From: CERB DO Correspondence / CEPRB Correspondance (HC/SC)
Sent: Tuesday, June 1, 2021 3:00 PM
To: Jean Marc Benoit
Subject: RE: Questions regarding Interim Approval for Pfizer-BioNTech vaccine in children ages 12-17

Dear Dr. Jean Marc Benoit,

Thank you for writing to Health Canada. Your inquiry dated May 10, 2021 was forwarded to the Biologic and Radiopharmaceutical Drugs Directorate (BRDD).

Please see below our responses to your questions.

Q1. On what basis is emergency interim authorization given for Covid-19 vaccination of children? What is the quantitative evidence of morbidity and mortality in Canadian children aged 12 to 17?

Q2. It is stated that the risk-benefit profile is “considered favourable” however, no quantification of risk for Canadian children is given. What is quantified risk for Canadian children for administration of this vaccine?

All of the authorized COVID-19 vaccines were tested in large phase 3 clinical trials with tens of thousands of participants. The key outcome assessed in those trials was the prevention of symptomatic COVID-19, and all of the authorized vaccines have also been shown to be effective in the prevention of hospitalization and death from COVID-19. Health Canada authorized the use of the Pfizer vaccine in children 12-15 years of age on May 5, 2021, after a thorough review of the available safety and efficacy data from a clinical trial in this age group, and building on all of the evidence which we had already reviewed. It is noteworthy that the vaccine was also approved by other regulatory jurisdiction for that age group (e.g. European Medicines Agency and the United States Food and Drugs Administration). COVID-19 is a serious disease that can have consequences for all age groups, including young people, particularly given the circulation of new variants of concern. Vaccinating younger adolescents will help protect them against severe COVID-19 outcomes and is expected to indirectly protect those around them, including vulnerable populations and those who are not eligible to receive a COVID-19 vaccine. The Pfizer-BioNTech vaccine will play an important role in protecting younger Canadians, their families, and their communities from COVID-19 illness, hospitalization and death.

You can find more information about the evidence on which Health Canada has based its decisions in the “Summary Basis of Decisions” documents available here: https://covid-vaccine.canada.ca.

Health Canada and the Public Health Agency of Canada also continue to monitor the safety of vaccines after authorization.

Q3. The cited literature which justifies this emergency interim authorization is an internal Pfizer document, which has yet to be published and subject to peer review. Given the known threat to validity of clinical studies carried out by the manufacturers of therapeutics, how does Health Canada justify proceeding on the basis of this material alone?

The health and safety of Canadians are the utmost priority for Health Canada, this is especially essential during the pandemic situation. Health Canada's Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19 provides for a mechanism to authorize vaccines and drugs for COVID-19 on an interim basis, similar to the emergency use authorization process used by the US FDA and other jurisdiction. The level of evidence submitted to support efficacy and safety for the authorization is similar across all international regulatory jurisdictions, and must meet a high standard of efficacy, safety and quality. In fact, Health Canada's requirements align with the published international statement on COVID-19 vaccines evidence.

Health Canada has a rigorous scientific review system in place to ensure vaccines are safe and effective throughout their lifecycle, from clinical trials to post-market surveillance. While Health Canada is expediting the approval process for COVID-19 drugs and vaccines, the Department only authorizes a vaccine once the data has demonstrated that the vaccine's benefits outweigh its risks for Canadians.

Specific information describing the information that Health Canada reviewed for the Pfizer-BioNTech COVID-19 Vaccine for 12 to 15 year olds and how the decision was made can be found at: https://covid-vaccine.canada.ca/info/regulatory-decision-summary-detailTwo.html?linkID=RDS00802

To ensure that the benefits of the vaccine continue to outweigh the risks, terms and conditions were imposed upon the authorization with respect to quality, clinical, labelling, and Risk Management Plan requirements: The manufacturer is required to provide safety data for all children 12 to 15 years of age in study C4591001, 6-months after Dose 2, when the data become available; to provide Study C4591001 report including safety, efficacy and immunogenicity data up to 2 years after Dose 2 in children 12 to15 years of age, when the data become available; and to provide the European Risk Management Plan with the Canadian Addendum adding information pertaining to the use in individuals 12 to 15 years of age to the safety specification, pharmacovigilance plan and risk minimization activities by May 25, 2021. Further, all post-market requirements including reporting of adverse reactions, monthly safety reports, patient information cards, signal assessment, etc. should continue to be submitted. Health Canada can also ask the manufacturer to submit additional safety information at any time.

As for all medicines, Health Canada continues to monitor the safety of the Pfizer-BioNTech COVID-19 vaccine in Canada closely. Along with the Public Health Agency of Canada and working in close collaboration with the provinces and territories and the manufacturer, we monitor for any adverse events that may develop after immunization.

In addition, the manufacturer (Pfizer Canada ULC and BioNTech Manufacturing GmbH) is legally required to submit reports of adverse events to Health Canada.

The manufacturer is planning to follow clinical trial participants for at least 2 years after the second dose of the vaccine is given. It must communicate any safety concerns to Health Canada.

The Department will take appropriate action, if required, to protect the health and safety of Canadians.

Q4. The cited literature to assess safety includes unpublished data on 1130 children. Given the extremely small sample size involved, how does Health Canada justify its decision that adequate data exists to evaluate safety in children?

The COVID-19 pandemic has created an unprecedented demand on Canada's health care system and has led to an urgent need for access to health products. As part of the government's broad response to the pandemic, Health Canada introduced new innovative and agile regulatory measures. These measures expedite the regulatory review of COVID-19 health products without compromising safety, efficacy and quality standards. These measures are helping to make health products needed for COVID-19, such as vaccines, available to Canadians.

Health Canada evaluates a vaccine for its safety, efficacy and quality based on scientific and clinical evidence, and authorizes vaccines that are safe, effective and of high quality, and whose benefits outweigh the risks. Health Canada will continue to monitor the quality of vaccines authorized for sale in Canada and conduct post-market surveillance of safety and effectiveness of vaccines authorized for sale in Canada.

Health Canada uses internal and international standards to evaluate vaccine (or preventive) products in pediatrics, using guidance documents from the World Health Organization, the European Agency for the Evaluation of Medicinal Products, the International Council for Harmonization of

Technical Requirements for Pharmaceuticals for Human Use, and the U.S. Food and Drug Administration.

The sample size of adolescents 12-15 years of age in the study is acceptable for authorization of vaccine under the Interim Order. The data set for adolescents 12-15 years of age is considered acceptable to establish a benefit-risk profile in this population. It is important to note that the use in adults also contributes to our knowledge on the vaccine. The safety assessment for 12-15 year olds indicated the following:

- Regarding reactogenicity, Tozinameran was well tolerated in subjects 12-15 years old and showed a similar pattern to that seen in 16-25 year olds. Pain at the injection site, fatigue, headaches, chills, joint pain and muscle pain were the most predominant as well as fever. Increased systemic events after dose 2 was similar to that seen with 16-25 year olds.

- The overall number of unsolicited adverse events, including severe adverse events, serious adverse events and adverse events of special interest, were few. The highest incidence was in the General Disorders and Administration Site Conditions, reflecting local and systemic reactogenicity events. Lymphadenopathy was identified as related to vaccination. There were no related SAEs. No deaths were reported. In addition, the updated safety follow-up in a large population in individuals 16-55 years of age did not identify new safety signals. This information was also supportive of the pediatric indication.

As stated above, the safety of the adolescents in the study is continued to be monitored, and post-marketing surveillance is in place for all populations.

Health Canada has placed terms and conditions on this authorization requiring Pfizer-BioNTech to continue providing information to Health Canada on the safety, efficacy and quality of the vaccine in this younger age group to ensure its benefits continue to be demonstrated once it is on the market. As with any therapeutic product, Health Canada will continue to closely monitor the safety of this vaccine, and will take action if safety concerns are identified.

Vaccines will play an essential role in the ability of Canadians to recover safely from the COVID-19 pandemic. The ongoing COVID-19 pandemic has a significant impact on public health. The availability of safe and effective vaccines will reduce the spread and severity of COVID-19 disease and reduce its social and economic consequences.

Q5. The United States has a Vaccine Adverse Events Reporting System (VAERS), and there are child death reports from Tozinameran, as well as reports of serious injury. The Health Canada report makes no mention of these reports, why not?

Health Canada and the Public Health Agency of Canada receive reports of adverse events following immunization with COVID-19 vaccines in Canada through the Canada Vigilance program and the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS). Adverse events following immunization are routinely monitored and information on adverse events following immunization with COVID-19 vaccines, including breakdowns of reports by vaccine name, age and sex, are published on the Government of Canada website on a weekly basis. As of May 7, 2021, no death or serious injury has been reported in people under the age 18 in Canada. These reports do not necessarily imply that a causal relationship between the event and the vaccine has been established. It can be expected that other, unrelated medical events will occur by chance after immunization, particularly when millions of people are being vaccinated.

Health Canada regularly reviews summary safety information for all COVID-19 vaccines authorized in Canada, which includes international data and data from other regulatory partners, including the United States. This information is taken into consideration as we examine and assess any new safety concerns. Should new safety information become available, Health Canada will assess it and take appropriate action. This could include communicating new risks to Canadians and healthcare providers or changing the recommended use of the product.

We hope that you will find this information helpful.

Thank you again for writing to Health Canada.

Sincerely,

Biologic and Radiopharmaceutical Drugs Directorate (BRDD)

From: Jean Marc Benoit
Sent: 2021-05-10 1:54 PM
To: BRDD ORA (HC/SC)
Subject: Questions regarding Interim Approval for Pfizer-BioNTech vaccine in children ages 12-17

To whom it may concern,

I am writing to request additional information regarding Tozinameran approval for children in Canada. It is my professional opinion that this approval was erroneously given based upon a highly

unfavourable risk-benefit profile in this population. I have reviewed the available documentation from Health Canada, most specifically the document with control number 251730, and am seeking clarification. I sincerely hope that it is I who have misunderstood the available information, and I trust that the answers to my questions will clarify and confirm the reasons for this approval.

1. On what basis is emergency interim authorization given for Covid-19 vaccination of children? What is the quantitative evidence of morbidity and mortality in Canadian children aged 12 to 17?
2. It is stated that the risk-benefit profile is “considered favourable” however, no quantification of risk for Canadian children is given. What is quantified risk for Canadian children for administration of this vaccine?
3. The cited literature which justifies this emergency interim authorization is an internal Pfizer document, which has yet to be published and subject to peer review. Given the known threat to validity of clinical studies carried out by the manufacturers of therapeutics, how does Health Canada justify proceeding on the basis of this material alone?
4. The cited literature to assess safety includes unpublished data on 1130 children. Given the extremely small sample size involved, how does Health Canada justify its decision that adequate data exists to evaluate safety in children?
5. The United States has a Vaccine Adverse Events Reporting System (VAERS), and there are child death reports from Tozinameran, as well as reports of serious injury. The Health Canada report makes no mention of these reports, why not?

I look forward to your responses, as do my patients and correspondents. I am including a news reporter with similar interests and concerns, in this email.

Sincerely,

Jean Marc Benoit MD CCFP EM