FDA Clears New Formula of Pfizer's COVID Vaccine for Kids and Adults Despite No Data on Safety or Efficacy

The U.S. Food and Drug Administration (FDA) on Oct. 29, 2021, approved emergency use authorization (EUA) of the Pfizer-BioNTech COVID vaccine for children aged 5 to 11, signing off on a new formula that contains tromethamine (Tris), without requiring animal or human data to assess safety or efficacy.

Instead, the FDA conducted "analytical comparability assessments" to see if Pfizer's COVID vaccine formulations containing Tris and phosphate-buffered saline (PBS) buffers were "analytically comparable," while assuring the public just 11 days before requesting EUA for the 5 to 11 age group the formula remained unchanged.

The formula for Pfizer's Comirnaty vaccine, fully approved by the FDA on Aug. 26 was not changed, despite the FDA stating at the time the two formulas were essentially the same. (What

this means, is that the Pfizer vaccine being given to everyone in the U.S. may not even contain the same formulation as the Pfizer vaccine that was actually licensed by the FDA.)

Pfizer and BioNTech submitted a request on Oct. 7, to amend its EUA to include use of a 2-dose primary series of the Pfizer-BioNTech COVID. vaccine – 10 µg each dose, administered 3 weeks apart – in individuals 5 to 11 years of age for active immunization to prevent COVID-19 caused by SARS-CoV-2.

On page 14 of the FDA's briefing document, it states "authorization is being requested for a modified formulation of the Pfizer-BioNTech COVID-19 Vaccine."

Under "vaccine formulation," it further states, "to provide a vaccine with an improved stability profile, the Pfizer-BioNTech COVID-19 vaccine for use in children 5-11 years of age uses tromethamine (Tris) buffer instead of the phosphate-buffered saline (PBS) as used in the previous formulation and excludes sodium chloride and potassium chloride."

The document states, "authorization and future licensure of the modified formulation is based on analytical comparability to the currently authorized PBS containing formulation."

Pfizer said the "change in buffer is not considered clinically significant," and is used to simplify administration and increase storage times in pharmaceutical products. The new formula is authorized for use in individuals 5 to 11 and in those 12 years of age and older, according to the Pfizer-BioNTech EUA letter of authorization (LOA) reissued by the FDA on Oct. 29.

Yet, Pfizer's COVID vaccine containing PBS – the formula actually used in the clinical trial for children aged 5 to 11– was not authorized for use in the 5 to 11 age group.

According to Cleveland Clinic, Tris is commonly used for the prevention and treatment of metabolic acidosis associated with

various clinical conditions such as heart bypass surgery or cardiac arrest. It is also used in other vaccines like dengue, smallpox and Ebola vaccines – none of which are routinely used in children – and a diabetes medication called Humalog.

The FDA categorizes tromethamine as a "category C" drug for pregnancy. It is not known whether tromethamine will harm an unborn baby, but animal reproduction studies have shown an adverse effect on the fetus, and "there are "no adequate and well-controlled studies in humans."

"The new formulation contains tromethamine, which is known as Tris buffer, and it's commonly used as a buffer in a variety of other FDA-approved vaccines and biologics, including products for use in children," Dr. Peter Marks, director of the Center for Biologics Evaluation and Research, said during a press briefing. "The FDA-evaluated manufacturing data [to] support the change in this inactive ingredient, and concluded it did not impact the safety or effectiveness of the product."

Yet, no human or animal trials were conducted to determine the safety or efficacy of the new formula and the FDA required no additional data to assure its safety or stability. According to the FDA's Letter of Authorization (LOA), reissued on Oct. 29, "analytical comparability assessments" showed the Pfizer-BioNTech COVID vaccine formulations containing Tris and PBS buffers were "analytically comparable."

"Analytical comparability assessments use laboratory testing to demonstrate that a change in product formulation does not impact a product's safety or effectiveness," the LOA states.

In conducting its assessment, the FDA said it compared the modified formulation with the Tris buffer to the originally-authorized formulation containing the PBS buffer – evaluating product appearance, size of the lipid-nanoparticle (LNP), integrity of the modRNA in the product, product composition and purity.

"The combination of release testing and characterization testing demonstrated that the modified formulation is analytically comparable to the original formulation," the FDA concluded.

Scientist says approval of new formula is 'simply outrageous'

During a meeting of the Vaccine and Related Biological Products Advisory Committee (VRBPAC) on Oct. 26, Dr. Steven Pergam, associate professor of vaccine and Infectious disease and clinical research at Fred Hutch, asked Dr. William Gruber, Senior Vice President of Pfizer Vaccine Clinical Research and Development [2:55:24] whether the "actual study" done in the 5 to 11 age group used the new Tris buffer.

Gruber responded, "the studies were done using the same volume 0.2 ml that is in the final presentation in terms of the dose but contained the PBS buffer. We obviously had extensive consultations with the FDA and it was determined that clinical studies were not required – again because the LNP and the mRNA are the same and the behavior in terms of the reactogenicity and efficacy are expected to be the same."

Dr. David Wiseman, a research scientist with a background in pharmaceutical research and product development, said the FDA's approval of Pfizer's new formula is "simply outrageous," without adequate studies to determine the safety or efficacy of the new formula.

"Whenever you've got an FDA regulated product – whatever the product is that the FDA regulates – and now they want to make even a minor manufacturing change, you have to justify to FDA why the proposed change you want to make does not impact safety or efficacy. That's the basic rule," Wiseman said.

"Potentially, it must go through all the kinds of testing you did with the old product. The company's objective is to get away with as little as possible. The FDA's objective, if they're being honest about it, is to do a reasonably good job

and to ask the company to do A, B or C types of studies in order to have some sort of assurance the proposed change doesn't affect the safety and efficacy of the product."

Wiseman said, as someone who works in the medical industry, it's inconceivable to him that animal studies were not performed to at least determine if the products are equivalent – and if he were changing the formula, he would be prepared to present animal studies or other types of studies to assure biological equivalence – not just analytical equivalence.

"All FDA did was evaluate the manufacturing data. They did not ask or apparently ask for animal data, and Pfizer apparently didn't provide it if they've done it," Wiseman said.

Wiseman stressed one might argue the buffer change is minor, but he's seen minor changes turn out not to be so minor, and "they would have needed to do animal toxicity studies, look how the product affects the reproductive system and conduct a biodistribution study – studying how the drug moves around the body," in addition to clinical studies.

"We could be very very clever and make all sorts of theories but at the end of the day I want to see it – and there could be chemical changes that weren't measured in a lab," Wiseman said.

Issues could arise from changing the PBS buffer to a Tris buffer, as the buffers affect storage conditions of the vaccine and there's a lot of quality control involved and opportunity for things to go wrong, Wiseman said. It could affect product stability and the potency of the dose – making it closer to the Moderna levels and it could result in people getting an effectively higher dose than they were before the formula was changed.

A different buffer may also affect the acidity of the local area and could change the charge, potentially affecting how the lipids are taken up in the body at the injection site and

how they are distributed around the body.

Moderna's COVID vaccine also contains tromethamine and has been restricted in Germany, France, Denmark, Sweden and Finland to people over the age of 30 due to an increased risk of myocarditis.

On Oct. 31, the FDA announced it was delaying its decision on whether to authorize Moderna's COVID vaccine for adolescents until the agency could determine whether the shot increases the risk of myocarditis. Yet, U.S. regulators have authorized the buffer change for everyone.

Pfizer, FDA said vaccine formula remained unchanged 11 days before requesting EUA for 5- to 11-year-olds

On Sept. 24, USA Today published an article, "Fact check: False claim that COVID-19 vaccine ingredients and formulas have changed since the rollout." In it, the news agency attempted to debunk theories Pfizer's formula had been changed.

"Once a COVID-19 vaccine has been granted EUA or is formally licensed and distributed for human use, there really is no changing its ingredients or formulation," said Dr. Paul Offit, director of the Vaccine Education Center at the Children's Hospital of Philadelphia and member of the FDA's COVID vaccine advisory panel.

"Every lot has to be exactly the same as the next lot, exactly the same," Offit told USA TODAY, explaining this consistency is baked into the vaccine's approval process, which also involves how the vaccine is manufactured.

Any change or addition to a vaccine for whatever reason would require vaccine developers to have their product reassessed by the FDA. "If a company ever decides to make a change … they have to essentially get a new license," Offit said.

In an emailed statement to USA TODAY, an FDA spokesperson said any major changes made to a vaccine or drug require “the submission of data, based on adequate and well-controlled clinical studies demonstrating safety and effectiveness.” The FDA must then approve any such changes.

Pfizer spokesperson Keanna Ghazvini confirmed in an email, the formulas and ingredients contained in their companies’ COVID vaccines had not been changed since their initial EUA issuance, while just 11 days later, disclosing during their request to amend EUA for 5 to 11 year-olds the formula had changed.