

Report to Congress

**REPORT ON EVIDENCE-BASED OPIOID ANALGESIC PRESCRIBING
GUIDELINES**

**Submitted Pursuant to Section 3002 of the Substance Use-Disorder Prevention
that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and
Communities Act of 2018**

U.S. Food and Drug Administration

A handwritten signature in black ink, appearing to read "S. Hahn". The signature is fluid and cursive, with the first letters of the first and last names being capitalized and prominent.

March 30, 2020

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Commissioner of Food and Drugs

Executive Summary

On October 24, 2018, the President signed into law the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act. The bipartisan legislation granted federal agencies additional authorities that will meaningfully advance efforts to combat the opioid crisis. Section 3002 requires the Commissioner of Food and Drugs to develop evidence-based opioid analgesic prescribing guidelines for indication-specific treatment of acute pain where such guidelines do not exist, and to submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate a report on how the U.S. Food and Drug Administration (FDA) will use those guidelines to protect the public health and a description of the public health need with respect to each such indication-specific treatment guideline.

Advancing the availability of evidence-based, indication-specific prescribing information has always been part of FDA's approach to ensuring the safe use of the products it regulates, including the safe use of opioid analgesic products. As part of its response to the U.S. opioid crisis, FDA is re-examining how opioid analgesics should be prescribed during an appropriate course of treatment for acute pain. It is critical that health care providers have the most current and comprehensive guidance on the appropriate management of acute pain.

Consistent with the requirements of section 3002 of the SUPPORT Act, FDA (or Agency) has launched an effort to develop a framework for evidence-based guidelines involving a contract with the National Academies of Science, Engineering, and Medicine (NASEM). By early 2020, NASEM will provide a consensus report that identifies the surgical procedures/medical conditions requiring research for the development of evidence-based guidelines to treat acute pain. Once this information becomes available, FDA will be able to describe the public health need with respect to each targeted indication-specific treatment guideline. In the meantime, as part of the multi-year, multi-phase project to implement section 3002, FDA is collaborating with stakeholders to collect available data and further facilitate the development of evidence-based guidelines. FDA also intends to seek stakeholder input into how the Agency can best use the guidelines to protect public health.

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Report on Evidence-Based Opioid Analgesic Prescribing Guidelines

I. Introduction

On October 24, 2018, the President signed into law the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act. Under section 3002, the Commissioner of Food and Drugs is required to develop evidence-based opioid analgesic prescribing guidelines for indication-specific treatment of acute pain for the relevant therapeutic areas where such guidelines do not exist. Furthermore, not later than one year after the date of enactment of the SUPPORT Act, the Commissioner of Food and Drugs is required to submit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate, and post on the public website of the Food and Drug Administration, a report on:

- (a) how the Food and Drug Administration will utilize the guidelines developed under section 3002(a) of the SUPPORT Act to protect the public health; and
- (b) a description of the public health need with respect to each such indication-specific treatment guideline.

In response to this directive, the U.S. Food and Drug Administration (FDA) prepared the following report.

II. Background

FDA is working to confront the staggering human toll of the opioid crisis. Ensuring the availability of evidence-based, indication-specific prescribing information has always been part of FDA's approach to ensuring the safe use of the products it regulates, including opioid analgesic products. However, the nation is facing a crisis: millions of Americans are misusing opioids,¹ and more than 40 people are dying every day from overdoses involving prescription opioids.² FDA is reassessing its approach to opioid products with the goal of reducing the opportunities for opioid misuse and abuse while ensuring that its actions are properly targeted, evidence-based, and serve the medical needs of patients.

Recognizing the critical role that health care providers play in addressing this public health priority, FDA is re-examining how opioid analgesics should be prescribed during an appropriate course of treatment for acute pain. Acute pain usually occurs suddenly and has a known cause like an injury, surgery, or infection. Examples of acute pain could be pain that occurs following a tooth extraction, broken arm, or

¹ Substance Abuse and Mental Health Services Administration. (2019). *Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health* (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHNationalFindingsReport2018/NSDUHNationalFindingsReport2018.pdf>. Accessed February 2020.

² Centers for Disease Control and Prevention. Overdose Deaths Involving Prescription Opioids. <https://www.cdc.gov/drugoverdose/data/prescribing/overdose-death-maps.html>. Accessed August 2019.

surgical procedure.³ By decreasing unnecessary and/or inappropriate exposure to opioid analgesics through prescribing practices for acute pain, health care providers may reduce the rate of new opioid use disorders (OUDs) as well as opioid-involved overdose, accidental poisoning, and death. To do this, health care providers need the most current and comprehensive guidance on the appropriate management of acute pain.

Some people who develop an OUD are first exposed to opioid analgesics through a lawful prescription from a health care provider. While the number of opioid prescriptions and opioid morphine milligram equivalents have been on a steady decline for the last few years, concerns remain about opioid analgesic prescriptions for larger quantities than appropriate for the medical need being addressed. Patients commonly report having unused opioid tablets, pills, or capsules following surgical procedures.⁴ Unused pills may be diverted to illicit markets or misused by friends or family members — 51% of people who report misuse of prescription pain relievers obtained the most recently misused drugs from a friend or relative.⁵ In addition, patients who are prescribed more medication than necessary themselves have increased opportunities for misuse— 37% of people who report misuse of prescription pain relievers obtained their most recently misused drugs through their own prescription.⁶ Progress has been made; drug overdose deaths in America declined by about five percent in 2018, the first decrease since 1990. This decline was almost entirely associated with a dip in deaths from prescription opioids. Fatal overdoses involving other drugs, especially fentanyl and methamphetamine, continued to rise.⁷

Consistent with the requirements of the SUPPORT Act, the Agency is supporting the development of a framework for evidence-based guidelines through a contract with the National Academies of Science, Engineering, and Medicine (NASEM) and working closely with stakeholders. The resulting framework will be used to help create evidence-based guidelines on appropriate opioid analgesic prescribing to treat acute pain resulting from specific medical conditions and common surgical procedures for which these drugs are prescribed. The guidelines are intended to inform clinical decisions by health care providers and patients.

III. Advancing Appropriate Prescribing of Opioid Analgesics for Acute Pain

Implementation of section 3002 of the SUPPORT Act is a multi-phase, multi-year project. The extent of its implementation depends on funding available in future years (see the section in this report on *Implementation Considerations*). A critical component outlined in each phase of the implementation plan

³ Centers for Disease Control and Prevention. Opioids for Acute Pain: What You Need to Know. Available at <https://www.cdc.gov/drugoverdose/pdf/patients/Opioids-for-Acute-Pain-a.pdf>. Accessed December 2019.

⁴ Bicket, M.C., et al., Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review. *JAMA Surg*, 2017. 152(11): p. 1066-1071.

⁵ Substance Abuse and Mental Health Services Administration. (2019). *Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health* (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHNationalFindingsReport2018/NSDUHNationalFindingsReport2018.pdf>. Accessed February 2020.

⁶ Ibid.

⁷ National Center for Health Statistics: Provisional Drug Overdose Death Counts. Available at <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>. Accessed December 2019.

is stakeholder engagement. FDA will seek input from a variety of stakeholders to facilitate the development, adoption, and assessment of evidence-based guidelines for acute pain where such guidelines do not exist.

Section A provides an overview of the implementation plan for section 3002. Section B describes Phase 1 in greater detail.

A. Section 3002 Implementation Plan

Implementation of section 3002 is divided into four phases.

Phase 1—NASEM contract and FDA projects to complement NASEM’s work. Key components include (and are described in greater detail below):

- The NASEM contract supports development of a framework for evidence-based guidelines and provides a list of indications for which prescribers would benefit from evidence-based guidelines.
- FDA undertakes research that complements NASEM’s work and develops a project plan for Phase 2, the development of evidence-based guidelines.
- Engagement with stakeholders (e.g., professional societies, government agencies, academic institutions, payers, etc.) contributes further to plans to develop the guidelines. See especially Phase 2.

Phase 2—Guideline development. FDA works with professional societies and other stakeholders to facilitate development of indication-specific, evidence-based guidelines. A strategic plan, or agenda, will be developed to facilitate expeditiously completing this phase and subsequent phases.

Phase 3—Adoption of guidelines. FDA works collaboratively with relevant professional societies and other stakeholders to ensure publication and adoption of these guidelines.

Phase 4—Assessment of guidelines. After adoption of indication-specific, evidence-based guidelines, FDA will determine how best to assess the effectiveness of the guidelines. Questions for consideration include the following.

- The extent of uptake and approaches for applying the guidelines by prescriber specialty, indication, and patient populations
- Whether prescribing patterns have moved closer to evidence-based guideline recommendations over time
- Whether the amount of medication has been appropriately prescribed so as to reduce or eliminate the excess medication, thereby decreasing the potential for accidental poisonings, misuse, and diversion
- Whether patients perceive adequate control over their acute pain when prescribers appropriately apply the guidelines; identification of any unintended consequences for patients with respect to limiting opioid analgesic quantities (e.g., barriers to getting additional medication if needed)
- The extent to which prescribers have knowledge of, attitudes about, and behaviors relating to guidelines; the extent guidelines may have been misapplied; identification of any barriers to implementation (e.g., lack of flexibility in adapting guidelines to treat individual patients)
- Whether the guidelines should be adjusted based on new evidence/analyses

B. NASEM Contract

In August 2018, FDA awarded a contract to NASEM to help advance the development of evidence-based guidelines for appropriate opioid analgesic prescribing for acute pain resulting from specific conditions or procedures where such guidelines do not exist.⁸ The primary scope of this work is (1) to gain an understanding of what evidence is needed to ensure that all current and future clinical practice guidelines for treating acute pain with opioid analgesics are evidenced-based to inform prescribing and (2) to determine what research is needed to generate that evidence in a practical and feasible manner.

NASEM is developing a framework that could be used to support the development of clinical practice guidelines or the evaluation of existing clinical practice guidelines for opioid analgesic prescribing. This framework will articulate a threshold level of evidence that should be available to support the development of and ensure consistency among guidelines.

As part of this work, NASEM is scanning the landscape of existing opioid analgesic prescribing guidelines, examining how they were developed, identifying any gaps in evidence for those guidelines, and outlining the research needed to generate the evidence to fill the gaps. Additionally, NASEM held a series of meetings and public workshops to engage a broad range of stakeholders, including the Centers for Disease Control and Prevention (CDC), which contributed expert knowledge on existing guidelines and on emerging evidence, or specific policy issues, related to the development and availability of opioid analgesic prescribing guidelines based on their specialties.

NASEM is developing a consensus report that includes a research agenda, not to exceed 10 clinical therapeutic areas (surgical procedures or medical conditions) for which either no prescribing guidelines for treating acute pain exist or for which evidence to support existing clinical practice guidelines for opioid analgesic prescribing is lacking. The report will also describe what evidence is needed.

As of July 2019, NASEM had established an ad hoc committee to (1) develop the framework for evaluating existing clinical practice guidelines for prescribing opioids for acute pain indications; (2) recommend indications for which new evidence-based guidelines should be developed; and (3) recommend a future research agenda to inform and enable professional societies to develop and disseminate evidence-based clinical practice guidelines for prescribing opioids to treat acute pain indications. In developing its evaluation framework, the committee is considering the standards established in the 2011 Institute of Medicine (IOM) report, *Clinical Practice Guidelines We Can Trust*.⁹

The NASEM committee has held three meetings:

- **November 13, 2018.** Public Session of the Committee on Evidence-based Clinical Practice Guidelines for Prescribing Opioids for Acute Pain.

The focus of this [public session](#) was for the committee to clarify the scope of the charge with the study sponsor (FDA) and initiate the process of gathering relevant information related to the study.

- **February 4, 2019.** Applying Clinical Practice Guidelines to Prescribing Opioids for Acute Pain: A Workshop

This [workshop](#) featured invited presentations and panel discussions on topics, including identifying and prioritizing surgical procedures and medical conditions associated with acute pain for which opioid analgesics are prescribed and considered clinically necessary (i.e., develop an initial list not to

⁸ See Activity Description of NASEM work, available at <http://nationalacademies.org/hmd/activities/mentalhealth/guidelinesforprescribingopioids.aspx>. Accessed August 2019.

⁹ See the IOM report, available at <https://www.ncbi.nlm.nih.gov/books/NBK209539/>. Accessed August 2019.

exceed 50 surgical procedures and medical conditions for consideration) where evidenced-based clinical practice guidelines would help inform prescribing practices and identifying what evidence is necessary or missing for each procedure or condition.

- **July 9, 2019.** Identifying Research Gaps in Clinical Practice Guidelines for Prescribing Opioids for Acute Pain: A Workshop

This [workshop](#) featured invited presentations and panel discussions on several topics, including identifying gaps and additional information required to bring the clinical guidelines for specific surgical or medical indications up to the standards indicated in the committee’s draft framework. The workshop also examined the use of various types of evidence for developing clinical practice guidelines.

FDA anticipates receiving the NASEM consensus report in early 2020.¹⁰ The report’s research agenda will help identify the surgical procedures/medical conditions that will require research for the development of evidence-based guidelines. Once this information becomes available, FDA will be able to describe the public health needs with respect to targeted indication-specific treatment guideline.

C. FDA Projects to Help Inform Development of Evidence-based Guidelines

While NASEM completes its work, FDA has been supporting projects to complement that work, including the following.

- University of Pennsylvania project

FDA is supporting an effort by the University of Pennsylvania to develop and implement an innovative and scalable approach to generating patient-centered opioid prescribing guidelines for specific procedures with acute pain. The project will build on previously successful efforts using patient telephone calls to implement an automated text-messaging platform that can collect data on patient-reported outcomes and opioid consumption. The data will be reported back to the health care providers and used to guide the creation of electronic health record defaults for further prescribing across specialties. The results will help inform health care providers and empower them to “right - size” opioid prescribing for specific procedures. The project will enroll patients in the orthopedic, neurosurgery, and other emergency medicine settings. Patients will be followed for 14 days following an opioid prescription for acute pain.

- FDA assessment of refills in primary care settings

FDA and external contractors assessed the relationship between the number-of-days supply of initial opioid analgesic prescriptions and additional refills in acute pain conditions treated in the primary care setting.¹¹ The study concluded that initial opioid analgesic prescriptions of ≤ 7 days’ duration appear sufficient for many patients seen in primary care settings with acute pain, consistent with recommendations from the 2016 Guideline from the Centers for Disease Control and Prevention targeting opioid analgesic prescribing in primary care settings. FDA investigators note that treatment strategies should account for varying patient- and condition-specific characteristics.

¹⁰ National Academies of Sciences, Engineering, and Medicine. Framing Opioid Prescribing Guidelines for Acute Pain: Developing the Evidence. Available at: <http://nationalacademies.org/hmd/Reports/2019/framing-opioid-prescribing-guidelines-for-acute-pain-developing-the-evidence>. Accessed February 2020.

¹¹ Mundkur M, Days' Supply of Initial Opioid Analgesic Prescriptions and Additional Fills for Acute Pain Conditions Treated in the Primary Care Setting - United States, 2014. MMWR Morb Mortal Wkly Rep. 2019 Feb 15;68(6):140-143. Available at <https://www.ncbi.nlm.nih.gov/pubmed/?term=mundkur+2019+primary+care>. Accessed June 2019.

- FDA assessment of refills after surgical procedures in Sentinel

FDA and external contractors assessed the relationship between the number-of-days supply of initial outpatient opioid analgesic prescriptions and additional refills after surgical procedures in the Sentinel distributed data system.¹² The study concluded that initial opioid analgesic prescription durations of 7 days or less may be sufficient for many opioid naive patients with post-surgical pain. For less invasive procedures, prescription durations of 1-3 days may also be sufficient, and many patients did not fill a prescription. FDA investigators note that treatment strategies should account for varying patient- and condition-specific characteristics.

- FDA/Yale-Mayo Clinic Centers of Excellence in Regulatory Science and Innovation Collaboration

FDA is collaborating with the Yale-Mayo Clinic Centers of Excellence in Regulatory Science and Innovation to gather real-world data on dose and duration of opioid analgesic use for various acute medical indications in diverse populations. The data obtained will be used to support evidence-based prescribing guidelines to help clinicians choose initial opioid analgesic amounts sufficient to treat pain while limiting unused supplies that can contribute to misuse, diversion, and accidental poisonings. Additionally, the data can help identify patient factors, such as demographics, social/cultural norms, co-morbid illness, and social determinants of health, that can help predict variations in opioid analgesic use and outcomes. The project aims to use an innovative smartphone application to provide patients with a platform to self-assess pain and to track opioid consumption. The project will enroll patients receiving care for new onset pain in the emergency department, primary care, or dental care offices. Patients will be followed for 180 days.

D. Stakeholder Engagement

FDA is engaging with stakeholders to seek input on the development of evidence-based guidelines. Early engagement and collaboration with stakeholders, such as professional societies, patients, health care systems, government agencies (e.g., CDC as directed by section 3002 of the SUPPORT Act) is critical to the success of the development, adoption, and assessment of evidence-based opioid prescribing guidelines.

Initial discussions with professional societies have focused on topics that will inform Phase 2, such as:

- Need for the development of indication-specific, evidence-based guidelines
- Availability of resources and tools for acute pain management (e.g., policy statements, guidelines, etc.)
- Availability of data related to opioid prescribing for a particular disease/condition/population
- Average length of time and cost to develop an evidence-based guideline

Leading into Phase 2, FDA envisions an Agency activity, such as a public workshop or call for comment from stakeholders through a notice published in the *Federal Register* on how FDA can best use the guidelines to protect the public health.

E. Implementation Considerations for Phases 2, 3, and 4

FDA will carefully consider how to accomplish program goals for Phase 2 (development of evidence-based guidelines), Phase 3 (guidelines adoption), and Phase 4 (assessment of effectiveness of guidelines).

¹² Estimating Optimal Quantities for Initial Opioid Analgesic Prescriptions for Acute Pain Conditions Presenting to Surgical Settings. Available at <https://www.sentinelinitiative.org/drugs/assessments/estimating-optimal-quantities-initial-opioid-analgesic-prescriptions-acute-pain>. Accessed March 2020.

In addition, there is uncertainty around if and how professional societies and health care systems will want to engage in the development and implementation of evidence-based guidelines following the NASEM framework, particularly in the absence of funding.

IV. Conclusion

The NASEM consensus report, expected in early 2020, will help identify the surgical procedures/medical conditions that will require research for the development of evidence-based guidelines to treat acute pain. In the meantime, FDA is collaborating with stakeholders to collect available data and further facilitate the development of evidence-based guidelines.

In summary, FDA's implementation of section 3002 of the SUPPORT Act will facilitate the development of evidence-based guidelines, helping to ensure patients receive appropriate medication to treat acute pain. Reducing unnecessary and/or inappropriate exposure to opioids — and the resulting opportunities for misuse— may translate into fewer people exposed to the risk of OUD. At the same time, FDA wants to ensure that patients with a clinical need for opioid analgesics under acute circumstances are able to appropriately manage their pain.