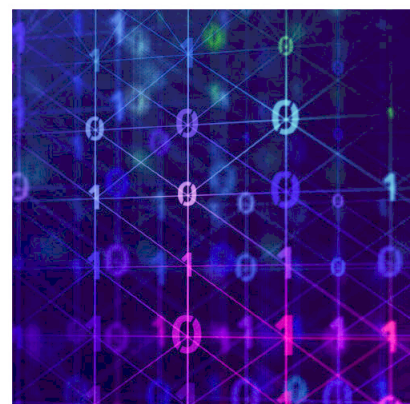
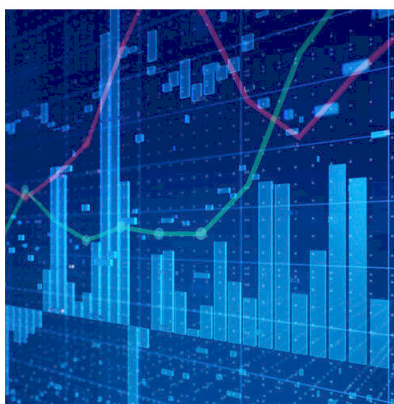




**U.S. FOOD & DRUG
ADMINISTRATION**

Cannabis Derived Products Data Acceleration Plan

Exploring Novel Data Sources to Help Inform Cannabis Derived Product
Safety and Quality Gaps



OCTOBER 2021

Introduction

Cannabis-derived products (CDP) and other emerging substances present unique challenges to one of the U.S. Food and Drug Administration's (FDA) core responsibilities: to protect public health by ensuring that products such as human and veterinary drugs, human and animal foods, dietary supplements, and cosmetics meet required safety and quality standards.¹ To best protect the public health, FDA needs robust information about potential safety problems or adverse events associated with FDA-regulated products, including CDPs. FDA also needs information about general patterns of product use and emerging trends—and it needs this information in close to real time, so that the Agency can deploy its limited resources quickly and effectively. We believe that new approaches to detecting safety signals and other insights using diverse data sources and rigorous analytical methods can contribute significantly to FDA's ability to respond to emerging and rapidly evolving product areas, like the CDP market.

Enhancing the FDA's safety surveillance and signal detection capabilities is critically important to understanding current and emerging CDP market segments. The FDA needs a suite of modern, flexible tools and processes that can be used across cannabinoids and other emerging substances to complement existing safety monitoring capabilities:

- **Cannabidiol (CBD):** The CBD market has grown rapidly since 2018 and is now estimated to be a \$4.6 billion market. Current forecasts predict the market will quadruple by 2026.² The current CBD market is complex, spanning thousands of products including one FDA approved drug containing CBD, Epidiolex, and unapproved products marketed as drugs, foods, beverages, cosmetics, dietary supplements, and products marketed for animals. Products are sold across a diverse set of distribution channels with a large percentage of sales occurring via e-commerce or dispensaries, channels that are not easily tracked by traditional third-party data providers or surveillance methods.
- **Emerging Cannabinoid Markets:** In addition to CBD, the current CDP market includes emerging cannabinoids such as delta-8-tetrahydrocannabinol (Delta-8 THC), delta-10 tetrahydrocannabinol (Delta-10 THC), cannabinal (CBN), tetrahydrocannabivarin (THCV), and cannabigerol (CBG), among others. While the emerging cannabinoid market is still nascent, it is a rapidly evolving digital-forward marketplace that is an emerging public health concern. The rise of Delta-8 THC products typifies many of the safety concerns FDA has with products that contain these other emerging cannabinoids: known or potential safety problems, lack of labeling information, potentially misleading product claims and product adulteration.³ We also note the rising rates of co-use of cannabis and CDPs together with nicotine products, which may pose unique public health concerns.⁴

Many CDPs are marketed by manufacturers for purported therapeutic or medical uses, even though the products have not been evaluated or approved by FDA. Selling unapproved products with unsubstantiated therapeutic claims is not only a violation of federal law, but also can put patients at risk, as these products have not been proven to be safe or effective. Many CDPs also

¹ <https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd>

² Brightfield Group 2020 CBD Market Data

³ <https://www.fda.gov/consumers/consumer-updates/5-things-know-about-delta-8-tetrahydrocannabinol-delta-8-thc>; <https://emergency.cdc.gov/han/2021/han00451.asp>

⁴ For example, see: Fataar F, Hammond D. The Prevalence of Vaping and Smoking as Modes of Delivery for Nicotine and Cannabis among Youth in Canada, England and the United States. *International journal of environmental research and public health*. 2019;16(21):4111.

violate the Federal Food, Drug, and Cosmetic Act in various other ways, for example by violating the various statutory and regulatory requirements for food additives.

Overall, the growth of the CDP market continues to outpace the growth in the science and our understanding of the public health implications of these products. The size and complexity of the CDP market—coupled with the public health concerns associated with CDPs—requires the efforts of diverse stakeholders, including FDA and other federal, state, local, territorial, and tribal government entities, academia, and industry, to identify new ways of detecting safety signals and accelerating appropriate research studies, including but not limited to rigorous toxicology studies.

To advance this work, FDA has developed a CDP Data Acceleration Plan.

FDA's CDP Data Acceleration Plan (DAP)

The CDP DAP (or DAP) is a portfolio of pilot initiatives and partnerships focused on advancing data-driven safety signal detection and building advanced technology capabilities. The DAP's primary goal is to leverage novel data sources and advanced data analytics to identify current and emerging safety vulnerabilities in the CDP market. The DAP is also focused on forging government data partnerships and championing scientific research to evaluate safety and consumer vulnerabilities.

Evaluating Current Data Sources

The first phase of the DAP focused on evaluating data sources to better understand how the current CDP data landscape can inform key data gaps outlined in the [FDA's CDP Public Docket](#) and additional gaps identified through an internal discovery process. The FDA's Cannabis Product Committee (CPC) evaluated over thirty data sources or providers to understand the key capabilities and limitations of the available data sets or data collection methods. Sources ranged from third party purchase data and surveys to traceability systems and mobile apps. The discovery process and analysis identified a key CDP capability and data gap for the FDA – *leveraging online data to help inform safety research and signal detection*. Improving this capability will allow the FDA to:

- Proactively identify CDP potential safety signals including adverse events from online activity and content
- Monitor and evaluate a digital-first market with thousands of companies across multiple product categories and forms
- Understand CDP usage motivations and patterns
- Understand how CDP safety misinformation impacts consumer behavior and identify opportunities for education and outreach
- Inform future social science, scientific and healthcare related CDP research

The discovery process also highlighted several opportunity areas from a healthcare perspective, including:

- Understanding the role of human and animal healthcare providers (HCPs) in promoting or preventing CDP consumption
- Determining if consumers are replacing approved prescription and over-the-counter drug products with CDPs, which can have serious consequences from a health perspective

- Evaluating if animal and human healthcare data can help to inform CDP safety gaps or identify consumer vulnerabilities
- Understanding HCP knowledge, practices, and needs related to improving reporting of CDP adverse events

Cultivation of Collaborative Partnerships

Critical to enriching the discovery process and path forward, is the development of opportunities for collaboration across stakeholders who offer varied experiences and resources, and who may contribute to these data sets. Over the past few years, the FDA has focused on strengthening working relationships with other federal agencies; various international regulatory bodies; and states, as well as state-based regulatory organizations. For example, the FDA is:

- exploring opportunities to partner with states, including to gain insights on important data that states may be gathering on CDP usage and adverse events
- developing an inter-Agency scientific agenda for CDP through a new [National Toxicology Program](#) pilot initiative
- growing capabilities for collaborative pursuit of CDP public health strategy and epidemiological intelligence with the CDC

Accelerating CDP Scientific Safety and Toxicology Research at the FDA

Improving safety signal detection through enhanced data science capabilities will help inform CDP safety data gaps. However, data gaps that require other scientific approaches, such as rigorous toxicology studies, still exist. The FDA is proactively conducting research in key areas to inform data gaps, including several toxicology, safety, and quality initiatives which currently include: the impact of CBD on the male reproductive system; transdermal penetration and pharmacokinetics of CBD; the impact of CBD on neurological development; further evaluation of the risk of liver injury from CBD; characterization of chemical constituents for smoked hemp flower and vaped cannabis products; various *in vivo and vitro* toxicity studies; and ingredient labeling accuracy. However, FDA continues to encourage industry and remind them of their responsibility to develop the needed data, aligned with FDA's current data standards, to ensure products are safe.

Piloting CDP Data Acceleration Initiatives

A key pillar of the DAP is piloting data science initiatives to test the feasibility of using advanced analytical tools and available data sources to detect safety signals associated with CDPs and generate other information on safety risks associated with specific products, or with categories of products. The pilot projects provide opportunities to:

- Build incremental capabilities to complement current FDA regulatory science and surveillance tools
- Capture actionable insights in short timeframes, typically <12 months
- Inform key CDP regulatory or policy-related data gaps
- Explore the utility of novel data sources and methods
- Test outputs to understand what type of online and healthcare data sources can meet the FDA's rigorous data standards for CDP data
- Help build flexible safety signal detection and surveillance capabilities that can be used beyond CDP—i.e., for other digital-forward marketplaces and emerging substances

The list below includes projects that are currently in the feasibility assessment phase as well as potential future projects. These projects involve FDA’s own scientific and regulatory programs, as well as a variety of stakeholders, including academics, data scientists (e.g., through our CERSI network), and industry (e.g., data providers) to execute these initiatives.

Sample Pilot Projects⁵	Overview
Analyze Online Certificates of Analysis (COA) to Evaluate Quality Communication vs. Actual Ingredients	<p><i>COAs are used by product manufacturers as a tool to communicate product quality to consumers and communicate that the product’s THC levels are below the 0.3% threshold set in the Farm Bill.</i></p> <p>Primary Objective: Map product COA data to the data collected via the FDA’s CBD product sampling project⁶, which is testing hundreds of hemp products for cannabinoids, toxic elements, pesticides, residual solvents, and microbial pathogens. Compare product COA data with the FDA analytical data on the product sold in-market to identify inconsistencies and quality issues.</p> <p>Secondary Objective: Determine how consumers access and use COA information. What are the hurdles to accessing COA documents? What are opportunities to improve COA access and communication to consumers?</p>
Identify CDP Safety Issues and Improve Safety Signal Detection via Online Data	<p><i>Consumer-generated online data for CDPs are potentially rich sources of information to identify safety issues and adverse events.</i></p> <p>Objective: Evaluate how online data (e.g., Reddit, consumer reviews) can complement traditional signal detection and adverse event surveillance systems (e.g., FAERS, CAERS, AERS) or identify issues that may not be easily captured via traditional systems.</p>
Pilot Real-time Surveillance Tools for Emerging Cannabinoids (e.g., Delta-8 THC, Delta-10 THC)	<p><i>The emerging cannabinoid market often starts online or via dispensaries – two channels where traditional safety, market and adverse event reporting systems do not have data-driven surveillance capabilities.</i></p> <p>Objectives: Detect safety signals and usage patterns associated with emerging CDPs in real-time. Inform future surveillance capability development for emerging trends beyond CDPs and identify potential safety issues before the issues become mainstream. Create actionable dashboards and data sets that can be used to inform regulatory science and enforcement (when appropriate) across the unapproved CDP market.</p>

⁵ Protecting consumer privacy is always a top FDA priority. All projects will use publicly available data or data sets where the FDA is able to legally access the data (e.g., through contracts, interagency agreements) and apply appropriate privacy-preserving approaches to protect any potential identifiable information.

⁶ <https://sam.gov/opp/7990bed5f9aa450c9e279ea37de3e1aa/view>

<p>Understand the Current CDP Market Landscape to Inform Enforcement</p>	<p><i>The current online CDP market spans thousands of products marketed as foods, beverages, cosmetics, dietary supplements, and products marketed for animals. For example, over 40% of CBD products are sold via e-commerce channels¹. In addition, a high percentage of delta-8 THC and other emerging cannabinoid product categories often originate online.</i></p> <p>Objective: Identify automated processes and technical solutions to evaluate the online product landscape and identify products to prioritize for enforcement. Pilot one category to evaluate technical feasibility and enforcement application.</p>
<p>Evaluate the Impact of Online Misinformation on CDP Quality and Safety Perceptions</p>	<p><i>Many products that purport to contain CBD and other cannabinoids are marketed for unsubstantiated therapeutic or medical uses, even though the products have not been evaluated nor approved by FDA.</i></p> <p>Objective: Develop a data-driven framework and process to understand how online safety misinformation may create consumer safety vulnerabilities and impact consumer behavior (e.g., replacing FDA approved drugs with unproven CDPs)</p>
<p>Determine the Impact of Healthcare Providers' CDP Perceptions on Usage and Safety</p>	<p><i>Based on a recent cannabis study, "Over two-thirds (68.9%) of clinicians surveyed believe that cannabis has medicinal uses and just over a quarter (26.6%) had ever recommended cannabis to a patient."⁷ While this study is focused on cannabis, it raises many questions about the impact of HCPs on CDP usage and safety.</i></p> <p>Objective: Leverage qualitative and quantitative data sources to understand HCP's CDP safety perceptions, usage perceptions and current CDP patient interactions. Leverage insights to identify potential consumer safety issues, inform an overall CDP education and outreach strategy and improve reporting of CDP adverse events.</p>
<p>Determine if Healthcare Data Can Inform CDP Safety and Usage Gaps</p>	<p><i>Consumers are using CDPs for a variety of health-related concerns. A key gap is to understand if usage is being captured in healthcare data systems. If so, can the data help to inform regulatory science and safety signal detection?</i></p> <p>Objective: Identify specific initiatives and key research questions to test if healthcare data can be used to inform safety signal detection and identify consumer vulnerabilities across a variety of potential health topics including chronic pain and mental health.</p>

⁷Gillian L. Schauer, Rashid Njai, and Althea M. Grant. Clinician Beliefs and Practices Related to Cannabis. Cannabis and Cannabinoid Research, <https://www.liebertpub.com/doi/abs/10.1089/can.2020.0165>.

Looking Forward: Modernizing Signal Detection Capabilities is Critical to Keeping Pace with Emerging Substances

The current CBD market is complex, spanning thousands of products including one FDA approved drug containing CBD, Epidiolex, and unapproved products marketed as drugs, foods, beverages, cosmetics, dietary supplements, and products marketed for animals. The diversity of consumer motivations and experiences with CDP is critical to understanding and identifying quality and safety issues. The fragmented and dynamic CDP market, with hundreds of small manufacturers selling products online, is rife with potential quality and safety concerns. The FDA needs a better understanding of the quality and safety systems that are currently in place across the overall supply chain from origin, manufacturing, and distribution to consumer usage. Leveraging novel data sources and partnering across the government to enhance our market knowledge will help the FDA keep pace with emerging digital-forward industries. Ultimately, these efforts will support the FDA in its mission to promote the public health and keep consumers safe.