COMMITTEE ON
ENERGY & COMMERCE
CHAIRMAN FRANK PALLONE, JR.

MEMORANDUM

January 24, 2020

To: Subcommittee on Health Members and Staff

Fr: Committee on Energy and Commerce Staff

Re: Hearing on "Improving Safety and Transparency in America's Food and Drugs"

On **Wednesday, January 29, 2020, at 10 a.m. in room 2322 of the Rayburn House Office Building**, the Subcommittee on Health will hold a legislative hearing entitled, "Improving Safety and Transparency in America's Food and Drugs."

I. H.R. 4712, THE "FAIRNESS IN ORPHAN DRUG EXCLUSIVITY ACT"

A. Background

The Orphan Drug Act was enacted in 1983 to incentivize the development of drugs for rare diseases by providing manufacturers with exclusive marketing rights for seven years from the date of approval, during which time the same drug produced by other manufacturers are barred from the market.[1] Drugs may be designated as an "orphan drug" and thus accorded market exclusivity if either the disease or condition affects less than 200,000 people, or drug research and development (R&D) costs are not likely to be recovered through sales. Few drugs have received "orphan drug" designation under the second criterion; this criterion has been recently criticized due to an "orphan drug" designation that was awarded to a buprenorphine product to treat opioid use disorder. Under the exclusivity terms of the designation, future approvals of generic competitors could be blocked.[2,3]

In response to a petition by a competing drug company and upon review of the agency's administrative record, the Food and Drug Administration (FDA) revoked the buprenorphine product's orphan drug status, stating that the agency had "erroneously granted Indivior's orphan-

[1] Pub. L. No. 97-414.

[2] *In Midst Of Opioid Crisis, FDA May Block New Addiction Drug From Market*, NPR (May 24, 2019) (www.npr.org/sections/health-shots/2019/05/24/722076165/in-midst-of-opioid-crisis-fda-may-block-new-addiction-drug-from-market).

[3] Diane Dorman, *Don't let the maker of a buprenorphine drug abuse the Orphan Drug Act*, Stat News (May 28, 2019) (www.statnews.com/2019/05/28/buprenorphine-drug-abu.s.ing-orphan-drug-act/).

drug designation request because… it was unreasonable to conclude that there would be no cost recovery from sales of buprenorphine in the United States."[4]

B. Legislation

H.R. 4712, the "Fairness in Orphan Drug Exclusivity Act", introduced by Reps. Dean (D-PA), Veasey (D-TX), Carter (R-GA), and McKinley (R-WV), updates the Orphan Drug Act to require drug manufacturers seeking orphan drug designations to demonstrate the absence of any reasonable expectation that the costs they incur in developing and making those drugs available in the United States for such disease or condition, and to make such demonstrations annually for the duration of the seven-year period of market exclusivity of an approved orphan drug. The bill directs FDA and the drug manufacturer to take into consideration the sales of all drugs for the rare disease or condition developed by the same manufacturer as well as all drugs containing the same active molecular components.

II. H.R. 4866, THE "NATIONAL CENTERS OF EXCELLENCE IN CONTINOUS PHARMACEUTICAL MANUFACTURING ACT"

A. Background

Continuous manufacturing is an advanced manufacturing technique where the finished drug product is produced in a continuous stream rather than traditional batch manufacturing that includes breaks or stops for different steps in the process.[5] According to testimony before the Subcommittee on Health from Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research at FDA, advanced manufacturing "can be used to reduce the Nation's dependence on foreign sources of APIs [active pharmaceutical ingredients], increase the resilience of our domestic manufacturing base, and reduce quality issues that trigger drug shortages or recalls."[6]

The 21st Century Cures Act, which was signed into law on December 13, 2016, authorized FDA to issue grants to institutions of higher education and nonprofit organizations to study and make recommendations regarding improvements to the process of continuous manufacturing of drugs and biologics.[7] Utilizing this authority, FDA has awarded five grants to institutions of

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[4] Response Letter from FDA, to Lassman Law + Policy (Nov. 7, 2019) (www.regulations.gov/document?D=FDA-2019-P-1679-0079).

[5] Sau "Larry" Lee, Ph.D., *Modernizing the Way Drugs Are Made: A Transition to Continuous Manufacturing* (www.fda.gov/drugs/news-events-human-drugs/modernizing-way-drugs-are-made-transition-continuous-manufacturing).

[6] House Committee on Energy and Commerce, Testimony of Janet Woodcock (Oct. 30, 2019). (energycommerce.house.gov/sites/democrats.energycommerce.house.gov/files/documents/Testimony-Woodcock-API_103019).

[7] 21st Century Cures Act, Pub. L. No.114-25, Sec. 3016 (www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf).

higher education and non-profits pertaining to biologics products.[8] The awardees are Harvard University, Carnegie-Mellon University, Rutgers University, Georgia Institute of Technology, and Massachusetts Institute of Technology.

B. Legislation

H.R. 4866, the "National Centers of Excellence in Continuous Pharmaceutical Manufacturing Act of 2019", was introduced by Chairman Pallone (D-NJ) and Rep. Guthrie (R-KY).

This legislation would amend the 21st Century Cures Act to direct FDA to designate National Centers of Excellence in Continuous Pharmaceutical Manufacturing (NCEs), which would work with FDA and industry to craft a national framework for continuous manufacturing implementation, including supporting additional research and development of this technology, workforce development, standardization, and collaborating with manufacturers to support adoption of continuous manufacturing. The bill authorizes $80,000,000 to be appropriated for NCEs from fiscal years 2021 through 2025.

III. H.R. 5663, THE "SAFEGUARDING THERAPEUTICS ACT"

A. Background

The Food and Drug Administration Safety and Innovation Act (FDASIA) authorized FDA to destroy certain imported drugs in instances where FDA believes such drugs are adulterated, misbranded, or unapproved and may pose a threat to the public health.[9] This authority enables FDA to prevent drugs that pose a threat to consumers from being further exported, thereby preventing further distribution or use of these products.[10]

B. Legislation

H.R. 5663, the "Safeguarding Therapeutics Act", introduced by Reps. Guthrie (R-KY) and Engel (D-NY), would extend FDA's administrative destruction authority to medical devices.

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[8] U.S. Food and Drug Administration, *FDA In Brief: FDA awards grants to foster innovation for advanced manufacturing technology as part of the agency's efforts to ensure a robust and reliable supply of biological products* (Sept. 20, 2019) (www.fda.gov/news-events/fda-brief/fda-brief-fda-awards-grants-foster-innovation-advanced-manufacturing-technology-part-agencys-efforts).

[9] Food and Drug Administration Safety and Innovation Act, Pub. L. No.112-144, Sec. 709 (www.congress.gov/112/plaws/publ144/PLAW-112publ144.pdf).

[10] U.S. Food and Drug Administration, *FDA's Administrative Destruction Authority* (www.fda.gov/industry/import-program-resources/fdas-administrative-destruction-authority).

IV. H.R. 5668, THE "MAKING OBJECTIVE DRUG EVIDENCE REVISIONS FOR NEW LABELING ACT OF 2020" OR THE "MODERN LABELING ACT OF 2020"

A. Background

Prescription drug product labeling contains information regarding the product based on an FDA analysis of the sponsor's new drug application or biologics license application. Labeling approved by FDA must contain all relevant information needed to support the safe and effective use of that product, such as conditions of use (including dosage and administration), warnings, contraindications, and any adverse reactions. Drug sponsors are required to update a marketed product's label as new information about the drug, such as new indications or safety-related information, becomes available. Generic drugs are generally required to have the same labeling as the brand drug they reference and generic drug manufacturers are not permitted to independently update labeling of their product to include new safety-related information if that information does not follow the approved labeling of the brand drug product.

Labeling for drug products does not always reflect new information about those products, such as new uses or safety information discovered after post-market use.[11] This may be due to the lack of sufficient incentives for manufacturers to submit supplements to continually update their product labeling, or once a brand drug has left the market.[12] A recent study found that most oncology drugs do not contain all relevant uses, leaving providers and patients without labeling information reflecting all relevant efficacy information.[13]

B. Legislation

H.R. 5668, the "MODERN Labeling Act of 2020", was introduced by Reps. Matsui (D-CA) and Guthrie (R-KY). This legislation gives authority to FDA to require modifications of outdated labeling for generic drugs and requires that FDA report any actions under the legislation taken to update labeling for covered drugs, including the number of drugs, description of the changes and the rationale, as well as any FDA recommendation to modify the program, among other items.

V. H.R. 961, THE "SAFEGUARD AMERICAN FOOD EXPORTS ACT OF 2019"

A. Background

In the United States, where horses, or formally referred to as equines, are not raised as food animals, there are currently no American slaughter houses processing horses for

[11] Shea, M; Stewart, M; Van Dyke, H; Ostermann, L; Allen, J; Sigal, E. 2018. *Outdated Prescription Drug Labeling: How FDA- Approved Prescribing Information Lags Behind Real-World Clinical Practice. Therapeutic Innovation and Regulatory Science*. DIA. (doi.org/10.1177/21684 79018759662).

[12] *Id.*

[13] *Id.*

consumption, and since 2014, including most recently in December 2019, federal appropriations legislation has restricted funding for the U.S. Department of Agriculture (USDA) to inspect horse meat.[14] Thousands of American horses, nonetheless, are exported to Canada and Mexico for slaughter each year.[15]

In addition to animal cruelty concerns, some observers have noted that horses are routinely treated with phenylbutazone and other drugs, which are banned by FDA for use in horses or other animals intended for human consumption.[16] Due to phenylbutazone's toxicity in bone marrow and association with aplastic anemia, the practice of slaughtering horses for human consumption has raised public health concerns.

B. Legislation

H.R. 961, the "Safeguard American Food Exports Act of 2019", introduced by Reps. Schakowsky (D-IL) and Buchanan (R-FL), amends the Federal Food, Drug, and Cosmetic Act (FFDCA) to deem equine parts, or horse parts, as unsafe, and to prohibit the knowing sale or transport of equines or equine parts in interstate or foreign commerce for purposes of human consumption.

VI. H.R. 1769, THE "DEFENDING AGAINST IMITATIONS AND REPLACEMENTS OF YOGURT, MILK, AND CHEESE TO PROMOTE REGULAR INTAKE OF DAIRY EVERYDAY ACT" OR THE "DAIRY PRIDE ACT"

A. Background

Current FDA regulations define "milk" as "the lacteal secretion, practically free from colostrum, obtained by the complete milking of one or more healthy cows".[17] This definition is used to define several other dairy products, including cheese and yogurt – though goat's or sheep's milk can be substituted for or mixed with cow's milk in making some dairy products.[18] Plant-based beverages and foods, including those marketed as soy milk, almond milk, oat milk, and others, have grown in popularity in recent years, with data showing an eight percent increase in sales of plant-based milk alternatives in 2018.[19] Under former FDA Commissioner Scott

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[14] *See* Nicholas Dodman, Nicholas Blondeau, and Ann Marini, *Association of Phenylbutazone Usage with Horses Bought for Slaughter: A Public Health Risk*, 48 FOOD & CHEMICAL TOXICOLOGY 1270 (2010).

[15] *See* USDA Market News, *Weekly Livestock Export Summary* (www.ams.usda.gov/mnreports/al_ls635.txt).

[16] *See* note 15; 21 CFR 520.1720e.

[17] 21 CFR 131.110.

[18] *See, e.g.*, 21 CFR 133.187 (defining "semisoft cheeses").

[19] Nielsen, *A Showdown in the U.S. Milk Aisle Continued at the End of July* (Aug. 3, 2018) (www.nielsen.com/us/en/insights/article/2018/a-showdown-in-the-us-milk-aisle-continued-at-the-end-of-july/).

Gottlieb, the agency stated concerns that labeling of some plant-based products "may lead consumers to believe that these products have the same key nutritional attributes as dairy products, even though these products can vary widely in their nutritional content."[20] FDA subsequently issued a request for information seeking comment on approaches to modernize standards of identity for plant-based products, for which the comment deadline was extended to January 28, 2019; however, the agency has not yet taken further action in response to the comments received.[21]

B. Legislation

H.R. 1769, the "DAIRY PRIDE Act", introduced by Rep. Welch (D-VT), would define in statute that a food is only a dairy product if the food (1) is, (2) contains as a primary ingredient, or (3) is derived from, the lacteal secretion (practically free from colostrum) obtained by the complete milking of one or more hooved mammals. The bill would also prohibit a food from being marketed as a dairy product if the food does not meet this definition. FDA would be required to issue final guidance on enforcement of these provisions not later than 180 days after enactment and would be required to report on enforcement of these provisions no later than two years after enactment.

VII. H.R. 2117, THE "FOOD ALLERGY SAFETY, TREATMENT, EDUCATION, AND RESEARCH ACT of 2019" OR THE "FASTER ACT of 2019"

A. Background

An estimated eight percent of children in the United States, which is approximately one in 13 children or two students in every classroom, are affected by food allergies.[22] Studies suggest that there has been a dramatic increase, over the past few decades, in children affected by allergies.[23] According to the Centers for Disease Control and Prevention (CDC), a food allergy occurs when the body has a specific and reproducible immune response, such as anaphylaxis, to certain foods.[24] Currently, the FFDCA defines major food allergens as milk, eggs, fish, crustacean shellfish, tree nuts, wheat, peanuts, and soybeans.

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[20] U.S. Food and Drug Administration, *Statement from FDA Commissioner Scott Gottlieb, M.D. on Modernizing Standards of Identity and the Use of Dairy Names for Plant-based Substitutes* (Sept. 27, 2018) (www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-modernizing-standards-identity-and-use-dairy-names).

[21] U.S. Food and Drug Administration, *FDA Extends Comment Period on Use of the Names of Dairy Foods in Labeling Plant-Based Products* (www.fda.gov/food/cfsan-constituent-updates/fda-extends-comment-period-use-names-dairy-foods-labeling-plant-based-products).

[22] Centers for Disease Control and Prevention, *Food Allergies* (May 29, 2019) (www.cdc.gov/healthyschools/foodallergies/index.htm).

[23] Jennifer Protudjer and Elissa Abrams, *Sesame the New Priority Allergen?*, JAMA Network Open (Aug. 2, 2019) (jamanetwork.com/journals/jamanetworkopen/fullarticle/2740776).

[24] *See* note 4.

Although sesame is an allergen of growing concern, affecting 0.23 percent of the population of U.S. children and adults, it is not required to be listed as an allergen on food products.[25] In fact, in some cases, sesame may not be listed at all on ingredients labels, being referred to instead through nonspecific terms such as "flavors," or included as the basis of other listed ingredients such as "tahini".[26] In response to a growing concern about sesame allergy, the FDA released a request for information in 2018, seeking comment on the prevalence and severity of sesame allergies in the United States and the prevalence of sesame-containing foods in the United States that are not required by law to disclose sesame in the ingredient list on food packages.[27]

B. Legislation

H.R. 2117, the "FASTER Act OF 2019", introduced by Rep. Matsui (D-CA), would require the CDC to expand the collection of information as to the prevalence of food allergies for specific allergens and to include that information in reports to Congress. The bill would also amend the FFDCA to include sesame as a major allergen and allow FDA, through regulation, to add other food ingredients as major allergens based on the prevalence and severity of allergic reactions to the food ingredient. Additionally, the bill would require the FDA to include patient experience data on treatments for patients with food allergies in its reports on patient experience data as well as a study by the National Academies of Sciences, Engineering, and Medicine on the economic costs of food allergies.

VIII. H.R. 2267, THE "INFANT FORMULA PROTECTION ACT of 2019"

A. Background

CDC advises consumers against purchasing expired infant formula.[28] Formula loses nutrient quality over time, putting infants consuming expired product at risk. Currently, FFDCA deems infant formula to be adulterated if it (1) does not provide appropriate nutrients; (2) does not meet the quality factor requirements prescribed by the Secretary; or (3) its processing does not comply with the good manufacturing practices and quality control procedures prescribed by the Secretary.[29] The FFDCA also specifies specific nutrients required to be included in infant

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[25] Christopher M. Warren et al., *Prevalence and Severity of Sesame Allergy in the United States*, JAMA Network Open

(Aug. 2, 2019) (jamanetwork.com/journals/jamanetworkopen/fullarticle/2740786).

[26] *Id.*

[27] Food and Drug Administration, *FDA Asks for Input on Sesame Allergies and Food Labeling* (Oct. 29, 2018) (www.fda.gov/food/cfsan-constituent-updates/fda-asks-input-sesame-allergies-and-food-labeling).

[28] Centers for Disease Control and Prevention, *Choosing an Infant Formula* (2019) (www.cdc.gov/nutrition/infantandtoddlernutrition/formula-feeding/choosing-an-infant-formula.html).

[29] 21 USC 350a.

formula.[30] Federal regulations require infant formula containers to include a "use by" date, which indicates that, on the basis of tests or other information, the formula will "(1) when consumed, contain not less than the quantity of each nutrient, as set forth on its label; and (2) otherwise be of an acceptable quality (e.g., pass through an ordinary bottle nipple)."[31]

B. Legislation

H.R. 2267, the "Infant Formula Protection Act of 2019", introduced by Reps. Meng (D-NY) and Kuster (D-NH), amends the FFDCA to additionally define infant formula as adulterated if its "use by" date has passed.

IX. H.R. 2827, THE "KEEP FOOD CONTAINERS SAFE FROM PFAS ACT OF 2019"

A. Background

A class of manmade chemicals known as perfluorinated substances (PFAS), including perfluroalkyl and polyfluoroalkyl substances, has been used in consumer products including cleaning products, paints, water-resistant fabrics, and cosmetics.[32] PFAS, such as perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) have also found use in providing nonstick, waterproof, or grease-resistant properties to cookware, food containers and wrappers.[33]

PFAS are extremely resistant to degradation and remain intact in the environment, which has resulted in the accumulation of PFAS in humans and animals. Although the FDA states that the science surrounding PFAS health effects is developing, the agency warns that bioaccumulation of certain PFAS may have serious adverse effects on human health.[34] PFAS exposure has been linked to several medical conditions including, but not limited to, thyroid dysfunction, liver disease, immunotoxicity, reproductive problems, and cancer.[35]

While PFOA and PFOS have been voluntarily phased out by most manufacturers, preliminary studies have also raised concerns about the continued use of PFAS in common

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[30] *Id.*

[31] 21 C.F.R. 107.20.

[32] Agency for Toxic Substances and Disease Registry, *Per- and Polyfluoroalkyl Substances (PFAS) and Your Health* (www.atsdr.cdc.gov/pfas/pfas-exposure.html).

[33] *Id.*

[34] U.S. Food and Drug Administration, *Per and Polyfluoroalkyl Substances* (2019) (www.fda.gov/food/chemicals/and-polyfluoroalkyl-substances-pfas).

[35] U.S. Environmental Protection Agency, PFOA Stewardship Program (www.epa.gov/assessing-and-managing-chemicals-under-tsca/fact-sheet-20102015-pfoastewardship-program).

products.[36,37,38] In 2019, FDA began its own PFAS testing of a select sample of food representing a typical consumer diet.[39] While FDA detected PFAS chemicals in a minority of foods, the agency maintains that the detected levels are not a human health concern.[40, 41] FDA has further found that PFAS that has been approved for use in some food contact substances does not migrate to food or pose a safety risk; however, the agency continues to review emerging research to make certain the continued use of PFAS in food contact applications is safe.[42]

B. Legislation

H.R. 2827, the "Keep Food Containers Safe from PFAS Act of 2019", introduced by Rep. Dingell (D-MI), amends the FFDCA to deem the use of PFAS in food contact substances unsafe, beginning January 1, 2022.

X. H.R. 4487, THE "CODIFYING USEFUL REGULATORY DEFINITIONS ACT" OR THE "CURD ACT"

A. Background

The term "natural cheese" has been placed by manufacturers on product labels to identify cheese made directly from milk or cream. Manufacturers of natural cheese distinguish their

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[36] Danish Environmental Protection Agency. *Short-chain Polyfluroalkyl Substances (PFAS): A Literature Review of Information on Human Health Effects and Environmental Fate and Effect Aspects of Short-Chain PFAS. Environmental Project 1707*, Danish Ministry of the Environment: Copenhagen (2015).

[37] Rosenmai et al. *Fluorinated Alkyl Substances and Technical Mixtures Used in Food Paper-Packaging Exhibit Endocrine-Related Activity*. Andrology, Vol. 4, Issue 4, 662-672 (2016).

[38] Birnbaum and Grandjean, *Alternatives to PFASs: Perspectives on the science*, Environmental Health Perspectives, Vol. 123, Issue 5, A104-A105 (2015).

[39] Food and Drug Administration, *Statement on FDA's scientific work to understand per- and polyfluoroalkyl substances (PFAS) in food, and findings from recent FDA surveys* (June 11, 2019) (www.fda.gov/news-events/press-announcements/statement-fdas-scientific-work-understand-and-polyfluoroalkyl-substances-pfas-food-and-findings).

[40] Food and Drug Administration, *FDA Makes Available Testing Method for PFAS in Foods and Final Results from Recent Surveys* (Oct. 21, 2019) (www.fda.gov/food/cfsan-constituent-updates/fda-makes-available-testing-method-pfas-foods-and-final-results-recent-surveys).

[41] Food and Drug Administration, *FDA Makes Available Results from Second Round of Testing for PFAS in Foods from the General Food Supply* (Dec. 20, 2019) (www.fda.gov/food/cfsan-constituent-updates/fda-makes-available-results-second-round-testing-pfas-foods-general-food-supply).

[42] Food and Drug Administration, *Questions and Answers on Per and Polyfluoroalkyl Substances (PFAS) in Food* (accessed Jan. 23, 2020). (www.fda.gov/food/chemicals/questions-and-answers-and-polyfluoroalkyl-substances-pfas-food).

product from pasteurized process cheese, which is made by blending different types of cheese together. However, "natural cheese" has not been officially defined under Federal statute.

B. Legislation

H.R. 4487, the "CURD Act", introduced by Reps. Kind (D-WI), Long (R-MO), and Schrader (D-OR), amends the FFDCA to define the term "natural cheese" as cheese produced by coagulating the protein of milk, skimmed milk, partly skimmed milk, cream, whey cream, or buttermilk, or any combination of such ingredients. The bill further specifies that this must be done through the action of rennet or other suitable coagulating agents, and by partially draining the whey resulting from the coagulation. The bill distinguishes "natural cheese" from pasteurized process cheese and restricts the use of the term "natural cheese" on product labeling to foods defined as such.

XI. WITNESSES

Panel I:

Jeff Allen, Ph.D.
President and CEO
Friends of Cancer Research

Richard Kaeser
Vice President, Global Brand Protection
Johnson & Johnson

Fernando Muzzio, Ph.D.
Distinguished Professor, Chemical and Biochemical Engineering
Rutgers, the State University of New Jersey

Kao-Ping Chua, M.D., Ph.D.
Assistant Professor, Department of Pediatrics
University of Michigan Medical School

Panel II:

Melanie Benesh
Legislative Attorney
Environmental Working Group

Tom Balmer
Executive Vice President
National Milk Producers Federation

J. David Carlin
Senior Vice President of Legislative Affairs and Economic Policy
International Dairy Foods Association

Douglas Corey, D.V.M.
Past President
American Association of Equine Practitioners

Talia Day
Patient Advocate

Paul C. DeLeo, Ph.D.
Principal
Integral Consulting, Inc.

Mardi Mountford
President
Infant Nutrition Council of America

Nancy Perry
Senior Vice President, Government Relations
American Society for the Prevention of Cruelty to Animals

Sara Sorscher
Deputy Director of Regulatory Affairs
Center for Science in the Public Interest