June 16, 2026

VIA EMAIL AND FDA DOCKET

Members, Vaccines and Related Biological
Products Advisory Committee
Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061,
Rockville, MD 20852
CBERVRBPAC@fda.hhs.gov
FDA-2026-N-4162

Re: *Docket No. FDA-2026-N-4162 for "Vaccines and Related Biological Products Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments – Safety and Effectiveness of MFLUSIVA (Influenza Vaccine, mRNA) manufactured by Moderna TX Inc.*

Dear VRBPAC Members:

We write on behalf of Informed Consent Action Network ("**ICAN**") regarding the upcoming VRBPAC (the **"Committee"**) meeting on June 18, 2026, during which the Committee will consider Moderna's mRNA influenza vaccine, Mflusiva (mRNA-1010).

ICAN respectfully urges the Committee to seriously consider the issues raised herein when making any recommendation concerning Mflusiva. As a threshold matter, this is the first influenza vaccine built on the mRNA platform—a technology that warrants heightened scrutiny given, *inter alia*, the established cardiac signals associated with mRNA-based Covid-19 vaccines. Moreover, as detailed below, significant unresolved questions remain regarding: (1) the unfavorable benefit-risk balance; (2) a concerning pattern of death, cardiac, and hematologic safety signals in the clinical trials; (3) the still unknown long-term risks of the mRNA platform; (4) the inability to generalize from single-season data; (5) the absence of head-to-head efficacy comparisons with the enhanced vaccines that constitute the current standard of care for older adults; and (6) questionable efficacy for frail and vulnerable adults.

I. UNFAVORABLE BENEFIT-RISK RATIO

In Mflusiva's Phase 3 efficacy and safety clinical trial,[1] the primary endpoint results showed a purported reduction in confirmed influenza-like illness from 2.8% to 2.0%, **yielding an**

[1] A Study of mRNA-1010 Compared with a Licensed Influenza Vaccine in Adults ≥50 Years of Age, https://clinicaltrials.gov/study/NCT06602024; *See also* Israel Leroux-Roels et al. *Efficacy and safety of an mRNA seasonal influenza vaccine in adults*. N Engl J Med. (May 7, 2026), https://pubmed.ncbi.nlm.nih.gov/42090792/ (hereinafter "**Leroux-Roels et al.**").

absolute risk reduction of only 0.8%.[2] These modest purported gains must be weighed against the safety profile: a reported **6.4% of Mflusiva recipients experienced a Grade 3 (severe) adverse reactions** in the Phase 3 efficacy trial, compared to only 1.0% of comparator recipients of a licensed standard-dose flu vaccine[3]—meaning for every 100 people vaccinated, about 6 people in the mRNA-1010 group had a severe short-term reaction, compared with about 1 person in the standard flu shot group. That means about 5 extra people per 100 had a severe reaction with mRNA-1010. Despite this disparity, the published study characterized the reactions as "mild to moderate and transient,"[4] raising concern that the severity of the reactogenicity profile has been inadequately acknowledged.

The Phase 3 immunogenicity trial data[5] admit that **8 participants experienced a Grade 4 (potentially life-threatening) adverse reaction**. Four of these reactions occurred in adults aged 65 years or older,[6] the very population for whom influenza vaccination is most critical. Notably, this trial used a quadrivalent (50 µg) formulation, rather than the trivalent (37.5 µg) formulation studied in the efficacy trial,[7] and the Grade 4 reactions in older adults raise serious questions about whether the vaccine can be safely scaled to a quadrivalent formulation for the older adult population.

Additionally, the reported serious adverse events ("**SAEs**") were higher in the Mflusiva arm compared to the flu vaccines given in the comparator arms in both Phase 3 trials. In the Phase 3 efficacy trial, the data claims that SAEs occurred in 2.2% of Mflusiva recipients versus 1.9% of comparator recipients.[8] In the Phase 3 immunogenicity trial, the data shows that the SAE imbalance was even more pronounced: 6 (0.5%) mRNA-1010 recipients versus 1 (<0.1%) comparator recipient in Part A; 10 (0.7%) versus 2 (0.1%) in Part B; and 9 (0.6%) versus 6 (0.4%) in Part C.[9] A signal that appears once may be chance. A signal that appears in the same direction across every independent dataset is a pattern—and one that demands investigation before the Committee endorses licensure.

Beyond the clinical data, the public health implications of this safety profile deserve consideration. If post-licensure experience confirms the elevated reactogenicity purportedly

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[2] Leroux-Roels et al., *supra* note 1 at Table 2 (primary endpoint events occurred in 411 of 20,179 mRNA-1010 recipients (2.0%) and 557 of 20,124 standard-dose comparator recipients (2.8%)).

[3] Leroux-Roels et al., *supra* note 1 at 1810.

[4] Leroux-Roels et al., *supra* note 1 at 1809.

[5] ModernaTX, Inc., *Study of mRNA-1010 Seasonal Influenza Vaccine in Adults*, No. NCT05827978, https://clinicaltrials.gov/study/NCT05827978; *See also* Mieke Soens et al. *A phase 3 randomized safety and immunogenicity trial of mRNA-1010 seasonal influenza vaccine in adults*. Vaccine (Feb. 7, 2025), https://pubmed.ncbi.nlm.nih.gov/39919447/ (hereinafter "**Soens et al.**").

[6] Soens et al., *supra* note 5 at 4.

[7] Soens et al., *supra* note 5 at 2 (mRNA-1010 included mRNAs encoding for the hemagglutinin surface glycoproteins of four influenza virus strains formulated in lipid nanoparticles.); Leroux-Roels et al., *supra* note 1 at 1803 (trivalent mRNA-1010 (37.5 µg, which includes 12.5 µg of each strain)).

[8] Leroux-Roels et al., *supra* note 1 at 1810.

[9] Soens et al., *supra* note 5 at Table 2.

observed in trials, it could further erode public confidence in influenza vaccination and reduce overall uptake.

II. CONCERNING AGGREGATE PATTERN OF DEATHS

In the Phase 1/2 trial, one participant was reported as experiencing a fatal cardiac arrest 15 days after vaccination with Mflusiva.[10] In Part A of the Phase 3 immunogenicity trial, the reported death imbalance is striking: five deaths reportedly (0.4%) occurred among Mflusiva recipients versus one death (<0.1%) among SD-IIV4 recipients during the study period.[11] In Part C of the same study, one death from acute myocardial infarction was reported from the Mflusiva group.[12] In the Phase 3 efficacy trial, the data claim that fatal events occurred at a rate of 0.2% in the Mflusiva and control arms, meaning there is no evidence the vaccine prevents deaths.[13]

Individually, each death except one was assessed by the study investigators as purportedly unrelated to vaccination. However, the 5:1 death ratio in Phase 3 immunogenicity Part A, combined with the cardiac-specific nature of several events across trials, raises a critical concern: the substantial systemic inflammatory response purportedly induced by Mflusiva—fever, myalgia, fatigue, and chills—may precipitate acute cardiovascular events in elderly patients with pre-existing cardiovascular disease. This potential mechanism demands rigorous evaluation *before* the Committee recommends licensure.

III. CARDIAC AND HEMATOLOGIC RISKS ASSOCIATED WITH MRNA PLATFORM

One recipient of Mflusiva in the Phase 3 efficacy trial was reported to have **developed cardiomyopathy 95 days after vaccination**.[14] Additionally, the Phase 1/2 trial reported a **fatal cardiac arrest, a case of angina pectoris, and a case of congestive cardiac failure**,[15] and the Phase 3 efficacy trial included a death from a reported **acute myocardial infarction**.[16] Although most of these events were classified by study investigators as "not related" to the vaccine, the clustering of reported cardiac SAEs across trials demands heightened scrutiny—particularly given the well-established association between myocarditis and the mRNA platform in the Covid-19 context.

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[10] Ivan Lee et al. *Safety and immunogenicity of a phase 1/2 randomized clinical trial of a quadrivalent, mRNA-based seasonal influenza vaccine (mRNA-1010) in healthy adults: interim analysis*. Nat Commun. (June 19, 2023), https://www.nature.com/articles/s41467-023-39376-7 at 4 (**hereinafter "Lee et al.**"]. Note that the Phase 1/2 interim analysis reported one participant who experienced a fatal cardiac arrest 15 days after vaccination with Mflusiva. Although the final results of that trial, published separately, reported no vaccine-related serious adverse events or deaths, the investigators "unrelated" classification of the cardiac arrest warrants scrutiny given the participant's proximity to vaccination and the broader pattern of cardiac events observed across trials.

[11] Soens et al., *supra* note 5 at Table 2.

[12] Soens et al., *supra* note 5 at 6.

[13] Leroux-Roels et al., *supra* note 1 at 1810.

[14] Leroux-Roels et al., *supra* note 1 at 1811.

[15] Lee et al., *supra* note 10 at 4.

[16] Soens et al., *supra* note 5 at 6.

In the Phase 3 trials, one recipient of Mflusiva was reported to have **developed thrombocytopenia 84 days post-vaccination,[17] and another purportedly developed deep vein thrombosis (onset Day 128) followed by a reported pulmonary embolism (onset Day 132)**.[18] These hematologic events raise additional questions about the mRNA platform's potential to provoke immune-mediated coagulation and platelet disorders—a class of adverse events that warrants dedicated monitoring in any post-licensure safety framework.

IV. UNKNOWN LONG-TERM EFFECTS OF THE MRNA PLATFORM, INCLUDING POTENTIAL CANCER RISK

The mRNA platform is still in its relative infancy as a licensed technology for widespread human use. The Committee is obligated to demand adequate long-term safety data before endorsing a novel mRNA product for routine annual use, especially in a non-emergency context.

There is a growing body of peer reviewed scientific literature that identifies potential biologically plausible oncogenic or tumor-promoting mechanisms and purported preliminary population-level cancer signals.[19] Certain authors have proposed hypothetical mechanisms by which repeated mRNA exposure could warrant additional study. The Committee should consider that licensing Mflusiva for routine annual use would effectively commit millions of Americans to repeated mRNA exposure without any data on the long-term immunological consequences of that regimen. Prudence demands that these questions be investigated *before*—not after—licensure.

V. LACK OF PLACEBO ARM AND CLINICAL RELEVANCE OF THE COMPARATOR USED

Mflusiva represents the first influenza vaccine built on the mRNA platform. The novel mechanism of action arguably justifies an even more rigorous safety assessment than that required of conventional influenza vaccines, including clinical trials with a true saline placebo to establish a baseline safety profile unconfounded by comparator reactogenicity.

Notably, the Phase 3 efficacy trial used standard-dose inactivated influenza vaccines as its comparator.[20] However, the CDC already preferentially recommends enhanced influenza

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[17] Leroux-Roels et al., *supra* note 1 at 1811.

[18] Soens et al., *supra* note 5 at 4.

[19] *See* Alberto Rubio-Casillas et al., *Review: N1-Methyl-pseudouridine (m1Ψ): Friend or foe of cancer?,* Int'l J. Biological Macromolecules, v. 267, 131427 (May 2024), https://doi.org/10.1016/j.ijbiomac.2024.131427; Charlotte Kuperwasser & Wafik S. El-Deiry, *COVID Vaccination and post-infection cancer signals: Evaluating patterns and potential biological mechanisms*, Oncotarget, vol. 17, 1 (Jan. 3, 2026), https://pubmed.ncbi.nlm.nih.gov/41498242/; and Makoto Abue et al., *Repeated COVID-19 Vaccination as a Poor Prognostic Factor in Pancreatic Cancer: A Retrospective, Single-Center Cohort Study*, Cancers vol 17, 12 (June 16, 2025), https://doi.org/10.3390/cancers17122006. Note that while the Abue study is retrospective, single-center, and observational—and therefore cannot establish causation—its findings raise a biologically plausible hypotheses warranting investigation. The fact that repeated mRNA vaccination correlated with elevated IgG4 levels and shorter survival in pancreatic cancer patients, even if confounded, is precisely the kind of signal that should be characterized before committing millions of Americans to annual mRNA exposure—not after.

[20] Leroux-Roels et al., *supra* note 1 at 1803.

vaccines—including high-dose, adjuvanted, and recombinant formulations—for adults 65 and older.[21] While the Phase 3 immunogenicity trial did use an enhanced vaccine as a comparator, it measured only antibody titers, not clinical outcomes. A head-to-head clinical efficacy trial demonstrating that Mflusiva prevents more illness than the enhanced vaccines already in use in those 65 and older remains the appropriate standard, and it has not been met.

Moderna has publicly stated that CBER previously advised that use of a licensed standard-dose influenza vaccine as the comparator in its Phase 3 study would be "acceptable," while nevertheless recommending use of a vaccine preferentially recommended for older adults. Even assuming the comparator was procedurally acceptable from a regulatory standpoint at the protocol-design stage, that does not answer the separate scientific question before the Committee. The issue is not whether Moderna complied with an acceptable study design, but whether the resulting data demonstrate a clinically meaningful benefit relative to the enhanced influenza vaccines that currently constitute the standard of care for adults aged 65 years and older. The available evidence does not do so.[22]

VI. SINGLE-SEASON EFFICACY LIMITATION AND ABSENCE OF ANTIGENIC MATCH DATA

The Phase 3 efficacy trial published results cover only the 2024–2025 Northern Hemisphere influenza season.[23] Influenza vaccine effectiveness is known to vary substantially from season to season depending on circulating strains and antigenic drift. A single-season result cannot establish the vaccine's ability to perform consistently across multiple seasons and varying epidemiological conditions.

Compounding this limitation, the published trial results did not report relative vaccine efficacy stratified by antigenic match to the vaccine strains.[24] This is a critical omission. One of the primary theoretical advantages of the mRNA platform is the avoidance of egg-adaptive mutations that reduce antigenic fidelity in conventional vaccines.[25] Without antigenic match data, the trial fails to validate the core scientific rationale for choosing the mRNA platform over existing alternatives.

VII. GENERALIZABILITY AND POPULATION CONSIDERATIONS

The Phase 3 efficacy trial population was reported to be 82.6% White, 70.4% from North America, and predominantly female (56.9%).[26] While these demographics may roughly reflect the U.S. population of adults 50 and older who typically receive influenza vaccines, they limit the

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[21] CDC, Flu and People 65 Years and Older, https://www.cdc.gov/flu/highrisk/65over.htm.

[22] *See* https://www.sec.gov/Archives/edgar/data/1682852/000168285226000012/exhibit991-02102026.htm.

[23] Leroux-Roels et al., *supra* note 1 at 1804.

[24] Leroux-Roels et al., *supra* note 1 at 1808.

[25] Colin Russell et al. *Seasonal influenza vaccine performance and the potential benefits of mRNA vaccines*. Hum Vaccine Immunotherapeutics. vol 20, 1 (April 15, 2024), https://pmc.ncbi.nlm.nih.gov/articles/PMC11020595/.

[26] Leroux-Roels et al., *supra* note 1 at Table 1.

Committee's ability to draw confident conclusions about efficacy and safety in racial and ethnic populations that are disproportionately affected by influenza complications.

Most critically, among participants aged 65 years and older in the Phase 3 efficacy trial, published subgroup analyses revealed troubling results. Frail participants showed a purported relative vaccine efficacy of only 30.3% (95% CI, −37.1 to 64.6), and vulnerable participants showed a purported relative vaccine efficacy of only 28.9% (95% CI, −15.5 to 56.3).[27] Because the confidence intervals in both subgroups cross zero, **the trial did not demonstrate a statistically significant benefit to the populations most in need of improved influenza protection**.

Nor should these deficiencies be deferred to post-marketing study. Public reporting indicates that Moderna may seek traditional approval for adults 50 to 64 years old and accelerated approval for adults 65 years and older, coupled with a post-marketing study in the older-adult population. But the 65-and-older population is precisely the group for whom the comparator, frailty, vulnerability, and severe-outcome limitations matter most. Those evidentiary gaps should be resolved before licensure, not after widespread annual administration.

VIII. UNDERPOWERED SEVERE DISEASE ENDPOINTS

The exploratory analyses of medically-attended influenza illness in the Phase 3 efficacy trial are based on small absolute numbers: only 4 reported hospitalizations in the Mflusiva group versus 8 in the comparator group, and 6 reported emergency department visits versus 12.[28] These numbers are too small to support reliable inferences about severe disease prevention and are highly susceptible to chance variation. They cannot form the basis of a regulatory claim that Mflusiva prevents serious influenza outcomes.

CONCLUSION

The currently available evidence does not support a favorable benefit-risk determination for Mflusiva at this time. The vaccine demonstrated only a purported modest absolute reduction in influenza illness, while exhibiting substantially increased reactogenicity and persistent safety signals that warrant further investigation. At the same time, the available data fail to establish a clinically meaningful advantage over the enhanced influenza vaccines already recommended for older adults—the population at greatest risk of severe influenza outcomes and the group most likely to receive this product.

Critically, the principal uncertainties identified throughout this letter are not peripheral issues that can be deferred until after licensure. Rather, they concern the fundamental questions that should be answered before a novel mRNA influenza vaccine is recommended for widespread use: whether the vaccine offers a meaningful clinical benefit beyond existing standards of care, whether its safety profile is adequately characterized, and whether the evidence supports use in the populations for whom vaccination is most consequential.

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[27] Leroux-Roels et al., *supra* note 1 at Figure 1.

[28] Leroux-Roels et al., *supra* note 1 at 1809.

The Committee's responsibility is not merely to determine whether Mflusiva performs better than a standard-dose comparator, but whether the totality of the evidence demonstrates that its benefits clearly outweigh its risks. Based on the current record, that showing has not been made. We therefore respectfully urge the Committee to recommend that additional clinical investigation be completed before licensure is granted.

Very truly yours,

/s/ Elizabeth A. Brehm
Elizabeth A. Brehm, Esq.
Erin Bello, Esq.
Marina Resciniti, Esq.
ebrehm@sirillp.com