Center for U.S. Policy

April 28, 2023

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

The Center for U.S. Policy ("Petitioner") submits this Citizen Petition under the Federal Food, Drug and Cosmetics Act ("FD&C Act") to request the Commissioner of the U.S. Food and Drug Administration ("FDA") to deem the Bamboo Health ("Bamboo") NarxCare software a misbranded device and take administrative action to prevent serious, adverse health consequences and death.

I. Action Requested

The Petitioner asks FDA to (1) deem Bamboo's NarxCare software a misbranded device; (2) issue a Warning Letter to Bamboo; (3) commence mandatory recall procedures with respect to the NarxCare software; and (4) take any other prompt action the agency deems appropriate to prevent serious, adverse health consequences or death.

NarxCare is a clinical decision support ("CDS") software product that meets the definition of a "device" under the FD&C Act. Yet, based on a search of FDA's publicly available databases, it appears that the device's manufacturer, Bamboo, is in violation of several provisions of the Act and its implementing regulations. Specifically, before introducing NarxCare into interstate commerce, Bamboo did not comply with the establishment registration, device listing, or premarket notification requirements set forth in Section 510 of the Act.[1] Therefore, FDA should deem NarxCare a misbranded device and take appropriate administrative action to prevent serious, adverse health consequences or death. As explained herein, such administrative action is particularly important given that Bamboo's software has fundamentally altered the practice of medicine in the U.S. to the detriment of patients with a legitimate need for controlled prescription medications and the health care providers who treat such patients.

II. Statement of Grounds

A. PDMPs as a Response to the Drug Poisoning Crisis

The number of drug poisoning deaths in the United States has quintupled since 1999.[2] Recent data indicate that more than 101,750 fatal drug poisonings occurred in the U.S. in the 12

[1] Federal Food, Drug and Cosmetics Act, 21 U.S.C. § 360(b),(j)-(k).
[2] Ryan D'Souza, et al., *Prescription Drug Monitoring Program*, STATPEARLS PUBLISHING, https://www.ncbi.nlm.nih.gov/books/NBK532299/ (last updated Jun. 23, 2022).

months ending in October 2022.[3] Policy makers have suggested a variety of strategies to address the drug poisoning crisis, including implementation of state Prescription Drug Monitoring Programs ("PDMPs") designed to collect, report, and monitor controlled medication dispensing data and help reduce the misuse and diversion of such medications. PDMPs consist of independent statewide electronic databases that track controlled medications dispensed by prescription in a particular state.[4] The data is used by state regulatory authorities to understand prescribing practices and patient behaviors.[5]

The concept of PDMPs is not new. The oldest continuously operating PDMP was established in California in 1939.[6] Like today's programs, early models were used as a regulatory tool by officials enforcing drug laws.[7] However, these early programs were paper-based and collected and stored limited information.[8] In the early 2000s, the U.S. Department of Justice ("DOJ") and the Drug Enforcement Administration ("DEA") started advocating for the establishment and expansion of more sophisticated PDMPs.[9] Unsurprisingly, the majority of state legislation implementing PDMPs has been enacted in the last twenty years.[10]

Many states' PDMP laws require health care providers ("HCPs") and pharmacists to query the PDMP under certain circumstances, such as the first time an opioid prescription is issued, upon issuing an opioid prescription with a dose exceeding a specified level, or upon set intervals for patients treated for pain.[11] As recognized by Bamboo, "[m]any PDMPs started as law enforcement tools, but most have migrated to a clinical decision support focus with hopes that providers and pharmacists will more carefully consider and manage the risks and benefits of opioids and other controlled substances."[12] Indeed, today's PDMPs are no longer passive data collection and storage programs, but rather sophisticated electronic databases that store and analyze vast amounts of information and apply algorithms to score patient risk for controlled substance misuse and to guide treatment decisions.[13]

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[3] Centers for Disease Control and Prevention, *Provisional Drug Overdose Death Counts*, NATIONAL CENTER FOR HEALTH STATISTICS (Feb. 15, 2023), https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm.
[4] D'Souza, et al., *Prescription Drug Monitoring Program*.
[5] *Id.*
[6] *Id.*
[7] Substance Abuse and Mental Health Services Admin., *Prescription Drug Monitoring Programs: A Guide for Healthcare Providers,* 10 IN BRIEF, 1, 1 (2017), https://store.samhsa.gov/sites/default/files/d7/priv/sma16-4997.pdf.
[8] Jennifer Oliva, *Dosing Discrimination: Regulating PDMP Risk Scores*, 110 CALIFORNIA LAW REVIEW 47, 75 (2022) *(*citing Substance Abuse and Mental Health Services Administration, IN BRIEF*, Prescription Drug Monitoring Programs: A Guide for Healthcare* Providers 1,1 (2017)).
[9] *Id*. at 75 (citing Prescription Drug Monitoring Program Training & Tech. Assistance Ctr., *History of Prescription Drug Monitoring Programs* 1, 3 (Mar. 2018), https://perma.cc/X3KX-GE4F).
[10] D'Souza, et al., *Prescription Drug Monitoring Program*.
[11] Appriss Health, *Up Front, Every Patient, Every Time* 1, 3, https://perma.cc/K2S4-Z88Z.
[12] *Id*.
[13] Oliva, *supra* note 8, at 76 (citing Substance Abuse & Mental Health Serv. Admin., *Prescription Drug Monitoring Programs: A Guide for Healthcare Providers,* at 1).

B. Overview of Bamboo Health's NarxCare Software

In 2014, Bamboo (formerly Appriss Health) acquired NARxCHECK, the first computer-generated drug use software to calculate "risk scores".[14] Bamboo manages more than 40 state PDMP databases through its AWARxE PDMP platform, PMP Gateway enhancement, and NarxCare.[15] The AWARxE PDMP platform presents providers information on controlled substance dispensing by prescription;[16] the PMP Gateway brings PDMP data to the point of care within the electronic health record;[17] and NarxCare generates additional analytics by calculating patient-specific "risk scores" for opioids, sedatives, and stimulants, collectively called "Narx Scores."[18]

According to product information published online, "NarxCare is a substance use disorder [("SUD")] platform that can be integrated into a PDMP, and also into workflow . . ."[19] The software "aids care teams in clinical decision-making . . . [and] provides support to help prevent or manage [SUD] . . ."[20] "The NarxCare platform is used to inform providers millions of times a month across the nation. It has been integrated into workflow and used as the default portal platform at the state PDMP level."[21]

The NarxCare software analyzes PDMP and non-PDMP data to generate a report setting forth a Narx Score, predictive risk scores, and red flags, among other things.[22] According to NarxCare's product materials, Narx Scores are "based on a complex algorithm factoring in" various data points that can be pulled from a PDMP.[23] These PDMP risk factors include the number of providers, number of pharmacies, morphine milligram equivalents ("MMEs") dispensed, overlapping prescription days, and potentiating medications (*e.g.,* a benzodiazepine prescription that could increase the depressant effects of an opioid medication).[24] Narx Scores "are quantified representations of the data in the PDMP and range from 000 - 999 with higher scores equating to higher risk and misuse, and the last digit always represents the number of active prescriptions."[25] In other words, NarxCare generates Narx Scores by analyzing vast

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[14] *Appriss Acquires NARxCHECK from the National Association Boards of Pharmacy Foundation* (Nov. 11, 2014), https://apprisshealth.com/pressrelease/appriss-acquires-narxcheck-from-the-national-association-boards-of-pharmacy-foundation/ [https://perma.cc/C5VG-2MXC].)

[15] Kristine Whalen and Katrina Sitkovits, *Evaluating the Impact: NarxCare and Gateway Effectiveness*, APPRISS HEALTH 1, 2 (Oct. 2020), https://go.bamboohealth.com/rs/228-ZPQ-393/images/Gateway-Effectiveness-White-Paper.pdf.

[16] *Id.*

[17] *Id.*

[18] Jim Huizenga, et al., *NARxCHECK® Score as a Predictor of Unintentional Overdose Death*, APPRISS HEALTH 1, 3 (Oct. 2016), https://apprisshealth.com/wp-content/uploads/sites/2/2017/02/NARxCHECK-Score-as-a-Predictor.pdf.

[19] Bamboo Health*, Up Front, Every Patient, Every Time* 1, 7 (May 2019), https://bamboohealth.com/wp-content/uploads/2022/10/Whitepaper_Maximizing-PDMP-Effectiveness-PDMP.pdf.

[20] Appriss Health, *NarxCare* 1,1, https://perma.cc/CSX9-NTGQ.

[21] Bamboo Health, *Up Front, Every Patient, Every Time,* at 10.

[22] Appriss Health, *NarxCare*, at 1.

[23] *Id.*

[24] Bamboo Health, *Up Front, Every Patient, Every Time*, at 8.

[25] Appriss Health, *NarxCare*, at 1.

amounts of information collected by PDMP databases to identify and weigh various data points that the software's designers have deemed indicators for substance misuse.[26]

With respect to predictive risk scores, "[t]hese composite risk scores incorporate relevant . . . PDMP and non-PDMP . . . [data] into advanced and customized predictive models to calculate a patient's risk of a host of outcomes, including overdose and addiction."[27] Bamboo has explained that these non-PDMP data sets "may include medical claims data, electronic health records, EMS data and criminal justice data."[28] According to several other sources, non-PDMP data may also include prescription payment method[29] and distance traveled for treatment.[30] In addition to generating risk scores for substance misuse, NarxCare purports to the likelihood of a patient developing a substance use disorder or experiencing a drug poisoning.[31]

Bamboo's position is that incorporation of non-PDMP data into NarxCare increases its effectiveness; thus, the company plans to continue to incorporate such data into the platform.[32] For example, Bamboo established a collaboration with a data aggregation company named hc1, whose software "automatically compar[es] lab results with state PDMP data" to provide "automated, intelligent data" that "make[s] useful comparisons in real-time with a single click."[33] Additionally, it has been suggested that risk score metrics should incorporate "contributory databases," including CLUE (auto industry), SIRIS (banking), MIDEX (real estate), and information provided from other businesses.[34] It is unclear whether Bamboo currently uses such data.

Bamboo has published several white papers online describing NarxCare in basic terms, including a plain language description of the five PDMP inputs used by its complex algorithm to compute Narx Scores and a basic outline of how the algorithm uses these data points.[35] These white papers also include citations to literature that purportedly supports the use of these five PDMP inputs disclosed by Bamboo. However, outside of passing references to non-PDMP

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[26] Oliva, *supra* note 8, at 50.
[27]Appriss Health, *NarxCare*, at 1.
[28] *Id*.
[29] *Id*. at 98 (citing Appriss Health, *Up Front, Every Patient, Every Time*, at 6; Ind. Bd. Pharmacy Prescription Monitoring Program, *Indiana's Prescription Drug Monitoring Program* 1, 3 https://web.archive.org/web/20161221053014/https://www.in.gov/ipac/files/Brady.pdf.); Indiana State Medical Association, *2022 Focused Update on INSPECT and Indiana Opioid Prescribing Laws* (Dec. 15, 2022), https://www.ismanet.org/ISMA/Events/Event_Display.aspx?EventKey=LWEB121522
[30] *Id*. at 100 (citing Appriss Health, *A Balanced Approach to Opioids and Chronic Pain: Part X – Machine Learning* (Sept. 19, 2018), https://web.archive.org/web/20210409004410/https://apprisshealth.com/blog/machine-learning/.
[31] Appriss Health, *NarxCare*, at 1.
[32] Appriss Health, *Up Front, Every Patient, Every Time*, at 10.
[33] Hc1, *Opioid Advisor*, https://web.archive.org/web/20221128143442/https://hc1.com/solutions/opioid-advisor-2 (last visited Mar. 20, 2023).
[34] Oliva, *supra* note 8*,* at 84.; citing Tony Schueth, et al., *PDMP Alerts, Analytics and the Pharmacy Workflow,* NAT. COUNCIL FOR PRESCRIPTION DRUG PROGRAMS (May 9, 2017), https://pocp.com/wpcontent/uploads/PDMP_FinalNCPDP_2017AC.pdf.
[35] *See, e.g.,* Kristine Whalen and Katrina Sitkovits*, NarxCare and PMP Gateway Effectiveness*, BAMBOO HEALTH (Oct. 2020), *https://bamboohealth.com/wp-content/uploads/2022/10/Whitepaper_NarxCare-PMP-Gateway-Effectiveness.pdf;* Bamboo Health*, Up Front, Every Patient, Every Time;* Kristine Whalen and Katrina Sitkovits, *Risk Scoring in the PDMP to Identify At-Risk Patients*, APPRISS HEALTH (Aug. 2020), https://go.bamboohealth.com/rs/228-ZPQ-393/images/AH-NarxCare-White-Paper.pdf..

inputs in Bamboo's publicly available documents, Petitioner did not identify any meaningful description published by Bamboo about how other PDMP and non-PDMP data points are incorporated into and used by NarxCare's algorithms. For example, factoring into the algorithm the distance traveled from home to a prescriber is likely based on the assumption that patients who travel farther are more likely to be engaged in suspicious drug-seeking behaviors.[36] However, there is no information published on how the algorithm "scores" this and similar metrics (*e.g.,* distance traveled to treatment), what such metrics suggest or prove, and the medical literature or other rationale that supports their use in NarxCare's algorithms.[37]

C. Serious, Adverse Health Consequences and Death

Bamboo's software has fundamentally altered the practice of medicine and disproportionately impacts certain patient populations. PDMPs were not designed to replace prescribers' professional judgement, diagnose health conditions, or dictate patients' course of care. Yet, law enforcement agencies like the DEA utilize PDMP data to surveil HCPs' prescribing habits, dispensers' practices, and patients' controlled substance histories.[38] If deemed an "over-prescriber" or "over-dispenser" by the DEA, individuals may be subject to administrative and criminal investigation, controlled substance registration suspension and revocation, and in some cases, arrest, asset seizure, prosecution, and incarceration.[39] Out of fear of being labeled as an opioid over-prescriber and having to defend against administrative and criminal allegations, providers are pressured to change their prescribing habits.[40] Indeed, "research demonstrates that PDMP risk scoring coerces clinicians to force medication tapering, discontinue prescriptions, and even abandon patients without regard for the catastrophic collateral consequences that attend to those treatment decisions."[41] This fear has provoked prescribers to drop or decline patients with pain and other patients for whom opioids and other controlled substances are medically necessary.[42] In 2020, the opioid dispensing rate reached its lowest point in 15 years.[43] Effectively, the software has played a significant, and often unwarranted, role in the choice not to prescribe opioids. As a result, many patients have been left without access to medically necessary treatments.[44]

In recent years, the percentage of patients undergoing opioid dose tapering has increased substantially.[45] Specifically, a study published in 2019 found that the "percentage of patients

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[36] Oliva, *supra* note 8, at 100.
[37] *Id.*
[38] *Id*. at 51.
[39] *Id*.
[40] *Id*. at 79 (citing Kelly K. Dineen & James M. Dubois, *Between a Rock and a Hard Place: Can Physicians Prescribe Opioids to Treat Pain Adequately While Avoiding Legal Sanction?*, 42 AM. J. L. & (2016)).
[41] *Id*. at 1.
[42] *Id*. at 78 (citing Rebecca Haffajee et al., *Mandatory Use of Prescription Drug Monitoring Programs*, 313 JAMA 891, 891–92 (2015)).
[43] Ctr. For Disease Control & Prevention, *U.S. Opioid Dispensing Rate Maps Print*, https://www.cdc.gov/drugoverdose/rxrate-maps/index.html (last reviewed Nov. 10, 2021).
[44] Oliva, *supra* note 8, at 78 (citing Cato Institute, *The Myth of an Opioid Prescription Crisis* (Sept.-Oct. 2017), https://www.cato.org/sites/cato.org/files/serials/files/policy-report/2017/9/cpr-v39n5-4.pdf
[45] Joshua Fenton, *Trends and Rapidity of Dose Tapering Among Patients Prescribed Long-term Opioid Therapy*, 2008-2017, 2 JAMA NETWORK OPEN 1,1 (Nov. 5, 2019), https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2755492.

tapering daily opioid doses increased from 12.7% in 2008 to 16.2% in 2015, before increasing to 18.6% in 2016 and 23.1% in 2017."[46] Tapering of patients' long-term opioid therapy results in adverse health consequences, including disruption of clinical stability, worsened pain control, and harm to the practitioner-patient relationship. Researchers reported in 2023 that "opioid tapering was associated with more emergency department visits and hospitalizations, [and] fewer primary care visits."[47] The researchers partially attributed the reduction in primary care visits to "ruptures in relationships" with providers.[48]

Rapidly tapering or discontinuing opioids has also been associated with an increased risk for drug poisoning and self-harm, particularly among persons with OUD.[49] A study published in 2021 reported a 68 percent increase in poisonings and a doubling of mental health crises in tapered compared to untapered individuals, among patients prescribed stable, long-term, higher-dose opioid therapy.[50] In 2019, the FDA issued a warning, cautioning practitioners not to abruptly discontinue or rapidly taper patients taking opioid pain medication.[51] The agency indicated that it had received reports of serious harm in patients, including withdrawal symptoms, uncontrolled pain, psychological distress, and suicide, who were rapidly tapered or discontinued from opioid medicines.[52] As such, patients' health and safety are at risk when they are denied medically necessary treatments.[53]

Patients with unmet medical needs may be driven to the illegal market, where counterfeits and illicit substances are increasingly being adulterated with fentanyl and other potentially lethal substances.[54] In 2021, the DEA released a public safety alert warning the public of the alarming increase in the lethality and availability of fake prescription pills containing fentanyl and methamphetamine.[55] Their laboratory found that six out of 10 analyzed fentanyl-

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[46] *Id*. at 5.
[47] Elizabeth Magnan, et al., *Association Between Opioid Tapering and Subsequent Health Care Use, Medication Adherence, and Chronic Condition Control*, 6 JAMA NETWORK OPEN 1,1 (Feb. 7, 2023), https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2801014.
[48] *Id*. at 2.
[49] Tami Mark & William Parish, *Opioid medication discontinuation and risk of adverse opioid-related health care events*, 103 J. SUBSTANCE ABUSE TREATMENT (May 2019), https://www.researchgate.net/publication/332957084_Opioid_medication_discontinuation_and_risk_of_adverse_opioid-related_health_care_events.
[50] Mark Rothstein & Julia Irzyk, *Physician Liability for Suicide after Negligent Tapering of Opioids*, 50 J. L., MED. & ETHICS 184, 185 (Mar. 4 2022) (citing Alicia Agnoli et al., *Association of Dose Tapering With Overdose or Mental Health Crisis Among Patients Prescribed Long-term Opioids*, 326 JAMA 411 (2021)).
[51] U.S. Food & Drug Admin., *FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering* (Apr. 9, 2019), https://www.fda.gov/drugs/drug-safety-and-availability/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes?utm_campaign=FDA%20MedWatch-Opioid%20Pain%20Medicines%3A%20Drug%20Safety%20Communication&utm_medium=email&utm_source=Eloqua.
[52] *Id*.
[53] Oliva, *supra* note 8, at 79 (citing Cato Institute, *supra* note 44, at 9, 11).
[54] *Id*.
[55] U.S. Drug Enforcement Agency, *Public Safety Alert: Sharp Increase in Fake Prescription Pills Containing Fentanyl and Meth* (Sept. 27, 2021), https://www.dea.gov/alert/sharp-increase-fake-prescription-pills-containing-fentanyl-and-meth.

adulterated counterfeit prescription pills contained a potentially lethal dose of fentanyl in 2022.[56] According to the DEA, the only safe medications are ones prescribed by a trusted medical professional and dispensed by a licensed pharmacist.[57] Yet, the use of NarxScores incentivizes providers to reduce and align their prescribing to correspond with patients' calculated risk scores, potentially forcing patients to decide whether to turn to illicit sources for symptom relief.[58] Inversely, poisonings due to illicit fentanyl, fentanyl analogs, and methamphetamine continue to increase.[59] In 2021, there were over 71,000 deaths from synthetic opioid poisoning (primarily fentanyl) in the United States, the highest per year on record.[60]

Despite the risk of such adverse outcomes, one critique of NarxCare points out that the software:

> neither tracks nor assesses patient health outcomes related to opioid deprescribing and tapering . . . NarxCare does not evaluate whether clinical deprescribing decisions improve or worsen patients' pain, mental health, daily functioning, or quality of life. NarxCare neither "flags" prescribers nor sends clinicians an alert when a medication-discontinued or force-tapered patient dies by suicide or is admitted to the emergency room with debilitating pain or depression . . . Best practices demand that opioid deprescribing "be undertaken with care, so as to alleviate adverse outcomes and avoid exacerbating health care inequities."

Oliva, supra note 8, at 98. Internal citations omitted.

Instead, Bamboo apparently measures NarxCare's effectiveness in a clinical setting through outcomes such as changing prescribing habits and reducing prescription quantities and MMEs.[61]

In addition to people with pain, marginalized patient groups are disproportionately harmed by prescribers' use of various "risk-indicators" reported by NarxCare. As noted above,

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[56] U.S. Drug Enforcement Agency, *Public Safety Alert: EA Laboratory Testing Reveals that 6 out of 10 Fentanyl-Laced Fake Prescription Pills Now Contain a Potentially Lethal Dose of Fentanyl*, https://www.dea.gov/alert/dea-laboratory-testing-reveals-6-out-10-fentanyl-laced-fake-prescription-pills-now-contain#:~:text=%E2%80%9CMore%20than%20half%20of%20the,%2C%E2%80%9D%20said%20Administrator%20Anne%20Milgram (last visited Jan. 30, 2023).

[57] U.S. Drug Enforcement Agency, *Public Safety Alert: Sharp Increase in Fake Prescription Pills Containing Fentanyl and Meth,* (Sept. 27, 2021).

[58] Oliva, *supra* note 8, at 106 (citing Stefan Kertesz, et al., *Nonconsensual Dose Reduction Mandates Are Not Justified Clinically or Ethically: An Analysis,* 48 J.L. MED. & ETHICS 259, 262; *International Stakeholder Community of Pain Experts and Leaders Call for an Urgent Action on Forced Tapering*, 20 PAIN MED. 429, 429–30 (2019)).

[59] National Institute on Drug Abuse, *Overdose Death Rates* (Jan. 20, 2022), https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates.

[60] Centers for Disease Control and Prevention, *U.S. Overdose Deaths In 2021 Increased Half as Much as in 2020 – But Are Still Up 15%,* (May 11, 2022), https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/202205.htm.

[61] *Oliva, supra* note 8*,* at 89.

data may include a patient's criminal history,[62] prescription payment method,[63] and distance traveled for treatment.[64] As such, these factors could discriminate against ethnic and racial minorities, and low-income and rural individuals. For example, ethnic and racial minorities, compared to White patients, are more likely to have criminal histories and not have insurance; and low-income patients are more likely to be uninsured and reside in health care deserts, requiring them to travel far distances for treatment.[65] As a result, certain patient groups may be more likely to turn to the illicit drug market for relief. In 2020, death rates from drug poisonings among Black Americans "overtook those of White Americans for the first time since the 1990s," signifying "a sharp reversal from 2010, when White Americans were over twice as likely to die" from drug poisonings.[66] Moreover, since 2011, Black Americans, when compared to any other racial group, have experienced the highest increase in deaths resulting from poisonings involving illicit synthetic opioids.[67]

The CDC emphasized this concern in its updated opioid prescribing guideline issued in 2022 as follows:

> Experts from OWG [Opioid Workgroup] had concerns about PDMP risk scores or other algorithmic interpretations from software platforms that can lead to distrust between clinicians and patients and stigmatization, particularly for patients with conditions such as opioid use disorder. Risk scores are reportedly generated by applying proprietary algorithms that are not publicly available to information from patient EHRs and other sources such as court records and criminal histories; these algorithms might disparately affect women, persons of color, and persons who live in poverty []. Importantly, whereas one PDMP-generated risk measure has shown fair concurrence with the WHO Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST), these scores have not been externally validated against clinical outcomes []. Such risk scores should not take the place of clinical judgment. Rather, clinicians should use specific PDMP information about medications prescribed to their patient in the context of other clinical information, including their patient's history, physical findings, and other relevant testing, to help them communicate with and protect their patient.

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[62] Oliva, supra note 8, at 101 (citing Leo Beletsky, *Deploying Prescription Drug Monitoring to Address the Overdose Crisis: Ideology Meets Reality*, 15 IND. HEALTH L. R. 139, 169 (2018); Regional Judicial Opioid Initiative, *Leveraging Social, Behavioral, and Health Data Harold Rogers PDMP – National Meeting* (Jun. 26, 2019)); *see also* Bamboo Health, *Up Front, Every Patient, Every Time*, at 14.

[63] *Id*. at 98 (citing Appriss Health, *Up Front, Every Patient, Every Time*; Indiana Board of Pharmacy Prescription Monitoring Program, Indiana's Prescription Drug Monitoring Program); Indiana State Medical Association, *2022 Focused Update on INSPECT and Indiana Opioid Prescribing Laws*.

[64] *Id*. at 100 (citing Appriss Health, *A Balanced Approach to Opioids and Chronic Pain: Part X - Machine Learning* (Sept. 19, 2018), https://web.archive.org/web/20210409004410/https://apprisshealth.com/blog/machine-learning/.

[65] *Id*. at 51, 101.

[66] *Id*. at 95 (citing Joseph Friedman & Helena Hansen, Opinion, *Surging Overdose Deaths Are a Tragic Racial Justice Issue,* L.A. TIMES (Nov. 23, 2021), https://www.latimes.com/opinion/story/2021-11-23/overdoses-u-s-black-white-native-americans).

[67] *Id*. (citing Substance Abuse & Mental Health Serv. Admin. Off. of Behavioral Health Equity*, The Opioid Crisis and the Black/African American Population: An Urgent Issue* 1, 4 (2020)).

Deborah Dowell, et al., *CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States*, 71 MORBIDITY & MORTALITY WEEKLY REPORT 1, 49 (Nov. 4, 2022) (citing Oliva, *supra* note 8, at 1-47; Cochran G, et al. *Validation and threshold identification of a prescription drug monitoring program* clinical *opioid risk metric with the WHO alcohol, smoking, and substance involvement screening test*, 228 DRUG ALCOHOL DEPEND (Nov. 1, 2021)).

D. NarxCare Validation Studies

Bamboo has published information online about studies attempting to validate the effectiveness of NarxCare. Until recently, these studies largely consisted of surveys and internal case studies.[68] In November 2021, a peer-reviewed study was published to externally validate NarxCare as a useful clinical decision support tool. The study evaluated the validity of the NarxCare narcotic score metric relative to the World Health Organization's Alcohol, Smoking, and Substance Involvement Screening Test ("ASSIST") and to identify risk level cutoff thresholds.[69] The study did not assess the validity of the software's sedative score, stimulant score, or the composite overdose risk score.[70] The study sample was drawn from adults picking up opioid prescriptions at a national pharmacy chain. It concluded that the narcotic score "could serve as a useful initial universal prescription opioid-risk screener."[71]

Petitioner anticipates that a more thorough critique of the November 2021 validation study will soon be published, explaining that the validation study was critically flawed and did not meet its own specified threshold for acceptable accuracy. For example, it was inappropriate to use ASSIST as the gold-standard to which the narcotic score metric was compared. ASSIST was not developed for use in the same population for whom narcotic scores are calculated. ASSIST is a questionnaire used to screen for non-medical use of various substances, including opioids, and to determine whether a conversation (or "brief intervention") should take place with the patient about the substance use. It is used in primary care settings and assigns a score for non-medical use of a particular substance into a risk category of low, moderate, or high.[72] ASSIST was both developed and validated using study populations drawn from SUD treatment centers and primary care settings.[73] ASSIST's opioid subscale classifies patients who have taken opioid pain relievers in the past 90 days as being at least at moderate risk for nonmedical opioid use and in need of an intervention. The study failed to incorporate the ASSIST developers' attempts to correct for scoring that has the potential to erroneously elevate risk scores for patients who receive opioid medication refills for pain relief.

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[68] *See, e.g.,* Appriss Health, *Up Front, Every Patient, Every Time*; Huizenga J.E., et al., *supra* note 18; Kristine Whalen and Katrina Sitkovits, *NarxCare and PMP Gateway Effectiveness*.

[69] Gerald Cochran, et al., *Validation and threshold identification of a prescription drug monitoring program clinical opioid risk metric with the WHO alcohol, smoking, and substance involvement screening test*, 228 DRUG & ALCOHOL DEPENDENCE 1, 1 (Nov. 1, 2021) https://www.sciencedirect.com/science/article/pii/S0376871621005627

[70] *Id*.

[71] *Id*.

[72] World Health Organization, *The Alcohol, Smoking and Substance Involvement Screening Test* (Jan. 1 2010), https://www.who.int/publications/i/item/978924159938-2.

[73] *Id*.

E. FDA Regulation of CDS Medical Devices

FDA is "responsible for protecting the public health by ensuring the safety, efficacy, and security of . . . medical devices . . ."[74] A "device" subject to FDA regulation includes "an instrument . . . , machine . . . , or other similar or related article . . . which is . . . intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease . . ."[75] FDA has long regulated software that qualifies a "device," referred to as "Software as a Medical Device" ("SaMD").[76] SaMD is "software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device."[77] SaMD includes software that provides "decision support for the diagnosis, treatment, prevention, cure, or mitigation of diseases or other conditions," or "CDS" software.[78]

1. Device vs. Non-Device CDS Determinations

The FDA divides CDS software into two categories: "Device" and "Non-Device." "Non-Device CDS" refers to decision support software functions that do not meet the statutory definition of a device.[79] In 2016, the 21st Century Cures Act added section 520(o) to the FD&C Act, which established criteria to determine whether software is "Non-Device CDS."[80] Section 520(o) (21 U.S.C. § 360j(o)) states:

> (1) The term device, as defined in section 201(h), shall not include "software function that is intended—
>
> > (A) for administrative support of a health care facility, including the processing and maintenance of financial records, claims or billing information, appointment schedules, business analytics, information about patient populations, admissions, practice and inventory management, analysis of historical claims data to predict future utilization or cost-effectiveness, determination of health benefit eligibility, population health management, and laboratory workflow;
> >
> > (B) for maintaining or encouraging a healthy lifestyle and is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;
> >
> > (C) to serve as electronic patient records, including patient-provided information, to the extent that such records are intended to transfer, store, convert formats, or display the equivalent of a paper medical chart, so long as—

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[74] U.S. Food & Drug Admin., *What We Do*, https://www.fda.gov/about-fda/what-we-do#mission (last revised Mar. 28, 2018).
[75] 21 U.S.C. § 321(h).
[76] U.S. Food & Drug Admin., Guidance, *Clinical Decision Support Software: Guidance for Industry and Food and Drug Administration Staff* (Sept. 28, 2022), https://www.fda.gov/media/109618/download [hereinafter 2022 Clinical Decision Support Software Guidance).
[77] U.S. Food & Drug Admin., *Software as a Medical Device (SaMD)*, https://www.fda.gov/medical-devices/digital-health-center-excellence/software-medical-device-samd (last revised Dec. 4, 2018).
[78] 2022 Clinical Decision Support Software Guidance, *supra* note 76, at 1.
[79] *Id*. at 4.
[80] *Id*. at 5.

(i) such records were created, stored, transferred, or reviewed by health care professionals, or by individuals working under supervision of such professionals;
(ii) such records are part of health information technology that is certified under section 3001(c)(5) of the Public Health Service Act; and
(iii) such function is not intended to interpret or analyze patient records, including medical image data, for the purpose of the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;

(D) for transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results, findings by a health care professional with respect to such data and results, general information about such findings, and general background information about such laboratory test or other device, unless such function is intended to interpret or analyze clinical laboratory test or other device data, results, and findings; or

(E) unless the function is intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system, for the purpose of-
(i) displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines);
(ii) supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition; and
(iii) enabling such health care professional to independently review the basis for such recommendations that such software presents so that it is not the intent that such health care professional rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient.[81]

As discussed in Section F below, FDA has published separate guidance documents regarding its interpretation of sections 520(o)(1)(A)-(D) and 520(o)(1)(E).[82]

2. Responsibilities of CDS Device Manufacturers

If software qualifies as a medical device under the FD&C Act, manufacturers of the device must satisfy several regulatory requirements based on the classification of the device (*i.e.*, Class I, II, or III).[83] Devices are classified based on their risk of use.[84] Class I devices carry the least amount of risk, while Class III devices (those that sustain or support life; implants) carry

[81] 21 U.S.C. § 360j(o)(1).
[82] U.S. Food & Drug Admin., *Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act* (Sept. 27, 2019), https://www.fda.gov/media/109622/download [hereinafter, Changes to Existing Medical Software Policies]; 2022 Clinical Decision Support Software Guidance, *supra* note 76).
[83] *See* 21 C.F.R. § 800 *et seq.*
[84] *See* 21 C.F.R. § 860.7.

the greatest amount. As such, regulatory controls are the least stringent for Class I devices and are the most stringent for Class III devices.[85]

All devices regardless of class are subject to "general controls." "General controls are the basic authorities . . . that provide the FDA with the means of regulating devices to ensure their safety and effectiveness," and include provisions related to misbranding; establishment registration and device listing; premarket notification; banned devices; notification, including repair, replacement, or refund; records and reports; restricted devices; and good manufacturing practices.[86] Given their higher risks, Class II and III devices are subject to additional controls to provide reasonable assurances of safety and effectiveness.[87]

All device manufacturers must register as an "establishment" with the FDA and submit listing information for all devices in commercial distribution.[88] However, prior to introducing a device into interstate commerce for commercial distribution, the manufacturer must (unless exempt) first notify the FDA by providing "premarket notification."[89] The premarket notification must set forth the device classification; for certain Class II devices, the actions taken to satisfy special regulatory controls that specifically apply to the device; and, if applicable, clinical trial data.[90]

3. FDA's Enforcement Authority for Misbranded Devices

The FDA can deem devices misbranded that (1) are manufactured by establishments that are not registered with the FDA; (2) are not listed with the FDA; or (3) were not the subject of a required premarket notification.[91] If the FDA finds that a device is misbranded, it may consider taking administrative action, including, but not limited to, issuing a Warning Letter or instituting mandatory recall procedures.[92]

The Warning Letter is the FDA's primary means of notifying regulated industry of violations and achieving prompt voluntary correction requiring the manufacturer to take corrective action.[93] In determining whether to issue a Warning Letter, FDA considers whether: (1) evidence shows that a firm, product, and/or individual is in violation of the law or regulations

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[85] U.S. Food & Drug Admin., *General Controls for Medical Devices*, (Mar. 22, 2018), https://www.fda.gov/medical-devices/regulatory-controls/general-controls-medical-devices.
[86] *Id*.
[87] Class II devices are also subject to "special controls" to provide reasonable assurances of device safety and effectiveness. Special controls are device specific and may include premarket data requirements, special labeling requirements, performance standards, and post-market surveillance. Class III devices must receive premarket approval from the FDA prior to marketing. U.S. Food & Drug Admin., Regulatory Controls, (Mar. 27, 2018), https://www.fda.gov/medical-devices/overview-device-regulation/regulatory-controls.
[88] 21 C.F.R. § 807.20.
[89] 21 U.S.C. § 360(k).
[90] *Id*.
[91] 21 U.S.C. § 352(o).
[92] U.S. Food & Drug Admin., *Regulatory Procedures Manual, Chapter 7: RECALL PROCEDURES* (Jul. 2021), https://www.fda.gov/media/71814/download.
[93] U.S. Food & Drug Admin., *Regulatory Procedures Manual, Chapter 4: ADVISORY ACTIONS* (Jul. 2021), https://www.fda.gov/media/71878/download.

and that failure to achieve adequate and prompt correction may result in agency consideration of an enforcement action; (2) the violation(s) are determined to be of regulatory significance, and the issuance of a Warning Letter is appropriate and consistent with agency policy; and (3) there is a reasonable expectation that the responsible firm and persons will take prompt corrective action.[94]

FDA may also issue a cease distribution and notification order (*i.e.,* a mandatory recall) if, after providing the appropriate person with an opportunity to consult with the agency, FDA finds that there is a reasonable probability that a device intended for human use would cause serious, adverse health consequences or death. The person named in the order must (1) cease distribution of the device; (2) notify health professionals and device user facilities of the order; and (3) instruct these professionals and device user facilities to cease use of the device.[95]

F. Petitioner's Position

It is Petitioner's position that NarxCare does not meet the criteria for non-device CDS set forth in the FD&C Act and, therefore, is a misbranded medical device subject to FDA regulation. FDA should take administrative action to prevent serious, adverse health consequences and death.

1. NarxCare is not non-device CDS.

NarxCare does not satisfy any of the criteria set forth in section 520(o)(1)(A)-(E) of the FD&C Act for non-device CDS products.

a. NarxCare does not satisfy section 520(o)(1)(A).

Section 520(o)(1)(A) applies to a software function that is intended to provide certain types of administrative support for health care facilities. NarxCare is not intended to provide administrative support of a health care facility, including "the processing and maintenance of financial records, claims or billing information, appointment schedules, business analytics, information about patient populations, admissions, practice and inventory management, analysis of historical claims data to predict future utilization or cost effectiveness, determination of health benefit eligibility, population health management, and laboratory workflow." Rather, it is integrated into PDMPs and used as clinical decision support with respect to prescribing and dispensing controlled prescription medications. Therefore, NarxCare does not satisfy 520(o)(1)(A) of the FD&C Act.

[94] *Id*.
[95] 21 C.F.R. § 810.10(a).

b. NarxCare does not satisfy section 520(o)(1)(B).

Section 520(o)(1)(B) applies to a software function that is intended for maintaining or encouraging a healthy lifestyle and that is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition. NarxCare is not intended for maintaining or encouraging a healthy lifestyle, and its intended use is related to the mitigation or prevention of disease.

As FDA explains in its guidance on 520(o)(1)(A)-(D), FDA considers a product with an intended use for maintaining or encouraging a "healthy lifestyle" to mean a product with an intended use that encourages or maintains a "general state of health or healthy activity," as defined in FDA's General Wellness Guidance.[96] The General Wellness Guidance defines general wellness products as those that (1) are intended for *only* general wellness use, and (2) present a low risk to the safety of users and other persons (*i.e.*, are not invasive, not implanted, and do not involve intervention or technology that poses a risk of safety, such as risks from lasers or radiation exposure).[97]

There are two categories of general wellness intended uses: (1) an intended use that relates to maintaining or encouraging a general state of health or a healthy activity (*e.g.,* apps with healthy lifestyle claims, such as weight management, physical fitness, or stress management, that do not relate to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition); and (2) an intended use that relates the role of healthy lifestyle in helping to reduce the risk or impact of certain chronic diseases or conditions and where it is well understood and accepted that healthy lifestyle choices may play an important role in health outcomes for the disease or condition.[98] Given that the second category makes reference to diseases or conditions, to avoid device designation, such products must have an intended use to: (1) "promote, track, and/or encourage choice(s), which, as part of a healthy lifestyle, may help to reduce the risk of certain chronic diseases or conditions"; or (2) "promote, track, and/or encourage choice(s) which, as part of a healthy lifestyle, may help living well with certain chronic diseases or conditions."[99] An example is a product that "tracks activity sleep patterns and promotes healthy sleep habits, which, as part of a healthy lifestyle, may help reduce the risk for developing type 2 diabetes."[100]

NarxCare analyzes PDMP and non-PDMP data to produce patient risk scores that influence health care providers' prescribing decisions in an effort to mitigate or prevent SUDs, including the disease of opioid use disorder. Furthermore, the software does not relate to the role of a healthy lifestyle by the end user, unlike the examples set forth in FDA's General Wellness Guidance. As such, NarxCare does not satisfy section 520(o)(1)(B) of the FD&C Act.

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[96] U.S. Food & Drug Admin., *Changes to Existing Medical Software Policies*, *supra* note 82; U.S. Food & Drug Admin., *General Wellness: Policy for Low Risk Devices* (Sept. 27, 2019), https://www.fda.gov/media/90652/download.

[97] U.S. Food & Drug Admin., *General Wellness: Policy for Low Risk Devices, supra* note 96.

[98] U.S. Food & Drug Admin., *Changes to Existing Medical Software Policies, supra* note 82; *General Wellness:* Policy for Low Risk Devices*, supra* note 96.

[99] U.S. Food & Drug Admin., *General Wellness: Policy for Low Risk Devices, supra* note 96.

[100] *Id.*

c. NarxCare does not satisfy section 520(o)(1)(C).

Section 520(o)(1)(C)(iii) applies to a software function intended to serve as electronic patient records, so long as, among other things, "such function is not intended to interpret or analyze patient records, including medical image data, for the purpose of the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition." However, NarxCare is intended to interpret or analyze patient records for the purpose of the mitigation or prevention of SUDs, including the disease of opioid use disorder. Therefore, the software does not satisfy section 520(o)(1)(C).

d. NarxCare does not satisfy section 520(o)(1)(D).

Section 520(o)(1)(D) applies to a software function intended for "transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results . . . unless such function is intended to interpret or analyze clinical laboratory test or other device data, results, and findings." NarxCare does not satisfy 520(o)(1)(D) because, to the extent it could be construed as incorporating data from a clinical laboratory or other medical device, the software is intended to interpret or analyze PDMP and non-PDMP data to produce predictive risk scores for SUDs, including the disease of opioid use disorder.

e. NarxCare does not satisfy section 520(o)(1)(E).

Section 520(o)(1)(E) sets forth four additional criteria a software function must satisfy to be considered non-device CDS and excluded from regulation as a medical device. FDA's guidance on Subsection (E) summarizes the four criteria and establishes defined terms as follows:

> Non-Device CDS software functions do not acquire, process, or analyze images, signals from an in vitro diagnostic device (IVD), or patterns or signals from a signal acquisition system (Criterion 1). Non-Device CDS software functions display, analyze, or print medical information (Criterion 2) in order to provide recommendations about a patient's care to an HCP user (Criterion 3) . . . Non-Device CDS software functions provide sufficient information about the basis for the recommendations to the HCP user, so that the user does not rely primarily on any of the recommendations to make a clinical decision about an individual patient (Criterion 4).[101]

The guidance also explains that certain CDS functions are excluded from the definition of a device by subsection (E) only "if the software functions meet *all* of the . . . [subsection's] four criteria . . ."[102] However, NarxCare does not satisfy "Criterion 3" (section 520(o)(1)(E)(ii)) or "Criterion 4" (section 520(o)(1)(E)(iii)).

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[101] 2022 Clinical Decision Support Software Guidance, *supra* note 76.
[102] *Id*. (Emphasis added).

i. Criterion 3

With respect to Criterion 3—software functions "intended for the purpose of supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition"—FDA's guidance states:

> FDA interprets Criterion 3 to refer to software that provides condition-, disease-, and/or patient specific recommendations to an HCP to enhance, inform and/or influence a health care decision but is not intended to replace or direct the HCP's judgment . . . [I]n cases where a software function provides a specific preventive, diagnostic or treatment output or directive, the software function fails Criterion 3 because it is not intended for the purpose of supporting or providing recommendations under section 520(o)(1)(E)(ii) . . .
>
> FDA considers [the level of software automation] when determining whether a software function is being used to enhance, inform and/or influence an HCP's decision-making (satisfying Criterion 3) or rather, to substitute, replace, or direct the HCP's judgment (failing Criterion 3).
>
> Automation bias is the propensity of humans to over-rely on a suggestion from an automated system . . . Automation bias may be more likely to occur if software provides a user with a single, specific, selected output or solution rather than a list of options or complete information for the user to consider. In the former case, the user is more likely to accept a single output as correct without taking into account other available information to inform their decision-making.
>
> This understanding of automation bias informs FDA's interpretation of "support or provide recommendations" in Criterion 3, as well as FDA's interpretation that Non-Device CDS software functions allow an HCP to independently review the basis for the recommendations presented by the software so that they do not rely primarily on such recommendations, as described in Criterion 4 . . .
>
> [S]oftware that provides a specific preventive, diagnostic, or treatment output or directive . . . would not satisfy Criterion 3. FDA interprets the purpose of such software functions as not supporting or providing recommendations to an HCP, but rather as directing the HCP to take a specific action and substituting for their judgment . . .
>
> Note that FDA considers software that provides information that a specific patient "may exhibit signs" of a disease or condition or

> *identifies a risk probability or risk score for a specific disease or condition* as providing a specific preventive, diagnostic, or treatment output. Therefore, such software would not satisfy Criterion 3. . .
>
> [A] [s]oftware function that identifies patients with *possible diagnosis of opioid addiction based on analysis of patient-specific medical information, family history, prescription patterns, and geographical data . . . is a device function*. It does not meet Criterion 3 because it provides a specific diagnostic or treatment output or directive.[103]

Similar to the examples emphasized above, NarxCare's algorithms analyze patient-specific medical history and prescription patterns drawn from the PDMP (*i.e.*, number of providers, number of pharmacies, MMEs dispensed, overlapping prescription days, and potentiating medications) and non-PDMP information, which may include criminal history, payment method, and geographical data, to "calculate a patient's risk of a host of outcomes, including overdose and addiction."[104] In other words, the software produces risk score outputs intended to prevent accidental drug poisonings and the disease of opioid use disorder and other SUDs.

NarxCare's risk scores are also susceptible to automation bias given that prescribers increasingly fear potential legal repercussions related to prescribing opioids and other controlled medications. For example, a prescriber who sees a report with a moderate to high NarxScore or overdose risk score very likely could, without further investigation of the patient's health record, interpret the score as a "do not prescribe" directive and decide to not prescribe an opioid medication to a patient with pain. In short, NarxCare does not just influence prescribers and dispensers when determining whether a controlled medication is appropriate for a patient and the associated risks to that individual—it often replaces their judgement altogether. Therefore, NarxCare cannot satisfy section 520(o)(1)(E)(ii) of the FD&C Act.

ii. Criterion 4

With respect to Criterion 4—"enabling such health care professional to independently review the basis for such recommendations . . ."—FDA's guidance provides:

> In order to be excluded from the definition of a device under section 520(o)(1)(E) of the FD&C Act, the software function must be intended to enable HCPs to independently review the basis for the recommendations presented by the software so that they do not rely primarily on such recommendations, but rather on their own judgment, to make clinical decisions for individual patients . . .

[103] *Id*. (emphasis added).
[104] Appriss Health, *NarxCare*, at 1.

> FDA does not consider software functions intended for a critical, time-sensitive task or decision to meet Criterion 4, because an HCP is unlikely to have sufficient time to independently review the basis of the recommendations . . .
>
> In order to describe the basis for the recommendations, regardless of the complexity of the software and whether or not it is proprietary, the software output or labeling should provide adequate background information in plain language on the input(s), algorithm logic or methods, datasets, and validation. Relevant sources should be identified and available to the intended user (*e.g.*, clinical practice guidelines with the date or version, published literature, or information that has been communicated by the CDS developer to the intended user) and understandable by the intended user (*e.g.*, data points whose meaning is well understood by the intended user). In order to enable independent evaluation of its basis, the recommendation should be based on information whose meaning could be expected to be independently understood by the intended HCP user (*e.g.*, the inputs used to generate the recommendations are identified, the recommendations are based on inputs that do not omit material information, and the quality and robustness of the datasets or clinical studies are described).

Bamboo does publish materials setting forth plain language explanations of how the five principal PDMP inputs are used to compute NarxScores and literature supporting the use of such inputs. It has also published an (albeit flawed) external validation study of its narcotic score. However, as explained above, Petitioner has not identified published materials setting forth adequate background, rationale, evidence, or validation on the use of other data inputs, including non-PDMP inputs used in calculating predictive risk scores. Furthermore, the narcotics score is the only risk score that is purported to have been externally validated, while NarxCare's sedative score, stimulant score, and composite overdose risk score apparently have not been externally validated. As a result, HCPs and dispensers cannot independently evaluate the basis of such scores and, therefore, NarxCare does not satisfy section 520(o)(1)(E)(iii) of the FD&C Act.

In short, because the NarxCare score is "simply presented to prescribers… without any way to independently evaluate its veracity,"[105] who may rely on it in decision making, the software does not satisfy section 520(o)(1)(E) of the FD&C Act, which requires that non-device CDS software functions provide sufficient information to allow for independent review of the basis for the recommendations to the HCP user, so that the user does not rely primarily on any of the recommendations to make a clinical decision about an individual patient.

[105] Cathleen London, *Predicting Drug Diversion: The Use of Data Analytics in Prescription Drug Monitoring*, The Student Journal of Information Privacy Law (citing Jennifer D. Oliva*, Prescription Drug Policing: The Right to Health-Information Privacy Pre and Post Carpenter*, 69 DUKE L.J. 775 (Jan. 2020)).

2. NarxCare is a misbranded CDS device subject to FDA regulation.

NarxCare is a medical device because the software is intended for use in the mitigation or prevention of SUDs, including the disease of opioid use disorder, and does not satisfy the criteria for non-device CDS. Yet, a search by the Petitioner of FDA's publicly available establishment registration and device listing databases, unique device identification database, and premarket notification (510(k)) database, did not yield any relevant results using search terms such as *Bamboo*, *Bamboo Health*, *Appriss Health*, and *NarxCare*. Furthermore, a search of FDA's device product classification database using terms such as *opioid* and *software* did not yield any results for NarxCare-type software that identifies patients with potential opioid addiction. However, the search did yield results for CDS software that, like NarxCare, uses algorithms to analyze data inputs to produce predictive clinical decision support. For example, a partial product category listing for "Burn Resuscitation Decision Support Software" states:

> Definition: The burn resuscitation decision support system (BRDSS) is intended for use in *prediction* of hourly fluid volume during initial 24 hours of burn resuscitation. It is intended for patients who have greater than 20% total body surface area burn.
>
> Technical Method: BRDSS is a *software based calculator that uses an algorithm* to calculate resuscitation volume *using* physiological *data inputs*. The algorithm used is developed by the manufacturer and may not be the typical algorithm used in standard practice to calculate fluid management for burn patients.
>
> Submission Type: 510(k) [premarket notification required]
>
> Device Class: 2[106]

Given these results, the Petitioner has reason to believe that Bamboo is required to, but has not yet registered as an establishment, listed NarxCare as device, and submitted a premarket notification.[107] Therefore, NarxCare is misbranded and subject to enforcement action by the FDA.

Most importantly, Bamboo's failure to comply with the FD&C Act and FDA regulations means that FDA has not substantiated NarxCare's safety and effectiveness. Yet, the software has been integrated into PDMPs across the country, is used "millions of times" per day, and continues to have a significant impact on medical decision making to the detriment of patients with pain and other marginalized groups.

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[106] U.S. Food & Drug Admin., Product Classification, https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm?id=PDT (last updated March. 13, 2023) (emphasis added).

[107] Based on the comparative partial listing set forth above, there is no reason to believe that NarxCare would be exempt from submitting a premarket notification.

3. FDA should take prompt action to prevent serious, adverse health consequences or death.

The FDA should promptly take appropriate action within its authority, including issuing a Warning Letter and commencing mandatory recall procedures, to prevent serious adverse health consequences or death.

There is evidence that Bamboo is in significant violation of the FD&C Act and FDA regulations that could justify FDA enforcement action if not promptly resolved. Therefore, FDA should issue Bamboo a Warning Letter requiring it to comply with all applicable provisions of the Act and FDA regulations to prevent serious, adverse health consequences and death.

Additionally, there is a reasonable probability that NarxCare could cause serious, adverse health consequences or death for people with a legitimate need for controlled prescription medications given that (1) NarxCare is used millions of times per day; (2) the software has a significant impact on prescribers' and dispensers' judgment regarding treatment with controlled medications; and (3) reducing access to medically necessary treatments can have devastating outcomes, as described in Section II-C above, especially in light of the nation's drug poisoning crisis. Therefore, FDA should commence mandatory recall procedures to limit the threat of serious adverse health consequences and death of patients who are negatively impacted by NarxCare.

III. Conclusion

For the reasons discussed above, the Petitioner asks FDA to deem NarxCare a misbranded device and promptly take appropriate administrative action to prevent serious, adverse health consequences and death.

IV. Environmental Impact

The Petitioner claims a categorical exclusion from the requirements of an environmental assessment or environmental impact statement pursuant to 21 C.F.R. § 25.30.

V. Economic Impact

The Commissioner has not requested that the Petitioner submit an economic impact statement.[108]

VI. Certification

I, the undersigned Petitioner, certify that, to the best of my knowledge and belief, this petition includes all information and views upon which this petition relies, and that it includes representative data and information known to me that is unfavorable to the petition.

[108] 21 C.F.R. § 10.30(b)(3).

Thank you for your attention to this important public health matter. We look forward to your prompt responsive actions and written reply.

Sincerely,

/s/ Lynn Webster

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Senior Fellow

Michael C. Barnes
Chairman