Use of Orally Ingestible Unapproved Prescription Drug Products Containing Fluoride in the Pediatric Population

Public Meeting Summary Report

REAGAN-UDALL FOUNDATION FOR THE FDA

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Executive Summary

On July 23, 2025, the Reagan-Udall Foundation for the FDA (the Foundation), in collaboration with the Food and Drug Administration (FDA), hosted a public meeting titled "Use of Orally Ingestible Unapproved Prescription Drug Products Containing Fluoride in the Pediatric Population."

The meeting brought together a diverse group of stakeholders including clinicians, researchers, parents, and patient advocates to discuss the use of orally ingestible unapproved prescription drug products containing fluoride in pediatric populations. The goal was to collect information illustrative of all perspectives on clinical use, safety concerns, and implications of the continued availability or removal of ingestible fluoride drug products (tablets and drops) that have been used since the 1940s to help prevent tooth decay. The meeting was not a decision-making meeting, nor was it about adding fluoride to drinking water. The meeting format included scientific presentations, parental experiences, and panel discussions, followed by comments from members of the public.

The discussions revealed two central tensions. Some viewed ingestible fluoride drug products as a vital preventive tool against pediatric dental caries, especially in communities lacking access to fluoridated water. Parental and clinical experiences underscored how these products can help bridge gaps in oral health, particularly for children in underserved areas. Other clinicians and researchers highlighted evidence that ingestible fluoride drug products may pose systemic risks, including neurocognitive and endocrine side effects. Some emphasized the lack of randomized controlled trials, the limited scope of existing research, and uncertainties about safe exposure thresholds.

Panel discussions emphasized the need for rigorous, evidence-driven evaluation of both risks and benefits. While some experts argued that available data support modest reductions in cavities with fluoride use, others cited reviews and longitudinal studies pointing to possible harm, especially in developing brains.

Public comment comprised over 4,000 written submissions to the Federal Register Docket and 20 oral comments during the public meeting, reflecting a wide range of perspectives. Many comments emphasized the role of ingestible fluoride drug products in preventing tooth decay and improving access to preventive oral health care, particularly in under-resourced communities. Others highlighted safety uncertainties, lack of FDA approval, and availability of topical alternatives. Additional themes included parental autonomy, gaps in professional education, and broader links between oral health, quality of life, and public trust. Collectively, public input revealed persistent polarization that extends beyond clinical practice into broader debates over public health, institutional credibility, and regulatory standards.

Overall, the meeting and public input demonstrated the current reliance on ingestible fluoride drug products in certain pediatric populations, as well as the urgent need for stronger evidence to determine their safety and efficacy in modern contexts.

Introduction and Opening Remarks

In May 2025, the U.S. Food and Drug Administration (FDA) initiated a review of orally ingestible unapproved prescription drug products containing fluoride. These ingestible fluoride drug products, available as tablets and drops, have been prescribed to children since the 1940s for the prevention of dental caries. Despite their long-standing use, they remain unapproved because these drugs have never been formally evaluated by FDA for safety, effectiveness, or quality.

At the FDA's request, the Reagan-Udall Foundation for the FDA (the Foundation) convened, on July 23, a public meeting titled "Use of Orally Ingestible Unapproved Prescription Drug Products Containing Fluoride in the Pediatric Population." The goal was to gather a wide range of perspectives and input from parents, advocates, clinicians, researchers, and members of the public on the use, safety, and role of these products in children.

Opening remarks provided by Dr. Jacqueline Corrigan-Curay from the FDA's Center for Drug Evaluation and Research (CDER) highlighted that the meeting was convened to collect information on orally ingestible unapproved prescription drug products containing 0.25 to 1 milligram of sodium fluoride. These products are prescribed for the prevention of pediatric dental caries. Dr. Corrigan-Curay emphasized that the meeting was not a decision-making forum and would not address water fluoridation, topical fluoride products, or over-the-counter fluoride-containing products.

Background data show that prescriptions for ingestible fluoride declined by approximately 40% between 2020 and 2024, with the steepest reductions occurring in children aged three to nine. Children between three and nine years old continue to account for about two thirds of all prescriptions (Figure 1a).[1] Prescribing is concentrated among pediatricians (43%), followed by dentists, with family practitioners, nurse practitioners, and other specialties contributing smaller shares (Figure 1b).[1] This context framed the central challenge of the meeting: discussing whether and for whom these long-relied-upon products remain appropriate, given current scientific knowledge about risks and benefits.

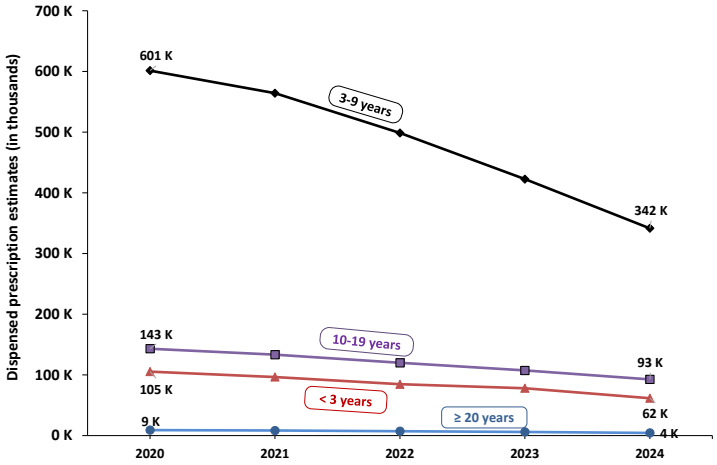

Figure 1a: From Jacqueline Corrigan-Curay's Opening Remarks
Nationally estimated number of prescriptions dispensed for ingestible prescription sodium fluoride products, by patient age, from U.S. outpatient pharmacies, 2020 – 2024. K represents thousands.

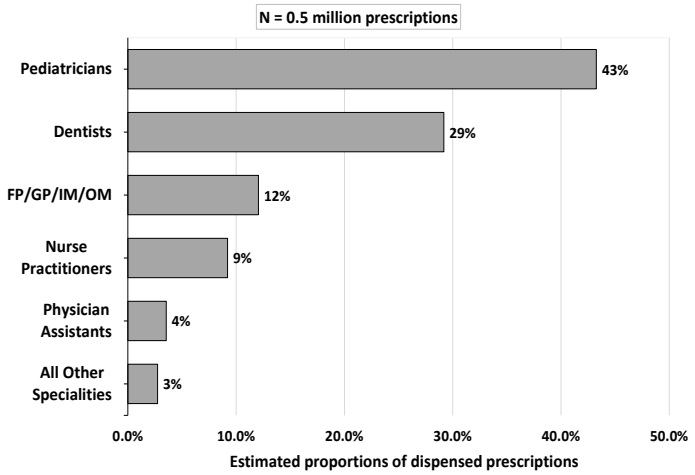

Figure 1b: *From* Jacqueline Corrigan-Curay's Opening Remarks
Nationally estimated proportions of prescriptions dispensed for ingestible sodium fluoride products, by prescriber specialties, from U.S. outpatient pharmacies, 2024

[1] IQVIA National Prescription Audit New to Brand™, time period 2020-2024, data extracted May 2025

Session 1: Scope of Product Use in Clinical Practice

The first session of the meeting examined how ingestible fluoride drug products are used in pediatric practice, what experiences patients and families have had with these products, and how clinicians and researchers assess their current role in oral health. The session focused on the necessity of ingestible fluoride drug products, especially in communities without water fluoridation; the clinical decision-making processes guiding their prescription; and the extent to which current evidence supports or challenges their continued use. The session sought to establish a picture of how the products function in practice, with the intent of addressing safety concerns in later discussions.

Clinical, Academic, and Advocacy Perspectives

Clinician presentations opened with a perspective emphasizing fluoride as a naturally occurring mineral, comparable to other essential nutrients, with its benefits and risks determined by dosage. This view stressed that insufficient systemic fluoride exposure during childhood tooth development results in weaker enamel and heightened vulnerability to cavities, while excessive intake may lead to dental fluorosis. The clinical challenge is to evaluate whether a child's environment through access to fluoridated water, naturally occurring fluoride in groundwater, and diet provides adequate exposure. When it does not, clinicians prescribe ingestible fluoride drug products at appropriate dosages to ensure proper enamel formation and long-term oral health.

This approach was further illustrated by experiences in states such as Utah, where local fluoridation policies vary county by county, requiring case-by-case assessments. In communities with fluoridated water, ingestible fluoride drug products are generally not prescribed; however, in non-fluoridated areas, drops and tablets were presented as indispensable tools for preventing dental caries. Population-level studies were cited to show that children from non-fluoridated communities experienced higher rates of untreated decay, greater reliance on costly hospital-based dental procedures, and more frequent school absences due to dental pain. In the Utah case study, children in fluoridated communities exhibited stronger enamel and fewer cavities, whereas children from non-fluoridated communities faced significantly higher burdens of preventable disease. These disparities were used to support the premise that ingestible fluoride drug products are critical in places where water fluoridation is not available.

From this perspective, eliminating access to ingestible fluoride drug products would disproportionately harm low-income and rural families. Children in these populations often lack routine preventive dental care, and systemic supplements help offset barriers by strengthening enamel from within during development. Without these tools, the gap in oral health outcomes between children in areas with fluoridated and non-fluoridated water would widen further. The presenter noted that systemic fluoride has been safely and effectively used for decades and remains an essential preventive measure to reduce avoidable suffering, costly interventions, and poor outcomes in pediatric oral health.

The discussion also included an alternative view of the clinical assessment that framed fluoride not as a nutrient but as a drug requiring the highest evidentiary standards. From this perspective, despite decades of widespread use, there are no randomized controlled trials that conclusively

demonstrate the efficacy of ingestible fluoride drug products in preventing cavities. Instead, most available evidence comes from observational studies, which are inherently limited by confounding factors such as socioeconomic status, diet, and access to dental care. Without high-quality trial data, the preventive value of ingestible fluoride drug products remains unproven.

This viewpoint also highlighted safety concerns. Rising rates of dental fluorosis were presented as evidence of overexposure, given the multiple sources of fluoride (Figure 2).[2] Potential neurodevelopmental risks cited in recent literature were raised as additional concerns, suggesting that cumulative exposure may exceed safe thresholds. The presenter also pointed to labeling inconsistencies: toothpaste products carry clear warnings against ingestion, yet ingestible fluoride drug products are prescribed to children at comparable doses. Such contradictions would undermine the rationale for systemic prescribing, the presenter noted. Discontinuation was recommended as the more scientifically defensible and ethically responsible course of action until stronger evidence emerges.

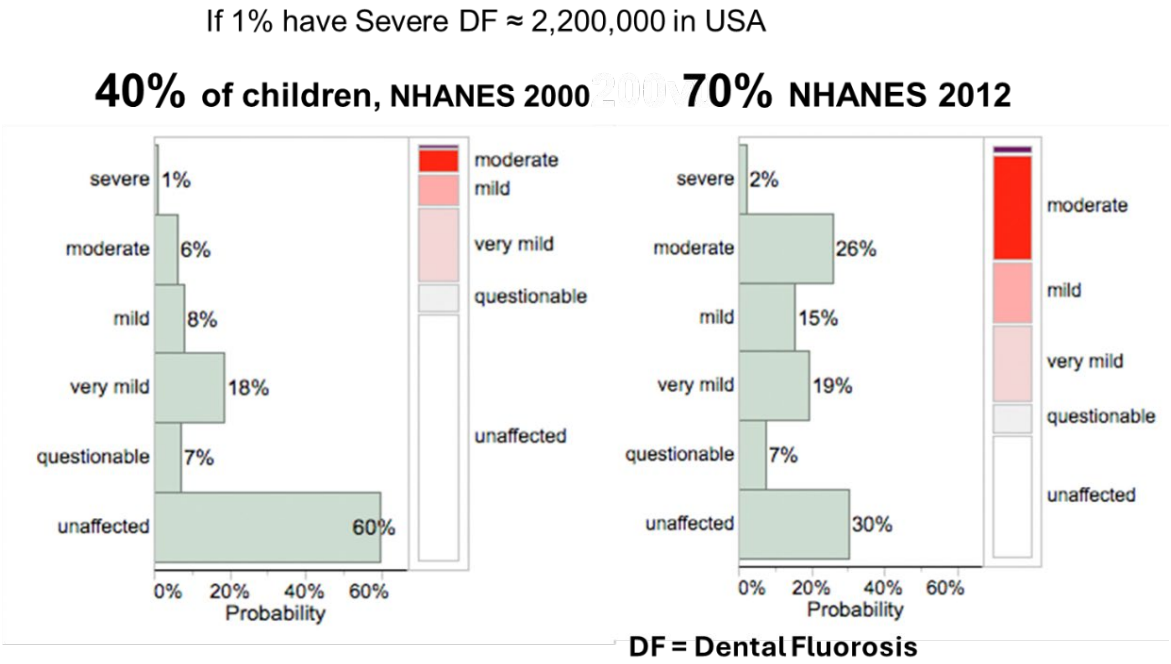

Figure 2: *From Bill Osmunson's Presentation titled*, **"Use of Orally Ingestible Unapproved Prescription Drug Products Containing Fluoride in the Pediatric Population 7/23/2025."** *Increase in dental fluorosis (DF) among U.S. children. According to NHANES data, the prevalence of dental fluorosis rose from approximately 40% in 2000 to 70% in 2012.*

Together, the two perspectives highlighted the central divide in the debate over ingestible fluoride drug products. The first perspective framed systemic fluoride as an established, essential preventive measure, backed by decades of clinical practice, epidemiological studies, and endorsement from professional organizations. Advocates emphasized that ingestible fluoride drug products are especially critical in non-fluoridated areas and that fluoride has proven safe when used at recommended levels. In contrast, the second perspective urged regulators to re-examine systemic fluoride through the lens of modern evidence standards. Without randomized controlled trials confirming efficacy, and with concerns about fluorosis and possible neurodevelopmental

[2] Wiener, R. C., Shen, C., Findley, P., Tan, X., & Sambamoorthi, U. (2018). Dental Fluorosis over Time: A comparison of National Health and Nutrition Examination Survey data from 2001-2002 and 2011-2012. *Journal of dental hygiene: JDH*, *92*(1), 23–29

effects resulting from overexposure, use of ingestible fluoride drug products was described as an insufficiently evidence-supported medical practice that should be discontinued.

At its core, the debate illustrated the challenge facing the FDA, as well as a broader tension in public health policy: How to weigh decades of practice-based and population-level evidence against standards for modern trial data when risks are identified, and how best to incorporate parental choice and clinical judgment in regulatory decision making.

Panel Discussion

To set the stage for further discussion, Dr. George Tidmarsh, Director of CDER, emphasized the FDA's responsibility: Regulatory decisions must be based on the strength of scientific evidence rather than tradition, belief, or anecdote. He acknowledged the importance of parental perspectives and clinical experience but cautioned that these cannot substitute for rigorous data. Citing a 2011 Cochrane review,[3] he highlighted the lack of clear evidence that ingestible fluoride drug products prevent cavities in primary teeth, questioning their effectiveness for the youngest children. He also noted an NIH-supported meta-analysis,[4] which reported an association between community water fluoridation and reductions in cognitive performance among children. The absence of definitive trial evidence demonstrating benefits in young children, combined with emerging data suggesting possible neurodevelopmental risks, highlighted the complexity of weighing risks and benefits. Dr. Tidmarsh tasked the panel with examining these competing dimensions and offering input on how best to weigh evidence for public health policy.

Balancing Evidence and Uncertainty. A few panelists emphasized that any regulatory decision must be guided by a rigorous assessment of both risks and benefits. While anecdotal parental experiences and clinical impressions provide valuable context, such information cannot substitute for robust scientific data. Reference was made to the previously mentioned Cochrane review, which questioned whether prescribing ingestible fluoride drug products to very young children is justified in the absence of robust trial data. Without strong trial data, claims of benefit remain uncertain and cannot serve as a reliable foundation for national policy.

Population-Level Benefits. Other panelists underscored decades of community water fluoridation research demonstrating population-level reductions in dental caries of approximately 25-30%. Although these data come from cross-sectional studies with inherent limitations, the evidence remains meaningful, especially given the consistency of findings across time and populations. From this perspective, ingestible fluoride drug products, though not a perfect substitute, may serve as a practical tool to extend the well-documented benefits of fluoridation to children living in communities without fluoridated water. The panel highlighted that this is particularly important in areas where children already face barriers to preventive dental care, as ingestible fluoride drug products may represent the only feasible option to reduce risk.

Toxicologic and Safety Considerations. A toxicology-focused viewpoint emphasized potential harms with ingestible fluoride drug products, particularly neurodevelopmental effects. Reference

[3] Tubert-Jeannin S, Auclair C, Amsallem E, et al. Fluoride supplements (tablets, drops, lozenges or chewing gums) for preventing dental caries in children. Cochrane Database Syst Rev. 2011;2011(12):CD007592. Published 2011 Dec 7. doi:10.1002/14651858.CD007592.pub2

[4] Taylor KW, Eftim SE, Sibrizzi CA, et al. Fluoride Exposure and Children's IQ Scores: A Systematic Review and Meta-Analysis. JAMA Pediatr. 2025;179(3):282–292. doi:10.1001/jamapediatrics.2024.5542

was made to systematic reviews, including those conducted by the National Toxicology Program, that reported inverse associations between fluoride exposure and cognitive outcomes. While many of these studies were conducted outside the U.S. and involved populations exposed to higher natural fluoride levels than typically seen domestically, panelists noted the consistency of results across multiple countries and exposure pathways. The use of urinary fluoride as a biomarker was cited as supportive evidence that the observed associations may reflect a true biological signal rather than random variation. These concerns were presented as important cautionary notes, particularly given the difficulty of reversing harm once exposure has occurred.

Overexposure Concerns. Panelists also considered the issue of overexposure. Rising rates of dental fluorosis were highlighted as evidence that children may be receiving fluoride from multiple sources including toothpaste, processed foods, and certain bottled waters in addition to prescribed ingestible fluoride drug products. This trend was interpreted by some as suggesting a narrower margin of safety than traditionally assumed, underscoring the importance of re-evaluating dosing standards in the context of modern fluoride exposure. The labeling paradox arose again as well: While topical toothpaste labels warn against swallowing any amount, ingestible fluoride drug products deliver comparable doses to children.

Clinical and Access Considerations. Participants also highlighted the realities faced in clinical practice. In communities without fluoridated water, ingestible fluoride drug products were described as modest but tangible tools to reduce dental caries and prevent invasive or costly dental procedures, particularly for families with limited access to dental care. Several panelists cautioned that eliminating ingestible fluoride drug products could disproportionately affect underserved populations, widening disparities in oral health outcomes between children in areas with fluoridated and non-fluoridated water.

Overall Takeaways. Session 1 highlighted several themes and tensions. First, ingestible fluoride drug products were described by some panelists as an important tool for specific and limited populations, while others contended these ingestible products could be replaced by alternative topical products. Second, the quality of evidence for both benefits and risks came into question, with participants calling for investment in higher-quality research to generate stronger, more generalizable evidence to guide updated regulatory decisions.

Session 2: Identifying Safety Concerns and Potential Risks

Building on the Session 1 discussion, Session 2 focused on whether use of ingestible fluoride drug products may pose risks to children's health. Discussions centered on the known and potential risks of ingestible fluoride drug products and their effects on children's oral and systemic health. Speakers considered how emerging evidence, particularly in areas such as neurocognition and endocrine function, should inform future evaluation and use of these products.

Ongoing NIH Studies on Fluoride Exposure & Health Outcomes

HEALTHY BRAIN AND CHILD DEVELOPMENT (HBCD) STUDY

PARTICIPANTS: 7,000 mother–child pairs

FOCUS: Tracks fluoride exposure from pregnancy through age 10

ENVIRONMENTAL INFLUENCES ON CHILD HEALTH OUTCOMES (ECHO) PROGRAM

PARTICIPANTS: >60,000 children across 44 states

FOCUS: Evaluates fluoride exposure alongside outcomes such as thyroid health, microbiome shifts, and systemic inflammation

ADOLESCENT BRAIN COGNITIVE DEVELOPMENT (ABCD) STUDY

PARTICIPANTS: >11,000 children across 21 U.S. sites

FOCUS: Examines how fluoride exposure interacts with biological and social factors to influence long-term brain and health outcomes

The session opened with remarks from Dr. Tidmarsh, who framed the discussion by reminding participants that ingestible fluoride drug products are unapproved drugs that have never undergone FDA's formal review of benefits and risks. He emphasized the importance of evidence-based analysis and noted that, if these products were removed, manufacturers could still pursue formal studies and reapply for approval. Dr. Tidmarsh also underscored the need for collaboration with dental and pediatric communities to identify and advance alternative strategies for promoting oral health.

Next, Dr. Jennifer Webster-Cyriaque, Acting Director of the National Institute of Dental and Craniofacial Research, provided an overview of the National Institutes of Health's research on fluoride. She highlighted ongoing large-scale federal efforts to clarify both benefits and risks of fluoride exposure, including dental fluorosis, potential systemic toxicity, and nutrition and dietary studies. Dr. Webster-Cyriaque emphasized that this multi-level research agenda aims to move beyond polarized debates and build an evidence base showing that fluoride is not a "magic bullet" but part of a broader prevention framework that must integrate oral hygiene, diet, community fluoride exposures, and access to dental care.

Oral and Gut Microbiome

The first scientific focus was on the oral and gut microbiome, where fluoride is suspected to have both potentially beneficial and potentially disruptive effects. Presenters outlined how fluoride at low levels can suppress cavity-causing bacteria, promote healthier oral flora, and alter biofilm structure to reduce susceptibility to decay. In this sense, ingestible fluoride drug products and other fluoride sources may strengthen the ecological defenses of the mouth.

The initial presentation highlighted the oral cavity as a collection of distinct microbial habitats: Tongue, cheeks, and dental plaque, each colonized with unique microbial communities and responses to interventions. Fluoride at therapeutic doses (0.25 mg – 1 mg) was described as selectively suppressing acid-producing bacteria, preventing cavity-causing organisms from dominating, and shifting biofilm composition in ways that protect enamel. It was noted that microbial interventions developed for the gut, such as probiotics, cannot be assumed to function in the same way in the oral cavity, underscoring the uniqueness of oral microbial ecology.

The second presentation turned attention to the gastrointestinal tract, where ingested fluoride interacts with the gut microbiome. The speaker reiterated that ingested fluoride first encounters the oral microbiome, where it can inhibit acid-producing bacteria that contribute to dental caries,

before being largely absorbed in the stomach and small intestine, limiting exposure (less than half of the original dose) to the colonic microbiota.

Most evidence on gut effects is derived from animal models. Animal studies show that very high concentrations (75-100 mg/L) of fluoride can disrupt microbial diversity and function, though the speaker noted that in general, these levels far exceed levels that would be encountered through ingestible fluoride drug products or fluoridated water.[5] More moderate-dose studies (4 mg/L) found beneficial shifts in the oral microbiome (fewer acid-producing bacteria) and minimal gut effects.[6]

The presenter reported on the limited human data available, including studies in areas with severe dental fluorosis, where exposure occurs through groundwater or inhaled fluoride-rich coal smoke. These studies report microbial shifts characterized by altered bacterial diversity and species abundance, particularly in individuals with skeletal fluorosis, though as noted by the presenter, such exposures are well above levels relevant to U.S. use.[7,8] Lastly, the presenter described a retrospective study that found children who had ingested fluoride through salt or tablets showed subtle differences in adult oral microbiota.[9] The clinical significance of these findings remains uncertain.

Together, these presentations emphasized dose as the critical variable: At controlled levels (low levels typical of community water fluoridation or ingestible fluoride drug products), fluoride appears to support microbial balance, whereas excessive or prolonged exposure may disrupt microbial composition and other systemic processes. Although the evidence remains preliminary, these potential systemic effects at higher doses could influence the overall risk-benefit profile of fluoride use.

Neurocognitive Concerns

The neurocognition session explored emerging evidence on fluoride exposure and brain development, highlighting a range of perspectives and underscoring the importance of exposure context, biomarkers, and study design.

Multiple presenters discussed emerging data linking fluoride exposure in early childhood, and in some cases prenatal exposure, to cognitive outcomes. Several longitudinal studies from Canada, Mexico, and Europe reported associations between elevated fluoride exposure and lower IQ scores in children. These studies frequently used urinary fluoride levels to capture total exposure

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[5] Zhong, N., Ma, Y., Meng, X., Zhang, J., Chen, D., & Zhou, J. (2022). *Effect of fluoride in drinking water on fecal microbial community in rats. Biological Trace Element Research, 200*(1), 238–246. https://doi.org/10.1007/s12011-021-02642-2

[6] Yasuda, K., Hsu, T., Gallini, C. A., Mclver, L. J., Schwager, E., Shi, A., DuLong, C. R., Schwager, R. N., Abu-Ali, G. S., Franzosa, E. A., Garrett, W. S., Huttenhower, C., & Morgan, X. C. (2017). *Fluoride Depletes Acidogenic Taxa in Oral but Not Gut Microbial Communities in Mice*. *mSystems*, *2*(4), e00047-17. https://doi.org/10.1128/mSystems.00047-17

[7] Wang, J., Yu, C., Zhang, J., Liu, R., & Xiao, J.-H. (2023). Aberrant gut microbiota and fecal metabolites in patients with coal-burning endemic fluorosis in Guizhou, China. *Environmental Science and Pollution Research International, 30*(27), 69913–69926. https://doi.org/10.1007/s11356-023-27051-9

[8]Zhou, G., Li, Q., Hou, X., Wu, H., Fu, X., Wang, G., Ma, J., Cheng, X., Yang, Y., Chen, R., Li, Z., Yu, F., Zhu, J., & Ba, Y. (2023). Integrated 16S rDNA sequencing and metabolomics to explore the intestinal changes in children and rats with dental fluorosis. *Ecotoxicology and Environmental Safety, 251*, 114518. https://doi.org/10.1016/j.ecoenv.2023.114518

[9] Wolff, D., Frese, C., Schoilew, K., Dalpke, A., Wolff, B., & Boutin, S. (2019). Amplicon-based microbiome study highlights the loss of diversity and the establishment of a set of species in patients with dentin caries. *PLoS ONE, 14*(7), e0219714. https://doi.org/10.1371/journal.pone.0219714

from all sources, including ingestible fluoride drug products, incidental toothpaste ingestion, dietary products, and water. Some presenters noted that across multiple cohorts, investigators observed an inverse relationship between urinary fluoride concentrations and IQ scores, suggesting a possible dose-response trend in which higher fluoride exposure corresponds to lower mean IQ. Some speakers characterized these studies as among the strongest to date because they measured exposure prospectively and directly, with results replicated across populations, lending weight to concerns that fluoride can cross the placental barrier and affect the developing brain. These presenters observed that the consistency of results across multiple populations lends credibility to the concern that fluoride can cross the placental barrier and affect the developing brain.

The first presentation observed that the benefits of fluoride are topical rather than systemic and emphasized that ingestible fluoride drug products lack adequate safety or efficacy data. The presentation cited widespread dental fluorosis and a growing body of studies linking fluoride exposure to lower IQ. The speaker argued that systemic ingestion confers risk without additional preventive benefit and pointed to dose-response data indicating neurocognitive effects at or below 1.5 mg/L (upper limit for fluoride in drinking water), though the reliability of low-dose data was debated.[10]

The second presentation focused on methodological limitations and exposure measurement. The speaker emphasized that results from endemic high-fluoride regions are not directly comparable to U.S. contexts.[11] Concerns were raised about relying on spot urinary fluoride as a long-term measure of exposure and on IQ as the sole endpoint, given its sensitivity to many social and environmental variables and poor reflection of long-term exposure. Similarly, IQ testing was characterized as an imperfect and variable endpoint, sensitive to socioeconomic, cultural, and environmental confounders. Meta-analyses that separated endemic from non-endemic populations found no changes in IQ associated with fluoride levels typical of community water fluoridation.

A third presentation emphasized balancing benefits and risks from a clinical perspective. One of the presentation slides summarized comparative studies from national cohorts in New Zealand, Canada, Spain, and Australia, showing no measurable neurocognitive differences between children in fluoridated and non-fluoridated communities. In this view, fluoride was framed as one of several preventive tools, with mild fluorosis described as a cosmetic side effect.

The fourth presentation examined a systematic review and meta-analysis that concluded with moderate confidence that higher fluoride exposures are associated with lower IQ in children. Specifically, the review found an inverse association between fluoride exposure and IQ across both water and urinary fluoride levels, with a linear dose-response relationship evident below 1.5mg/L.

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[10] Grandjean, P., & Choi, A. L. (2023). Updated dose–response assessment and meta-analysis of fluoride developmental neurotoxicity studies rated higher quality by National Toxicology Program. *Environmental Health Perspectives, 131*(9), 97001. https://doi.org/10.1289/isee.2023.EP-044

[11] Kumar, J. V., Moss, M. E., Liu, H., & Fisher-Owens, S. (2023). Association between low fluoride exposure and children's intelligence: a meta-analysis relevant to community water fluoridation. *Public Health*, *219*, 73–84. https://doi.org/10.1016/j.puhe.2023.03.011

The presenter emphasized the need for additional longitudinal studies in low-exposure settings to clarify the magnitude of and thresholds at which potential neurocognitive effects might occur.[12]

Despite differences in interpretation, the neurocognitive discussion underscored a critical theme: Though uncertainty remains about the magnitude of risk, the potential for harm to child brain development carries significant weight in any risk-benefit assessment. Presenters agreed that the evidence, though not conclusive, demands continued U.S.-based research investment.

Thyroid Health

The discussion then turned to the thyroid, another area where fluoride exposure has been suggested to exert systemic effects. Presenters noted that the thyroid gland produces key hormones thyroxine (T4) and triiodothyronine (T3), which regulate metabolism and are essential for normal growth and brain development, especially during pregnancy and infancy. They summarized existing studies suggesting that fluoride exposure may interfere with thyroid hormone regulation, potentially contributing to subclinical hypothyroidism or other endocrine dysfunction.[13,14,15] While the body of evidence remains relatively small, the biological plausibility of these effects was noted because fluoride is known to interact with iodine metabolism, an essential process for thyroid hormone synthesis.

One presentation provided new epidemiologic findings of pregnant women in Canada, linking fluoride exposure in drinking water to maternal hypothyroidism.[16] Stronger associations were observed when women who had autoimmune thyroid disease and women who had lived in their home for under a year were excluded, suggesting a link between chronic exposure and thyroid disruption. Notably, a 0.5 mg/L difference in water fluoride levels – the approximate difference between fluoridated and non-fluoridated communities – was associated with 65% greater odds of hypothyroidism. The speaker emphasized that fetal brain development in early pregnancy is entirely dependent on maternal thyroid hormone and cited evidence showing that boys born to mothers with hypothyroidism may have lower IQ. Possible mechanisms were described, including interference with iodine metabolism and disruption of thyroid-regulating enzymes.

A second presentation framed the thyroid discussion within a broader risk-benefit perspective, noting that fluoride is not nutritionally required and that its dental benefits are achieved primarily through topical exposure, not systemic. The presentation reviewed evidence that systemic fluoride

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[12] Taylor, K. W., Eftim, S. E., Sibrizzi, C. A., Blain, R. B., Magnuson, K., Hartman, P. A., Rooney, A. A., & Bucher, J. R. (2025). Fluoride Exposure and Children's IQ Scores: A Systematic Review and Meta-Analysis. *JAMA Pediatrics*, *179*(3), 282–292. https://doi.org/10.1001/jamapediatrics.2024.5542

[13] Iamandii, I., De Pasquale, L., Giannone, M. E., Veneri, F., Generali, L., Consolo, U., Birnbaum, L. S., Castenmiller, J., Halldorsson, T. I., Filippini, T., & Vinceti, M. (2024). Does fluoride exposure affect thyroid function? A systematic review and dose-response meta-analysis. *Environmental Research, 242*, 117759. https://doi.org/10.1016/j.envres.2023.117759

[14] Waugh, D. T. (2019). Fluoride exposure induces inhibition of sodium/iodide symporter (NIS) contributing to impaired iodine absorption and iodine deficiency: molecular mechanisms of inhibition and implications for public health. *International Journal of Environmental Research and Public Health, 16*(6), 1086. https://doi.org/10.3390/ijerph16061086

[15] Chaitanya, N. C. S. K., Karunakar, P., Allam, N. S. J., Priya, H. M., Alekhya, B., & Nauseen, S. (2018). A systematic analysis on possibility of water fluoridation causing hypothyroidism. *Indian Journal of Dental Research, 29*(3), 358-363. https://doi.org/10.4103/ijdr.IJDR_235_17

[16] Hall, M., Lanphear, B. P., Chevrier, J., Hornung, R., Green, R., Goodman, C. V., Ayotte, P., Angeles Martinez-Mier, E., Zoeller, R. T., & Till, C. (2023). Fluoride exposure and hypothyroidism in a Canadian pregnancy cohort. *Science of the Total Environment, 869*, 161149. https://doi.org/10.1016/j.scitotenv.2022.161149

exposure, at levels comparable to those achieved through fluoride tablet use or community water fluoridation, has been associated with reduced thyroid function; subclinical hypothyroidism; and increased prevalence of goiter, an enlargement of the thyroid gland often linked to iodine deficiency. Subclinical hypothyroidism, defined by elevated TSH with normal T4 and T3 levels, was emphasized as having potential clinical consequences, such as associations with increased risks of cardiovascular disease, depression, and cognitive dysfunction, including lower offspring IQ.

The speaker also noted that the fluoride intake levels linked to thyroid effects (≈0.05–0.1 mg/kg/day) overlap with those reached by children taking fluoride tablets according to current recommendations, particularly when combined with other dietary and environmental exposures. The risk may be amplified among individuals with low iodine or calcium intake, chronic kidney disease, or other conditions that reduce fluoride excretion. From this standpoint, systemic ingestion introduces risk without providing added benefit. This argument highlighted fluoride's potential role in endocrine dysfunction, with dental fluorosis serving as visible evidence that fluoride reaches developing tissues.

As with neurocognition, the overall body of thyroid research remains limited, though the available evidence supports a biologically plausible link between fluoride exposure and altered thyroid function. Presenters emphasized that more targeted research is needed to establish causal relationships and determine whether the levels of exposure associated with use of ingestible fluoride drug products are sufficient to pose a risk.

Panel Discussion

The panel discussion weaved together evidence from toxicology, epidemiology, clinical dentistry, and public health practice, offering a variety of perspectives on fluoride exposure and its health implications.

Evidence on Neurodevelopmental Impact and Public Health Interpretation. One line of discussion emphasized that accumulating data linking fluoride exposure to potential neurodevelopmental harm cannot be dismissed as incidental or premature. Drawing parallels to lead research, several panelists noted that similar epidemiologic evidence, though imperfect, was sufficient for agencies like the Centers for Disease Control and Prevention and the World Health Organization to act on childhood lead exposure. Urinary fluoride, despite its variability, was defended as an appropriate biomarker in large-scale studies, and panelists stressed that consistent inverse associations between fluoride exposure and IQ scores across multiple populations provide a concerning signal that warrants attention. From this perspective, claims that exposure levels in U.S. communities are too low to be relevant were challenged, with the argument that adverse effects have been observed even at or below current averages for fluoridated areas.

Limitations in Methodology and Emerging Research Approaches. Other panelists highlighted the limitations of existing research. Concerns were raised that many studies rely on spot urinary samples, which may not accurately capture exposure over time or reflect individual variation. Methodological variability, dietary influences, and lack of adjustment for dilution were cited as potential sources of error. One counterargument was that such imprecision typically biases findings toward the null, meaning that observed associations could underestimate the true effect. Researchers also described new approaches, such as using toenails and exfoliated teeth as cumulative biomarkers, which may eventually provide stronger evidence. While these refinements

are underway, panelists acknowledged the urgent need for U.S.-based, well-controlled cohort studies to clarify risks under domestic exposure conditions.

Balancing Dental Benefits and Fluorosis Risk. The discussion then shifted to fluoride's well-established role in preventing dental caries. Several panelists underscored decades of data from community water fluoridation programs showing reduced caries rates, suggesting that systemic exposure during early childhood may contribute to lasting protection even after children move away from fluoridated areas. They disputed the idea that swallowing fluoride has no benefit, pointing out that mild dental fluorosis is itself evidence of systemic uptake and can confer greater resistance to decay. The panel also called for a more nuanced understanding of fluorosis, noting that mild cases may be difficult to diagnose accurately, can resemble cosmetic whitening effects, and are not typically considered harmful. At the same time, panelists recognized that overexposure in early life remains a valid concern and requires closer monitoring of cumulative fluoride sources, including toothpaste ingestion and processed foods.

Considering Potential Alternatives to Ingestible Fluoride Drug Products. The panel addressed the role of ingestible fluoride drug products compared to topical alternatives. Some participants argued that systemic fluoride sources offer limited additional benefit beyond topical sources such as toothpaste, which are safer, cheaper, and more practical for broad use. Ingestible fluoride drug products were described as burdensome due to cost, prescription requirements, and daily adherence, while contributing more significantly to fluorosis risk. From this standpoint, emphasis should shift to promoting topical fluoride and addressing other caries risk factors, such as sugar consumption, vitamin D deficiency, and low-level lead exposure. Others noted that in non-fluoridated areas, ingestible fluoride drug products remain one of the few tools available to address stark differences in oral health outcomes, particularly for underserved children with limited access to preventive services.

Overall Takeaways. While the first session highlighted current use of ingestible fluoride drug products for oral health, the second session illuminated the current state of research about systemic risks. From microbiome disruption to potential neurocognitive and endocrine effects, the evidence presented was concerning but not conclusive. Some urged precautionary action now, warning that failure to act in the face of credible signals would repeat mistakes of past toxic exposures. Others emphasized the need for patience and scientific rigor, arguing that policy should not shift until better U.S.-based evidence clarifies the true balance of risks and benefits. Despite divergent views, panelists converged on one conclusion: High-quality, comprehensive studies are urgently needed to resolve lingering uncertainty and guide regulatory decisions that protect both children's health and public trust.

Perspectives from the Public

Invited Parent Perspectives

To complement the scientific and clinical presentations and panels, the meeting included invited remarks from parents, offering insight into how fluoride guidance and access affect families' real-world decisions. These perspectives grounded the discussion in everyday experiences where choices about fluoride use are shaped by local water conditions, clinician recommendations, and generational perceptions of dental health. Through these personal accounts, panelists and

attendees heard how community context, clinician advice, and family experience intersect to shape oral health outcomes across generations.

One parent described being prescribed fluoride drops for her son when they lived in an area with uncertain water fluoridation. She observed no side effects and attributed her son's strong dental health to early use of fluoride drops, combined with later access to fluoridated water. This contrasted with her parents' and grandparents' experiences prior to fluoridation, which involved widespread tooth loss and reliance on dentures. Her account underscored the uneven availability of community water fluoridation across the country, which leaves some populations more dependent on these products than others.

Another parent, a nurse and mother of nine children, shared her experience living in an area with non-fluoridated water. She highlighted her decision-making process regarding fluoride tablets and the influence that family members and other sources had at various points in time, resulting in only some of her children receiving fluoride tablets. Ultimately, decades later, her children had divergent dental outcomes: A daughter who likely did not receive fluoride tablets experienced frequent cavities and soft enamel, while siblings who received fluoride tablets avoided cavities well into adulthood.

Public Comment and Docket Analysis

The public comment session highlighted a wide range of perspectives, with parents, advocates, and clinicians offering remarks both for and against the use of ingestible fluoride drug products. Registration for public comment was open to the public. Twenty members of the public submitted requests to speak, and all were able to present their perspectives on their first-choice topic in person or virtually during the session. The four topics for public comment were as follows:

- **Topic 1:** Clinical Use and Prescribing Considerations for Pediatric Tooth Decay Prevention
- **Topic 2:** Safety Concerns
- **Topic 3:** Appropriateness of Pediatric Use Considering Additional Sources of Exposure
- **Topic 4:** Impact of Removal of Orally Ingestible Unapproved Prescription Drug Products and Potential Alternatives

Topic 1: Clinical Use and Prescribing Considerations for Pediatric Tooth Decay Prevention. Commenters discussed the long-standing role of ingestible fluoride drug products in pediatric dental care. Supporters of the currently available, unapproved products emphasized their role as essential tools to prevent cavities, especially for children from low-income or rural families who lack access to fluoridated water. These commenters described these products as indispensable for addressing gaps in oral health and support as a means of preserving clinical judgment and parental choice. By contrast, opponents underscored unresolved safety concerns, the unapproved regulatory status of these products, and the risk of cumulative exposure from multiple sources of fluoride. They questioned the scientific basis for systemic use and argued that in a modern context with widespread access to fluoridated toothpaste and topical varnishes, ingestible fluoride drug products are outdated, unnecessary, and potentially harmful.

Clinical use and prescribing considerations were central to the discussion. Pediatric dentists, epidemiologists, and public health experts testified that ingestible fluoride drug products are supported by decades of research and endorsed by professional organizations such as the

American Academy of Pediatrics, the American Dental Association, and the U.S. Preventive Services Task Force. They stressed that both systemic and topical fluoride contribute to caries prevention, particularly in children without access to fluoridated water. Some highlighted real-world evidence showing substantial reductions in caries when both sources are combined. Others argued instead that the scientific consensus now supports only topical benefits, rendering ingestion obsolete. Several cited international guidelines that favor topical sources, such as toothpaste and varnish, over ingestible products, questioning whether a product whose mechanism of action does not justify systemic exposure should be prescribed.

Topic 2: Safety Concerns. Safety concerns were among the most polarizing themes. Parents shared personal stories of children experiencing autism, ADHD, hypothyroidism, and chemical sensitivities they attributed to fluoride exposure; others cited draft findings from the National Toxicology Program and epidemiological studies linking fluoride ingestion to lowered IQ and other developmental risks. Some framed fluoride as a potential neurotoxin and compared its use to past regulatory failures such as thalidomide. Others countered that at recommended levels, ingestible fluoride drug products are safe and effective, with mild fluorosis the only well-documented side effect, and argued that anecdotal reports and studies from high-exposure settings outside the U.S. should not guide U.S. regulatory action.

Topic 3: Appropriateness of Pediatric Use Considering Additional Sources of Exposure. The question of appropriateness of pediatric use given cumulative exposures was also contested. Some argued that children are already exposed to fluoride through drinking water, food, toothpaste, and other sources, with rising rates of fluorosis serving as evidence of overexposure. They contended that ingestible fluoride drug products add unnecessary risk. Others responded that prescribing allows for careful adjustment based on measured water levels and a child's individual risk profile, ensuring that ingestible fluoride drug products are only prescribed where needed. They emphasized that professional oversight provides the flexibility necessary to manage cumulative exposure safely.

Topic 4: Impact of Removal of Orally Ingestible Unapproved Prescription Drug Products and Potential Alternatives. The discussion of the impact of removal and alternatives underscored the stakes of potential regulatory action. Some commenters warned that discontinuing ingestible fluoride drug products would worsen outcomes in oral health, increase untreated dental caries, and shift families and health systems toward costly restorative and emergency care, undoing decades of preventive progress. They characterized fluoride as part of the nation's preventive health infrastructure, likening it to vaccines or iodine in salt, and described removal as a step backward in public health. Others welcomed removal, describing ingestible fluoride drug products as relics of a discredited paradigm. They pointed to topical strategies such as fluoridated toothpaste, varnish, and sealants, as well as improved diet and nutrition, as sufficient alternatives, arguing these approaches protect children without the systemic risks associated with ingestion.

Docket Analysis

The docket received 4,604 written submissions, reflecting significant public engagement and extending the themes raised in the live session. Comments reinforced fluoride's role as a critical equalizer in underserved areas, where shortages of pediatric dentists, underfunded Medicaid programs, and financial barriers already limit access to preventive care. These submissions highlighted structural barriers, stressing that ingestible fluoride drug products are sometimes the

only affordable and practical preventive measure for families who would otherwise rely on emergency dental care. Parents and clinicians described the issue in intergenerational terms, recalling how lack of fluoride access in their own childhoods resulted in lifelong oral health problems, and urging FDA not to limit care options for their children that would result in similarly poor outcomes. Others emphasized the economic implications, warning of rising Medicaid expenditures, increased insurance claims, and heavy financial burdens on the families least able to afford restorative care.

Other docket submissions highlighted regulatory and ethical concerns, noting that ingestible fluoride drug products remain unapproved drugs never formally evaluated for safety or efficacy by the FDA. Critics invoked the agency's history with unapproved products as reason for caution and argued that permitting continued use without robust review undermines the FDA's credibility and public trust. These submissions often extended beyond questions of efficacy to include broader allegations of institutional bias, portraying fluoride as an industrial byproduct promoted by professional organizations and government agencies for political or financial reasons.

In addition, global comparisons were raised on both sides. Opponents pointed to European countries that discourage or ban ingestible fluoride drug products, framing this as evidence that systemic fluoride is unnecessary. Supporters highlighted evidence from Canada and the U.S. showing increased decay rates following the removal of water fluoridation, suggesting similar risks if products are withdrawn.

Other themes in the docket went beyond those raised in oral comments. Several submissions underscored the professional and parental autonomy afforded by ingestible fluoride drug products, which allow for individualized, opt-in preventive care unlike community water fluoridation. Some raised concerns about professional education, arguing that dental training treats fluoride benefits as unquestioned fact and does not adequately engage with emerging risks. Others noted that fluoride's role in oral health is tied to broader issues of nutrition, lifestyle, and systemic disease, linking oral health outcomes to self-esteem, employability, and overall quality of life.

Taken together, the public comment session and the docket submissions reveal entrenched and highly polarized perspectives. Oral testimony largely centered on clinical practice, safety debates, and the immediate consequences of removing unapproved products, while the docket expanded the discussion to include structural barriers to care, economic burdens, regulatory legitimacy, global comparisons, distrust of institutions, and the ethical balance between individual choice and collective public health. Both sources demonstrate that the debate over ingestible fluoride drug products extends far beyond a narrow scientific dispute to encompass fundamental questions regarding regulatory credibility and the role of public health infrastructure.

Closing Summary

The meeting underscored both the complexity of the scientific and clinical questions at hand and the depth of public interest in the FDA's review of ingestible fluoride drug products. Across sessions, participants converged on the importance of preventing childhood cavities but diverged sharply on whether systemic fluoride remains a safe and appropriate means to do so. Discussions revealed several areas of agreement: All parties acknowledged the persistent burden of pediatric

dental caries, the uneven distribution of fluoridated water across the United States, the importance of healthy diet and nutrition to prevent child dental caries and promote health overall, and the urgent need for high-quality research to clarify the risks and benefits of fluoride exposure during critical developmental windows. There was also consensus that regulatory decisions should rest on rigorous, transparent evaluation of available evidence rather than anecdote or tradition. Yet the divisions were equally pronounced. Clinicians, advocates, researchers, and families supportive of ingestible fluoride drug products emphasized decades of use, endorsements from professional societies, and the role of these products in advancing health, particularly in rural and low-income communities. Other clinicians, advocates, researchers, and families challenged the adequacy of the evidence base, pointing to the absence of randomized controlled trials, the emergence of safety uncertainties, and the contradiction of permitting prescribing of unapproved drugs while fluoride's primary benefits are acknowledged as topical. The debate around neurocognitive and endocrine risks highlighted a persistent gap between precautionary and evidentiary standards, with some urging immediate action and others calling for patience until U.S.-based studies can more definitively resolve questions of potential harm.

The oral public comment session and 4,604 written docket submissions reinforced these themes while also surfacing broader considerations, including the economic burden of untreated caries, intergenerational impacts of access to fluoride, regulatory legitimacy, and public trust in institutions. These contributions reflected not only polarized views but also deep engagement from stakeholders across the country.

In sum, the meeting highlighted a shared recognition of the need to address preventable oral disease but also revealed enduring disagreements about the role of systemic fluoride in child health. The central challenge for FDA moving forward is to reconcile the reliance of some families and communities on these products with the need for modern, trial-quality evidence and clear risk assessments. Closing the current evidence gaps will be critical for building consensus, guiding future policy, and ensuring that any regulatory pathway both safeguards children's health and sustains public confidence in science-based decision-making.

The full meeting transcript, accompanying slide deck, meeting recording, and speaker biographies are publicly available on the Reagan-Udall Foundation for the FDA website.

Appendix

Use of Orally Ingestible Unapproved Prescription Drug Products Containing Fluoride in the Pediatric Population

Hybrid Public Meeting

Wednesday, July 23, 2025 | 9:30am – 4pm (eastern)

In-person: 10903 New Hampshire Ave, Bldg. 31 Conference Center, Great Room, Silver Spring, MD 20993-0002
Virtual: Link to follow

Meeting Description

This hybrid public meeting, convened by the Reagan-Udall Foundation for the FDA in collaboration with the FDA, aims to gather input on the clinical use and safety of ***orally ingestible unapproved prescription fluoride drug products*** in children, such as drops and tablets. Some of these products have been used since the 1940s to prevent tooth decay in areas with low or no water fluoridation. This meeting is ***not*** about adding fluoride to drinking water and is ***not*** a decision-making forum.

Draft Agenda

9:30am **Welcome**

- Susan C. Winckler, RPh, Esq.
  CEO, Reagan-Udall Foundation for the FDA

9:35am **Opening Remarks**

- Jacqueline Corrigan-Curay, JD, MD
  Principal Deputy Center Director, Center for Drug Evaluation and Research, FDA

9:45am **Session 1: Scope of Use of Orally Ingestible Unapproved Prescription Drug Products Containing Fluoride in Clinical Practice**

Session Description: *This session will explore the current scope and patterns of use of orally ingestible unapproved prescription drug products containing fluoride within clinical practice settings*

Presentations:

- Sally Greenberg, JD, Lived Patient Experience
- James H. Bekker, DMD, University of Utah School of Dentistry
- Bill Osmunson, DDS, MPH, Fluoride Action Network

Reactor Panel (30 min)

- Linda Birnbaum, PhD, DABT, ATS, Duke University, National Institute of Environmental Health Sciences
- David Krol, MD, MPH, FAAP, American Academy of Pediatrics
- Scott Tomar, DMD, MPH, DrPH, University of Illinois Chicago College of Dentistry

10:45am **Break**

11am **Session 2: Identifying Safety Concerns and Potential Risks Associated with the Use of Orally Ingestible Unapproved Prescription Drug Products Containing Fluoride**

Session Description: *This session will examine safety concerns and potential risks related to the use of orally ingestible unapproved prescription drug products containing fluoride*

Presentations:

- Valerie Heaton, Lived Patient Experience
- Jennifer Webster-Cyriaque, DDS, PhD, National Institutes of Health

Oral and Gut Microbiome

- Purnima Kumar, BDS, MDS, PhD, University of Michigan School of Dentistry
- Gary Moran, BA (Mod), PhD, FTCD, Trinity College Dublin

Neurocognitive

- Griffin Cole, DDS, NMD, MIAOMT, International Academy of Oral Medicine and Toxicology
- Jayanth Kumar, DDS, MPH*, formerly at* California Department of Public Health
- Susan Fisher-Owens, MD, MPH, University of California San Francisco
- Kyla Taylor, PhD, National Institutes of Health

Thyroid

- Christine Till, PhD, C.Psych, York University
- Kathleen Thiessen, PhD, Oak Ridge Center for Risk Analysis

Reactor Panel (30 min)

- Bruce Lanphear, MD, MPH, Simon Fraser University
- Charlotte W. Lewis, MD, MPH, University of Washington School of Medicine

1pm **Lunch Break**

2pm **Public Comment on 4 Topics**

- Clinical Use and Prescribing Considerations for Pediatric Tooth Decay Prevention
- Safety Concerns
- Appropriateness of Pediatric Use Considering Additional Sources of Exposure
- Impact of Removal of Orally Ingestible Unapproved Prescription Drug Products/ Potential Alternatives

3:55pm **Adjourn**

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