veklury	remdesivir
39.	Viltepso	viltolarsen
40.	Winlevi	clascoterone
41.	Xeglyze*	abametapir*
42.	Xeglyze*	abametapir*
43.	Zeposia	ozanimod hydrochloride
44.	Zepzelca	lurbinectedin
45.	Zokinvy	lonafarnib

*FDA approved NMEs that was repeated on the FDA website.

Appendix C: FDA-Approved NMEs (2010 and 2020) Included in Study

Number	FDA Approved NME in 2010	FDA Approved NME in 2020
1.	Ampyra (dalfapridine)	Ayvakit (avapritinib)
2.	Gilenya (fingolimod hydrochloride)	Barhemysys (amisulpride)
3.	Laftacaft (alcaftadine)	Byfavo (remimazolam besylate)
4.	Latuda (lurasidone hydrochloride)	Detectnet (copper dotatate cu-64)
5.	Pradaxa (dabigatran etexilate mesylate)	Dojolvi (triheptanoin)
6.	Teflaro (ceftaroline fosamil)	Evrysdi (cisdiplam)
7.	Victoza (liraglutide recombinant)	Gavreto (pralsetinib)
8.		Gemtesa (vibegron)
9.		Imcivree (setmelanotide acetate)
10.		Inqovi (cedarudine; decitabine)
11.		Isturisa (osilodrostat phosphate)
12.		Klisyri (tirbanibulin)
13.		Nexletol (bempedoic acid)
14.		Nexlizet (bempedoic acid; ezetimibe)
15.		Nurtec ODT (remegepant sulfate)
16.		Olinvyx (oliceridine)
17.		Orladeyo (berotralstat hydrochloride)
18.		Ongentys (opicapone)
19.		Oxlumo (lumasiran sodium)
20.		Pemazyre (pemigatinib)
21.		Pizensy (lactitol)
22.		Qinlock (ripretinib)
23.		Retevmo (selpercatinib)
24.		Rukobia (fostemsavir tromethamine)
25.		Tabrecta (captatimib hydrochloride)
26.		Tauvid (flortaucipir f-18)
27.		Tazverik (tazemetostat)
28.		Tukysa (tucatinib)
29.		Veklury (remdesivir)
30.		Winlevi (clastcoterone)
31.		Xeglyze (abametapir)
32.		Zeposia (ozanimod hydrochloride)
33.		Zepleca (lurnonafarnib binectedin)

Appendix D: FDA-Approved NMEs (2010): Name and Indication

1. AMPYRA (dalfampridine): is a potassium channel blocker indicated to improve walking in adult patients with multiple Sclerosis (MS). This was demonstrated in walking speed.
2. ASCLERA (polidocanol): Age: 18 years or older, it is a sclerosing agent indicated to sclerose uncomplicated spider veins (varicose veins ≤1mm in diameter) and uncomplicated reticular veins (varicose veins 1 to 3 mm in diameter) in the lower extremity. Asclera has not been studied in varicose veins more than 3 mm in diameter.
3. CARBAGLU (carbaglu): Age- Pediatric and Adult patients. It is a carbamoyl phosphate synthetase 1 (CPS 1) activator indicated in pediatric and adult patients as: Adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to N-acetylglutamate (NAGS) deficiency. Maintenance therapy for the treatment of chronic hyperammonemia due to NAGS deficiency. Adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to propionic acidemia (PA) or methyl malonic acidemia (MMA).
4. ELLA (ulipristal acetate): Age group, 16 years and over. It is a progesterone agonist/ antagonist emergency contraceptive for prevention of pregnancy following unprotected intercourse or unknown or suspected contraceptive failure. Ella is not intended for routine use as a contraceptive.
5. GILENYA (figolimod hydrochloride): Age for 10 years and older. It is a sphingosine 1-phosphate receptor modulator indicated for the treatment of patients with relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

6. HALAVEN (eribulin mesylate): Age- Adults. It is a microtubule inhibitor indicated for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.
7. JEVTANA (cabazitaxel): Age: Adults, men. It is a microtubule inhibitor indicated in combination with prednisolone for treatments of patients with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing treatment regimen.
8. LAFTACAFT* (alcaftadine): Age- 2 years and older. It is a H1 histamine receptor antagonist indicated for the prevention of itching associated with allergic conjunctivitis.
9. LATUDA (lurasidone hydrochloride): Age- 13 years and older. It is an atypical antipsychotic for the treatment of Schizophrenia, depressive episodes associated with Bipolar I disorder (bipolar depression), as monotherapy and as adjunctive therapy with lithium or valproate.
10. NATAZIA (estradiol valerate; dienogest): Age- Women of child bearing age. It is an estrogen/progestin COC, indicated for use by women to prevent pregnancy. The efficacy of Natazia in women with a body mass index (BI) of >30 kg/m2 has not been evaluated.
11. PRADAXA* (dabigatran etexilate mesylate): Age- Adults and Paediatric patients aged 8 years or older. It is a direct thrombin inhibitor indicated to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation.
12. TEFLARO* (ceftaroline fosamil): Age- Adult and Pediatric patients (at least 34 weeks gestational age and 12 days postnatal age and older). It is a cephalosporin antibacterial

indicated for the treatment of the following infections caused by designated susceptible bacteria: Acute bacterial skin and skin structure infections (ABSSSI), community-acquired bacterial pneumonia (CABP).

13. VICTOZA (liraglutide recombinant): Age- Adults and children (10 years of age and older). It is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus, to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease.

*The FDA approved NMEs that were repeated twice on the FDA website.

Appendix E: FDA-Approved NMEs (2020): Name and Indication

1. ARTESUNATE* (artesunate): Age- Adult and pediatric patients, it is an antimalarial indicated for the initial treatment of severe malaria in adult and pediatric patients. Treatment of severe malaria with Artesunate for injection should always be followed by a complete treatment course of an appropriate oral antimalarial regimen.
2. AYVAKIT (avapritinib) is a kinase inhibitor indicated for: Age- 18 years and older. It is used for: Gastrointestinal Stromal Tumor (GIST): the treatment of adults with unresectable or metastatic GIST harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon18 mutation, including PDGFRA D842V mutations. Advanced Systemic Mastocytosis (AdvSM): the treatment of adult patients with AdvSM. AdvSM includes patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM AHN), and mast cell leukemia (MCL)."
3. BARHEMSYS (amisulpride): Age- 18 years and older. It is a dopamine-2 (D2) antagonist indicated in adults for Prevention of postoperative nausea and vomiting (PONV) either alone or in combination with an antiemetic of a different class. Treatment of PONV in patients who have received antiemetic prophylaxis with an agent of a different class or have not received prophylaxis.
4. BYFAVO (remimazolam besylate): Age- Adults 18 years and older, it is for injection is a benzodiazepine indicated for the induction and maintenance of procedural sedation in adults undergoing procedures lasting 30 minutes.
5. CERIANNA (fluoroesteadiol f-18): is a drug for the visual detection of estrogen receptor (ER)-positive lesions in addition to tissue biopsy in patients with recurrent or metastatic breast cancer.

6. DETECTNET (copper dotatate cu-64): Age- Adult patients. DETECTNET is a drug for detection of the specific type of tumors called somatostatin receptor positive neuro-endocrine tumors (NETs) in adults. NETs are rare tumors that develop in certain hormone-producing cells of the body's neuro-endocrine system.
7. DOJOLVI (triheptanoin): Age- pediatric and adult patients. DOJOLVI is a drug that provides calories and fatty acids for pediatric and adult patients with long-chain fatty acid oxidation disorder. Long-chain fatty acid oxidation disorders (LC-FAOD) are a group of rare, genetic, life threatening disorders caused by defects in the enzymes needed to produce the energy from fatty acids. Patients with LC-FAODs can suffer from muscle pain, fatigue, and heart failure because their bodies break down muscle as a source of energy as fat cannot be used as an energy source.
8. EVRYSDI (risdiplan): is a drug for the treatment of spinal muscular atrophy (SMA) in patients 2 months of age and older. Spinal muscular atrophy is a rare genetic disease that affects mostly children and young adults. It is caused by a low level of protein in the motor neurons that are responsible for normal muscle functioning. The lack of protein causes motor neuron loss, progressive muscle weakness, and may lead to premature death from respiratory failure.
9. GALLIUM GA 68 PSMA-11* (gallium ga-68 psma-11): Ga 68 PSMA-11 is a drug used for detection of specific cancer lesions in men with prostate cancer whose newly diagnosed cancer could be cured with the initial treatment, or who have been treated for prostate cancer but have high prostate-specific antigen (PSA) in their blood. High PSA in the blood of these patients is a suspicious sign that cancer is coming back or spreading.

10. GAVRETO* (pralsetinib): is a drug used to treat adult patients with non-small cell lung cancer (NSCLC) which has spread to other parts of the body (metastatic) and is caused by abnormal RET (rearranged during transfection) genes.
11. GEMTESA (vibegron): Age range: Adults patients. It is used to treat the following symptoms due to a condition called overactive bladder (OAB): a strong need to urinate with leaking or wetting accidents, the need to urinate right away, and the need to urinate often.
12. IMCIVREE (setmelanotide acetate): is a drug used for long-lasting weight management in patients 6 years and older who are obese because of a specific enzyme deficiency [(proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency)].
13. INQOVI (cedazuridine; decitabine): is used to treat adults with myelodysplastic syndromes (MDS) including chronic myelomonocytic leukemia. MDS is a type of blood cancer in which blood cells in the bone marrow are defective leading to a low number of one or more types of blood cells.
14. ISTURISA (osilodrostat phosphate): is a drug for the treatment of adults with Cushing's disease: who cannot have pituitary gland surgery, or who have had pituitary gland surgery, but the surgery did not cure their Cushing disease. Cushing's disease is a rare disease in which the adrenal glands make too much of the cortisol hormone because of stimulation from a pituitary tumor.
15. KLISYRI (tirbanibulin): Age- 18 years and older. It is used on the skin to treat patients with actinic keratosis on the face or scalp. Actinic keratosis is a common skin disease

caused by long-term exposure to the sun and/or indoor tanning. If left untreated, AK may progress to skin cancer.

16. KOSELUGO (selumetinib sulfate): is used to treat children 2 years of age and older with a type of tumor called plexiform neurofibroma or PN that occurs in a rare disease called neurofibromatosis type 1 (NF1). It is used in patients whose tumors cause symptoms and could not be surgically removed.
17. LAMPIT (nifurtimox): It is drug used to treat Chagas disease in children less than 18 years old. Chagas disease is an infectious disease caused by a parasite (Trypanosoma [T.] cruzi). After years of infection, the parasites may cause serious and sometimes deadly heart conditions as well as serious gut and nerve damage.
18. NEXLETOL (bempedoic acid): Age- Adults. It is a drug for the treatment of high LDL cholesterol, which is sometimes referred to as “bad cholesterol”. NEXLETOL is to be used in the following two groups of patients: (1) Adult patients with an inherited condition called heterozygous familial hypercholesterolemia (HeFH) or (2) patients with complications from too much cholesterol (known as atherosclerotic cardiovascular disease – ASCVD), such as hearts and strokes.
19. NEXLIZET (bempedoic acid; ezetimibe): Age- 18 years and older. It contains an adenosine triphosphate-citrate lyase (ACL) inhibitor and a cholesterol absorption inhibitor, is indicated as an adjunct to diet and maximally tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C.
20. NURTEC ODT (rimegepant sulfate): Age- 18 years and older. NURTEC ODT is a drug used for treatment of acute migraine with or without aura in adults.

21. OLINVYK (oliceridine): Age- Adult patients, 18 years and older. It is a drug for the treatment of acute pain in adults when the pain is severe enough to require an intravenous opioid.
22. ORGOVYX (relugolix): is a drug for the treatment of adults with advanced prostate cancer.
23. ORLADEYO (berotralstat hydrochloride): is a drug used to prevent attacks of hereditary angioedema (HAE) in patients 12 years and older. Hereditary angioedema is a rare, inherited and sometimes life-threatening condition with repeat episodes (attacks) of severe swelling in various parts of the body, including stomach, limbs, face and throat.
24. ONGENTYS (opicapone): Age- Adults. It is a drug used to treat patients with Parkinson's disease (PD) who are having "off" episodes while taking drugs (levodopa and carbidopa) for the treatment of Parkinson's disease. An "off" episode is a time when a patient's medications are not working well, leading to an increase in Parkinson's symptoms, such as tremor and difficulty walking.
25. OXLUMO (lumasiran sodium): is a drug used to lower the level of urine oxalate in children and adults with primary hyperoxaluria type 1 (PH1). PH1 is a rare, inherited disorder in which the liver makes too much oxalate. Excess oxalate can lead to kidney stones and kidney damage. Over time, oxalate can also build up in the body and damage other organs, including the heart, bones and eyes.
26. PEMAZYRE (pemigatinib): is a drug used for treatment of adults with bile duct cancer (cholangiocarcinoma) that has spread to other parts of the body (metastatic) or cannot be removed by surgery. It should be used in patients who have been previously treated with chemotherapy and whose cancer has a certain type of abnormality in the FGFR2 gene.

27. PIZENSY (lactitol): is used to treat a type of constipation called chronic idiopathic constipation (CIC) in adults.
28. QINLOCK (ripretinib): is drug used to treat adult patients with gastrointestinal stromal tumor (GIST) whose disease: cannot be surgically removed or, has spread throughout the body (metastatic GIST), and has been treated with at least three prior treatments. GIST is type of stomach, bowel, or oesophagus tumour.
29. RETEVMO (selpercatinib): is a drug used to treat certain cancers caused by abnormal RET (rearranged during transfection) genes in: Adult patients with non-small cell lung cancer (NSCLC) which has spread to other parts of the body (metastatic). Adults and children 12 years of age and older with advanced or metastatic medullary thyroid cancer (MTC). Adults and children 12 years of age and older with advanced or metastatic thyroid cancer who have received radioactive iodine that did not work or is no longer working.
30. RUKOBIA (fostemsavir tromethamine): Age- 18 years and older. It is a drug for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults who have received several anti-HIV-1 regimens in the past, and have HIV-1 virus that is resistant to many antiretroviral medicines, and who are failing their current antiretroviral therapy because it is not effective, have intolerable side effects or other safety problems.
31. TABRECTA (capmatinib hydrochloride): TABRECTA is a drug used to treat adult patients with a type of non-small cell lung cancer (NSCLC) which: has a specific gene mutation (mesenchymal epithelial transition or MET mutation) and, has spread to other parts of the body (metastatic).

32. TAUVID (flortaucipir f-18): Tauvid is a drug for the visual detection of aggregated neurofibrillary tangles or NFTs in the brain of adult patients with suspected Alzheimer's disease (AD). NFTs are deposits of tau protein that are present in the brains of patients with AD. Alzheimer's disease is a common degenerative disease of the brain that starts with mild thinking, judging and memory problems and progresses to dementia and death.
33. TAZVERIK (tazemetostat hydrochloride): is a drug used to treat a type of cancer called advanced epithelioid sarcoma. It is to be used in patients 16 years and older when cancer has spread and cannot be completely removed by surgery. Epithelioid sarcoma is a rare, slow growing type of cancer that begins in the soft tissues of the body (most commonly under the skin of an extremity)
34. TUKYSA (tucatinib): is a drug for treatment of adults with human epidermal growth factor receptor (HER) 2-positive breast cancer that has spread to other parts of the body including the brain (metastatic) or cannot be removed by surgery. It should be used in patients who have been previously treated for their metastatic disease with at least one anti-HER2 regimen and in combination with two other medications for the treatment of metastatic breast cancer (trastuzumab and capecitabine).
35. VEKLURY (remdesivir): Age: 12 years and older, it is for use in adult and pediatric patients 12 years and older weighing at least 40 kg (88 lbs) for the treatment of coronavirus disease 2019 (COVID-19) requiring hospitalization.COVID-19 is an infectious, potentially serious or life-threating respiratory disease caused by a coronavirus called SARS-CoV-2 virus.
36. VILTEPSO (viltolarsen): Age- ages 4 years to 17 years old. It is a drug for the treatment of a particular type of Duchenne muscular dystrophy (DMD). It is to be used only in

patients who have a specific mutation of the dystrophin gene. DMD is a rare disease that primarily affects boys. It is caused by low levels of a muscle protein called dystrophin. The lack of dystrophin causes progressive muscle weakness and premature death.

37. WINLEVI (clascoterone): is used on the skin to treat acne vulgaris in patients 12 years and older. Acne vulgaris is a skin disease characterized by oily skin, blackheads or whiteheads, pimples, and sometimes scarring.
38. XEGLYZE* (abametapir): Age- 6 months of age and older. For topical use only, It is a lotion applied once to dry hair." "It is should be used in the context of an overall lice management program: Wash (with hot water) or dry-clean all recently worn clothing, hats, used bedding and towels. Wash personal care items such as combs, brushes and hair clips in hot water. Use a fine-tooth comb or special nit comb to remove dead lice and nits.
39. ZEPOSIA (ozanimod hydrochloride): is a drug used for the treatment of adults with relapsing forms of multiple sclerosis (RMS) including: clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease.
40. ZEPZELCA (fluoroesteadiol f-18): is a drug used to treat adult patients with small cell lung cancer (SCLC) which has spread to other parts of the body (metastatic) on or after treatment with platinum-containing therapy.
41. ZOKINVY (lonafarnib): is a drug used in patients one year of age and older with a certain body surface area to lower the risk of death in Hutchinson-Gilford Progeria Syndrome (HGPS), or to treat certain processing-deficient progeroid laminopathies.

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