Our STN: BL 125408/675

NOTIFICATION
SAFETY LABELING CHANGE
January 9, 2026

Seqirus, Inc.
Attention: Caroline Beauregard
475 Green Oaks Parkway
Holly Springs, NC 27540

Dear Ms. Beauregard:

Please refer to your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for Influenza Vaccine (FLUCELVAX).

Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and licensed biological product applications to make safety related labeling changes based upon new safety information that becomes available after approval of the drug or biological product.

Since FLUCELVAX was approved on November 20, 2012, we have become aware of the following: In two postmarketing observational studies conducted in the Biologics Effectiveness and Safety System (BEST) an increased risk of febrile seizures was observed during the first day following vaccination with standard dose trivalent (2024-2025 Formula) and quadrivalent (2023-2024 Formula) influenza vaccines in children 6 months through 4 years of age.[1] The risk of febrile seizures following vaccination with any influenza vaccine was assessed during the 2023-2024 and 2024-2025 respiratory influenza seasons using three commercial insurance claims data sources in self-controlled case series (SCCS) analyses. The risk of febrile seizures within a risk window of 0 to 1 day postvaccination was compared to the risk within a control window of 8 to 63 days postvaccination. The SCCS analyses from the 2023-2024 and 2024-2025 seasons identified a significantly increased risks of febrile seizures in the first day following influenza vaccination. The incidence rate ratio (IRR) for febrile seizure following quadrivalent vaccine (2023-2024) in one data partner was 1.97 [95% CI: 1.09, 3.54] with an estimated attributable risk of 21.2 excess febrile seizure episodes per million standard dose quadrivalent vaccinations. In the same data partner, the IRR following trivalent vaccine (2024-2025) was 2.94 [95% CI: 1.72, 5.01] with an

[1] Lloyd PC, Acharya G, Zhao H, et al. Safety monitoring of health outcomes following influenza vaccination during the 2023–2024 season among U.S. Commercially-insured individuals aged 6 months through 64 years: Self-controlled case series analyses. Vaccine. Sep 17 2025;63:127614. doi: https://doi.org/10.1016/j.vaccine.2025.127614.

attributable risk of 44.2 excess febrile seizure episodes per million standard dose trivalent vaccinations.We consider this information to be “new safety information” as defined in section 505-1(b)(3) of the FDCA.

In accordance with section 505(o)(4) of the FDCA, we are notifying you that based on the new safety information described above, we believe that the new safety information should be included in the labeling for influenza vaccines with an approved indication extending to less than 5 years of age as follows:

HIGHLIGHTS OF PRESCRIBING INFORMATION

RECENT MAJOR CHANGES

Warnings and Precautions, Febrile seizures (5.x) Month/Year

WARNINGS AND PRECAUTIONS

In two separate postmarketing observational studies, an increased risk of febrile seizures was observed during the first day following vaccination with standard dose trivalent (2024-2025) and quadrivalent (2023-2024) influenza vaccines in children 6 months through 4 years of age. (5.x, 6.2)

FULL PRESCRIBING INFORMATION

5 WARNINGS AND PRECAUTIONS

5.x. Febrile Seizures

In two postmarketing observational studies, an increased risk of seizures was observed in the first day following vaccination among children 6 months to <5 years of age *[see Adverse Reactions (6.2)]*.

Under section 6.2

6.2 Febrile Seizures.

Postmarketing Observational Study of the Risk of Febrile Seizure following Vaccination with trivalent/quadrivalent influenza vaccines.

The association between influenza vaccine and febrile seizures was evaluated in children ages 6 months through 4 years during the 2023-2024 and 2024-2025 respiratory seasons using three commercial health insurance claims data sources.

A self-controlled case series (SCCS) analyses compared the risk of febrile seizures within a risk window of 0 to 1 day postvaccination to a control window of 8 to 63 days postvaccination. The 2023-2024 and 2024-2025 season SCCS analyses found significantly increased risks of febrile seizures in the first day following influenza

standard dose quadrivalent and trivalent vaccinations, respectively. The estimated attributable risk from one data partner was 21.2 per million excess febrile seizure episodes or a 97% increase in relative risk (IRR: 1.97 [95% CI: 1.09, 3.54]) after the standard dose quadrivalent vaccine and a 44.2 per million excess febrile seizure episodes or a 194% increase in relative risk (IRR: 2.94 [95% CI: 1.72, 5.01]) following the standard dose trivalent vaccine. The results of this type of observational study suggest a causal relationship between standard dose influenza quadrivalent and trivalent vaccines and febrile seizures in children 6 months through 4 years of age.

In accordance with section 505(o)(4), within 30 calendar days of the date of this letter, you must submit a supplement proposing changes to the approved labeling in accordance with the above direction or notify FDA that you do not believe a labeling change is warranted and submit a rebuttal statement detailing the reasons why such a change is not warranted. If you submit a supplement that includes only language identical to that specified above, the supplement may be submitted as a changes being effected (CBE-0) supplement. If the supplement includes proposed language that differs from that above, submit a prior approval supplement (PAS).

Under section 505(o)(4), if you fail to submit a response within 30 calendar days, you would be in violation of the FDCA that may deem your product to be misbranded under section 502(z) and may subject you to enforcement action, including civil monetary penalties under section 303(f)(4)(A) and an order to make whatever labeling changes FDA deems appropriate to address the new safety information.

Please submit your safety labeling submission to STN 125408.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

SAFETY LABELING CHANGES UNDER 505(o)(4) - PRIOR APPROVAL SUPPLEMENT

OR

SAFETY LABELING CHANGES UNDER 505(o)(4) – CHANGES BEING EFFECTED

OR

SAFETY LABELING CHANGES UNDER 505(o)(4) – REBUTTAL (CHANGE NOT WARRANTED)."

Prominently identify subsequent submissions related to the safety labeling changes supplement with the following wording in bold capital letters at the top of the first page of the submission:

SAFETY LABELING CHANGES UNDER 505(o)(4) - AMENDMENT

If you have any questions, please contact the Regulatory Project Manager, Jeffy Mattathil, PhD, by email (Jeffy.Mattathil@fda.hhs.gov).

Sincerely,

Vinay Prasad, MD, MPH
Director
Center for Biologics Evaluation and Research