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Scott Gottlieb, M.D.
Commissioner
Food and Drug Administration (FDA)
Division of Dockets Management
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Docket No. FDA-2017-N-6502

**Opioid Policy Steering Committee: Prescribing Intervention- Exploring a Strategy for Implementation:
Public Hearing Request for Comments**

Dear Dr. Gottlieb:

On behalf of 40,000 general dentists, the Academy of General Dentistry (AGD) is pleased to provide comments on exploring a prescribing intervention for opioid prescription medications. As an educational organization, the AGD provides continuing education courses on best prescribing practices for opioids. The AGD is committed to delivering quality dental care to patients of all ages and to advocate for optimal oral health.

This nation has been facing the deadliest pharmaceutical epidemic in history. As the scourge of opioid abuse wears on, no part of the U.S. has been left untouched by the human toll this epidemic has left behind. No sector comes off unscathed and is free from blame of the opioid crisis the U.S. Mistakes were surely made by pharmaceutical companies in their aggressive marketing campaigns for opioid sales. Additionally, the Joint Commission declared pain as the fifth vital sign that ultimately resulted in having adverse consequences of increased opioid prescribing.

The AGD appreciates the federal government's all-hands-on-deck approach of countering opioid abuse as the Department of Health and Human Services (DHHS) agencies are working with the Drug Enforcement Agency (DEA)/ Federal Bureau of Investigation (FBI)/ Department of Justice (DOJ), Department of Homeland Security (DHS), the White House, and the legislative branches to put an end to this crisis.

The latest data demonstrate that the opioid drug epidemic has evolved from a legal drug problem into an *illegal*¹ drug problem. In 2016, 63,632 drug overdose deaths occurred, a 21.4% increase from 2015.^{2,3} Heroin, illicit fentanyl, and fentanyl analogues are now major contributors to overdose deaths.

As a nation, we must be committed to prosecute those responsible for criminal actions to the fullest extent of the law. We must all learn from mistakes made and not allow them to occur in the future. It is incumbent on all of us to find solutions to the opioid epidemic.

Inappropriate Prescribing

Inappropriate opioid prescribing has contributed to accidental death from opioid overdoses. In order to counter deficiencies from the past, federal agencies, clinicians, insurance companies, and state dental boards have developed opioid prescribing guidelines. Some states, such as Pennsylvania have very prescriptive dispensing guidelines for opioids.⁴

Developed in 2017, the CDC Guideline for Prescribing Opioids for Chronic Pain⁵, is under attack by some in the chronic pain community. Notably, the CDC has not produced a guideline for prescribing opioids for acute pain.

Some speakers/commenters suggest that more authority should be given to pharmacists. The AGD does not agree with that premise. While pharmacists can be instrumental in notifying authorities if they witness excessive or inappropriate prescribing of opioids, pharmacies were also party to some pill mill schemes. As state law regulates the practice of dentistry and medicine, state laws and regulations are being enacted to draw strict limits to the number of opioids that can be dispensed in any given opioid prescription.

Chronic and Acute Use of Opioids

Chronic Use

Certain patients, particularly those suffering intractable pain often caused by chronic spinal conditions, are in need of a constant supply of pain relief. As was evident from January 30, 2018 meeting

¹ Vivolo-Kantor, A, Seth, P, Gladden, M, Mattson, C, Baldwin, G, Kite-Powell, A, Coletta, C. Vital Signs: Trends in Emergency Department Visits for Suspected Opioid Overdoses—United States, July 2016–September 2017. Centers for Disease Control MMWR. March 6, 2018.

https://www.cdc.gov/mmwr/volumes/67/wr/mm6709e1.htm?s_cid=mm6709e1_w

² Ibid.

³ CDC. Wide-ranging online data for epidemiological research (WONDER) Atlanta, GA: U.S. Dept. of Health and Human Services, CDC, National Center for Health Statistics; 2016. <https://wonder.cdc.gov>

⁴ Prescribing Guidelines for Pennsylvania. Opioid Dispensing Guidelines. Revised January 14, 2016.

<http://www.health.pa.gov/My%20Health/Diseases%20and%20Conditions/A-D/Documents/PA%20Guidelines,%20on%20the%20Dispensing%20of%20Opioids.pdf>

⁵ Dowell, D, Haegerich, T, Chou, R. CDC Guideline for Prescribing Opioids for Chronic Pain

<https://www.cdc.gov/drugoverdose/prescribing/guideline.html>

presentations and comments received from patients suffering from chronic pain conditions, accommodations must be made for this subset of patients.

A study⁶ on long term use of opioid medications to treat moderate to severe chronic back pain or hip or knee osteoarthritis concluded that treatment with opioids was not superior to treatment with non-opioid medications. Since this study's duration was 12 months long, this raises questions on the efficacy of opioids for long-term use.

Acute Use

The Institute of Medicine (IOM) noted that opioids can be safe and effective for acute postoperative pain, procedural pain, and patients nearing the end of life who desire more pain relief, when used as prescribed.⁷ Most prescriptions written by general dentists and dental specialties are for acute pain. Data demonstrate that the risk of opioid addiction among people who are prescribed opioids from a doctor is quite low.⁸

State PDMPs

Federal dollars continue to be scarce. Instead of starting up a new national system, perhaps federal dollars and efforts could be used to augment and interconnect state programs. The system needs the ability to integrate with all of the states. Prescription drug monitoring program (PDMP) Interconnect exists but policy issues are preventing data from being shared with all states. As was discussed at the open public meeting, the use of PDMPs usually takes approximately 30 minutes by health care professionals and are not operational within a clinician's work flow.

Data from Florida demonstrate the prescription drug monitoring programs and a pill mill law are associated with a large relative reduction in prescription opioid use for high-risk patients.⁹

Electronic Health Records

There is minimal data on the use of certified electronic health records (EHR) by dentists. One study by the Dental Practice-based Research Network reported electronic dental record implementation at 14.3%

⁶ Krebs, E, Gravelly, A, Nugent, S. Effect of Opioid vs. Nonopioid Medications on Pain-Related Function in Patients with Chronic Back Pain or Hip or Knee Osteoarthritis. JAMA. 2018; 319(9):872-882.

⁷ Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research. Institute of Medicine. June 29, 2011. <http://www.nationalacademies.org/hmd/Reports/2011/Relieving-Pain-in-America-A-Blueprint-for-Transforming-Prevention-Care-Education-Research.aspx>

⁸ Satel, S. The Myth of What's Driving the Opioid Crisis. Politico Magazine. February 21, 2018. <https://www.politico.com/magazine/story/2018/02/21/the-myth-of-the-roots-of-the-opioid-crisis-217034>

⁹ Chang, HY, Murimi, I, Faul, M, Rutkow, L, Alexander, GC. Impact of Florida's prescription drug monitoring program and pill mill law on high-risk patients: A comparative interrupted time series analysis. Pharmacoepidemiol Drug Saf. 2018 Feb 28.

for solo practitioners and 15.9% for group practitioners.¹⁰ Since most dentists are not significant users of the Medicare program, there are not financial incentives for using electronic dental records for payment initiatives. Dentists, by and large, did not meet the eligibility criteria to receive incentive payments from the Centers for Medicare & Medicaid Services (CMS) to establish an electronic health records system in their offices, as did many physicians.

While many dentists use a type of electronic records, efforts to mandate electronic dental records and e-prescribing of opioids would, at this time, be problematic for dentists. The AGD looks forward to improved capability and overall interoperability of software systems in order to increase patient safety.

Law Enforcement

The largest opioid-related fraud enforcement action occurred on July 13, 2017.¹¹ Four hundred and twelve defendants were charged with opioid health care actions. In 2017, federal prosecutors charged more than 300 defendants in opioid-related crimes.¹² It is imperative that law enforcement continue to close off illegal avenues of opioid distribution and fraud. Moreover, law enforcement partners including the Department of Homeland Security and the United Postal Service are seeking to prevent importation of fentanyl and carfentanil from China and other countries. Law enforcement must be a strong and willing partner to stem the tide of opioid abuse in the U.S.

Mental, Social, Cultural and Other Considerations

One of every six adults in the United States has a mental illness.¹³ The National Institute on Drug Abuse finds that people with severe mental illness are 4.6 times more likely to use drugs at least 10 times in their lives.¹⁴ Mental health concerns cannot be discounted as a factor in the abuse of opioid drugs.

¹⁰ Schleyer, T, Song, M, Gilbert, GH, Rindal, DB, Fellows, VV, Gordan, VV, Funkouser, E. Electronic dental record use and clinical information management patterns among practitioner-investigators in the Dental Practice-Based Research Network. J Ma Dent Assoc. 2013;144:49-58.

¹¹ Department of Justice. National Health Care Fraud Takedown Results in Charges Against Over 412 Individuals Responsible for \$13 Billion in Fraud Losses <https://www.justice.gov/opa/pr/national-health-care-fraud-takedown-results-charges-against-over-412-individuals-responsible>

¹² Department of Justice. Deputy Attorney General Rosenstein Delivers Remarks at the America's Health Insurance Plans' National Health Policy Conference. Washington, D.C. March 7, 2018. <https://www.justice.gov/opa/speech/deputy-attorney-general-rosenstein-delivers-remarks-america-s-health-insurance-plans>

¹³ National Institute of Mental Health <https://www.nimh.nih.gov/health/statistics/mental-illness.shtml>

¹⁴ National Institute on Drug Abuse <https://www.drugabuse.gov/news-events/news-releases/2014/01/severe-mental-illness-tied-to-higher-rates-substance-use>

Moreover, if our nation is to make progress on turning around this nation's terrible opioid epidemic, we must ensure that we are looking at the problems holistically. The Social Capital Project¹⁵ found that of the 42,249 opioid related deaths in 2016, 67 percent were men. Additionally, in 2015, 32 percent of the population (aged 25 or older) was either never married or divorced but accounted for 71 percent of all opioid overdose deaths. Further, opioid casualties appear to affect the least educated disproportionately. In 2015, among those 25 and older, "forty percent of the population had no more than a high school diploma or equivalent, but they accounted for 68 percent of all opioid overdose deaths."

These data would seem to indicate that social and cultural influences may be significant factors in driving this national opioid overdose crisis. Lastly, genetic propensity for addiction may play a role in opioid abuse.

Alternative Approaches to Pain Relief

More research is needed on alternative approaches of pain relief. Instead of using opioids, some emergency rooms are employing alternative approaches to treat pain. Dry needling¹⁶ followed with a shot of local anesthetic, lidocaine patches, nitrous oxide,¹⁷ ibuprofen, acetaminophen, warm compresses, and ketamine¹⁸ are all approaches that some hospital systems are using to treat pain instead of issuing opioid prescription drugs.

The FDA is soliciting feedback on the following questions:

Prescriber Documentation

1. *If a REMS were to specify threshold drug amounts for opioid analgesic prescriptions above which prescribers would be required to provide additional documentation of medical necessity, what should the amounts be and how should they be determined for various clinical indications? What data are there to support such amounts? What additional data would be useful?*

¹⁵ Social Capital Project SCP Report No. 2-17. The Numbers Behind the Opioid Crisis
<https://www.lee.senate.gov/public/cache/files/b54a2abb-978d-4bbb-a868-531cdfaeae7a/the-numbers-behind-the-opioid-crisis-final.pdf>

¹⁶ Wang, Hansi Lo. ER Reduces Opioid Use by More than Half with Dry Needles, Laughing Gas. National Public Radio. February 20, 2018. <https://www.npr.org/sections/health-shots/2018/02/20/577139699/er-reduces-opioid-use-by-more-than-half-with-dry-needles-laughing-gas>

¹⁷ Balkman, Jaleesa. ER Doctors Cut Opioid Prescriptions by More than Half by Treating Pain with Laughing Gas and Dry Needles. Daily Mail. February 23, 2018. <http://www.dailymail.co.uk/health/article-5419247/ER-reduces-opioids-half-using-LAUGHING-GAS.html>

¹⁸ Daley, John. Ten ERs in Colorado tried to Curtail Opioids and Did Better than Expected. Kaiser Health News. February 23, 2018. <https://khn.org/news/ten-ers-in-colorado-tried-to-curtail-opioids-and-did-better-than-expected/>

The health care community is working towards ensuring that the right patient has the appropriate medication for their dental or medical condition. The AGD would not impose additional constraints on clinicians, at this time. Many states have enacted mandated maximum limits on opioid prescribing, such as New Jersey and Pennsylvania.

Express Scripts, a pharmacy benefit manager, imposed a maximum fill of 7 days for initial opioids for acute conditions. Additionally, Express Scripts¹⁹ fills short-acting opioids rather than long-acting opioids in an enhanced prior authorization program. In light of the restrictions on the use of opioid medications by state law, medical and dental boards, pharmacy benefit managers, and the proposal from Centers for Medicare & Medicaid Services (CMS), we do not believe the further addition of federal prescribing intervention is warranted, at this time. Instead, DEA quotas must be reassessed and updated, as appropriate.

2. If such measures were required, how should prescribers be made aware of them? Within the Agency's statutory REMS authority, how should the Agency require sponsors to ensure compliance with them? How should the Agency require sponsors to assess their effect in reducing misuse, abuse, and new addictions?

The AGD believes that clinicians should make the final decision on medication for their specific patient's health concern. We do not think that additional steps are warranted from clinicians. The FDA must adequately assess the potential for addiction and the abuse of pain medications when they are reviewing applications for a new drug application (NDA).

Additional REMS Approaches

3. The Steering Committee requests input from the public on whether, in addition to, or in conjunction with the above described prescriber intervention, and to the extent consistent with its statutory authority, the Agency should consider requiring sponsors to create a system that utilizes a nationwide prescription history database to facilitate safe use of opioid analgesics.

The Food and Drug Administration Amendments Act of 2007 (FDAAA) granted authority to the FDA for Risk Evaluation and Mitigation Strategies (REMS) to be used to ensure that the benefits outweigh the risks of certain medications. The FDA's current proposal to require manufacturers of drugs to create a national PDMP or database seems to be broadening the constraints of the agency's REMS authority. The intention of Congress when including the REMS provision in FDAAA, was to create a legal mechanism to add medication guides and other requirements for select medications, not to create a new national prescription database.

4. If this approach were adopted, how should the Agency require sponsors to assess the impact of such requirements?

¹⁹ Snezana Mahon, Pharm D. "The Opioid Crisis: The Role of Technology and Data in Preventing and Treating Addiction" U.S. Senate Committee on Health, Education Labor and Pensions, February 27, 2018. <https://www.help.senate.gov/imo/media/doc/Mahon.pdf>

The AGD is not certain that sponsors should be assessing the impact of a national PDMP on opioids. The inherent conflicts-of-interests of manufacturers would seem to be apparent that it would be inappropriate to conduct an assessment of this nature. Furthermore, health care privacy is another major concern. The FDA should work with federal and local public health officials to evaluate statistics on successful pain mitigation cases, addiction, death, and overdoses attributed to the use of opioids.

Additional Considerations

5. The proposed Opioid Analgesics REMS includes a Medication Guide and a Patient Counseling Document to educate patients. It also includes a Blueprint for Health Care Providers Involved in the Management or Support of Patients with Pain that contains information on counseling patients and caregivers about the safe use of opioid analgesics. Consistent with its statutory authority, should FDA require sponsors to take additional measures to ensure that health care providers, their patients, and patient caregivers and family members are educated on safe storage and disposal and the risks of misuse, abuse, and addiction associated with opioid analgesics (e.g., a public health campaign targeted at these groups)?

The AGD wholeheartedly supports a public health education campaign on the safe use and potential of abuse of opioid medications. We do not believe that the public is sufficiently aware of the potential harm these drugs may pose towards addiction. Notwithstanding other efforts, dentists, physicians, pharmacy benefit managers, and pharmacists may also choose to counsel patients about the safe use of opioids.

6. Should the Agency consider additional measures intended to improve the safety of patient storage and handling of opioid analgesics?

Some groups have advocated for smart pill bottles to be used in conjunction with the long term use of opioids. An education campaign about the safety hazards of sharing medications with family and friends would be appropriate and warranted given the propensity of addiction occurrences from the sharing of medications.

7. How might use of unit-of-use packaging play a role in encouraging appropriate prescribing of opioid analgesics?

The AGD is not certain what benefits would be accomplished through unit-of-use packaging for opioid medications. As we understand unit-of-use packaging, the drug product is intended to be dispensed without modification, except for patient labeling. However, patients use opioids for both acute and chronic conditions. As a result, the needs of medication duration can vary considerably. Since some states are now imposing a maximum fill on opioid medications and some states are not, unit-of-use packing would need to be tailored to the specific needs of each state law. From a manufacturing standpoint, it would seem to be very difficult to accommodate each state's needs circumventing a standardization in the manufacturing process.

8. Should the Agency require sponsors to create a mechanism by which patients could return unused pills, and if so, to whom?

Public and private efforts are underway to dispose of unused medications. The DEA Take Back Day is quite effective. According to their statistics, a record-breaking 912,305 pounds –or 456 tons²⁰ – of potentially dangerous expired, unused, and unwanted prescription drugs were collected during the 14th annual Prescription *Drug Take Back Day* in October 2017.

Express Scripts supplies drug deactivation disposal bags for patients to destroy unused medications. The bags use carbon to neutralize the active ingredients in the drugs and this can be accomplished in the patient’s home and safely disposed in their trash.

Walmart uses a DisposeRX™ packet which contains a polymer blend when added to warm water and prescription drugs that converts the mixture into a biodegradable gel. Additionally, CVS provides medication disposal kiosks inside CVS Pharmacy and CVS Health locations to collect unused medications. CVS has removed more than 100 metric tons²¹ of unused medications through collection in their boxes and in police stations.

In light of the governmental and private sector efforts to safely dispose of unused medications, the AGD does not believe it is necessary for the FDA to mandate that sponsors create a mechanism to return unused medications.

Conclusion

Thank you for considering our comments. The AGD will continue to convey information and educational offerings to our membership in order to reduce the use of opioid prescription medications. We stand ready with the FDA and other federal agencies to be part of the solution to the deadliest drug epidemic in our nation’s history.

Sincerely,



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AGD President

²⁰ U.S. Drug Enforcement Administration, 14th National Take Back Day, October 28, 2017:
https://takebackday.dea.gov/sites/default/files/NTBI_XIV_Totals-Oct2017.pdf

²¹ CVS Health Press Release: Oct. 25, 2017. CVS Introduces Safe Medication Disposal Inside CVS Pharmacy, Marking National Prescription Drug Take Back Day. <https://cvshealth.com/newsroom/press-releases/cvs-health-introduces-safe-medication-disposal-inside-cvs-pharmacy-marking>