Dear Ms. Davies:

On behalf of the 3,500 individual and 98 institutional members of the American Association for Dental Research (AADR), we applaud the efforts by the FDA to bring an end to the opioid epidemic that has touched every part of the United States. Specifically, we applaud the inclusion of dental health providers in this effort and in the recent National Academies of Medicine report “Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use” (hereon, “NAM report”), which included orofacial pain researcher Dr. Eli Eliav. AADR supports the implementation of the recommendations in the NAM report, especially those regarding investing in research to better understand pain and opioid use disorder (Recommendation 3-1); characterization of the opioid epidemic (Recommendation 4-3) and public health considerations to better inform the regulatory process (Recommendation 6-2).

The purpose of this response is to provide a perspective from dental, oral and craniofacial research on the use of opioids to treat orofacial pain. The dental research community is concerned with both acute dental pain and chronic orofacial pain. It is important for the Opioid Policy Steering Committee to appreciate that opioid prescribing in dentistry is almost exclusively for acute dental pain. The most common type of pain that a dentist will encounter is acute postoperative pain, e.g. following third molar, or “wisdom”, tooth extraction. Conversely, very few dentists treat chronic orofacial pain, but chronic orofacial pain is an active area of study in the dental, oral and craniofacial research community. Furthermore, the dental perspective is important in chronic orofacial pain because even standard dental treatment may exacerbate orofacial pain and occasionally lead to chronic orofacial pain, and chronic orofacial pain patients may undergo oral surgery that causes acute pain on top of chronic pain that will need to be managed. To summarize our recommendations, the FDA should focus its efforts on increasing the use of nonopioids as first-line treatment in pain management and proper use of opioids when necessary through proper regulation, monitoring and provider and patient training.
Regarding specific questions posed by the Opioid Policy Steering Committee:

**What more can or should FDA do to ensure that the full range of available information, including about possible public health effects, is considered when making opioid-related regulatory decisions?**

Opioid-related regulatory decisions should be as specific as possible. Most opioid prescriptions from dentists are for acute postoperative pain—primarily oral combinations of hydrocodone/acetaminophen (APAP) and oxycodone/APAP. A benefit-risk framework that applies to the use of opioids for chronic pain should not be applied to these cases. The current guideline from the American Dental Association is for first-line treatment using nonsteroidal anti-inflammatory drugs (NSAIDs), which have been shown to be just as effective as opioids in acute cases. FDA regulations should encourage providers to try NSAIDs first or indicate that they are contraindicated for the patient by including simple reminders or nudges in electronic prescribing systems. For patients who are unable to take nonopioids for a variety of reasons or whose acute pain is not well-controlled by nonopioids alone, efforts should focus on ensuring that prescriptions for acute postoperative pain are for the proper duration to reduce the amount of leftover medication that could be subject to diversion or misuse.

In the case of chronic orofacial pain, the FDA should consider and minimize the adverse public health effects of widespread opioid prescription use while making patient-centered regulatory decisions. Create sufficiently flexible regulations that allow the provider and the patient to make the best decision. Regulations should have proper exceptions for those who cannot take nonopioids or achieve a reasonable level of pain relief using nonopioids within the safe dosing range and therefore may require opioids. The FDA needs to consider the public health consequences of untreated or inadequately treated chronic pain in addition to the consequences of opioid overprescription. Regulations should not create a situation in which opioids are underprescribed for those who need them because of a misplaced fear of addiction.

**Should FDA consider adding a recommended duration of treatment for specific types of patient needs (e.g., for specific types of surgical procedures) to opioid analgesic product labeling? Or, should FDA work with prescriber groups that could, in turn, develop expert guidelines on proper prescribing by indication?**

The FDA should work with prescriber groups to develop professional guidelines and appropriate labeling for the duration of use.

**If opioid product labeling contained recommended duration of treatment for certain common types of patient needs, how should this information be used by FDA, other state and Federal health agencies, providers, and other intermediaries, such as health plans and pharmacy benefit managers,**
as the basis for making sure that opioid drug dispensing more appropriately and consistently aligns with the type of patient need for which a prescription is being written?

If the FDA adds the duration of treatment to opioid product labeling, the FDA should be clear that this is a recommendation and allow flexibility for the prescriber to meet individual patient needs.

**Are there steps FDA should take with respect to dispensing and packaging (e.g., unit of use) to facilitate consistency of and promote appropriate prescribing practice?**

For acute postoperative pain, pills should be dispensed for the likely time that pain will endure. However, proper flexibility should be built into the system because the practitioner does not know how much pain is likely to occur with any individual following a surgical procedure. The 2016 CDC recommendation (#6) regarding the use of opioids for acute pain that indicates that 2-3 day supply is usually sufficient and a need for more than 7 days is rare. It has been reported repeatedly that 7-10 hydrocodone/APAP pills are the median number used following impacted third molar extractions, although many patients may take none and other as many as twenty.

**Should FDA require some form of mandatory education for health care professionals who prescribe opioid drug products, and if so, how should such a system be implemented?**

Yes, FDA should require continuing education training on opioid use for the treatment of pain. This should be monitored by the Drug Enforcement Administration (DEA) by requiring prescribers to check a box during DEA registration indicating that such training has been completed. Training should be provider-specific. In other words, requirements should be tailored to dentists and not identical to training for physicians or other health care professionals. Training should be focused on acute pain and opioid-sparing alternatives. Training elements and goals should include:

1) Creating a habit of using nonopioids as a first-line of treatment for patients who can take NSAIDs and APAP.
   a) There should be a heavy focus on options to opioid prescribing, especially when there is good scientific evidence that nonopioids are just as or more efficacious than opioids, such as NSAIDs as first-line therapy for acute postoperative pain. However, prescribers should be acutely aware of contraindications and adverse effects of nonopioids. This is especially a concern for chronic pain sufferers who may have to use NSAIDs over a long period of time and may suffer renal or gastrointestinal toxicity, for patients with comorbidities such as heart failure or high blood pressure and for patients at risk of liver damage from use of APAP.
   7-10

2) Pain management in patients that are currently chemically-dependent or have a history of abuse.

3) Increase provider comfort with screening, knowledge of treatment resources and referral. Management of addiction is generally considered beyond the scope of practice for dentists.
4) Proper use and cessation of use of opioids, especially differentiation between symptoms of withdrawal from stopping a short prescription of opioids versus increased pain from the surgery and the possible need for tapering.11

5) How to properly counsel patients on the risks of opioid use and properly securing and disposing of opioids.

6) Understanding that both patient and provider demographic characteristics (race, age and sex) influence clinician’s assessments of a patient’s pain and their decisions regarding pain treatment, as well as the recommendations for the use of opiate and non-opiate analgesics.12, 13

To implement mandatory education for providers, the FDA should conduct outreach by sending representatives to professional society meetings to educate providers about new policies and regulatory considerations and to get feedback from providers.

**What other steps should FDA take to operationalize the above described goals?**

Although outside the FDA’s authority, prescription drug monitoring programs have been shown to be extremely effective in limiting prescribing and should be required and supported.14 A national database should be instituted rather than being limited as state programs. As suggested recently, this could be funded through surcharges to the pharmaceutical companies marketing scheduled drugs. Some but not all states require prescribers to check monitoring databases before prescription. This should be required by all states or by the national database if one is created.

FDA should work with other federal and state agencies and private stakeholders given the FDA’s limited mandate and authority. For example, the NAM report noted the frequency of prescribing opioids in emergency rooms for nontraumatic acute dental pain when these conditions could be treated simply with standard dental procedures, thereby avoiding opioid prescriptions. This is a larger problem about access to proper dental care both during and outside of normal dental office hours that FDA cannot address. However, FDA can bring such issues to the attention of other regulating and governing bodies. FDA should also work with entities that provide continuing education and set education and curriculum standards for students.

In addition to the recommendations for research outlined in the NAM report, we also encourage research on opioid abuse in special populations (youth, women, etc.) given recent studies suggesting that teenagers are at increased risk for opioid abuse.

**Are there additional policy steps FDA should consider relating to the OPSC that are not identified in this notice?**
Secure electronic prescribing could eliminate the rules regarding written prescriptions for Schedule II drugs. Currently there is a belief that written prescriptions are offered to patients as a matter of convenience if unexpected need arises. This may take time, but is an obvious answer to prescribing Schedule II opioids.

Disposal of hydrocodone/APAP (Vicodin®, Norco®, Lorcet®) by flushing should be added to the current list of approved opioid disposal procedures.

With the requirement to reduce APAP dose in combination formulations from 500 or 750 mg APAP to 350 mg instituted by FDA several years ago, clinical research that compares current APAP-opioid combination formulations with full dose NSAIDs should be encouraged and funded. There is little to support the use of these combinations when risks and benefits are evaluated. Interestingly, these studies (Vicodin® vs ibuprofen vs ibuprofen/APAP) are not available.15

In conclusion, regulators have the difficult task of reducing the availability of opioids to the public that can be used for nonmedical purposes while ensuring that opioids are available to those who require them for medical purposes. These tasks must be accomplished simultaneously.

Thank you for the opportunity to provide comments to the Opioid Steering Policy Committee on this important issue. AADR members stand ready to work with FDA and other government agencies to accomplish the task at hand. Please contact Dr. Seun Ajiboye, Director of Science Policy and Government Affairs, at sajiboye@iadr.org or 703-299-8099 should you have any questions.

Sincerely,

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References