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Attorneys for Defendants
CITY AND COUNTY OF SAN FRANCISCO, ET AL.

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF SAN FRANCISCO

UNLIMITED JURISDICTION

UNITED SF FREEDOM ALLIANCE, BHANU VIKRAM, CARSON R. SCHILLING, CHRISTA L. FESTA, CHRISTIANNE T. CROTTY, DENNIS M. CALLAHAN, JR., FAIMING CHEUNG, and JESSICA KWOK-BO LINDSEY,

Plaintiffs,

vs.

CITY AND COUNTY OF SAN FRANCISCO, a municipal corporation and administrative division of the State of California, et al., and Does 1 through 100, inclusive,

Defendants.

Case No. CGC-22-597428

EXHIBIT J, PART 7–EXHIBIT M TO REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF DEFENDANTS CITY AND COUNTY OF SAN FRANCISCO, ET AL.'S DEMURRER TO THE SECOND AMENDED COMPLAINT FOR VIOLATION OF CIVIL RIGHTS AND DECLARATORY AND INJUNCTIVE RELIEF

Hearing Date: June 21, 2022
Hearing Judge: Judge Richard B. Ulmer
Time: 9:30 a.m.
Place: Dept. 302

Date Action Filed: January 4, 2022
Trial Date: None set

N.12. May an employer voluntarily provide accommodations requested by an applicant or employee due to COVID-19, even if not required to do so under the ADA? *(12/14/21)*

Yes. Employers may choose to provide accommodations beyond what the ADA mandates. Of course, employers must provide a reasonable accommodation under the ADA, absent undue hardship, if the applicant or employee meets the definition of disability, requires an accommodation for the disability, and is qualified for the job with the accommodation. Accommodations might consist of schedule changes, physical modifications to the workplace, telework, or special or modified equipment. See, e.g., **WYSK Section D** or U.S. Department of Labor Blog, **Workers with Long COVID-19: You May Be Entitled to Workplace Accommodations (https://blog.dol.gov/2021/07/06/workers-with-long-covid-19-may-be-entitled-to-accommodations)** for more information.

Applicability of Definition of Disability

N.13. If an employer subjected an applicant or employee to an adverse action, and the applicant or employee is covered under any one of the three ADA definitions of disability, does that mean the employer violated the ADA? *(12/14/21)*

No. Having a disability, alone, does not mean an individual was subjected to an unlawful employment action under the ADA.

For example, the fact that an applicant or employee has a current disability, or a record of disability, does not mean that an employer violated the ADA by not providing an individual with a reasonable accommodation. As discussed in **Section D**., there are several considerations in making reasonable accommodation determinations, including the employee's need for the accommodation due to a disability and whether there is an accommodation that does not pose an undue hardship to the employer.

Similarly, the fact that an employer regarded an applicant or employee as an individual with a disability does not necessarily mean that the employer engaged in unlawful discrimination. For example, the ADA does not require an employer to hire anyone who is not qualified for the job. Moreover, in some instances, an employer may have a defense to an employment action taken based on an actual impairment, such as where the individual poses a **direct threat (https://www.eeoc.gov**

/wysk/what-you-should-know-about-covid-19-and-ada-rehabilitation-act-and-other-eeo-laws) to the health or safety of themselves or others in the workplace.

N.14. Do any ADA protections apply to applicants or employees who do not meet an ADA definition of disability? *(12/14/21)*

Yes. The ADA's requirements about disability-related inquiries and medical exams, **medical confidentiality**, **retaliation, and interference** apply to all applicants and employees, regardless of whether they have an ADA disability. By contrast, an individual must have a "disability" to challenge employment decisions based on disability, denial of reasonable accommodation (see **N.10**), or disability-based harassment.

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EXHIBIT K

TO

REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF DEFENDANTS CITY AND COUNTY OF SAN FRANCISCO, ET AL.'S DEMURRER TO SECOND AMENDED COMPLAINT FOR VIOLATION OF CIVIL RIGHTS AND DECLARATORY AND INJUNCTIVE RELIEF

Why You Should Not Use Ivermectin to Treat or Prevent COVID-19

Español (/consumers/articulos-en-espanol/por-que-no-debe-utilizar-ivermectina-para-tratar-o-prevenir-el-covid-19)

Português (/consumers/consumer-updates/por-que-voce-nao-deve-usar-ivermectina-para-tratar-ou-prevenir-covid-19)

中文 (/consumers/consumer-updates/weishenmebuyinggaishiyongyiweijunsuzhiliaohuoyufang2019xinguanfeiyan)

Tagalog (/consumers/consumer-updates/bakit-hindi-ka-dapat-gumamit-ng-ivermectin-upang-gamutin-o-maiwasan-ang-covid-19)

Tiếng Việt (/consumers/consumer-updates/tai-sao-ban-khong-nen-su-dung-ivermectin-de-dieu-tri-hoac-ngan-ngua-covid-19)

한국어 (/consumers/consumer-updates/kobideu-19-covid-19leul-chilyohago-yebanghagi-wihayeo-ibeomegtineul-sayonghaji-malaya-haneun-iyu)

COVID-19. We've been living with it for what sometimes seems like forever. Given the number of deaths that have occurred from the disease, it's perhaps not surprising that some consumers are turning to drugs not approved or authorized by the Food and Drug Administration (FDA).

One of the FDA's jobs is to carefully evaluate the scientific data on a drug to be sure that it is both safe and effective for a particular use. In some instances, it can be highly dangerous to use a medicine for the prevention or treatment of COVID-19 that has not been approved by or has not received emergency use authorization from the FDA.

There seems to be a growing interest in a drug called ivermectin for the prevention or treatment of COVID-19 in humans. Certain animal formulations of ivermectin such as pour-on, injectable, paste, and "drench," are approved in the U.S. to treat or prevent parasites in animals. For humans, ivermectin tablets are approved at very specific doses to treat some parasitic worms, and there are topical (on the skin) formulations for head lice and skin conditions like rosacea.

However, the FDA has received multiple reports of patients who have required medical attention, including hospitalization, after self-medicating with ivermectin intended for livestock.

Here's What You Need to Know about Ivermectin

- The FDA has not authorized or approved ivermectin for use in preventing or treating COVID-19 in humans or animals. Ivermectin is approved for human use to treat infections caused by some parasitic worms and head lice and skin conditions like rosacea.

- Currently available data do not show ivermectin is effective against COVID-19. Clinical trials (https://www.clinicaltrials.gov/ct2/results?cond=COVID-19&term=ivermectin&cntry=&state=&city=&dist=&Search=Search) assessing ivermectin tablets for the prevention or treatment of COVID-19 in people are ongoing.
- Taking large doses of ivermectin is dangerous.
- If your health care provider writes you an ivermectin prescription, fill it through a legitimate source such as a pharmacy, and take it *exactly* as prescribed.
- Never use medications intended for animals on yourself or other people. Animal ivermectin products are very different from those approved for humans. Use of animal ivermectin for the prevention or treatment of COVID-19 in humans is dangerous.

What is Ivermectin and How is it Used?

Ivermectin tablets are approved by the FDA to treat people with intestinal strongyloidiasis and onchocerciasis, two conditions caused by parasitic worms. In addition, some topical forms of ivermectin are approved to treat external parasites like head lice and for skin conditions such as rosacea.

Some forms of animal ivermectin are approved to prevent heartworm disease and treat certain internal and external parasites. It's important to note that these products are different from the ones for people, and safe only when used in animals as prescribed.

When Can Taking Ivermectin Be Unsafe?

The FDA has not authorized or approved ivermectin for the treatment or prevention of COVID-19 in people or animals. Ivermectin has not been shown to be safe or effective for these indications.

There's a lot of misinformation around, and you may have heard that it's okay to take large doses of ivermectin. It is not okay.

Even the levels of ivermectin for approved human uses can interact with other medications, like blood-thinners. You can also overdose on ivermectin, which can cause nausea, vomiting, diarrhea, hypotension (low blood pressure), allergic reactions (itching and hives), dizziness, ataxia (problems with balance), seizures, coma and even death.

Ivermectin Products for Animals Are Different from Ivermectin Products for People

For one thing, animal drugs are often highly concentrated because they are used for large animals like horses and cows, which weigh a lot more than we do— up to a ton or more. Such high doses can be highly toxic in humans. Moreover, the FDA reviews drugs not just for safety and effectiveness of the active ingredients, but also for the inactive ingredients. Many inactive ingredients found in products for animals aren't evaluated for use in people. Or they are included in much greater quantity than those used in people. In some cases, we don't know how those inactive ingredients will affect how ivermectin is absorbed in the human body.

Options for Preventing and Treating COVID-19

The most effective ways to limit the spread of COVID-19 (https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html) include getting a COVID-19 vaccine when it is available to you and

following current CDC guidance.

Talk to your health care provider about available COVID-19 vaccines and treatment options. Your provider can help determine the best option for you, based on your health history.

FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems

Does not affect FDA-approved uses for malaria, lupus, and rheumatoid arthritis

July 1, 2020 Update: A summary of the FDA review of safety issues (https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/OSE%20Review_Hydroxychloroquine-Cholorquine%20-%2019May2020_Redacted.pdf) with the use of hydroxychloroquine and chloroquine to treat hospitalized patients with COVID-19 is now available. This includes reports of serious heart rhythm problems and other safety issues, including blood and lymph system disorders, kidney injuries, and liver problems and failure.

June 15, 2020 Update: Based on ongoing analysis and emerging scientific data, FDA has revoked the emergency use authorization (EUA) to use hydroxychloroquine and chloroquine to treat COVID-19 in certain hospitalized patients when a clinical trial is unavailable or participation is not feasible. We made this determination based on recent results from a large, randomized clinical trial in hospitalized patients that found these medicines showed no benefit for decreasing the likelihood of death or speeding recovery. This outcome was consistent with other new data, including those showing the suggested dosing for these medicines are unlikely to kill or inhibit the virus that causes COVID-19. As a result, we determined that the legal criteria for the EUA are no longer met. Please refer to the Revocation of the EUA Letter (/media/138945/download)and FAQs on the Revocation of the EUA for Hydroxychloroquine Sulfate and Chloroquine Phosphate (/media/138946/download) for more information.

[4-24-2020] FDA Drug Safety Communication

What safety concern is FDA announcing?

The FDA is aware of reports of serious heart rhythm problems in patients with COVID-19 treated with hydroxychloroquine or chloroquine, often in combination with azithromycin and other QT prolonging medicines. We are also aware of increased use of these

medicines through outpatient prescriptions. Therefore, we would like to remind health care professionals and patients of the known risks associated with both hydroxychloroquine and chloroquine. We will continue to investigate risks associated with the use of hydroxychloroquine and chloroquine for COVID-19 and communicate publicly when we have more information.

Hydroxychloroquine and chloroquine have not been shown to be safe and effective for treating or preventing COVID-19. They are being studied in clinical trials for COVID-19, and we authorized their temporary use during the COVID-19 pandemic for treatment of the virus in hospitalized patients when clinical trials are not available, or participation is not feasible, through an Emergency Use Authorization (EUA) (/media/136784/download). The medicines being used under the hydroxychloroquine/chloroquine EUA (/media/136534/download) are supplied from the Strategic National Stockpile, the national repository of critical medical supplies to be used during public health emergencies. This safety communication reminds physicians and the public of risk information set out in the hydroxychloroquine (/media/136537/download) and chloroquine healthcare provider fact sheets (/media/136535/download) that were required by the EUA.

Hydroxychloroquine and chloroquine can cause abnormal heart rhythms such as QT interval prolongation and a dangerously rapid heart rate called ventricular tachycardia. These risks may increase when these medicines are combined with other medicines known to prolong the QT interval, including the antibiotic azithromycin, which is also being used in some COVID-19 patients without FDA approval for this condition. Patients who also have other health issues such as heart and kidney disease are likely to be at increased risk of these heart problems when receiving these medicines.

What is FDA doing?

To decrease the risk of these heart problems that can be life-threatening, we are warning the public that hydroxychloroquine and chloroquine, either alone or combined with azithromycin, when used for COVID-19 should be limited to clinical trial settings or for treating certain hospitalized patients under the EUA. FDA will continue to investigate risks associated with the use of hydroxychloroquine and chloroquine for COVID-19, and we will communicate publicly when we have more information.

What are hydroxychloroquine and chloroquine and how can they help me?

Hydroxychloroquine and chloroquine are FDA-approved to treat or prevent malaria. Hydroxychloroquine is also FDA-approved to treat autoimmune conditions such as chronic discoid lupus erythematosus, systemic lupus erythematosus in adults, and rheumatoid arthritis.

The EUA was based upon limited evidence (/media/136784/download) that the medicines may provide benefit, and for this reason, we authorized their use only in hospitalized patients under careful heart monitoring.

What should patients and parents/caregivers do?

Patients taking hydroxychloroquine or chloroquine for FDA-approved indications to treat malaria or autoimmune conditions should continue taking their medicine as prescribed. The benefits of these medicines outweigh the risks at the recommended doses for these conditions. Do not stop taking your medicine without first talking to your health care professional, and talk to them if you have any questions or concerns.

Be aware that there are no proven treatments for COVID-19 and no vaccine. If you are receiving hydroxychloroquine or chloroquine for COVID-19 and experience irregular heartbeats, dizziness, or fainting, seek medical attention right away by calling 911.

Do not buy these medicines from online pharmacies without a prescription from your health care professional. Consumers should not take any form of chloroquine that has not been prescribed for them by a healthcare professional. Serious poisoning and death have been reported after mistaken use of a chloroquine product not intended to be taken by humans (/animal-veterinary/product-safety-information/fda-letter-stakeholders-do-not-use-chloroquine-phosphate-intended-fish-treatment-covid-19-humans). If you have these medicines in your home, keep them in childproof containers out of the reach of children to prevent accidental poisoning (https://www.poison.org/18002221222) (http://www.fda.gov/about-fda/website-policies/website-disclaimer).

What should health care professionals do?

We recommend initial evaluation and monitoring when using hydroxychloroquine or chloroquine under the EUA or in clinical trials that investigate these medicines for the treatment or prevention of COVID-19. Monitoring may include baseline ECG, electrolytes, renal function and hepatic tests. Be aware that hydroxychloroquine or chloroquine can:

- cause QT prolongation
- increase the risk of QT prolongation in patients with renal insufficiency or failure
- increase insulin levels and insulin action causing increased risk of severe hypoglycemia
- cause hemolysis in patients with Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency
- interact with other medicines that cause QT prolongation even after discontinuing the medicines due to their long half-lives of approximately 30-60 days

If a healthcare professional is considering use of hydroxychloroquine or chloroquine to treat or prevent COVID-19, FDA recommends checking www.clinicaltrials.gov (http://www.clinicaltrials.gov/) for a suitable clinical trial and consider enrolling the patient. Consider using resources (https://crediblemeds.org/healthcare-providers/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) available to assess a patient's risk of QT prolongation and mortality.

What did FDA find?

We have reviewed case reports in the FDA Adverse Event Reporting System database (/drugs/surveillance/questions-and-answers-fdas-adverse-event-reporting-system-faers), the published medical literature, and the American Association of Poison Control Centers National Poison Data System concerning serious heart-related adverse events and death in patients with COVID-19 receiving hydroxychloroquine and chloroquine, either alone or combined with azithromycin or other QT prolonging medicines. These adverse events were reported from the hospital and outpatient settings for treating or preventing COVID-19, and included QT interval prolongation, ventricular tachycardia and ventricular fibrillation, and in some cases death. We are continuing to investigate these safety risks in patients with COVID-19 and will communicate publicly when more information is available.

How do I report side effects from hydroxychloroquine and chloroquine?

To help FDA track safety issues with medicines, we urge patients and health care professionals to report side effects involving hydroxychloroquine and chloroquine or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

en Español (/drugs/drug-safety-and-availability/la-fda-advierte-en-contra-del-uso-de-la-hidroxicloroquina-o-la-cloroquina-para-el-tratamiento-del)

Drug Safety Communication (/media/137250/download) (PDF - 140KB)

Related Information

- Coronavirus (COVID-19) Update: FDA Revokes Emergency Use Authorization for Chloroquine and Hydroxychloroquine (/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-chloroquine-and)
- COVID-19 FAQs (/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-frequently-asked-questions)
- FAQs on Emergency Use Authorization for Chloroquine and Hydroxychloroquine (/media/136784/download)
- Poison Control (https://www.poison.org/18002221222) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)
- CredibleMeds: QT Drugs Database (https://www.crediblemeds.org/healthcare-providers/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)
- NIH COVID-19 Treatment Guidelines (https://covid19treatmentguidelines.nih.gov/introduction/)
- The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective (/drugs/information-consumers-and-patients-drugs/fdas-drug-review-process-ensuring-drugs-are-safe-and-effective)
- Think It Through: Managing the Benefits and Risks of Medicines (/drugs/information-consumers-and-patients-drugs/think-it-through-managing-benefits-and-risks-medicines)

Contact FDA

For More Info

855-543-DRUG (3784) and press 4
druginfo@fda.hhs.gov (mailto:druginfo@fda.hhs.gov)

Report a Serious Problem to MedWatch

Complete and submit the report Online (https://www.accessdata.fda.gov/scripts/medwatch/).
Download form (/about-fda/medwatch-consumer-voluntary-reporting-pdf) or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.

Back to Top

Lou Kennedy
CEO and Owner
Nephron Pharmaceuticals Corporation
4500 12th Street Extension
West Columbia, SC 29172

RE: ANDA 78202
Budesonide Inhalation Suspension, for inhalation suspension
MA 1, 3

WARNING LETTER

Dear Mr. Kennedy:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has become aware of emails that you and your sales representative sent on July 14, 2020 and July 7, 2020, respectively, in your capacity as employees of Nephron Pharmaceuticals Corporation (Nephron) regarding Budesonide Inhalation Suspension, for inhalation suspension (Budesonide). These emails were submitted as complaints to the FDA Bad Ad Program. The emails provide evidence that Budesonide is intended for a new use for which it lacks approval, specifically treatment of symptoms associated with "Coronavirus Disease 2019" (COVID-19), and for which its labeling does not provide adequate directions for use. This renders Budesonide misbranded within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and makes its distribution violative. 21 U.S.C. 352(f)(1); 331(a). *See* 21 CFR 201.5; 201.100; 201.115; 201.128.

The emails are also false or misleading in that they represent that Budesonide has certain benefits, but fail to include **any** risk information about the drug. Thus, the emails misbrand Budesonide within the meaning of the FD&C Act and make its distribution violative. 21 U.S.C. 352(a) & (n); 321(n), 331(a). *See* 21 CFR 202.1(e)(5). These violations are concerning from a public health perspective because they create a misleading impression about the safety and effectiveness of Budesonide for the treatment of COVID-19 and suggest a use for which the labeling does not provide adequate directions for safe and effective use of the product.

There is currently a global outbreak of respiratory disease caused by a novel coronavirus that has been named "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2). The disease caused by the virus has been named COVID-19. On January 31, 2020, the Department of Health and Human Services (HHS) issued a declaration of a public health

emergency related to COVID-19 and mobilized the Operating Divisions of HHS.[1] The declaration has been renewed for an additional 90 days twice, with the most recent renewal going into effect on July 25, 2020.[2] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[3]

Background

Below are the indication and summary of the most serious and most common risks associated with the use of Budesonide.[4] According to the FDA-approved product labeling (PI):

> Budesonide inhalation suspension is indicated for the maintenance treatment of asthma and as prophylactic therapy in children 12 months to 8 years of age.
>
> Limitations of Use
>
> Budesonide inhalation suspension is NOT indicated for the relief of acute bronchospasm.

Budesonide is contraindicated for primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required and in patients with hypersensitivity to budesonide or any of the ingredients of budesonide inhalation suspension. The PI for Budesonide includes warnings and precautions regarding local effects, deterioration of disease and acute asthma episodes, hypersensitivity reactions including anaphylaxis, immunosuppression, transferring patients from systemic corticosteroids therapy, hypercorticism and adrenal suppression, reduction in bone mineral density, effects on growth, glaucoma and cataracts, paradoxical bronchospasm and upper airway symptoms, eosinophilic conditions and Churg-Strauss Syndrome, and drug interactions with strong cytochrome P450 3A4 inhibitors. The most common adverse reactions reported with use of Budesonide include respiratory infection, rhinitis, coughing, otitis media, viral infection, moniliasis, gastroenteritis, vomiting, diarrhea, abdominal pain, ear infection, epistaxis, conjunctivitis, and rash.

Lack of Adequate Directions for Use

The emails that you and your sales representative sent include claims and representations about the use and/or benefits of Budesonide as a treatment for symptoms associated with

[1] Secretary of Health and Human Services Alex M. Azar II, Determination that a Public Health Emergency Exists. Jan. 31, 2020. (Accessible at https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx).
[2] Secretary of Health and Human Services Alex M. Azar II, Renewal of Determination that a Public Health Emergency Exists. July 23, 2020. (Accessible at https://www.phe.gov/emergency/news/healthactions/phe/Pages/covid19-23June2020.aspx).
[3] President Donald J. Trump, Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19). Mar. 13, 2020. (Accessible at https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/).
[4] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece(s) cited in this letter.

COVID-19. For example, the email that you sent on July 14, 2020 includes the prominent headline claim, "**BUDESONIDE** RELIEVES RESPIRATORY SYMPTOMS ASSOCIATED WITH COVID-19" (emphasis original), in conjunction with an image of your product and what appears to be SARS-CoV-2. This email also states, "Over the last few weeks, doctors and researchers have touted the benefits of using Budesonide as a treatment for symptoms associated with COVID-19. One physician, who went viral this month, called Budesonide a 'silver bullet.'" Additionally, the email that your sales representative sent on July 7, 2020, with the subject line, "COVID-19 – Budesonide – Video," links to a YouTube video that the sales representative says is of a physician discussing "treating COVID patients successfully with Budesonide and an antibiotic. . . . You may want to share this with your respiratory team and pulmonary docs. Cost effective way to treat Coronavirus!"

These claims and representations provide evidence that Nephron is promoting Budesonide for a new use for which it lacks approval and for which its labeling does not provide adequate directions for use. Budesonide is not approved as a treatment for symptoms associated with COVID-19, and its labeling does not contain adequate directions for such use, thereby rendering the drug misbranded. These claims and representations, which misleadingly suggest that Budesonide is safe and effective for a use for which it is not approved and for which you have provided no evidence to support, are particularly alarming from a public health perspective because COVID-19 has caused significant morbidity and mortality, and because there is currently no FDA-approved treatment for symptoms associated with COVID-19.[5]

False or Misleading Risk Presentation

Promotional materials misbrand a drug if they are false or misleading with respect to risk. The determination of whether promotional materials are misleading includes, among other things, not only representations made or suggested in promotional materials, but also failure to reveal facts material in light of representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the materials.

The emails cited above include claims and representations about the use and/or benefits of Budesonide, but they fail to communicate **any** risk information about the product. By omitting the risks associated with Budesonide, the emails fail to provide material information about the consequences that may result from the use of the drug and create a misleading impression about the safety of Budesonide.

Conclusion and Requested Action

For the reasons discussed above, the emails provide evidence that Budesonide is intended for a new use for which it lacks approval, and for which its labeling does not provide adequate directions for use. This renders Budesonide misbranded within the meaning of the FD&C Act and makes its distribution violative. 21 U.S.C. 352(f)(1); 331(a); see 21 CFR 201.5; 201.100; 201.115; 201.128. The emails are also false or misleading and therefore misbrand

[5] https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap.

Budesonide within the meaning of the FD&C Act and make its distribution violative. 21 U.S.C. 352(a) & (n); 321(n), 331(a). *See* 21 CFR 202.1(e)(5).

OPDP requests that Nephron immediately cease misbranding Budesonide and/or cease introducing the misbranded drug into interstate commerce. Please submit a written response to this letter on or before October 6, 2020, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Budesonide that contain statements such as those described above, and explaining your plan for discontinuing use of such materials, or, in the alternative, for ceasing distribution of Budesonide. Because the violation/violations described above are serious, we request, further, that your submission include a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about the issues discussed in this letter to the audience(s) that received the violative promotional materials. In order to clearly identify the violative promotional piece(s) and/or activity and focus on the corrective message(s), OPDP recommends that corrective piece(s) include a description of the violative promotional piece(s) and/or activity, include a summary of the violative message(s), provide information to correct each of the violative message(s), and be free of promotional claims and presentations. To the extent possible, corrective messaging should be distributed using the same media, and generally for the same duration of time and with the same frequency that the violative promotional material was disseminated. If you believe that your product is not in violation of the FD&C Act, include your reasoning and any supporting information for our consideration.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266**. A courtesy copy can be sent by facsimile to (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA 1, 3 in addition to the ANDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Warning Letter.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Budesonide comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Failure to correct the violations discussed above may result in FDA regulatory action, including seizure or injunction, without further notice.

Sincerely,

{See appended electronic signature page}

Robert Dean
Director
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

ROBERT T DEAN
09/22/2020 03:22:53 PM

EXHIBIT L

TO

REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF DEFENDANTS CITY AND COUNTY OF SAN FRANCISCO, ET AL.'S DEMURRER TO SECOND AMENDED COMPLAINT FOR VIOLATION OF CIVIL RIGHTS AND DECLARATORY AND INJUNCTIVE RELIEF

City and County of San Francisco

Department of Public Health

San Francisco General Hospital and Trauma Center

Roland Pickens, Interim Chief Executive Officer

Occupational Health Service - San Francisco General Hospital and Trauma Center
1001 Potrero Avenue ◦ Building 9 – Room 115 ◦ San Francisco, CA 94110
Telephone: 415.206.6581 ◦ Fax: 415.206.3669

OCCUPATIONAL HEALTH REQUIREMENTS

In accordance with Centers for Disease Control and Prevention Guidelines, Centers for Medicare and Medicaid Services (CMS), California Occupational Safety and Health Administration, (Cal/OSHA) and California State Infection Control Laws, all applicants (new and reappointments) are now required to submit proof of immunity from certain communicable diseases. The San Francisco General Hospital (SFGH) Medical Center requires that you also have annual Tuberculosis screening and N95 fit testing to work in-patient care areas.

You are required to sumbit the following to SFGH Occupational Health Services (OHS):

Proof of immunity (i.e. titer results or immunization records from your primary care provider, training program, or Employee Health program from previous position) for the following:

Measles
Mumps
Rubella
Varicella
Tetanus, Diphtheria, Pertussis (Tdap) documentation or declination
Hepatitis B vaccine documentation of 3 vaccinations AND positive titer or declination
Annual Flu Shot – vaccination or declination (During influenza season only – October through March, SFGH imposes a mandatory masking policy for all unvaccinated patient caregivers).

Documentation for Tuberculosis Testing: Acceptable Documentation includes a typed letter on formal letterhead, legibly signed note from personal physician. The letter must describe the reaction in millimeters which has occurred within the preveious 12 months.

For previous negative results:

Documentation of a previous two-step Tuberculosis skin test (TST) with ongoing annual surveillance *AND* most recent in last 12 months
OR
Tuberculosis skin test - One within last 12 months AND one within previous 90 days.
OR
IGRA Results - T-Spot or Quantiferon Gold (previous 12 months)
OR
Printout from previous occupational health provider (previous employer in the previous 12 months)

For previous positive results: Acceptable documentation includes a typed letter on formal letterhead, legibly signed note from personal physician. The letter must describe proof of previous medication treatment or the reaction in millimeters.

For new appointments: SFGH Symptom review form and Chest x-ray films within last 90 days.

For reappointments: SFGH Symptom review form and Chest x-ray, as determined necessary.

If you do not have all the immunization/TB records, you are required to make an appointment with Occupational Health Services to have titers drawn, TB testing, or N-95 Mask Fit testing as needed.

SFGH Occupational Health Services Location:
1001 Potrero Ave, Building 9, Room 115
(415) 206-6581 -- press 2 for appointment

You will be notified by Medical Staff services if you are not compliant for credentialing. Medical Staff Services will notify you when you are in compliance.

EXHIBIT M

TO

REQUEST FOR JUDICIAL NOTICE IN SUPPORT OF DEFENDANTS CITY AND COUNTY OF SAN FRANCISCO, ET AL.'S DEMURRER TO SECOND AMENDED COMPLAINT FOR VIOLATION OF CIVIL RIGHTS AND DECLARATORY AND INJUNCTIVE RELIEF

TOMÁS J. ARAGÓN, M.D., Dr.P.H.
State Public Health Officer & Director

State of California—Health and Human Services Agency

California Department of Public Health

GAVIN NEWSOM
Governor

February 22, 2022

TO: All Californians

SUBJECT: Health Care Worker Vaccine Requirement

Related Materials: Health Care Worker Vaccine Requirement Q&A | All Facilities Letter 21-30.3 | All Facilities Letter 21-29.3 | All Facilities Letter 21-34.3 | All Facilities Letter 21-27.3 | All Facilities Letter 21-28.3

Updates as of February 22, 2022:

- Allows for workers with completed primary series vaccination and recent infection to defer booster dose by up to 90 days from infection.

State Public Health Officer Order of February 22, 2022

Since the start of the pandemic, CDPH has led with science and data to better understand this disease. There has been a growing body of evidence suggesting that a combination of history of SarsCoV2 vaccination and infection can lead to a strong "hybrid" immunity after recovery from infection. Additionally, there is immunological data suggesting that allowing an adequate interval between an infection and a COVID-19 vaccination dose may be important to allow quality immune memory.

Vaccines continue to remain the most critical aspect of moving our communities out of this pandemic. They lower risk of getting and spreading the virus that causes COVID-19 and also prevent serious illness and death. They are critical for building a foundation of individual and herd immunity, especially while a portion of our population continues to be unvaccinated. According to the CDC "… getting a COVID-19 vaccination is a safer and more dependable way to build immunity to COVID-19 than getting sick with COVID-19. COVID-19 vaccination causes a more predictable immune response than infection with the virus that causes COVID-19." Conversely, the level of protection people get from COVID-19 infection alone may vary widely depending on how mild or severe their illness was, the time since their infection, which variant they were infected with, and their age. Increasing evidence shows that a combination of infection after completing the primary series of vaccination can build strong hybrid immunity. Thus CDPH is updating its order requiring health care workers to be fully vaccinated and boosted by March 1, 2022 to allow delay of the March 1, 2022 deadline for receiving a booster for covered workers with proof of a recent infection for up to 90 days from date of infection.

Accordingly, amendments to the original State Public Health Officer Order of December 22, 2021, are needed at

this time, to reflect current science and understanding as it relates to hybrid immunity in those who are fully vaccinated and then become infected. As we continue to learn more about post-Omicron infection immunity, hybrid immunity, waning immunity in general, and what new variants may evolve, we will continue to reassess COVID-19 vaccine requirements and recommendations.

Introduction from Original State Public Health Officer Order of December 22, 2021

Since Thanksgiving, the statewide seven-day average case rate has increased by 34% and hospitalizations have increased by 17%. In addition, the recent emergence of the Omicron variant (it is estimated that approximately 70% of cases sequenced, nationally, are Omicron and rapid increases are occurring globally) further emphasizes the importance of vaccination, boosters, and prevention efforts, including testing, are needed to continue protecting against COVID-19.

Early data also suggest the increased transmissibility of the Omicron variant is two to four times as infectious as the Delta variant, and there is evidence of immune evasion. Recent evidence also shows that among healthcare workers, vaccine effectiveness against COVID-19 infection is also decreasing over time without boosters. Consequently, current vaccine requirements of staff in health care settings are not proving sufficient to prevent transmission of the more transmissible Omicron variant. Boosters have been available in California since September 2021.

Although COVID-19 vaccination remains effective in preventing severe disease, recent data suggest vaccination becomes less effective over time at preventing infection or milder illness with symptoms, especially in people aged 65 years and older.

Based on the emergence of Omicron, additional statewide facility-directed measures are necessary to ensure we maintain adequate staffing levels within our healthcare delivery system. Additionally, given the current hospital census, even a moderate surge in cases and hospitalizations could materially impact California's health care delivery system within certain regions of the state. Accordingly, amendments to the original State Public Health Officer Order of August 5, 2021, to make boosters mandatory and to require additional testing of workers eligible for boosters who are not yet boosted, are necessary at this critical time.

Introduction from Original State Public Health Officer Order of August 5, 2021

The COVID-19 pandemic remains a significant challenge in California. COVID-19 vaccines are effective in reducing infection and serious disease. At present, 63% of Californians 12 years of age and older are fully vaccinated with an additional 10% partially vaccinated. California is currently experiencing the fastest increase in COVID-19 cases during the entire pandemic with 18.3 new cases per 100,000 people per day, with case rates increasing ninefold within two months. The Delta variant is highly transmissible and may cause more severe illness. In fact, recent data suggests that viral load is roughly 1,000 times higher in people infected with the Delta variant than those infected with the original coronavirus strain, according to a recent study. The Delta variant is currently the most common variant causing new infections in California.

Unvaccinated persons are more likely to get infected and spread the virus, which is transmitted through the air. Most current hospitalizations and deaths are among unvaccinated persons. Thanks to vaccinations and to measures taken since March 2020, California's health care system is currently able to address the increase in cases and hospitalizations. However, additional statewide facility-directed measures are necessary to protect particularly vulnerable populations, and ensure a sufficient, consistent supply of workers in high-risk health care settings.

Hospitals, skilled nursing facilities (SNFs), and the other health care facility types identified in this order are particularly high-risk settings where COVID-19 outbreaks can have severe consequences for vulnerable

populations including hospitalization, severe illness, and death. Further, the settings in this order share several features. There is frequent exposure to staff and highly vulnerable patients, including elderly, chronically ill, critically ill, medically fragile, and disabled patients. In many of these settings, the patients are at high risk of severe COVID-19 disease due to underlying health conditions, advanced age, or both.

Vaccinations have been available in California from December 2020 to the present, and from January 1, 2021, to July 12, 2021, a total of 9,371 confirmed COVID-19 outbreaks and 113,196 outbreak-related cases were reported to CDPH. Increasing numbers of health care workers are among the new positive cases, despite vaccinations being prioritized for this group when vaccines initially became available. Recent outbreaks in health care settings have frequently been traced to unvaccinated staff members.

Vaccination against COVID-19 is the most effective means of preventing infection with the COVID-19 virus, and subsequent transmission and outbreaks. As we respond to the dramatic increase in cases, all health care workers must be vaccinated to reduce the chance of transmission to vulnerable populations.

For these reasons, COVID-19 remains a concern to public health and, in order to prevent its further spread in hospitals, SNFs, and other health care settings, new public health requirements are necessary at this time.

NOW, THEREFORE, I, as State Public Health Officer of the State of California, order:

1. All workers who provide services or work in facilities described in subdivision (a) have their first dose of a one-dose regimen or their second dose of a two-dose regimen by September 30, 2021:

a. Health Care Facilities:

i. General Acute Care Hospitals
ii. Skilled Nursing Facilities (including Subacute Facilities)
iii. Intermediate Care Facilities
iv. Acute Psychiatric Hospitals
v. Adult Day Health Care Centers
vi. Program of All-Inclusive Care for the Elderly (PACE) and PACE Centers
vii. Ambulatory Surgery Centers
viii. Chemical Dependency Recovery Hospitals
ix. Clinics & Doctor Offices (including behavioral health, surgical)
x. Congregate Living Health Facilities
xi. Dialysis Centers
xii. Hospice Facilities
xiii. Pediatric Day Health and Respite Care Facilities
xiv. Residential Substance Use Treatment and Mental Health Treatment Facilities

b. Two-dose vaccines include: Pfizer-BioNTech or Moderna or vaccines authorized by the World Health Organization. The one-dose vaccine is: Johnson and Johnson [J&J]/Janssen. All COVID-19 vaccines that are currently authorized for emergency use can be found at the following links:

i. By the US Food and Drug Administration (FDA), are listed at the FDA COVID-19 Vaccines webpage.
ii. By the World Health Organization (WHO), are listed at the WHO COVID-19 Vaccines webpage.

c. "Worker" refers to all paid and unpaid individuals who work in indoor settings where (1) care is provided to patients, or (2) patients have access for any purpose. This includes workers serving in health care or other health care settings who have the potential for direct or indirect exposure to patients or SARS-CoV-2 airborne aerosols. Workers include, but are not limited to, nurses, nursing assistants, physicians, technicians, therapists, phlebotomists, pharmacists, students and trainees, contractual staff not employed by the health care facility, and persons not directly involved in patient care, but who could be exposed to infectious agents that can be transmitted in the health care setting (e.g., clerical, dietary, environmental services, laundry, security, engineering and facilities management, administrative, billing, and volunteer personnel).

2. All workers currently eligible for boosters, who provide services or work in facilities described in subdivision 1(a) must be "fully vaccinated and boosted" for COVID-19 receiving all recommended doses of the primary series of vaccines and a vaccine booster dose pursuant to Table A below.

Table A:

California Immunization Requirements for Covered Workers

COVID-19 Vaccine	Primary Series	When to get the vaccine booster dose	Which vaccine booster dose to receive
Moderna or Pfizer-BioNTech	1st and 2nd doses	Booster dose 6 mos after 2nd dose	Any of the COVID-19 vaccines authorized in the United States may be used for the booster dose, but either Moderna or Pfizer-BioNTech are preferred.
Johnson and Johnson [J&J]/Janssen	1st dose	Booster dose 2 mos after 1st dose	Any of the COVID-19 vaccines authorized in the United States may be used for the booster dose, but either Moderna or Pfizer-BioNTech are preferred.
World Health Organization (WHO) emergency use listing COVID-19 vaccine	All recommended doses	Booster dose 6 mos after getting all recommended doses	Single booster dose of Pfizer-BioNTech COVID-19 vaccine

A mix and match series composed of any combination of FDA-approved, FDA-authorized, or WHO-EUL COVID-19 vaccines	All recommended doses	Booster dose 6 mos after getting all recommended doses	Single booster dose of Pfizer-BioNTech COVID-19 vaccine

a. Those workers currently eligible for booster doses per the Table above must receive their booster dose by no later than March 1, 2022.[1] Workers who provide proof of COVID-19 infection after completion of their primary series [2] may defer booster administration for up to 90 days from date of first positive test or clinical diagnosis, which in some situations, may extend the booster dose requirement beyond March 1st. Workers not yet eligible for boosters must be in compliance no later than 15 days after the recommended timeframe above for receiving the booster dose. Workers with a deferral due to a proven COVID-19 infection must be in compliance no later than 15 days after the expiration of their deferral.

3. Workers may be exempt from the vaccination requirements under sections (1) and (2) only upon providing the operator of the facility a declination form, signed by the individual, stating either of the following: (1) the worker is declining vaccination based on Religious Beliefs, or (2) the worker is excused from receiving any COVID-19 vaccine due to Qualifying Medical Reasons.

a. To be eligible for a Qualified Medical Reasons exemption the worker must also provide to their employer a written statement signed by a physician, nurse practitioner, or other licensed medical professional practicing under the license of a physician stating that the individual qualifies for the exemption (but the statement should not describe the underlying medical condition or disability) and indicating the probable duration of the worker's inability to receive the vaccine (or if the duration is unknown or permanent, so indicate).

4. If an operator of a facility listed above under section (1) deems a worker to have met the requirements of an exemption pursuant to section (3) OR deems a booster-eligible worker to have not yet received their booster dose pursuant to section (2), the worker must meet the following requirements when entering or working in such facility:

a. Test for COVID-19 with either PCR or antigen test that either has Emergency Use Authorization by the U.S. Food and Drug Administration or be operating per the Laboratory Developed Test requirements by the U.S. Centers for Medicare and Medicaid Services. Testing must occur at least twice weekly for unvaccinated exempt workers and booster-eligible workers who have not yet received their booster in acute health care and long-term care settings, and at least once weekly for such workers in other health care settings. Facilities must begin testing of all booster-eligible workers who have not yet received their booster by December 27, 2021. CDPH strongly recommends that all workers in Skilled Nursing Facilities (including those that are fully vaccinated and boosted) undergo at least twice weekly screening testing.

b. Wear a surgical mask or higher-level respirator approved by the National Institute of Occupational Safety and Health (NIOSH), such as an N95 filtering facepiece respirator, at all times while in the facility.

5. Consistent with applicable privacy laws and regulations, the operator of the facility must maintain records of workers' vaccination or exemption status. If the worker is exempt pursuant to section (3), the operator of the facility then also must maintain records of the worker's testing results pursuant to section (4).

a. The facility must provide such records to the local or state Public Health Officer or their designee promptly upon request, and in any event no later than the next business day after receiving the request.

b. Operators of the facilities subject to the requirement under section (1) must maintain records pursuant to the CDPH Guidance for Vaccine Records Guidelines & Standards with the following information: (1) full name and date of birth; (2) vaccine manufacturer; and (3) date of vaccine administration (for first dose and, if applicable, second dose).

c. For unvaccinated workers: signed declination forms with written health care provider's statement where applicable, as described in section (2) above.

d. Testing records pursuant to section (4) must be maintained.

6. Nothing in this Order limits otherwise applicable requirements related to Personal Protective Equipment, personnel training, and infection control policies and practices.

7. Facilities covered by this Order are encouraged to provide onsite vaccinations, easy access to nearby vaccinations, use of work time to get vaccinated, and education and outreach on vaccinations, including:

a. access to epidemiologists, physicians, and other counselors who can answer questions or concerns related to vaccinations and provide culturally sensitive advice; and

b. access to online resources providing up to date information on COVID-19 science and research.

8. The July 26 Public Health Order will continue to apply.

9. This Order shall take effect on December 22, 2021, and facilities must be in compliance with the Order by February 1, 2022, with the exception of the deadlines set forth in section 2.a, which facilities must comply with as written.

10. The terms of this Order supersede the August 5, 2021 State Health Officer Health Care Worker Vaccine Requirement Order.

11. This Order is issued pursuant to Health and Safety Code sections 120125, 120140, 120175,120195 and 131080 and other applicable law.

Tomás J. Aragón, MD, DrPH

Director and State Public Health Officer

California Department of Public Health

[1] On January 25, 2022, this deadline for booster doses was updated from February 1, 2022, to March 1, 2022. This change was necessary because of challenges caused by the Omicron surge that made it difficult for some to obtain their booster doses by the initial deadline. For instance, impacted persons were unable to get boosted while ill. Further, there are critical staffing shortages in some areas and additional flexibility is needed due to the fact that boosting can cause missed time from work due to side effects related to receiving booster doses.

[2] To provide proof of prior infection, workers must provide documentation of previous diagnosis from a healthcare provider or confirmed laboratory results.

California Department of Public Health
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