manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- **MAIL/HAND DELIVERY/COURIER (FOR WRITTEN/PAPER SUBMISSIONS):** Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2019–D–0914 for ''Review and Update of Device Establishment Inspection Processes and Standards.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240–402–7500.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for a single hard copy of the guidance entitled ''Review and Update of Device Establishment Inspection Processes and Standards'' to the Office of Strategic Planning and Operational Policy, Office of Regulatory Affairs, Food and Drug Administration, 12420 Parklawn Dr., Element Building, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your request. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Tiffany Kelley, Office of Regulatory Affairs, Division of Operational Policy, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993–0002, 301–348–1970, *Tiffany.Kelley@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

FDA is issuing this guidance document to comply with section 702(b) of FDARA (Pub. L. 115–52). Section 702(b) of FDARA directs FDA to issue guidance that specifies how FDA will implement the processes and standards, applicable to inspections of domestic and foreign device establishments, described in section 704(h)(1)(A) through (D) of the FD&C Act (21 U.S.C. 374(h)(1)(A) through (D)), as added by section 702(a) of FDARA. FDARA 702(b) also requires the guidance to provide for standardized methods of communication when communication is required under section 704(h)(1) of the FD&C Act, establish a standard timeframe for inspections, and identify practices for investigators and device establishments to facilitate the continuity of inspections of such establishments.

In the **Federal Register** of March 29, 2019 (84 FR 11983), FDA announced the availability of the draft guidance of the same title. FDA received several comments on the draft guidance and those comments were considered as the guidance was finalized. The guidance announced in this notice finalizes the draft guidance dated March 29, 2019.

FDA is issuing this guidance consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

This guidance refers to currently approved FDA collections of information. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). The collections of information in 21 CFR part 803 have been approved under OMB control number 0910–0437. The collections of information in 21 CFR part 820 have been approved under OMB control number 0910–0073.

III. Electronic Access

Persons interested in obtaining a copy of the guidance may do so by downloading an electronic copy from the internet at either *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/search-general-and-cross-cutting-topics-guidance-documents* or *https://www.regulations.gov.* Persons unable to download an electronic copy of ''Review and Update of Device Establishment Inspection Processes and Standards; Guidance for Industry'' may send an email request to *ORAPolicyStaffs@fda.hhs.gov* to receive an electronic copy of the document.

Dated: June 24, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2020–13972 Filed 6–26–20; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–N–1046]

Use of Codeine-Containing Analgesics in Children Under 12 Years of Age Subsequent to CYP2D6 Genetic Testing; Establishment of a Public Docket; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; establishment of a public docket; request for comments.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing the establishment of a docket to solicit public comment on

specific questions pertaining to the use of codeine for analgesia in children under 12 years of age, and the use of cytochrome P450 2D6 (CYP2D6) testing in children under 12 years of age prior to treatment with codeine-containing analgesics. These questions are posed in section II.

DATES: Submit either electronic or written comments by August 28, 2020.

ADDRESSES: You may submit comments as follows:

Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before August 28, 2020. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of August 28, 2020. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2020–N–1046 for ''Use of Codeine-Containing Analgesics in Children Under 12 Years of Age Subsequent to CYP2D6 Genetic Testing.'' Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: LCDR Jessica Voqui, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 3121, 301–796–2280.

SUPPLEMENTARY INFORMATION:

I. Background

Codeine-containing prescription analgesic products approved by FDA are currently contraindicated in children under 12 years of age.[1] The Agency is considering a request for regulatory action to amend this contraindication to provide for use in children under 12 years of age who are shown to be cytochrome P450 isoenzyme 2D6 (CYP2D6) normal metabolizers (also known as ''extensive metabolizers'') or CYP2D6 intermediate metabolizers based on pharmacogenetic testing that includes CYP2D6 copy number or gene duplication detection. As discussed in section I.C., below, concerns have been raised in a citizen petition that children under 12 years of age in acute pain may not be able to access appropriate opioid analgesic drugs, and FDA is interested in understanding the scope and impact of any potential access issues. To properly assess the appropriateness and potential impact of making this amendment to the contraindication, the Agency seeks input from the healthcare community and the public on the following issues: (1) Pain management in children under 12 years of age; (2) availability and clinical utility of CYP2D6 genotyping tests; and (3) e-prescribing availability as a potential mitigation approach for opioid analgesic access in urgent situations.

Analgesic products with codeine as an active ingredient are opioids that are generally indicated for the relief of mild to moderate pain where the use of an opioid analgesic is appropriate and for which alternative treatments are inadequate. Codeine-containing products indicated for analgesia are marketed either as single ingredient codeine (a Controlled Substances Act (CSA) Schedule II drug) or in combination with other non-narcotic active ingredients, such as acetaminophen (the combination being a CSA Schedule III drug); most of the use is with the combination products.

[1] See April 20, 2017, Drug Safety Communication at *https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-restricts-use-prescription-codeine-pain-and-cough-medicines-and.* Codeine remains available through the over-the-counter (OTC) Drug Monograph for Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products (21 CFR 341.14, 21 CFR 341.74, 21 CFR 341.90) in combination with other medications for cough and cold symptoms.

There are also codeine-containing products indicated for the relief of cough, that contain a combination of codeine with other active ingredients in prescription products for cough and symptoms associated with upper respiratory allergies or common cold; however, the pediatric cough/cold indications were removed from prescription codeine cough/cold products in January 2018.[2] Codeine is partially metabolized to morphine, its most potent analgesic metabolite, through the CYP2D6 pathway. CYP2D6 is a polymorphic enzyme, leading to a high degree of variability for metabolism of codeine because of underlying genetic differences in CYP2D6 activity. Because of this variability, depending on CYP2D6 activity, patients may be at risk for therapeutic failure (''poor metabolizers'') or at risk for opioid-related toxicity (''ultra-rapid metabolizers'').

A. Regulatory History: 2007–2013

Given the variability in the metabolism of codeine, the safety of codeine use in children has been a concern, particularly the risk of life-threatening or fatal respiratory depression. Over the past several years, FDA has updated the labeling for codeine-containing prescription products regarding the risk of respiratory depression. In 2007, prescription codeine product labeling was updated with information regarding polymorphic metabolism and the risk of respiratory depression, specifically in breastfed infants of mothers who used codeine. In August 2012, FDA issued a Drug Safety Communication (DSC) about reports of death and respiratory depression in pediatric patients, primarily with use of codeine following tonsillectomy and/or adenoidectomy. In February 2013, after completing a review of the available safety data for codeine in the FDA Adverse Event Reporting System (FAERS) and the medical literature, FDA required a Boxed Warning and Contraindication regarding the use of codeine-containing prescription analgesics following tonsillectomy and/or adenoidectomy, highlighting the risk to those children who are ultra-rapid metabolizers of codeine due to CYP2D6 polymorphism. These children may be particularly sensitive to the respiratory depressant effects of codeine because ultra-rapid metabolizers metabolize standard doses of codeine in the liver to high circulating levels of morphine (codeine's active metabolite). As part of the review of this issue, in addition to codeine, FDA evaluated the FDA Adverse Event Reporting System (FAERS) and the medical literature for cases of death or overdose in children related to the therapeutic use of immediate-release morphine, oxycodone, or hydrocodone. This search did not reveal clear cases of unexplainable or unconfounded death or opioid toxicity.

In June 2013, following a review of the relevant data, the European Medicines Agency (EMA) made the determination that ''codeine-containing products indicated in the management of pain should only be indicated in children above 12 years of age and contraindicated in paediatric patients below 18 years of age undergoing tonsillectomy and/or adenoidectomy for obstructive sleep apnoea syndrome as well as in women during breast-feeding and in patients known to be CYP2D6 ultra-rapid metabolisers'' (*https://www.ema.europa.eu/en/medicines/human/referrals/codeine-containing-medicines*).

B. Regulatory History: 2015–2017

In April 2015, the EMA completed a review of the use of codeine for cough and cold indications. The EMA contraindicated the use of codeine-containing products in children under 12 years of age for cough and cold and recommended that codeine-containing cough and cold products not be used in children and adolescents ages 12 to 18 years of age who have breathing problems (see ''Codeine-containing medicinal products for the treatment of cough or cold in paediatric patients: Codeine not to be used in children below 12 years for cough and cold,'' available at *https://www.ema.europa.eu/en/medicines/human/referrals/codeine-containing-medicinal-products-treatment-cough-cold-paediatric-patients*).

Subsequent to the release of the EMA recommendations about use of codeine-containing products in children for cough and cold indications, FDA initiated a safety review of available data regarding respiratory depression and death with codeine-containing product use for cough in children. In addition, FDA also re-evaluated available safety data regarding codeine use for analgesia in children. Because of the potential for shifting use to other opioids if the scope of the February 2013 contraindication for codeine use in children was expanded (*i.e.,* beyond pain management following tonsillectomy and/or adenoidectomy), FDA also evaluated the safety of other opioid-containing potential treatments, including hydrocodone-containing cough and cold products, and tramadol products.

The Office of Surveillance and Epidemiology (OSE) within FDA's Center for Drug Evaluation and Research (CDER) completed a Pediatric Postmarketing Epidemiological, Pharmacovigilance, and Drug Utilization Review on November 13, 2015. The review identified 64 cases in the FAERS database from 1965 to May 2015 of serious respiratory depression, including 24 deaths, in children 18 years of age and below receiving codeine-containing products. Most of the cases (50 out of 64), including fatal cases (21 out of 24), involved children under 12 years of age. Among the 48 cases that reported the reason for use, 34 reported pain management (17 were post-adenotonsillectomy), and 14 reported cough and cold management; 12 of 21 deaths in children under 12 years of age occurred when a codeine-containing product was used unrelated to pain post-adenotonsillectomy (cough and cold, n=7; general pain, n=2; other postoperative pain, n=2; sore/strep throat pain, n=1). Ten of 64 cases mentioned CYP2D6 genotype (7 were ultra-rapid metabolizers and 3 were normal metabolizers); the remaining 54 cases did not report CYP2D6 genotyping. Of the three cases that occurred in normal metabolizers, two involved 3-year-old twin brothers who received inadvertent overdoses of codeine for treatment of a cold (one resulted in death) and one involved a 3-year-old female who underwent tonsillectomy for obstructive sleep apnea. Other risk factors for codeine toxicity were noted in several cases such as obesity, obstructive sleep apnea, and overdose. OSE concluded that there is case report evidence of respiratory depression following codeine use for both pain and cough and cold treatment, particularly in pediatric patients under 12 years of age.

FDA held a joint meeting of the Pulmonary and Allergy Drugs and the Drug Safety and Risk Management Advisory Committees (PADAC/DSaRM AC) on December 10, 2015 (80 FR 65770, October 27, 2015; minutes available at *https://www.fda.gov/media/95855/download*), to discuss the safety of codeine in pediatric patients. The issue of whether to add a recommendation to the labeling for prescription codeine drug products to genotype children prior to prescribing codeine was not raised as a specific topic of discussion for the AC. However,

[2] See January 11, 2018, Drug Safety Communication at *https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-requires-labeling-changes-prescription-opioid-cough-and-cold.* But see fn. 1, supra.

FDA did explain why a recommendation for routine genotyping prior to receiving codeine was not added to product labeling at the time of the 2013 labeling change. First, normal metabolizers, in some cases, convert codeine to morphine at levels similar to ultra-rapid metabolizers. Second, the positive predictive value of the genotyping tests is low; thus, the number needed to be screened in order to prevent one adverse event is very high. Third, genotyping may be logistically difficult to implement because preoperative lab tests are not routinely obtained before adenotonsillectomy.

There was some discussion at the AC meeting about patient access issues. The patient representative, a mother of a child with sickle cell disease (SCD), expressed concerns focused on her daughter being able to get any opioid for use at home, rather than codeine/acetaminophen specifically. The overall theme of her comments was the difficulty with accessing opioid medications for control of SCD-related intermittent painful crises if a patient has to go to the emergency department for care and see physicians who are not familiar with the patient or the patient's family.

Another issue raised at the 2015 PADAC/DSaRM AC meeting was that the pediatric pain specialists on the committee contended that codeine/acetaminophen was not an appropriate drug for the treatment of painful sickle cell crises because the acetaminophen limits the dose of codeine that can be administered.

Two-thirds of the AC panel (20 out of 29) recommended that FDA contraindicate use of codeine-containing drug products for analgesia in children under 18, and the same number (20 out of 29) recommended that FDA contraindicate use of codeine-containing drug products for cough in children under 18.

Subsequent to internal discussions about the AC's recommendations, in April 2017, the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) and the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP), both within CDER's Office of New Drugs, issued a Safety Labeling Change (SLC) notification letter related to the risk of life-threatening respiratory depression in children associated with the use of codeine-containing products and the risk of life-threatening respiratory depression in breastfed infants whose mothers were treated with codeine-containing products. Although the AC panel recommended contraindicating codeine-containing drug products for children under 18, FDA chose to limit the contraindication to children under 12 years of age. The Agency also included in the SLC notification letter a requirement to add warning language regarding use of codeine-containing products in children ages 12 to 18 years of age who may have risk factors (*e.g.,* obstructive sleep apnea, obesity, respiratory conditions) making them more susceptible to life-threatening or fatal respiratory depression with codeine.

These labeling changes were based upon the following considerations:

- Available data suggest that younger children (under 12 years of age) may be at highest risk of life-threatening or fatal respiratory depression.
- In addition to the risk factor of CYP2D6 ultra-rapid metabolizer status, some case reports suggested that other risk factors/conditions (*e.g.,* obesity, obstructive sleep apnea, oropharyngeal swelling (post-tonsillectomy)) may make patients more susceptible to respiratory depression with codeine.
- There was some sentiment from the AC that prescribing of codeine-acetaminophen combination drug products, which are CSA Schedule III drugs, for pain in children resulted in opioids with lower abuse or diversion potential being in the household compared to Schedule II opioids being prescribed.
- Contraindication of codeine-containing drug products in children under 12 years of age would support continued availability of codeine-containing drug products for use in children ages 12 to 18 years of age who rely on codeine for pain management.
- A contraindication of codeine-containing drug products in children under 12 years of age is consistent with decisions made by other regulatory authorities, such as EMA and Health Canada (see *https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/33915a-eng.php*).

On August 29, 2017, the supplements submitted in response to the SLC notification letter were approved with updated labeling that included new language in the sections outlined above.

C. Citizen Petition Submission—December 2017

A citizen petition (Petition) dated December 14, 2017 (Docket no. FDA–2017–P–6918), was submitted to FDA by Kelly Caudle, MD, Director, Clinical Pharmacogenetics Implementation Consortium, St. Jude Children's Research Hospital, Memphis, TN, along with other clinical pharmacologists (Petitioners) from around the country. The Petitioners requested that, with the exception of the post-adenotonsillectomy setting, the contraindication of codeine-containing analgesics be amended to provide for use of these products in children under 12 years of age who are known to be CYP2D6 normal metabolizers or intermediate metabolizers based on adequate pharmacogenetic testing (*i.e.,* capable of measuring copy number or detect gene duplications). The Petitioners suggest that the current contraindication may cause children under 12 years of age with recurrent acute pain to have decreased access to opioid analgesics, which may result in more emergency department and urgent care visits. According to the Petition, such decreased access could occur because codeine/acetaminophen combination drug products are CSA Schedule III (able to be prescribed by telephone) whereas other opioid analgesics that would be suitable to treat a patient's pain are Schedule II and cannot be prescribed by telephone.

In FDA's view, if Petitioners' proposed labeling were adopted, a CYP2D6 genotype/phenotype determination would be essential for the safe and effective use of codeine drug products. Thus, under the Agency's authorities governing prescription drug labeling, the approved labeling of codeine-containing analgesics would also need to specify that, with respect to use in children under 12 years of age, the products are intended for use only subsequent to the necessary genotype/phenotype determination using an appropriate, FDA-authorized companion diagnostic device.[3]

FDA is aware of several available CYP2D6 genotype tests, each of which assess different alleles of CYP2D6 and which may not uniformly assess gene copy number. FDA is also aware that these tests have been shown to vary in performance with respect to identifying the range of genotype combinations. For example, most CYP2D6 tests, the wild type (referred to as ''*1'') is typically a default result, *i.e.,* no variant is detected and therefore the allele is assigned as the wild type (*1). FDA is concerned that, if a test does not have the ability to detect rare genotype variants, then patients who have these rare variants would be called wild type, and the wrong genotype result (potentially

[3] For more information about relevant law and policy regarding companion diagnostics and the corresponding therapeutic products, see FDA's guidance titled, *In Vitro Companion Diagnostic Devices* (available at *https://www.fda.gov/media/81309/download*).

normal metabolizer) could be given for those patients.

Based on prescription dispensing data obtained from a proprietary drug utilization database available to FDA, the Agency understands that the number of patients ages 0 to 11 who were dispensed codeine-containing analgesic products decreased from an estimated 735,000 patients in 2013 to 230,000 patients in 2017. Following the addition of the contraindication of codeine-containing drug products in children under 12 years of age to the codeine product labeling in August 2017, FDA has seen the prescription use of codeine decline further to 84,000 patients ages 0 to less than 12 years of age in 2018.[4]

II. Additional Issues for Consideration and Request for Information

FDA is soliciting information and comment from stakeholders regarding the issues described in this document. In addition to any other aspects of these issues that stakeholders may care to comment upon, FDA is interested in answers to the following questions in particular:

Topic 1: Pain Management in Children Under 12 Years of Age (for Prescribers and Other Stakeholders, as Appropriate)

1. What factors do you consider in choosing to prescribe an opioid analgesic for children under 12 years of age who require treatment for recurrent episodes of acute pain (*e.g.,* severity of pain, lack of response to other analgesics, or the specific disease, such as children with sickle cell disease-related pain crises)?

2. Which pediatric populations, other than children with sickle cell disease, typically use an opioid analgesic for recurrent episodes of acute pain?

3. What role, if any, do you see for codeine/acetaminophen combination drug products in the treatment of children under 12 years of age with recurrent episodes of acute pain?

4. What is your institution/department/clinical practice's recommended approach (or specific formulary options) for selecting an opioid analgesic for a child under 12 years of age? Was your institution/department/clinical practice's current approach modified following FDA's August 2017 codeine labeling revision that contraindicated codeine-containing drug products in children under 12 years of age? If there is not a recommended approach, what opioid analgesics are typically prescribed in your practice to patients under 12 years of age?

5. In your view/experience, is the contraindication for use of codeine/acetaminophen combination drug products in children under 12 years of age hampering optimal patient care?

6. What are the issues you have faced regarding urgent access to opioid analgesics (*e.g.,* after hours, on weekends, and holidays) for a child under 12 years of age with recurrent episodes of acute pain requiring an opioid analgesic?

a. For clinicians: If you have had to face these issues, how do they impact prescribing decisions? For example, would you consider giving a hard copy prescription for a small amount of opioid analgesic to be used in urgent or after-hours situations so the patient can avoid making a visit for urgent/emergency care?

b. For caregivers/patient advocates: How have you handled these issues?

Topic 2: CYP2D6 Genotyping Tests (for Prescribers and Technical Experts)

1. Would amending the contraindication to provide for CYP2D6 genotyping for children under 12 years of age prior to prescription of codeine-containing drug products change your clinical practice?

2. Have you utilized a CYP2D6 genotyping test when determining which opioid analgesic to select for a child under 12 years of age who has recurrent acute pain severe enough to warrant treatment with an opioid analgesic? Describe why or why not.

3. Describe your experience with interpreting CYP2D6 genotyping test results and using those results to make drug prescribing decisions.

4. For a CYP2D6 genotyping test to appropriately identify patients who can safely receive a codeine-containing drug product, what is the minimum genotyping accuracy and minimum acceptable coverage of the currently known genotypes that typically result in a poor metabolizer or ultra-rapid metabolizer phenotype?

5. Regarding detection of ultra-rapid metabolizers, what is the type of test output that would be needed for copy number? Is a result of ''duplication present'' (*i.e.,* more than one copy) sufficient, or is specific quantitation of the number of copies needed?

Topic 3: E-Prescribing Availability (for Prescribers)

1. Is e-prescribing available in your institution/department/clinical practice?

2. What is your practice regarding e-prescribing of Schedule II opioids? Are there any limitations in your institution/department/clinical practice for e-prescribing of Schedule II opioids?

3. Would you e-prescribe a Schedule II opioid based on a telephone discussion with a child's caregiver? Would you e-prescribe any opioid (including those in Schedule III and Schedule IV) based on a telephone discussion with a child's caregiver? Describe why or why not.

4. If you do not have e-prescribing available, how does that impact your ability to prescribe Schedule II opioids for children under 12 years of age, particularly with recurrent acute pain episodes?

Dated: June 24, 2020.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2020–13974 Filed 6–26–20; 8:45 am]

BILLING CODE 4164–01–P

[4] Source: IQVIA Total Patient Tracker™, 2013–2018. Data extracted May 2018 and June 2019.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Information Technology Advisory Committee 2020 Schedule—Revised; Meeting

AGENCY: Office of the National Coordinator for Health Information Technology (ONC), HHS.

ACTION: Notice of meeting.

SUMMARY: The Health Information Technology Advisory Committee (HITAC) was established in accordance with section 4003(e) of the 21st Century Cures Act and the Federal Advisory Committee Act. The HITAC, among other things, identifies priorities for standards adoption and makes recommendations to the National Coordinator for Health Information Technology (National Coordinator). The HITAC will hold public meetings throughout 2020. See list of public meetings below.

FOR FURTHER INFORMATION CONTACT: Lauren Richie, Designated Federal Officer, at *Lauren.Richie@hhs.gov,* (202) 205–7674.

SUPPLEMENTARY INFORMATION: Section 4003(e) of the 21st Century Cures Act (Pub. L. 114–255) establishes the Health Information Technology Advisory Committee (referred to as the ''HITAC''). The HITAC will be governed by the provisions of the Federal Advisory Committee Act (FACA) (Pub. L. 92–463), as amended, (5 U.S.C. App.), which sets forth standards for the formation and use of federal advisory committees.