Organizational Audit Paper - Part 1-3 FINAL

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Organization Selected: The organization selected for the assigned organizational audit paper is the Food and Drug Administration (FDA). The FDA is a federal organization of the United States Department of Health and Human Services (HHS) responsible for protecting public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, food, and cosmetics (F. a. D. Administration, 2023b). According to the FDA's History webpage, "The Food and Drug Administration is the oldest comprehensive consumer protection organization in the U. S. federal government. (…) Although it was not known by its present name until 1930, FDA's modern regulatory functions began with the passage of the 1906 Pure Food and Drugs Act (…) Since then, the FDA has changed along with social, economic, political, and legal changes in the United States." (F. a. D. Administration, 2023c) With oversight of a wide range of consumer-based products, the scope of the FDA is broad and complex. This organizational audit will focus on the FDA's oversight of prescription drugs, specifically opioid prescription pain medication (OPPM). Focusing on the FDA's oversight of OPPMs will allow for a more focused organizational ethics audit of the FDA's role in the opioid epidemic (OE) that continues to have a substantial public health impact. This paper will prove that the FDA failed to uphold its ethical duties before and during the OE. Specifically, the presented evidence will support the claim that the FDA failed to prioritize public health and safety, as demonstrated by its approval of OPPMs without sufficient evidence and oversight, negligence in addressing the addictive nature and potential misuse of OPPMs, and susceptibility to industry influence, ultimately initiating and exacerbating the OE and its devastating consequences on individuals, families, and communities.

Organization's History: Created in 1906, the FDA has dramatically evolved and expanded its scope throughout its long history. The evolution and expansion of the FDA and its regulatory authority have been essential to protecting public health. In order to comprehensively address and review the FDA's organizational ethics, it is crucial to understand the history and functions of an organization. (Bowman & West, 2021) Many key historical references, specific to the FDA and OPPMs, are used to understand the context by which the FDA functions and its role in overseeing prescription drugs (F. a. D. Administration, 2023b).

Following the creation of the FDA, the first historical reference used to establish the history and context of the FDA's role in the OE was the establishment of the Harrison Narcotics Tax Act (HNTA) of 1914. The HNTA regulated the production and distribution of opioids (such as morphine, heroin, and codeine) by taxing those involved in the trade. It required registration with the Internal Revenue Service and furthered the FDA's ability to oversee the use of these drugs. (Suarez, 1969) Next was the passage of the Federal Food, Drug, and Cosmetic Act (FD&C Act) of 1938. Following an incident where an untested medication called Elixir Sulfanilamide contributed to over 100 deaths, the FD&C Act was passed to strengthen regulations on testing medications for safety. The FD&C Act required manufacturers to prove the safety of new drugs before they could be marketed and introduced more

rigorous labeling requirements (Cavers, 1939). Then the Kefauver-Harris Drug Amendments (KHDA) was established in 1953. In response to public health concerns about thalidomide, a drug used to treat nausea in pregnant women which were found to cause severe congenital disabilities (Kim & Scialli, 2011), the KHDA amendments were enacted to strengthen drug safety requirements. Drug manufacturers were now required to prove not only the safety but also the efficacy of their products. (Turner, 2012) The above-outlined historical references establish the regulatory function of the FDA related to prescription drugs and establish the responsibility of the FDA to ensure public safety.

Expanding on the FDA's regulatory authority, specific to OPPMs, was the Controlled Substances Act (CSA) of 1970, which created a drug scheduling system to classify drugs based on their potential for abuse, medical use, and safety. OPPMs were placed in different schedules, with Schedule II containing the most potent opioids like morphine, oxycodone, and fentanyl. The FDA continues to play a critical role in determining the scheduling of drugs under the CSA. (Lampe & Attorney, 2021) The next regulatory enhancement was the Prescription Drug User Fee Act (PDUFA) of 1992. The PDUFA allowed the FDA to collect fees from drug manufacturers to fund faster reviews of new drugs. The PDUFA aimed to speed up the approval process and improve access to life-saving medications. Recent concerns related to the potential influence of pharmaceutical manufacturers over the FDA caused by the PDUFA will be addressed later in this paper. These critical points in the FDA's history provide essential context to the ethical considerations for how the FDA has participated in the OE and the public trust required to maintain public health. (Phillips, Ford, & Bonnie, 2017) Research demonstrates that the most crucial action by the FDA associated with the OE occurred in 1995 (Van Zee, 2009) when, under its authority to approve prescription medication, the FDA approved OxyContin, a long-acting form of oxycodone which became one of the most widely marketed versions of OPPM for non-cancer chronic pain patients. While OxyContin was promoted as a safer alternative to other OPPMs because of its controlled-release formulation, it was eventually proven that the research used in the approval was insufficient. The FDA's approval of OxyContin became a significant factor in the OE due to its high potential for abuse and addiction (Theodore J Cicero, Inciardi, & Muñoz, 2005).

In 2000, as OxyContin abuse grew, the FDA began to face criticism for its role in approving and regulating the drug. In response, the FDA began implementing stricter regulations for OPPMs, including more robust warning labels and the Risk Evaluation and Mitigation Strategies (REMS) framework. (Theodore J Cicero et al., 2005) Twelve years later, in 2012, the FDA recommended rescheduling hydrocodone combination products (like OxyContin and Vicodin) from Schedule III to the more restrictive Schedule II, acknowledging their high potential for abuse and addiction. (Traynor, 2013) Most recently, in 2018, the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities

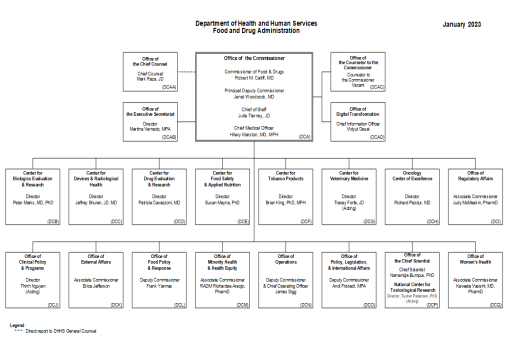
Act was signed into law, providing the FDA with additional tools and authorities to address the OE. This included measures to promote the development of non-addictive pain treatments and safer opioid formulations. (Act, 2018)

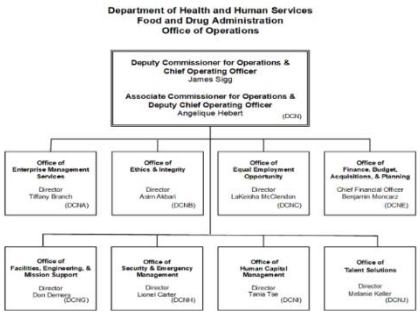
Throughout its history, the FDA has continually refined and expanded its oversight of OPPMs in response to the changing landscape of drug use. Despite this, the FDA has faced criticism of the timing and implementation of its regulatory authority. This criticism has since expanded to various ethical concerns. Future sections of this paper will focus on the ethical obligations imposed on the FDA based, in part, on the organization's history and well-established responsibilities specific to the approval and regulation of OPPMs.

Organization's Purpose and Mission: According to the FDA's website, their mission is as follows. "The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our Nation's food supply, cosmetics, and products that emit radiation (…) FDA is responsible for advancing public health by helping to speed innovations that make medical products more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medical products and foods to maintain and improve their health." (F. a. D. Administration, 2023b)

Specific to the FDA's role in the oversight and regulation of prescription drugs, the FDA regulates preclinical testing, Investigational New Drug (IND) applications, all phases of clinical trials, New Drug Applications (NDA), drug review and approval, post-marketing surveillance, and generic drug transitions, also known as Abbreviated New Drug Applications (ANDA). (Borchers, Hagie, Keen, & Gershwin, 2007) Each phase of the drug approval and regulation process listed above is focused on safety and efficacy, with ethical oversight incorporated into all process phases.

Staffing arrangements (organizational chart): According to the FDA's website, "effective March 31, 2019, FDA began operational implementation of an organization reorganization. FDA's reorganization reflects the organization's commitment to modernizing its structure to advance its mission to protect and promote public health and to meet the challenges of rapid innovation across the industries regulated by FDA." (F. a. D. Administration, 2023b) The two organizational charts, provided here and in Appendix A, were taken from the FDA's website and reflect the structure of the FDA and the organizational placement of its Office of Ethics and Integrity (OEI). According to the FDA's OEI website, its mission is to "provide advice and assistance to current and former employees to help ensure that decisions they make, and actions they





take, are not, nor appear to be, tainted by any question of conflict of interest." (Integrity, 2023) The FDA's OEI oversees all aspects of the organization's ethics and integrity policy, procedures, and enforcement. Based on the provided organizational chart, the FDA's OEI falls under the FDA's Office of Operations (OOO), which directly reports to the Commissioner of the FDA. This structure provides prominence and broad ethical oversight across the entire organization. (F. a. D. Administration, 2023b)

Ethics Management Infrastructure: The FDA's Ethics Management Infrastructure is crucial for maintaining the organization's and its employees' integrity and trustworthiness, both essential aspects of public trust. Due to the nature and scope of the FDA, ethical oversight is a central function that impacts all areas of the organization. According to the FDA's OEI website, the OEI states that "the ethics laws and regulations were established to promote and strengthen the public's confidence in the integrity of the Federal government. The Division of Ethics and Integrity strives to maintain a positive public perception in the way FDA conducts its business activities and to help employees perform the functions of their positions free from conflict of interest." (Integrity, 2023) The primary functions of the OEI include ethics training, advice and assistance, financial disclosure reporting, ethics liaison activities, and outside activities (Integrity, 2023). The FDA is guided by a well-established ethical infrastructure that helps ensure its actions are consistent with its mission and values. (Ethics, 2017) The OEI implements the components of the FDA's ethical infrastructure, which includes the following.

1. Ethics Training: To ensure that employees know their ethical obligations and maintain the highest standards of conduct, the FDA provides mandatory ethics training to its staff. This training covers conflicts of interest, gifts, financial disclosure, and post-employment restrictions. (Ethics, 2017)
2. Ethics Officials: The FDA has designated ethics officials responsible for providing guidance and support to employees on ethical issues. These officials help to interpret and apply federal ethics laws and regulations, resolve potential conflicts of interest, and ensure compliance with ethics requirements. (Ethics, 2017)
3. Enforcement and Compliance: The FDA investigates misconduct allegations and takes appropriate disciplinary action when necessary. Employees are encouraged to report potential ethical violations through various channels, including the FDA's Office of Internal Affairs or the HHS Office of Inspector General. (Ethics, 2017)
4. Public Trust and Transparency: The FDA is committed to maintaining public trust and ensuring transparency in its decision-making processes. The organization actively engages with stakeholders, including industry, academia, and patient advocacy

groups, to promote transparency and foster trust in its regulatory activities. This engagement is most commonly done by implementing advisory committees comprising internal and external subject matter experts. (Ethics, 2017)

5. Conflict of interest policy and financial disclosures: The FDA has policies to identify and manage conflicts of interest among its employees, contractors, and advisers. FDA employees must submit financial disclosure reports, which provide information about their financial interests and holdings. These policies require individuals to disclose potential conflicts of interest and for the organization to assess and manage them to ensure that its decisions are based on scientific and regulatory principles. (Ethics, 2017)
6. Regulatory process: The FDA ensures that products are safe and effective before being marketed to the public. This process includes a rigorous scientific review of product data, public input, and feedback to ensure that various perspectives inform the organization's decisions. (Ethics, 2017) The FDA has established stringent regulations and policies to approve, label, and monitor drugs to minimize potential abuse and misuse. One such strategy includes the REMS framework for certain drugs, which requires manufacturers to develop and implement plans to ensure the safe use of these medications. (Dabrowska, 2018)
7. Post-market surveillance: The FDA monitors products after they are approved to identify any safety concerns or other issues that may arise. This monitoring is a critical component of the organization's ethical oversight procedures, as it ensures that the FDA remains vigilant in protecting public health and safety. (Ethics, 2017). Specific tools used by the FDA to provide post-market surveillance include the Adverse Event Reporting System (FAERS), which collects information on adverse events and medication errors, and the Sentinel Initiative (SI), which uses electronic health data to monitor the safety of FDA-regulated products. (Edwards et al., 2013)

In summary, the FDA's Ethics Management Infrastructure is a comprehensive system that seeks to promote and maintain the highest ethical standards among its employees, ensuring that the organization's decision-making processes are transparent, unbiased, and trustworthy. This infrastructure is crucial in safeguarding public health and fostering public trust in the FDA. After initial review, the FDA's ethics management infrastructure has mechanisms to address critical ethical considerations. Future sections of this paper will further analyze if theories, such as the Ethics Triad, including deontology, utilitarianism, and virtue ethics, are fully considered in the design of the FDA’s ethical management infrastructure. (Bowman & West, 2021) In addition, it has been made clear that the FDA's ethics management infrastructure is constantly evolving. The FDA regularly reviews and updates its ethics policies and procedures to stay current with changing laws, regulations, and best practices in ethical conduct. (Ethics, 2017) Additionally, outside departments such as the United States Office of Government Ethics (USOFE) conduct regular reviews to

monitor compliance with the FDA's OEI. The most recent report by the USOFE was conducted in May of 2017 and was used to inform this paper. (Ethics, 2017) This all contributes to an ongoing commitment to ethical practices by the FDA and structurally serves as an example for public administrators on the importance of constant evaluation of ethics in the public sector. (Cooper, 2012) This audit will aim to determine if the ethical infrastructure of the FDA was sufficient in its application related to OPPM approval and monitoring.

The Case of Misconduct: The OE has been and continues to be a significant public health crisis in the United States (US). Over the past 23 years, the country has experienced sharp year-over-year increases in opioid-related drug overdoses and deaths. Research has demonstrated that in 1999, the age-adjusted rate of overdose deaths in the US was 6.1 per 100,000. In 2021, the age-adjusted drug overdose death rate rose to 32.4 per 100,000, which represents a percentage increase of 432%. (Spencer, Miniño, & Warner, 2022) More specifically, in 2021, overdose deaths rose to 106,699. (Spencer et al., 2022) This equates to over 1 million people in the US dying from a drug-related overdose since 2000 (Schwartz, 2022). While many compounding factors must be considered, evidence has shown that over-prescribing OPPMs was the current OE's initial driver (Wilkerson, Kim, Windsor, & Mareiniss, 2016). As the federally designated regulatory authority for all consumer products in the US, including drugs and medications, the FDA is responsible for approving and regulating OPPMs. The initial increase in drug-related overdose deaths directly correlates to the approval by the FDA of OPPMs, such as OxyContin, to treat chronic pain in non-cancer patients. Because of this, the FDA has faced criticism and allegations of ethical misconduct related to its approval of OPPMs, its lack of regulation of OPPMs, and the impact such actions have had on the OE. In an article published in the AMA Journal of Ethics, the author states that "In 2017, the President's Commission on Combatting Drug Addiction and the Opioid Crisis found that the opioid crisis was caused in part by "inadequate oversight by the Food and Drug Administration," and the National Academy of Sciences (NAS) publicly called on the FDA to overhaul its opioid policies." (Kolodny, 2020) (Bonnie, Kesselheim, & Clark, 2017) This paper will present the overall case of ethical misconduct by the FDA concerning its role in the OE, including critical areas in which the ethics infrastructure described above did not function as originally intended. Specific actions by key FDA administrators will also be provided to support the case.

As the FDA continues to face increased scrutiny over its culpability in the OE, many critics have raised concerns over key actions and inactions by the FDA. In their own admission, Dr. David Kessler, who was the FDA commissioner when the FDA approved OxyContin, acknowledged, "No doubt it was a mistake. It was certainly one of the worst medical mistakes, a major mistake." (Mitchell, 2018) Further demonstrating the failures of the FDA, a recent article by (Castronuovo, 2022) titled "OxyContin Decision Involved FDA' Miscalculation, Woodcock Says" outlines testimony by Janet Woodcock, the current Principal Deputy

Commissioner of the FDA. Woodcock admits that the FDA's approval of OxyContin included a "miscalculation about projected harms." (Castronuovo, 2022) The FDA first approved OxyContin when Woodcock was the FDA's Director of the Center for Drug Evaluation and Research. (Castronuovo, 2022) Woodcock admits that the FDA "failed to adequately predict the harms associated with the drug that has fallen into the center of the US opioid epidemic." (Castronuovo, 2022) Woodcocks' comments prove that the FDA and its officials incorrectly approved OxyContin, thus questioning the process of approving OPPMs. The actions taken by FDA officials, including Woodcock, were so concerning that in June of 2021, when Woodcock was being considered for the Commissioner of the FDA position, US Sen. Joe Manchin (D-W.Va.) strongly urged President Biden not to nominate Woodcock. Specifically, Sen. Manchin stated that the "FDA has played a critical role in this overdose epidemic by overseeing continuous approvals of stronger and more addictive opioids since the initial approval of OxyContin in 1995…and Dr. Woodcock has been there for all of it" (Castronuovo, 2022).

In an article by (Mitchell, 2018) titled "How the FDA helped pave the way for an opioid epidemic," the author lays out how the FDA failed to do its job correctly when it approved OPPMs with limited to no evidence for broad application to pain management. (Mitchell, 2018) It has been revealed that the sole research used to claim that OPPMs were safe, and was used to inform the FDA decision to approve OxyContin, came from a one-paragraph letter to the editor published in a 1980 edition of the New England Journal of Medicine. ("Addiction Rare in Patients Treated with Narcotics," 1980) Even though there was no confirmed or actual research-based evidence of OPPM's safety, the FDA still approved OxyContin and many other OPPMs. (Leung, Macdonald, Stanbrook, Dhalla, & Juurlink, 2017) In an article by (Kolodny, 2020) titled "How FDA failures contributed to the opioid crisis," the author examines the role of the FDA in the OE, arguing that the agency's failures contributed significantly to the problem. (Kolodny, 2020) identifies critical factors that led to the FDA's shortcomings.

First, (Kolodny, 2020), similar to (Mitchell, 2018), identifies the FDA's failed process of approving and properly labeling OPPMs for safety. Specifically, (Kolodny, 2020) explains that the FDA did not adequately investigate the safety and addictive properties of OPPMs prior to approval. Evidence shows that the FDA over-relied on insufficient data sponsored partly by the pharmaceutical manufacturers seeking approval for OPPMs. The FDA's quick, insufficient, and lenient approval allowed OPPM manufacturers to aggressively market their products as safe and non-addictive for chronic, non-cancer pain without the required evidence to make such a claim. Secondly, (Kolodny, 2020) suggests that the FDA ignored the risks of opioid dependence before and after approving OPPMs. Evidence shows that the FDA failed to recognize and address the risks associated with opioid dependence, even as evidence of the problem mounted. (Kolodny, 2020) suggests that the FDA took far too long to take

appropriate action to mitigate the risks of addiction or overdose, such as requiring manufacturers to develop abuse-deterrent formulations or implementing post-marketing surveillance to monitor the impact of OPPMs on public health. Evidence shows that the FDA, in many ways, has not taken, until recently, aggressive enough action to curtail the overprescribing of OPPMs or hold manufacturers accountable for their role in the OE. (Kolodny, 2020) concludes that the FDA's failures have significantly contributed to the OE, which has led to the deaths of over 1 million Americans.

To best understand the ethical misconduct of the FDA concerning the OE, we must consider specific areas in which the FDA failed to uphold its duties. The first consideration is the presence of regulatory capture within the FDA. (Haffajee, 2020) The FDA has been accused of being too close to the pharmaceutical industry, leading to a phenomenon known as regulatory capture. Critics argue that the FDA approved new OPPM too quickly, without adequate scrutiny of their safety and potential for abuse. (Mitchell, 2018) This may be due, in part, to the influence of the pharmaceutical industry on the FDA's decision-making process, such as through lobbying, funding of clinical trials, and the utilization of advisory committee members that were also paid by the same OPPM manufacturers applying for FDA approval. (Haffajee, 2020) In the article by (Kolodny, 2020), the author explains that the experts used by the FDA to establish the safety of OPPMs were financially incentivized by the pharmaceutical companies that manufactured OPPMs. Further supporting the potential influence of OPPM manufacturers on the FDA is the Prescription Drug User Fee Act (PDUFA) of 1992, which was mentioned earlier in this paper. The PDUFA allows the FDA to collect fees from drug manufacturers to fund faster reviews of new drugs. (Berndt, Gottschalk, Philipson, & Strobeck, 2005) Critics argue that while the PDUFA is intended to bring life-saving drugs to the market more efficiently, it also enables pharmaceutical manufacturers to influence the FDA. The continued controversies related to the PDUFA are outlined in the article by (Jewett, 2022) titled "FDA's Drug Industry Fees Fuel Concerns Over Influence." The article by (Jewett, 2022) explains that the pharmaceutical industry, through PDUFA fees, finances about 75 percent of the FDA's drug division. (Jewett, 2022) Critics have raised concerns over the FDA's ability to remain impartial while a substantial portion of its budget relies on the same industry it is funded to regulate. The use of potentially biased data and the pharmaceutical industry's influence contribute to the continued concerns around the FDA's ability to impartially determine the safety and approval of medications, such as OPPMs. (US Senate Homeland Security & Governmental Affairs Committee, 2017) (Fleming, 2018)

The ethical consideration of regulatory capture also relates to the FDA's failure to monitor and regulate OPPMs after approval. Critics suggest that the FDA did not adequately monitor the marketing and prescribing practices of OPPM manufacturers and providers, even after the high rates of addiction associated with OPPMs were made clear. In addition, critics argue that the FDA did

not consider or act on the public health impact of OPPMs not being used as prescribed. (Abrams, 2018) (Soelberg, Brown, Du Vivier, Meyer, & Ramachandran, 2017) Even as new evidence emerged regarding the risks and addictive potential of OPPMs, the FDA did not take decisive action to curb the prescribing and distribution of these drugs, such as implementing stricter regulations or revoking approvals of certain OPPMs. These factors contribute to the consideration of ethical misconduct and how regulatory capture could be a factor in this context. Critics suggest that the slow response from the FDA serves as evidence that OPPM regulations prioritized the industry's interests over public health concerns. (Kolodny, 2020) Additionally, this evidence highlights a failure in the FDA's ethical oversight, which was established to prevent unethical practices such as regulatory capture and external influence.

Using the evidence presented by (Kolodny, 2020), (Mitchell, 2018), and (Jewett, 2022), the close relationship between Purdue Pharma, the manufacturer of OxyContin, and the FDA raises substantiated concerns about the regulatory capture present within the FDA and its influence over the approval and monitoring of OPPMs. Critics have raised concerns about the established culture within the FDA that supports and normalizes regulatory capture. (Haffajee, 2020) Additionally, it has been made clear that the practices of the OPPM manufacturers were unethical and, in some cases, criminal. Specifically, in 2007, Purdue Pharma and three executives pleaded guilty to criminal charges related to their misleading marketing of OxyContin and agreed to pay over $600 million in fines. (Whalen, 2018) In 2020, 20 years after the start of the OE, Purdue pleaded guilty to additional criminal charges and agreed to pay over $8 billion in penalties while agreeing to dissolve the company and form a new public benefit company focused on addiction treatment and overdose reversal. (Dyer, 2020) The consequences placed on Purdue have since expanded to many other OPPM manufacturers. Known as the "The Opioid Settlement," a series of legal agreements have recently been reached between various US states, local governments, and pharmaceutical companies involved in producing, distributing, and selling OPPMs. (Dyer, 2022) Critics have continued to question if the OPPM manufacturers have been found liable in the OE, could the organization responsible for the oversight of these companies also be liable? (DeShazo, Johnson, Eriator, & Rodenmeyer, 2018) While many OPPM manufacturers have been held accountable for their actions, these settlements further expand the concern for regulatory capture within the FDA and its role in the OE.

The next and most egregious ethical consideration relates to conflict of interest. Many have accused the FDA of having conflicts of interest in multiple areas related to OPPMs. In 2016, a Senate investigation found that the FDA had relied on experts with financial ties to the pharmaceutical industry to help establish the safety standards used to approve OPPMs. (Demasi, 2022) According to multiple sources, OPPM manufacturers allegedly paid these experts to promote the use and safety of OPPMs, and

their recommendations directly influenced the FDA's decisions. (Kolodny, 2020) Research has also found that many FDA officials involved in approving OPPMs also had unethical financial ties to pharmaceutical companies producing OPPMs and later went on to work for those same companies. (Kolodny, 2020) (US Senate Homeland Security & Governmental Affairs Committee, 2017) (Fleming, 2018) These conflicts of interest raise questions about the impartiality of the FDA's decision-making process and the agency's ability to ensure conflicts of interest do not impact the approval and regulation of OPPMs.

A specific example of conflict of interest relates to Dr. Curtis Wright, who led the FDA effort to approve OPPMs in 1995. While at the FDA, Dr. Wright strongly supported and recommended the approval of OxyContin for moderate to severe pain for non-cancer patients. (Mitchell, 2018) Just two years after the FDA approved OxyContin, Dr. Wright took a very high-paying consulting job with Purdue Pharma, the manufacturer of OxyContin. (Mitchell, 2018) While the FDA has conflict of interest policies and oversight for employees, this case suggests that the FDA's ethics infrastructure, at the time, lacked effective oversight of employees who later worked for the same manufacturers they were charged with regulating. The case of Dr. Wright is an example of a phenomenon known as the "revolving door," where individuals move between roles in government agencies and the industries they regulate. Further investigation has shown that the revolving door phenomenon within the FDA is more common than expected. In a study from 2016, researchers found that more than 25% of FDA employees later went on to work for the same pharmaceutical companies they once regulated. (Bien & Prasad, 2016) As concerns about the revolving door culture at the FDA persist, it is essential for the FDA to continually evaluate and strengthen its policies to address potential conflicts of interest and maintain public trust. While the FDA's OEI (Integrity, 2023) states that the organizational culture of the FDA is shaped by its mission to protect and promote public health, ensuring the safety, efficacy, and security of drugs and other products it regulates, the presented examples of regulatory capture, conflict of interest, and revolving door employees serve as evidence that the culture in the FDA is not always aligned.

Lastly, the real-life implications of the ethical failures by the FDA must be recognized. While the evidence of ethical misconduct by the FDA related to the OE is still debated, the implications associated with overprescribing OPPMs are clear. For example, in a book by Beth Macy titled "Dopesick" (Macy, 2018), which was also produced as a Hulu mini-series in 2021 (Witter), outlines the real-life impact the OPPM-driven OE has had on millions of Americans. In addition, research into the history and function of the FDA indicates that the FDA is the established authority responsible for preventing public health epidemics such as this from occurring. So while the FDA, unlike many of the OPPM manufacturers involved in the OE, may not be directly

criminally liable, the FDA failed to uphold its duties to the public, and concise ethical considerations must be made to ensure a public health crisis like the OE does not happen again.

Reflected Issues in Ethics Infrastructure: Having established details on the ethical misconduct by the FDA and its officials related to the OE, it is vital to identify failures in the FDA's ethical infrastructure that allowed these incidences. The FDA's OEI is responsible for maintaining ethical standards and promoting a culture of integrity within the organization. (Integrity, 2023) However, several issues have been raised concerning the OE and the effectiveness of the FDA's ethics infrastructure.

1. Conflicts of interest: Concerns have been raised about potential conflicts of interest within the FDA, such as financial and post-employment relationships between FDA officials and pharmaceutical companies, conflicts of interest involving expert advisory committees used in the FDA's approval process, and the source of data utilized by the FDA. These direct conflicts of interest have and could continue to create biases in the decision-making process within the FDA. Therefore, the FDA's OEI must ensure that such conflicts of interest are identified and managed effectively to maintain public trust in the organization. This could be accomplished by better regulating the conflicts of interest among the advisory committees used in the approval process, expanding regulations on the current and post-employment of FDA employees, and validating the source of the research used to prevent an over-reliance on pharmaceutical industry data.
2. OPPM approval and regulation: The FDA failed to fulfill its regulatory obligations in approving and regulating OPPMs. The FDA's lenient approval and lack of regulation allowed for the aggressive marketing and distribution of OPPMs, thus leading to widespread abuse and addiction. The FDA's OEI must make sound, timely, and ethically justified decisions when approving and regulating OPPMs. While it is understood that the FDA must balance its dual roles of protecting public health and fostering innovation in the pharmaceutical industry, proper ethical approval and regulation must be established at all phases. In addition, the FDA's OEI should ensure that the agency's decision-making processes carefully consider all competing interests and prioritize public health. Specifically, the FDA and its OEI should prevent a culture that supports regulatory capture.
3. Cooling-off period and Post-employment restrictions: As of 2020, federal law imposes a "cooling-off" period, usually one to two years, during which former senior government employees are restricted from working for, representing, or engaging in lobbying activities for companies that were part of their prior responsibilities. (Administration, 2020) These cooling-off periods and post-employment restrictions were not in place when OPPMs were first approved. Now that these policies have been established, the FDA's OEI should consider which levels of FDA employees must follow the existing post-employment regulations and how long the cooling-off period should be.

Addressing these ethical concerns and improving the FDA's ethics infrastructure is essential to restore public trust in the agency and more effectively combat the OE. This may involve more effective ethics training, increasing transparency, strengthening regulations, improving post-marketing surveillance, and managing conflicts of interest.

Organization's Response to the Misconduct Case: To demonstrate the actions taken by the FDA to address and mitigate the OE, the FDA has created a website (https://www.fda.gov/drugs/information-drug-class/timeline-selected-fda-activities-and-significant-events-addressing-substance-use-and-overdose) outlining the FDA's activities and significant events to address substance use and overdose prevention. (U. F. a. D. Administration, 2023) This website is meant to increase transparency and public trust in the FDA's ability to fulfill its responsibilities. The FDA also publishes a blog called FDA Voices, where Robert M. Califf, MD, Commissioner of the FDA, provides updates on the actions of the FDA, with some specifically focused on how the FDA continues to address the OE. (Califf, 2022) The FDA also published, on 4/13/2023, an FDA Drug Safety Communication specifically focused on "prescribing information for all opioid pain medicines to provide additional guidance for safe use." (F. a. D. Administration, 2023a) An additional example of the FDA's efforts to fulfill its promise to monitor OPPMs includes a recall notice issued on 4/28/2023 outlining a labeling error issued by Teva Pharmaceutical based on its Fentanyl Buccal Tablets CII. (U. S. F. a. D. Administration, 2023) The FDA's recall notice demonstrates its commitment to ensuring all OPPMs include the required labeling to ensure public safety. These combined communications from the FDA help to outline how the FDA is now responding to the OE. From an ethical perspective, the FDA's response to the OE can be outlined as follows:

1. Reassessing its approach to OPPM approval, monitoring, and labeling: The FDA has committed to more thoroughly evaluating the risks and benefits of new OPPMs before approval and to monitor the post-market use of OPPMs more closely. The FDA has also revised the labeling requirements for OPPMs to more clearly communicate the risks of addiction, abuse, and overdose. Lastly, the FDA implemented the REMS program to manage known or potential risks associated with OPPMs to ensure that the benefits of the OPPMs outweigh their risks. (Alford et al., 2016) The REMS also helps to ensure that prescribers and patients are well-informed about the risks and benefits of OPPMs, thereby promoting informed decision-making. (Sekeres, 2022) Additionally, to be more benevolent, the FDA supports new research into understanding and addressing the root causes of the OE. The FDA also continues to act against companies that use misleading marketing practices, contributing to overprescribing OPPMs. (Dyer, 2022) (U. F. a. D. Administration, 2023)
2. Expanding access to medications designed to treat and prevent substance use disorder (SUD) and overdose: The FDA has prioritized developing and approving OPPMs with abuse-deterrent properties to make them less attractive for misuse. This

includes new OPPM formulations that make it "more difficult to solubilize or crush, thus discouraging abuse through injection and inhalation" (Theodore J. Cicero, Ellis, & Surratt, 2012). The FDA has also streamlined the approval process for medications used to treat SUD and overdose, including buprenorphine and naloxone. (U. F. a. D. Administration, 2023) The FDA recently approved naloxone, the drug used to reverse an overdose, for over-the-counter distribution to make the drug more available. (Tanne, 2023)

3. Ensuring Health Justice: The FDA has taken significant steps to ensure OPPMs are distributed and used fairly, equitably, and safely. This involves working with other government agencies to improve access to addiction treatment and promote alternative pain management options. The FDA has also started to take broad steps to address disparities in opioid prescribing and treatment access, disproportionately impacting specific disparate populations still impacted by OE. (Furr-Holden, Milam, Wang, & Sadler, 2021) (U. F. a. D. Administration, 2023)

Application of Organization-level Ethical Theories: This course has highlighted that understanding the theoretical background of ethical misconduct is vital. The organizational ethics theories presented by (Bowman & West, 2021), specifically the Ethics Triad, can be applied to the FDA's handling of the OE. First to consider is the ethical theory of deontology, also called the pertinent rules or duty ethics theories. (Bowman & West, 2021) Deontology posits that actions should be guided by moral principles or duties, irrespective of the consequences, and follows an established set of rules or principles. (Bowman & West, 2021) In the context of the OE, the rules, duties, and moral principles of the FDA should have prioritized public health. If this were the case, the FDA would have ensured a more thorough and unbiased approval process, stricter and more responsive regulation and oversight of OPPM manufacturers, and more accurate guidance for healthcare providers on appropriate prescribing practices. The theory of deontology also raises the question of whether employees at the FDA believed their decision to approve OPPMs was moral. In this context, the ethical dilemma faced by the employees at the FDA involved in approving and regulating OPPMs may have weighed the benefits of treating chronic pain in the short term over the potential for addiction long term. Further investigation should be focused on what could have prevented FDA employees from acting on their moral principles or duties at the point of OPPM approval and throughout OPPM regulation, even when the evidence of the dangers of OPPMs grew.

Second is the ethical theory of utilitarianism, also called the results of action, consequentialism, or teleology theories. (Bowman & West, 2021) Utilitarianism is the ethical theory that explains that actions should be judged by their consequences, aiming to maximize overall happiness and minimize suffering (Alkadry, Blessett, & Patterson, 2015). Applying utilitarianism's theory to the OE's handling, the FDA should have weighed the benefits of OPPMs for pain relief against the potential harm caused

by increased tolerance, dependence, addiction, and overdose. The FDA could have implemented policies and practices that balanced the need for pain relief with the risk of abuse, such as encouraging the development of abuse-deterrent formulations, encouraging the use of alternative pain management methods, enforcing stricter labeling requirements, and monitoring prescribing practices more closely. Could a culture within the FDA that normalizes regulatory capture also impact the FDA's ability to maximize overall happiness and minimize suffering? If so, could the theory of ethical relativism be at play where the morality of the FDA employees must be considered in the context of the cultural norms within the FDA? (Eiser, 2021) Additionally, we understand that utilitarianism focuses on the greater good for the most amount of people. Some could argue that, in the short term, OPPMs positively impacted many patients with chronic pain. The OE then proved that, in the long term, OPPMs, had a more significant negative impact on those with addiction. Did the FDA only weigh the benefits of approving OPPMs in the short term and not the long term? Further investigation should be focused on how, when the evidence of the dangers of OPPMs became apparent, the FDA and its officials did not see the dangers of OPPMs outweighing the benefits.

Third is the ethical theory of virtue ethics, also called personal rectitude, integrity, or character theory. (Bowman & West, 2021) Virtue ethics is the theory that explains the importance of personal character and virtues in ethical decision-making. (Bowman & West, 2021) In the case of the OE, the FDA did not utilize an ethical decision-making process to approve and regulate OPPMs. In an ethical decision-making process, the FDA would have ensured that the evidence was sound and that the advisory committees were free of conflicting interests. What could the FDA have done to foster a better culture of responsibility, empathy, and integrity among its employees, enabling them to make ethical decisions that prioritize the public's well-being over the interest of the OPPM manufacturers? By adhering to principles of the Ethics Triad, including deontological ethics, utilitarianism, ethical relativism, and virtue ethics, the FDA could have mitigated the severity of the crisis and better served the public interest.

Recommendations: As previously mentioned, the FDA continuously evaluates and monitors the effectiveness of its policies and structures. This paper clarifies that while the FDA has taken significant steps to address its failures in handling the OE, further improvements must be considered. As outlined by (Bowman & West, 2021) and (Cooper, 2012), for organizations to ensure sound ethical conduct, there must be a thorough understanding and application of the theoretical ethics framework. The previous section of this paper outlined specific areas, based on the Ethics Triad (Bowman & West, 2021), where the FDA failed to uphold its ethical duties. For this reason, the recommendations outlined in this section will be organized using the Ethics Triad (Bowman & West, 2021) as the framework to prioritize the presented recommendations. The FDA can use these recommendations to ensure better public health and safety specific to its oversight of OPPMs and similar medications. (Gostin, Hodge, & Noe, 2017).

First, the application of deontology, referred to as the pertinent rules or duty ethics theories (Bowman & West, 2021), focuses on following predefined moral rules and principles. (Songklin, 2016) (Bowman & West, 2021) The FDA can improve its ethics infrastructure to better address ethical failures in the handling of the OE by implementing the following steps based on rules-based ethics:

1. Establish a more comprehensive code of ethics and conflict of interest policies: While the FDA has an established code of ethics, the environment in which the FDA operates is constantly evolving. To best address this, the FDA should ensure that its code of ethics continues to cover every aspect of the FDA's responsibilities, including drug approval, monitoring, and regulation. In addition, this code and process should be transparent and accessible to all stakeholders, including the public. Finally, the FDA should continuously access its established conflict of interest policies and regulations. This will help mitigate conflicts of interest that could compromise the integrity of the FDA's decision-making process.
2. Enhance transparency and public engagement: The FDA is essential to public trust. As such, the FDA must ensure that decision-making processes are transparent and involve input from various stakeholders, including healthcare professionals, patients, and the public. This will help to establish and renew trust and accountability in the FDA's actions following its failures related to the OE.
3. Prioritize patient safety and public health: The organizational audit conducted for this paper revealed multiple scenarios where the FDA could be influenced by the industry it regulates. The FDA must emphasize the importance of patient safety and public health in the decision-making process. This can be done by creating and adhering to strict rules and guidelines and prioritizing these concerns over other external interests. This could include revising the PDUFA and other associated regulations that could create external influence over the FDA. The recent process to rapidly develop, approve, and distribute COVID-19 vaccines can provide additional evidence of how these regulations can be improved. (Boyle, Nowak, Kinder, Iachan, & Dayton, 2023)
4. Encourage enhanced whistleblower protection: This paper raised whether or not the FDA employees involved in approving OPPMs felt their actions were moral and ethical. Ineffective whistleblower protections can be one reason these concerns were not brought forward or addressed. Therefore, the FDA must focus on what could have prevented FDA employees from acting on their moral principles or duties at the point of OPPM approval and throughout OPPM regulation, even when the evidence of the dangers of OPPMs grew. To address this, the FDA must establish and reinforce rules that protect whistleblowers who report unethical conduct or practices within the FDA or pharmaceutical companies. This will help ensure that ethical concerns are brought to light and addressed promptly.

5. Enhance traditional ethics training and review: Similar to how the environment in which the FDA operates is constantly evolving and thereby requires continuous evaluation of policies and procedures, and the FDA must also conduct regular ethics training for its employees to ensure they are up-to-date on ethical guidelines and principles. This should include periodic assessments to evaluate employees' understanding and adherence to ethical rules. Improved ethics training also positively impacts utilitarianism and virtue-based ethics, discussed later in this paper.
6. Establish an independent ethics oversight committee: The FDA should consider establishing an independent committee responsible for overseeing the FDA's ethical practices and decision-making processes. This committee should fall under the authority of an external agency, such as the USOFE, and have the authority to investigate and address potential ethical violations. This external oversight can effectively address regulatory capture and external influence issues.
7. Foster a culture of ethics: This paper presents evidence that the FDA has an established culture that allows for regulatory capture, external influence, and post-employment incentives. To address this, the FDA must cultivate a culture that values ethical behavior and decision-making within the organization. This can be achieved by promoting open dialogue, recognizing ethical conduct, promoting and enforcing established policies and procedures, and holding individuals accountable for their actions.

Second, the application of utilitarianism also referred to as the results of action, consequentialism, or teleology theories (Bowman & West, 2021), focuses on the outcomes of actions to determine their ethical value. (Songklin, 2016) The FDA can improve its ethics infrastructure to better address ethical failures in the handling of the OE by implementing the following steps based on results-based ethics:

1. Develop a more precise and ethical framework: The current framework used by the FDA relies heavily on external influences, including financial support through the PDUFA and pharmaceutical industry experts. To ensure that decisions are made with the best possible outcomes, the FDA should create an ethical framework that emphasizes public health, patient well-being, and long-term consequences but does not rely so heavily on external factors. This framework should enable full autonomy based on unbiased research to guide all drug approval, regulation, and enforcement decisions. This may require new funding models to support the FDA.
2. Improve communication and collaboration: It is well understood that public health requires comprehensive communication and collaboration. This often includes multiple government agencies that serve particular functions. The FDA and all related government agencies must ensure that the roles of each agency are fully aligned and assigned most appropriately and ethically.

This requires the FDA to ensure its regulatory authority and procedures are ethically aligned internally and externally. In addition, the FDA must encourage open communication and collaboration between agencies and stakeholders, including pharmaceutical companies, healthcare providers, government agencies, and patients. This will help ensure that all parties are working toward the common goal of reducing the negative impacts of the OE most ethically. Improved communication and collaboration also positively impact virtue-based ethics discussed later in this paper.

3. Prioritize long-term public health outcomes: The FDA's handling of the approval and regulation of OPPMs highlights the urgent need to consider the long-term impacts verse the short-term benefits of certain drugs such as OPPMs. In evaluating the benefits and risks of pharmaceutical products, the FDA should ensure a complete understanding of the various uses and abuses of certain medications, not just the strictly prescribed utilization. This will best prioritize long-term public health outcomes over short-term financial gains or other considerations. In the context of the OE, this includes preventing addiction, reducing overdose deaths, and promoting responsible prescribing practices.
4. Enhance the development of alternative pain management options: Research is now clear that in most scenarios, non-opioid treatments are more effective in treating chronic pain. (Duncan, Smith, Maguire, & Stader III, 2019) To further reduce reliance on OPPMs and ensure the most effective and safe treatments for pain are widely available, the FDA should further promote the development of alternative pain management options, such as non-addictive medications and integrative medicine approaches. This includes expanding the FDA’s direct support of new research and incentivizing pharmaceutical companies to invest in research and development, similar to the SUPPORT Act of 2018. (Act, 2018)

Third, the application of virtue ethics, also called the personal rectitude, integrity, or character theory (Bowman & West, 2021), focuses on the moral character of individuals and organizations rather than specific actions or consequences. (Songklin, 2016) Applying virtue-based ethics to the FDA's handling of the OE can help improve its ethics infrastructure by promoting a culture that emphasizes moral virtues like integrity, transparency, and compassion by implementing the following steps based on virtue-based ethics:

1. Cultivating integrity: The examples of regulatory capture and conflicts of interest impact the integrity of the FDA's process and procedures. To best address this, the FDA should continuously prioritize acting with integrity in all its decision-making processes, ensuring its actions align with its core mission to protect public health. This includes increasing the OEI's scope and prominence to avoid conflicts of interest, promote unbiased scientific assessments, and diligently evaluate the safety and efficacy of all drugs and medical products.

2. Encouraging compassion: It is clear that the FDA was highly motivated to address chronic pain for non-cancer patients through its quick approval of OPPMs. While this could be seen as a compassionate response, the FDA must always take a compassionate approach that balances treating chronic pain while considering the suffering of individuals and families affected by addiction. A critical ethical principle that guides medicine and public health is included in the Greek Hippocratic oath, which states, "First, do no harm or injustice." (Miles, 2005) The FDA must always ensure it follows this ethical principle. Specific to the FDA's handling of the OE, this could involve better prioritizing developing and approving alternative pain management options, supporting evidence-based addiction treatment, and advocating for policies that reduce the stigma surrounding SUD.
3. Emphasizing humility: By their own admission, the FDA made fatal mistakes in handling the OE. Therefore, the FDA must continue recognizing and learning from its past ethical failures. By fostering a culture of humility, the FDA can encourage employees to admit mistakes, learn from them, and continually strive to improve their decision-making processes. This includes enhancing whistleblower protections and establishing mechanisms for employees to self-disclose errors without consequence. One framework used to accomplish this is the High-reliability Organizations Model (Desai, Madsen, & Roberts, 2012), which encourages a culture of humility and safety.
4. Establishing accountability: While the FDA has taken steps to hold itself accountable for its actions related to the OE, the FDA must continue to demonstrate its commitment to ethical conduct by transparently holding itself accountable. The FDA should also establish more transparent and precise mechanisms for holding individuals and the organization accountable for their actions. (Cooper, 2012) The increased accountability would foster greater public trust in the FDA overall.

Current Ethical Dilemmas Faced by Healthcare Providers: While the FDA continues to mitigate the OE's impact on the nation, new and emerging ethical dilemmas have become more prevalent. In response to the overprescribing of OPPMs, new restrictions, and regulations have been instituted to prevent the overuse and abuse of OPPMs. As a result, many patients with chronic pain, who have been treating their chronic pain with OPPMs for many years, are often inadequately or under-served. Healthcare providers are now faced with the complex challenge of balancing the compassionate care of patients with the need to prevent opioid misuse and addiction. (Cheraghi, Valizadeh, Zamanzadeh, Hassankhani, & Jafarzadeh, 2023) In addition to the internal improvements the FDA must make to ensure a more ethical approach to drug approval and regulation, it must also provide clear guidance and support to healthcare providers to maintain the standard of care for patients with chronic and acute pain. Evidence shows that many chronic pain patients who can no longer obtain maintenance doses of OPPMs often turn to illicit

sources, thus significantly increasing their chances of overdose. The following dilemmas are particularly significant and must be addressed by the FDA moving forward.

1. Beneficence, Non-maleficence, and Justice: Healthcare providers must provide effective pain relief (beneficence) while avoiding harm (non-maleficence). (Patel & Wright, 2019) In the context of the current OE, healthcare providers must carefully consider the risks and benefits of prescribing OPPMs within many new restrictive regulations, including the potential for addiction, overdose, and other side effects. An essential ethical principle is ensuring equitable access (justice) to pain relief. Over-regulation of OPPMs may disproportionately affect patients with chronic pain who legitimately require these medications, leading to undertreatment and reduced quality of life. (Morley, Chumbley, & Briggs, 2020) Healthcare providers must consider the potential consequences of restrictive prescribing practices, including the possibility that patients might seek illicit sources of OPPMs. The FDA and other government agencies must ensure that new policies and regulations provide the tools to treat patients with chronic and acute pain currently utilizing OPPMs.
2. Stigmatization and Education: Patients with chronic pain may experience stigmatization due to the association between the use of OPPMs and addiction. Healthcare providers must be careful not to reinforce stereotypes or contribute to the marginalization of these patients. Healthcare providers are also responsible for staying informed about best practices for managing chronic pain. This includes understanding non-opioid and non-pharmacological treatment options and recognizing and addressing signs of addiction. (Craig et al., 2020) The FDA and other government agencies must ensure that healthcare providers are provided with the tools and education required to eliminate stigma and provide safe standards of patient-centered care.
3. Societal responsibility, Structural Racism, and Implicit Bias: Healthcare providers, including the FDA, must contribute to the public good. This responsibility can be impacted by structural racism, disparities in access to care, and implicit bias. Research has shown that Black and Hispanic individuals often have less access to quality healthcare due to lower socioeconomic status, inadequate health insurance, or living in medically underserved areas. (Kennel, Withers, Parsons, & Woo, 2019) Racial disparities also exist in prescribing OPPMs, with research indicating that Black and Hispanic patients are often under-prescribed OPPMs compared to their White counterparts. (Kennel et al., 2019) This can lead to inadequate pain management and may contribute to long-term health consequences. Research has shown that unconscious or implicit bias is a cause of these disparities in care. Healthcare providers may have implicit biases affecting their perception of a patient's pain and subsequent prescribing decisions. (Craig et al., 2020) Research has shown that some healthcare providers may underestimate the pain levels of Black and Hispanic patients, leading to the under-prescribing of OPPMs. (Craig et al., 2020) Some healthcare

providers may hold false beliefs about the pain tolerance of different racial and ethnic groups or may be influenced by stereotypes about drug-seeking behavior, resulting in underprescribing OPPMs for Black and Hispanic patients. (Lee et al., 2019) Healthcare providers, including the FDA, must ensure that all policies and regulations are designed to eliminate and address these disparities and stigmas to provide socially responsible, equitable, effective care.

Conclusion: This paper has provided evidence that the FDA failed to uphold its ethical duties before and during the OE. Specifically, the presented evidence supports the claim that the FDA failed to prioritize public health and safety, as demonstrated by its approval of OPPMs without sufficient evidence and oversight, negligence in addressing the addictive nature and potential misuse of OPPMs, and susceptibility to industry influence, ultimately initiating and exacerbating the OE and its devastating consequences on individuals, families, and communities. While much has already been done to mitigate the broad impacts of the OE, public health continues to face challenges related to widespread addiction and the disparate impact that the subsequent over-regulation of OPPMs might cause. (Fallon et al., 2021) The current context of the OE relies significantly on the FDA's ability to function ethically and effectively. The recommendations included in this paper ensure that the FDA is best positioned to act in the best interests of public health more effectively, efficiently, and ethically in the future. As the OE continues to evolve, the FDA must balance the competing ethical principles presented in this paper to ensure patients have access to safe, effective, and equitable pain management options while minimizing the risks associated with addiction.

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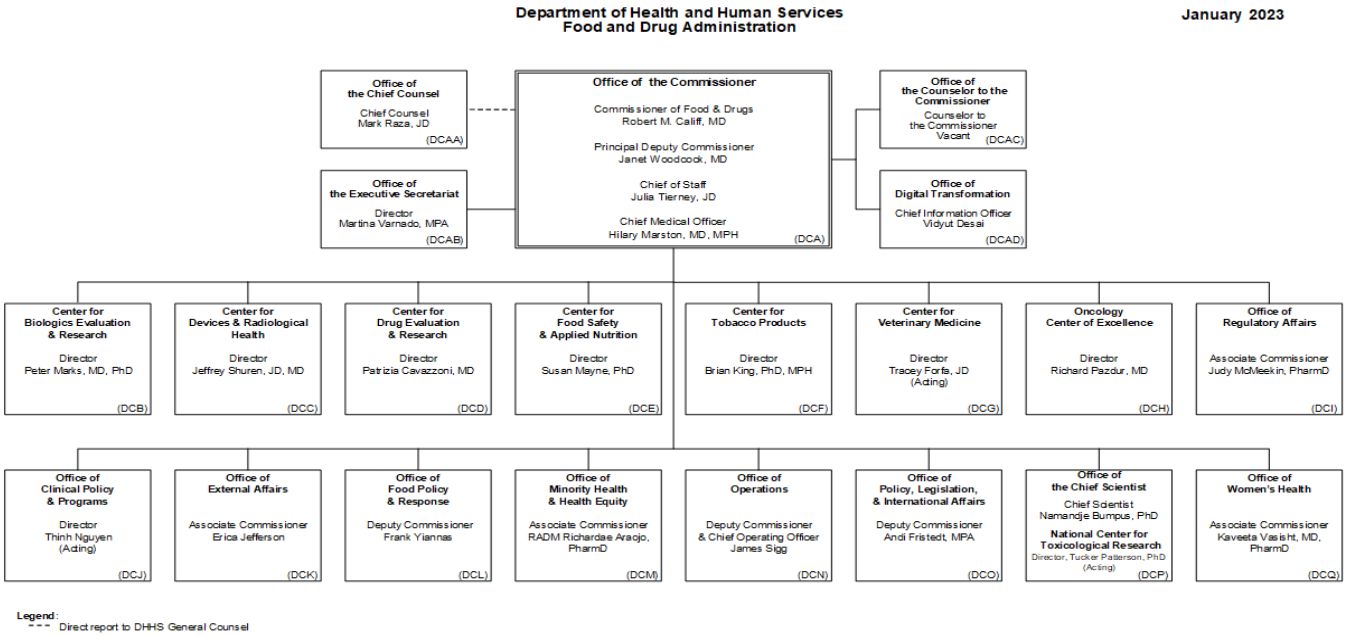
Appendix A:

Full FDA Organizational Chart



FDA Office of Ethics and Integrity Organizational Chart