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SUBMITTED VIA REGULATIONS.GOV

Division of Dockets Management (HFA-305)
U.S. Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Rm. 1061
Rockville, MD 20825

Re: FDA-2025-P-6831, Citizen Petition from Children's Health Defense – Alliance for mRNA Medicines Comments

The Alliance for mRNA Medicines submits these comments in response to the December 8, 2025, "Citizen Petition" from Children's Health Defense relating to the U.S. Food and Drug Administration's (FDA's) actions concerning COVID-19 vaccines developed and manufactured by Moderna, Inc. and Pfizer, Inc./BioNTech—specifically, authorization under Emergency Use Authorizations (EUAs) in December 2020 and, subsequently, licensure pursuant to Biologic License Applications (BLAs) in 2021 and 2022. The FDA should deny this frivolous and error-ridden petition outright.

I. Introduction

FDA-licensed COVID-19 vaccines—specifically Moderna's SPIKEVAX and Pfizer/BioNTech's Comirnaty—have helped prevent serious illness and death in millions of Americans, as well as millions of people around the world. From the early days of the COVID-19 pandemic, U.S. and global regulatory bodies exerted careful scrutiny and oversight over the authorization and subsequent licensing of these crucial vaccines. The two leading vaccines developed and manufactured by Moderna and Pfizer/BioNTech, respectively, went through rigorous and exhaustive review by the FDA at the EUA and, later, BLA stages of approval, with both companies submitting extensive data and information to support the vaccines' potency, safety, and purity.

Nothing in the Citizen Petition comes close to identifying a lawful basis for the FDA to revisit its approval of the BLAs for SPIKEVAX or Comirnaty or to take any of the other requested actions, which are themselves subject to various procedural and substantive safeguards. The Petition fails to identify credible regulatory deficiencies and does not undermine FDA's licensure determinations. In particular, it fails to set forth defensible facts that could support one of the limited bases available under FDA regulations to revoke a biologic license, including that a "product is not safe and effective for all of its intended uses," or that a product is misbranded. *See* 21 C.F.R. § 601.5(b)(1)(vi). Nor does the Petition adduce any plausible facts that could justify suspending a BLA. *See id.* § 601.6(a) (requiring "reasonable grounds to believe that" (a) a ground for revocation exists under § 601.5 and that, as a result, (b) "there is a danger to health"). The Petition paints a distorted picture of the FDA's regulatory framework,

the approval processes for the COVID-19 vaccines, and the rigorous and extensive documentation and studies supporting the COVID-19 vaccine applications submitted for FDA licensure. Its arguments are largely semantic, rely on non-existent or misinterpreted legal requirements, and are inconsistent with long-standing FDA practice governing biologics and vaccines.

Moreover, were the FDA to attempt to revoke a BLA on the basis of the Petition, the FDA would have to follow applicable processes and afford parties the due process required by FDA regulations. *See* 21 C.F.R. § 601.5(b)(2).

Although the Petition contains many flawed claims about the law and facts at issue, this response addresses six of the most significant flaws. For the reasons set forth below, the FDA should deny the Petition.

II. Moderna and Pfizer Satisfied the Applicable IRB, IND, and Clinical Trial Requirements

To start, the Petition fundamentally misconstrues what an EUA is, what its requirements are, and how it relates to clinical trials and informed consent. The Petition's fundamental confusion about the EUA, as well as BLA, processes underlies its entire argument and infects and undermines the Petition as a whole.

The contrast the Petition draws between (1) a "***non-investigational*** Emergency Use Authorization (EUA) pathway"—"meaning a product that is ***not part of a clinical investigation*** under an [IND] application and exemption"—and (2) "the ***investigational*** [BLA] pathway," Pet. at 4, is equally misleading and irrelevant.[1] Before the FDA authorized COVID-19 vaccines under an EUA, Moderna and Pfizer submitted Investigational New Drug (IND) applications. *See* 21 C.F.R. § 312.20(a). Moderna's Phase 1 study was conducted by NIH under an NIH IND application submitted on February 20, 2020 (IND 19635).[2] Moderna's Phase 2 study was conducted under its own IND submitted on April 27, 2020 (IND 19745).[3] Pfizer/BioNTech submitted an IND in April 2020.

FDA clearance of the IND applications allowed Moderna and Pfizer to move forward with rigorous randomized control trials (RCTs) with institutional review board (IRB) oversight and informed consent.[4] The Petition's claim that "[t]hese COVID-19 vaccines were

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[1] All emphases added unless otherwise noted.

[2] Press Release, *Moderna Announces IND Submitted to U.S. FDA for Phase 2 Study of mRNA Vaccine (mRNA-1273) Against Novel Coronavirus*, Nasdaq (Apr. 27, 2020), https://www.nasdaq.com/press-release/moderna-announces-ind-submitted-to-u.s.-fda-for-phase-2-study-of-mrna-vaccine-mrna; FDA, SPIKEVAX Summary Basis for Regulatory Action, at 6 (Jan. 30, 2022) ("Spikevax SBRA"), https://www.fda.gov/media/155931/download.

[3] Spikevax SBRA at 6.

[4] *See* Lindsey R. Baden et al., *Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine*, 384 NEJM 403, 404 (2021) ("The central institutional review board approved the protocol and the consent forms. All participants provided written

manufactured under EUA standards, ***without clinical trials***," Pet. at 5, is therefore inaccurate. The Petition itself later concedes that "Moderna initiated human clinical studies on March 16, 2020" and "Pfizer initiated human clinical studies in April 2020, and its pivotal Phase 3 trial on July 27, 2020." Pet. at 20. As the FDA confirmed, both Moderna and Pfizer carried out RCTs to provide supporting evidence for their EUAs.[5]

Moderna, for example, completed Phase 1 and 2 trials, as well as a 30,000-participant placebo-controlled Phase 3 trial for SPIKEVAX.[6] The Phase 3 (COVE) study started on July 27, 2020, and the primary efficacy analysis was announced on November 30, 2020. The Phase 3 study demonstrated that "[t]he mRNA-1273 vaccine [SPIKEVAX] showed 94.1% efficacy at preventing Covid-19 illness, including severe disease."[7] As the FDA explained, EUA approval for SPIKEVAX was based on a "Protocol-Specified, Event-Driven Primary Efficacy Analysis."[8] After assessing Moderna's and Pfizer's clinical trials, the FDA granted EUAs to Pfizer on December 11, 2020[9] and Moderna on December 18, 2020.[10] As the FDA explained regarding Pfizer's vaccine:[11]

- "The first EUA, issued Dec. 11, for the Pfizer-BioNTech COVID-19 Vaccine for individuals 16 years of age and older was based on safety and effectiveness data from a randomized, controlled, blinded ongoing clinical trial of thousands of individuals."
- "To support the FDA's approval decision today, the FDA reviewed updated data from the clinical trial which supported the EUA and included a longer duration of follow-up in a larger clinical trial population."
- "Based on results from the clinical trial, the vaccine was 91% effective in preventing COVID-19 disease."

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informed consent before enrollment."); Hana M. El Sahly et al., *Efficacy of the mRNA-1273 SARS-CoV-2 Vaccine at Completion of Blinded Phase*, 385 NEJM 1774, 1775 (2021) (same); *see also* ModernaTX, Inc., Protocol Number mRNA-1273-P301, *Informed Consent Form and Authorization To Use and Disclose Protected Health Information* (July 15, 2020) (noting IRB oversight of clinical trial), https://cdn.clinicaltrials.gov/large-docs/27/NCT04470427/ICF_002.pdf.

5 *See infra* notes 11 & 12 and accompanying text.

6 Stéphane Bancel, *Moderna's mRNA Vaccine Against COVID-19 Receives FDA Emergency Use Authorization*, Moderna (Dec. 18, 2020), https://www.modernatx.com/en-US/media-center/all-media/blogs/moderna-mrna-vaccine-against-covid-19-receives-fda-emergency-use.

7 Lindsey R. Baden et al., *Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine*, 384 NEJM 403, 403 (2021), https://www.nejm.org/doi/full/10.1056/NEJMoa2035389.

8 Spikevax SBRA at 19.

9 Press Release, Pfizer, *Pfizer-BioNTech COVID-19 Vaccine COMIRNATY® Receives Full U.S. FDA Approval for Individuals 16 Years and Older* (Aug. 23, 2021), https://www.pfizer.com/news/press-release/press-release-detail/pfizer-biontech-covid-19-vaccine-comirnatyr-receives-full.

10 Authorizations of Emergency Use of Two Biological Products During the COVID-19 Pandemic; Availability, 86 Fed. Reg. 5200 (Jan. 19, 2021), https://www.federalregister.gov/documents/2021/01/19/2021-01022/authorizations-of-emergency-use-of-two-biological-products-during-the-covid-19-pandemic-availability.

11 Press Release, FDA, *FDA Approves First COVID-19 Vaccine* (Aug. 23, 2021), https://www.fda.gov/news-events/press-announcements/fda-approves-first-covid-19-vaccine.

When granting approval for Moderna's SPIKEVAX BLA in January 2022, the FDA stated:[12]

- "The Spikevax biologics license application (BLA) builds upon the data and information that supported the EUA, such as preclinical and clinical data, as well as details of the manufacturing process and the sites where the vaccine is made."
- "'The FDA's medical and scientific experts conducted a thorough evaluation of the scientific data and information included in the application pertaining to the safety, effectiveness, and manufacturing quality of Spikevax. This includes the agency's independent verification of analyses submitted by the company, our own analyses of the data, along with a detailed assessment of the manufacturing processes, test methods and manufacturing facilities.'"
- "The updated analyses to determine effectiveness of Spikevax included 14,287 vaccine recipients and 14,164 placebo recipients 18 years of age and older who did not have evidence of SARS-CoV-2 infection prior to receiving the first dose.… These data demonstrated that Spikevax was 93% effective in preventing COVID-19, with 55 cases of COVID-19 occurring in the vaccine group and 744 COVID-19 cases in the placebo group. The vaccine was also 98% effective in preventing severe disease."

Finally, the Petition attempts (at 8) to contrast (1) FDA regulations governing the protection of human subjects in research (including informed consent requirements), 21 C.F.R. Part 50, and IRB oversight for research, 21 C.F.R. Part 56, with (2) statutory requirements for *administering* a product approved under an EUA, *see* 21 U.S.C. § 360bbb-3a(e)(1), *i.e.*, where individuals must be "informed" about certain facts and options. The latter requirements for administering a product approved under an EUA have nothing to do with obtaining an EUA on the front end, which is governed by standards under Section 564(c)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. § 360bbb-3(c). Investigational development leading up to an EUA (which requires informed consent and IRB approval) and administration of EUA-approved products (which does not require informed consent or IRB approval) are distinct issues. The fact that there was no IRB oversight for post-EUA administration of the COVID-19 vaccine is thus legally irrelevant from the vantage point of satisfying EUA standards.[13] Moreover, as

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[12] Press Release, FDA, *Coronavirus (COVID-19) Update: FDA Takes Key Action by Approving Second COVID-19 Vaccine* (Jan. 31, 2022), https://web.archive.org/web/20220131214048/https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-key-action-approving-second-covid-19-vaccine.

[13] For that reason, testimony by former FDA official Marion Gruber that "*[u]se* of an investigational COVID-19 vaccine under an EUA is not subject to informed consent requirements" but, rather, "vaccine recipients need to be provided a fact sheet, and that describes the investigational nature of the product, the known and potential benefits and risks of the product, available alternatives, and there is the option to refuse vaccination," in no way undermines the bases for EUA approval for SPIKEVAX or Comirnaty. Meeting Transcript, FDA, *Center for Biologics Evaluation and Research (CBER) 161st Vaccines and Related Biological Products Advisory Committee (VRBPAC) Meeting* (Oct. 22, 2020), at 36:5-12, https://www.fda.gov/media/143982/download. *See* Pet. at 30. The Petition, moreover, misidentifies the source of the statement that "[u]nder EUA, it is your choice to receive or not receive the vaccine." *See* Pet. at 30 & n.56. It comes directly from an FDA-approved vaccine information sheet. *See* FDA, *Vaccine Information Fact Sheet for Recipients and Caregivers About Spikevax (COVID-19 Vaccine, mRNA), Moderna COVID-19 Vaccine, and Moderna COVID-19 Vaccine, Bivalent (Original and Omicron Ba.4/Ba.5) To Prevent Coronavirus Disease 2019 (COVID-19)*, at 5-6 (updated Aug. 31, 2022),

explained above, the RCTs supporting the EUAs were conducted under INDs with IRB oversight and informed consent.[14]

III. Vaccines Distributed Under an EUA Can Later Satisfy the FDA's BLA Standards, as Moderna's and Pfizer's Vaccines Did

The Petition also claims that "[p]roducts that reach consumers as EUA countermeasures under a declared emergency cannot satisfy BLA labeling standards retroactively." Pet. at 28. This claim, too, is both misleading and irrelevant.

It is misleading because neither the Public Health Service Act (PHSA) nor the FD&C Act requires that a product be developed, manufactured, or distributed exclusively under BLA conditions from the outset to be licensed. An EUA is a lawful temporary mechanism for emergency access to biologics and does not preclude or invalidate subsequent BLA licensing. The FDA's BLA licensure determination is based on whether an application meets statutory standards at the time of the BLA review—including adequate evidence of safety, purity, and potency, and approved manufacturing conditions. *See, e.g.*, 21 C.F.R. § 601.2(a). Prior EUA distribution does not render a product incapable of later satisfying BLA labeling standards. If the Petition's legal theory were correct, no product initially studied under accelerated, adaptive, or emergency frameworks could ever be licensed. That is obviously wrong and would lead to absurd results that contravene the public health.

Moreover, the Petition's claim is irrelevant because neither Moderna nor Pfizer sought "retroactiv[e]" application of BLA standards for their vaccines, Pet. at 28, nor did the FDA grant it. No one contends that BLA licensure retroactively converted EUA-distributed vaccine lots into licensed product. What matters is whether the licensed product and labeling at approval met all of the statutory standards based on the supporting materials and data, and the FDA expressly concluded that they did so. The FDA applied BLA standards to assess and license the COVID-19 vaccines prospectively. After receiving EUA authorization in December 2020, Moderna and Pfizer began compiling full BLA packages and submitting them on a rolling basis to FDA based on voluminous additional documentation, consistent with applicable statutory and regulatory requirements—including those of demonstrating purity, potency, and efficacy. *See* 21 C.F.R. § 601.2(d); *id*. § 601.20(c) (manufacturing process). Pfizer completed its BLA submission on May 18, 2021, and the FDA granted priority review in July 2021[15] and full approval of August 23, 2021.[16] For its part, Moderna completed its BLA submission on August 24, 2021, and the FDA granted full approval on January 22, 2022.[17] In short, EUA authority under Section 564 of

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https://www.fda.gov/media/144638/download.

[14] *See supra* note 4.

[15] Press Release, Pfizer, *U.S. FDA Grants Priority Review for the Biologics License Application for Pfizer-BioNTech COVID-19 Vaccine* (July 16, 2021), https://cdn.pfizer.com/pfizercom/2021-07/BLA_Acceptance_Media_Statement_FINAL.pdf.

[16] FDA, BLA Approval Letter for Comirnaty (Aug. 23, 2021), https://www.fda.gov/media/151710/download.

[17] FDA, BLA Approval Letter for Spikevax (Jan. 31, 2022), https://www.fda.gov/media/155815/download.

the FD&C Act, and BLA licensure under the PHSA and 21 C.F.R. Part 601, are distinct legal mechanisms. An EUA provides temporary emergency access; it does not supplant or foreclose subsequent licensure. The relevant legal question for BLA approval is whether the application satisfied BLA standards at approval, something the FDA expressly found for SPIKEVAX, MNEXSPIKE, and COMIRNATY when it approved their respective BLAs.

The BLA approvals by the FDA for Moderna's and Pfizer's COVID-19 vaccines were prospective and fully supported. The FDA did not purport to retroactively grant BLA approval for the period when either vaccine had EUA authorization. Nor did the FDA grant BLA approval applying only EUA standards. Rather, the FDA applied the standards for BLA approval and found them fully satisfied.

The regulatory history, which highlights the sequential development of the EUA of the Moderna COVID-19 vaccine, followed by the full licensure of SPIKEVAX, is summarized in the following Table:

Regulatory History Regulatory Events / Milestones	**Date**
Pre-IND meeting	February 19, 2020
IND submission IND 19635 for Phase 1 Study	February 20, 2020
IND 19745 for Phase 2 Study	April 27, 2020
Fast Track designation granted	May 11, 2020
EUA Filed	November 30, 2020
EUA issued	December 18, 2020
Pre-BLA meeting - Clinical	April 28, 2021
Pre-BLA meeting – CMC/Regulatory	July 1, 2021
BLA 125752/0 submission	August 24, 2021
BLA filed	October 14, 2021
Mid-Cycle communication	The Applicant cancelled
Late-Cycle meeting	The Applicant cancelled
Action Due Date	April 24, 2022

The bottom line is clear: The Petition's assertion (at 30) that "the clinical trials for COVID-19 vaccines were not subject to IRB review and did not undergo clinical trials sufficient to satisfy the statutory BLA requirements" is fiction. Nor is there any truth in the allegation that the FDA committed an "egregious" "violation" in licensing vaccines whose supporting human clinical trials "lacked IRB oversight and were not legally compliant clinical investigations." Pet. at 5. In fact, as described above, Moderna and Pfizer complied fully with EUA requirements and then took extensive additional steps required for submitting full BLA applications, which the FDA duly approved in 2021-2022 after determining the BLA standards to be satisfied. There was no "retroactive" shoe-horning of the sort that the Petition alleges.

IV. FDA-Accepted Manufacturing Changes Made Between Phase 3 Studies and Commercial Sale Do Not Invalidate Clinical Data or Render a Product Unapprovable or Mislabeled

The Petition next erroneously contends that "the data from Phase 3 trials, which are included in several sections of Comirnaty and SPIKEVAX BLA labels (Sections 6, 8, 14), cannot be deemed representative of the commercially shipped SPIKEVAX and Comirnaty vials. This means that vials being distributed in interstate commerce today are mislabeled for purposes of BLA." Pet. at 19. Once again, the Petition misconstrues the law and FDA regulatory practice.

The FDA does not require the manufacturing processes for investigational products used in Phase 3 clinical trials to be identical to those used for commercial production. In fact, the Agency recognizes that manufacturing processes might be subject to evolution over time. The existing regulatory framework and detailed guidance provide the foundation for the FDA to routinely review and approve manufacturing changes through comparability assessments. For additional information, refer to 21 C.F.R. § 601.12 ("Changes to an approved application").[18] The Petition is thus wrong in claiming that manufacturing evolution following Phase 3 renders a product mislabeled or that such changes invalidate clinical evidence supporting licensure. The FDA's approval serves as confirmation that any manufacturing changes that have been reviewed by the Agency have no adverse impact on authorized product quality, efficacy, and safety.[19]

V. Use of EUA-Authorized Diagnostic Tests for Identifying SARS-COV-2 Does Not Render Clinical Assays "Unvalidated"

The Petition further asserts that "[b]oth Pfizer's and Moderna's pivotal studies in humans utilize unvalidated assays for primary efficacy endpoints" on the grounds that the diagnostic tests used to determine if subjects had SARS-COV-2 had been authorized only under the EUAs. Pet. at 26. But the Petition's premise that an EUA-authorized assay is unvalidated or invalid for clinical trial endpoint use is illogical and unsupported. EUA authorization for a diagnostic does

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[18] *See* FDA, *Guidance for Industry: Q5E Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process* (June 2005), https://www.fda.gov/media/71489/download.

[19] Moderna carried out various comparability analyses described by the FDA. *See* Spikevax SBRA at 7-10.

not preclude fitness-for-purpose validation/bridging in a specific trial setting.

Assays used to conduct SARS-CoV-2 testing for Moderna studies were appropriately validated and implemented in accordance with applicable regulatory frameworks and ICH E6 Good Clinical Practice guidelines. For Moderna's SPIKEVAX Phase 3 clinical trial (mRNA-1273-P301), the Viracor Eurofins SARS-CoV-2 RT-qPCR assay was analytically validated under FDA-recognized CLIA high-complexity COVID-19 policies and subsequently granted FDA EUA authorization prior to study initiation. For Moderna's MNEXSPIKE Phase 3 clinical trial (mRNA-1283-P301), the Roche SARS-CoV-2 RT-qPCR assay was fully FDA EUA-authorized, with site-level verification completed at all testing laboratories prior to sample analysis.

The above validation and verification steps ensured that all applicable assays were fit for their intended purpose, validated prior to use, and operated within qualified laboratory systems, consistent with ICH E6 expectations for validated systems, data reliability, and clinical trial quality oversight. Accordingly, the assays used to generate Moderna's clinical data in both SPIKEVAX and MNEXSPIKE clinical studies meet regulatory and GCP requirements.

Study	Assay	Validation & Regulatory Status	Key Validation Milestones	Public Reference
mRNA-1273-P301	Viracor Eurofins SARS-CoV-2 RT-qPCR (LDT)	Fully validated assay with FDA EUA	**March 2020:** Validation submitted to FDA **April 2, 2020:** EUA authorized by FDA	https://www.fda.gov/media/136740/download https://www.fda.gov/media/136739/download
mRNA-1283-P301	Roche SARS-CoV-2 RT-qPCR	Fully validated commercial assay with FDA EUA	**June 2022:** Validation submitted to FDA **June 14, 2022:** EUA authorized by FDA	https://www.fda.gov/files/medical%20devices/published/EUA-Roche-Duo-ifu.pdf https://www.fda.gov/media/159273/download

Moderna's submissions and the regulators' responses prove the point. Although the FDA's "Summary Basis for Regulatory Action" (SBRA) for SPIKEVAX does not specifically discuss validation of assays, the European Public Assessment Report (EPAR) does, stating that "[v]alidation data include various protocols and validation results for extraction PCR performance and stability of test samples using different matrices (swabs and saliva). Overall, the results indicate that the test method is acceptably validated."[20] In addition, as reviewers in the Division of Vaccines and Related Products Applications within FDA's Office of Vaccines Research and Review concluded in their 109-page assessment of January 28, 2022:

[20] European Medicines Agency, *Assessment Report: COVID-19 Vaccine Moderna*, EMA/15689/2021 Corr.1, at 86 (Mar. 11, 2021), https://www.ema.europa.eu/en/documents/assessment-report/spikevax-previously-covid-19-vaccine-moderna-epar-public-assessment-report_en.pdf.

> Two diagnostic assays were used for the assessment of the [Spikevax] Phase 3 clinical study efficacy endpoints. ... Both assays have FDA's authorization for emergency use. Assays used in the evaluation of secondary immunogenicity endpoints include the S-2P IgG binding antibody ELISA (validated; [redacted]) and SARS-CoV-2 pseudotyped virus neutralization assay (PsVNA) (validated; Duke University Medical Center). The information provided in the [Spikevax] BLA supported the suitability of the assays for their intended uses.[21]

Furthermore, the SBRA for SPIKEVAX, dated January 30, 2022, notes the EUA approval of the diagnostic method and concludes that "[t]he assay was adequately validated for the above described diagnostic and viral load assessments."[22]

In short, there is no merit to the Petition's assertion about inadequately validated diagnostic tests for detecting SARS-COV-2 after administration of the SPIKEVAX vaccine in Moderna's clinical trials.

VI. Pre-Clinical Studies Supporting Moderna's BLAs/SBLAs for SPIKEVAX and MNEXSPIKE Met All Applicable Standards

The Petition makes a number of allegations regarding compliance with the standards for pre-clinical studies. None of the arguments has merit.

To start, the Petition's attempts to cast doubt on Moderna's compliance with FDA's current Good Laboratory Practice (GLP) standards and regulations are unfounded. *See* Pet. at 19-26. FDA's GLP requirements, *see* 21 C.F.R. Part 58, apply to nonclinical laboratory studies intended to support the safety of regulated products, including vaccines, when submitted to the FDA in support of INDs or BLAs. Pivotal preclinical safety studies supporting the BLAs/SBLAs for SPIKEVAX and MNEXSPIKE—including repeat-dose toxicity studies (incorporating single-dose and local tolerance endpoints) and developmental and reproductive toxicity studies—were GLP-compliant and conducted with SPIKEVAX or MNEXSPIKE or a product deemed representative of SPIKEVAX or MNEXSPIKE with the same quality attributes.[23] Nor is the Petition right in asserting that "[t]here were no nonclinical or clinical data available for mRNA-1273 (later SPIKEVAX) … before 2020." Pet. at 20. To the contrary, a nonclinical toxicity study was conducted with mRNA-1273 and used to support the EUA for SPIKEVAX.[24]

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[21] FDA, *BLA Clinical Review Memorandum: Spikevax*, at 17-18 (Jan. 28, 2022), https://www.fda.gov/media/156342/download.

[22] *See* Spikevax SBRA at 15.

[23] *See* Spikevax SBRA at 14 ("The safety of SPIKEVAX is further supported by the aggregate rat repeat-dose toxicity profiles observed in six GLP toxicity studies of five vaccines formulated in SM-102 lipid particles containing mRNAs encoding various viral glycoprotein antigens, demonstrating tolerance of repeat doses of these vaccines without any detrimental effects."). Further support was provided by a non-GLP repeat-dose toxicity and immunogenicity study. *See id.*

[24] *See* FDA, *VRBPAC Briefing Document: Moderna COVID-19 Vaccine* (Dec. 17, 2020),

Although the original BLA for SPIKEVAX contained a non-GLP study conducted with mRNA-1273, GLP toxicity studies conducted with other products deemed to be representative of SPIKEVAX were reviewed and cited in this SBA. A GLP toxicity study was conducted with mRNA-1273 and included in SBLAs, as detailed in the Type II variation Assessment report for the bivalent mRNA-1273 containing Omicron BA.1 strain.[25] The results from this study were consistent with the GLP toxicity data from the representative products referenced in the SBA, providing evidence for suitability of those other products to support the BLA of SPIKEVAX. [26] In addition, a GLP toxicity study was conducted and included in the BLA with MNEXSPIKE.[27] Finally, single dose and local tolerance endpoints were deemed appropriately characterized by this body of data by all global health authorities, as specifically stated by Japan's regulatory authority in its report approving SPIKEVAX.[28]

The Petition's claim (at 23) that vaccine development requires standalone safety pharmacology studies is also incorrect. The FDA and other regulatory authorities applying WHO and International Council for Harmonisation (ICH) guidance use a risk-based approach, and vaccines generally do ***not*** warrant dedicated safety pharmacology testing absent a specific safety concern or high systemic exposure to the central nervous system, heart, or lung. The GLP repeat-dose toxicity studies conducted to support licensure of SPIKEVAX and MNEXSPIKE did not identify any of these vital organs as target organs and exposure of vaccine components to these tissues are low to negligible.[29] Thus, no safety pharmacology studies were warranted.

As to Moderna's biodistribution study, the Petition takes issue with the fact that it was conducted in male rats only, was non-GLP, and involved a different product, mRNA-1647

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https://www.fda.gov/media/144434/download.

[25] *See* European Medicines Agency, *Assessment Report: Spikevax*, EMA/896245/2022, at 104-109 (2022), https://www.ema.europa.eu/en/documents/variation-report/spikevax-previously-covid-19-vaccine-moderna-h-c-005791-ii-0075-g-epar-assessment-report-variation_en.pdf.

[26] *See supra* note 23.

[27] *See* FDA, *Toxicology Review of mRNA-1283 Vaccine (Final Report)*, BLA 125835 (mNEXSPIKE) (Original submission, Sept. 30, 2024), *available at* https://www.fda.gov/media/187340/download?attachment [document # 21].

[28] *See* Japanese Ministry of Health, Labour and Welfare, *Report on the Deliberation Results*, at 20 (May 20, 2021), https://www.pmda.go.jp/files/000243267.pdf.

[29] Susan M.G. Goody et al., *Biodistribution of mRNA Vaccines in Rats: Enrichment in Injection Site and Lymph Tissues and Rapid Clearance Without Tissue Persistence*, at 5, bioRxiv (posted Jan. 25, 2026), https://www.biorxiv.org/content/10.64898/2026.01.23.701408v1.full.pdf; Spikevax SBRA at 14; FDA, *Toxicology Review of mRNA-1283 Vaccine (Final Report)*, BLA 125835 (MNEXSPIKE) (Original submission, Sept. 30, 2024), https://www.fda.gov/media/187340/download?attachment [document # 21]; European Medicines Agency, *Assessment Report: COVID-19 Vaccine Moderna*, EMA/15689/2021 Corr.1, at 47 (Mar. 11, 2021), https://www.ema.europa.eu/en/documents/assessment-report/spikevax-previously-covid-19-vaccine-moderna-epar-public-assessment-report_en.pdf; European Medicines Agency, *Assessment Report: Spikevax*, EMA/896245/2022, at 104-109 (2022), https://www.ema.europa.eu/en/documents/variation-report/spikevax-previously-covid-19-vaccine-moderna-h-c-005791-ii-0075-g-epar-assessment-report-variation_en.pdf; Australian Department of Health, *Australian Public Assessment Report for Elasomeran* [Spikevax], at 14-15 (Aug. 2021), https://www.tga.gov.au/sites/default/files/auspar-elasomeran.pdf; Japanese Ministry of Health, Labour and Welfare, *Report on the Deliberation Results*, at 20 (May 20, 2021), https://www.pmda.go.jp/files/000243267.pdf.

(cytomegalovirus vaccine), rather than mRNA-1273 (SPIKEVAX). *See* Pet. at 20, 23-24. To begin with, biodistribution studies are ***not*** explicitly required by 21 C.F.R. Part 58, WHO, or ICH to be GLP-compliant.[30] Moreover, consistent with regulatory guidance, the need for and design of the biodistribution studies used to support SPIKEVAX and MNEXSPIKE were determined using a risk-based approach that considered the vaccine platform, formulation, route of administration, and how the data were used to support the safety assessment.

As to the criticism that the biodistribution study focused on mRNA-1647, it is meritless. As explained in one of the Moderna studies that the Petition itself cites (at 20 n.34),[31] because biodistribution will be driven by the lipid nanoparticle (LNP) structure of Moderna's vaccine platform, assessing biodistribution of mRNA-1647 will also be applicable to mRNA-1273.[32] Moreover, not only the FDA but regulatory bodies around the world accepted this study for licensure.[33] In sum, Moderna's FDA-approved methodology for assessing biodistribution does not call the SPIKEVAX BLA into question.

As to the fact that the biodistribution study with mRNA-1647 was conducted in male rats only, Pet. at 23-24, Moderna has conducted a biodistribution study using mRNA-1273 (SPIKEVAX) in male and female Sprague Dawley rats.[34] This study was conducted following engagement with the FDA and other global health authorities and performed in accordance with applicable international guidance, including the World Health Organization (WHO) guidelines on the nonclinical evaluation of vaccines and mRNA vaccines and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use. Detailed biodistribution datasets, including the mRNA-1273 biodistribution study, have been reviewed by multiple regulatory agencies worldwide to support licensure of SPIKEVAX and MNEXSPIKE.

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[30] *See, e.g.*, FDA, *S12 Nonclinical Biodistribution Considerations for Gene Therapy Products Guidance for Industry*, at 3 (May 2023) ("In principle, nonclinical BD studies that are not conducted in compliance with good laboratory practice (GLP) are acceptable."), https://www.fda.gov/media/167605/download; WHO, *Guidelines on Nonclinical Evaluation of Vaccines*, WHO Technical Report Series, No. 927, at 33 (2005) ("[T]here may be situations where full compliance with GLP is not possible."), https://cdn.who.int/media/docs/default-source/biologicals/vaccine-standardization/annex-1nonclinical.p31-63.pdf; ICH, *Nonclinical Biodistribution Considerations for Gene Therapy Products S12*, at 2 (Mar. 14, 2023) ("In principle, nonclinical BD studies that are not conducted in compliance with Good Laboratory Practice (GLP) are acceptable."), https://database.ich.org/sites/default/files/ICH_S12_Step4_Guideline_2023_0314_WithCorrection_0.pdf.

[31] The Petition incorrectly describes studies cited in footnote 34 as relating to Comirnaty rather than SPIKEVAX.

[32] HHS Response to Judicial Watch FOIA Request, at PDF p. 293 (Apr. 13, 2022) ("The biodistribution of mRNA-based vaccines in LNPs is predicted to be driven by the LNP characteristics. Therefore, mRNAs that are within an LNP of the same composition (e.g., mRNA-1273 and mRNA-1647) are expected to distribute similarly."), https://www.judicialwatch.org/wp-content/uploads/2022/08/JW-v-HHS-Biodistribution-Prod-4-02418.pdf; *see also id.* at 302, 308, 318, 332, 345, 362, 660, 669, 670, 678, 695 (same).

[33] *See, e.g.*, Spikevax SBRA at 14; European Medicines Agency, *Assessment Report: COVID-19 Vaccine Moderna*, EMA/15689/2021 Corr.1, at 47 (Mar. 11, 2021), https://www.ema.europa.eu/en/documents/assessment-report/spikevax-previously-covid-19-vaccine-moderna-epar-public-assessment-report_en.pdf; Swissmedic, *Swiss Public Assessment Report*, at 12 (Dec. 3, 2021), https://www.swissmedic.ch/dam/swissmedic/en/dokumente/zulassung/swisspar/68267-spikevax-01-swisspar-20211203.pdf.download.pdf/20211203_SwissPAR-Spikevax.pdf.

[34] *See* Susan M.G. Goody et al., *Biodistribution of mRNA Vaccines in Rats: Enrichment in Injection Site and Lymph Tissues and Rapid Clearance Without Tissue Persistence*, at 5, bioRxiv (posted Jan. 25, 2026), https://www.biorxiv.org/content/10.64898/2026.01.23.701408v1.full.pdf.

These detailed study reports and datasets are reviewed by health authorities as part of regulatory submissions, but they are not typically accessible to the public. Therefore, statements asserting that biodistribution data are not available in both male and female rats, based solely on the observation that they were not included in the FDA Summary Basis for Regulatory Action or EMA Assessment Report, are inaccurate. To enhance public understanding, biodistribution data for mRNA-1273 were recently made public.[35]

With regard to the Petition's claim (at 24) that about "significant increase in fetal abnormalities" in Moderna's GLP-compliant perinatal/postnatal developmental and reproductive toxicity study, regulatory authorities worldwide reviewed Moderna's complete study report for licensure of mRNA-1273, where the study was conducted at doses in rats that significantly exceeded the dose administered to humans when normalized to body weight. Regulatory authorities consistently concluded that the skeletal findings observed in rat offspring were not adverse and had no biological or toxicological consequence, as there were no effects on pup growth, viability, or postnatal development. Partly on that basis, the FDA and other health authorities all concluded that "no vaccine-related fetal malformations or variations and no adverse effect on postnatal development were observed in the study."[36] As summarized by the Swiss national regulatory authority Swissmedic:[37]

> A GLP-compliant developmental and reproductive toxicity (DART) study was performed in female Sprague Dawley rats with mRNA-1273. A human clinical dose [based on per dose basis] of the mRNA-LNP vaccine was administered twice before mating and twice during gestation. The only noteworthy findings were the development of wavy ribs and increased nodules on ribs, but these were not considered adverse as there was no effect on pup growth or viability. The wavy ribs and rib nodules resolve postnatally without medical intervention.

Regarding the Petition's claim (at 26) that "reproductive toxicity in males was not assessed for … Moderna's SPIKEVAX and MNEXSPIKE," both the FDA's vaccine guidance and the ICH S5(R3) describe reproductive toxicity testing for vaccines (including male fertility assessment) as risk-based and product-specific, rather than a routine requirement for all vaccines intended for adults of reproductive age.[38] Additional male fertility studies are recommended

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35 *See id.*

36 Spikevax SBRA at 14; *see also* FDA, *Toxicology Review of SPIKEVAX (mRNA-1273 COVID-19 Vaccine)*, BLA 125752/0 (May 28, 2021), *available at* https://www.fda.gov/media/156343/download?attachment.

37 Swissmedic, *Swiss Public Assessment Report*, at 14 (Dec. 3, 2021), https://www.swissmedic.ch/dam/swissmedic/en/dokumente/zulassung/swisspar/68267-spikevax-01-swisspar-20211203.pdf.download.pdf/20211203_SwissPAR-Spikevax.pdf.

38 *See* FDA, *Guidance for Industry: Considerations for Developmental Toxicity Studies for Preventive and Therapeutic Vaccines for Infectious Disease Indications* (Feb. 2006), https://www.fda.gov/files/vaccines%2C%20blood%20%26%20biologics/published/Guidance-for-Industry--Considerations-for-Developmental-Toxicity-Studies-for-Preventive-and-Therapeutic-Vaccines-for-Infectious-Disease-Indications.pdf; ICH, *ICH Harmonised Guideline: Detection of Reproductive and Developmental Toxicity for Human Pharmaceuticals S5(R3)* (adopted Feb. 18, 2020), https://database.ich.org/sites/default/files/S5-R3_Step4_Guideline_2020_0218.pdf.

only when triggered by meaningful exposure in reproductive organs, adverse histopathological findings, or a plausible biological mechanism for effects on fertility or germline cells. In the case of SPIKEVAX (mRNA-1273), biodistribution studies demonstrated little to no distribution to the testes,[39] and GLP repeat-dose toxicity studies with mRNA-1273, mRNA-1283, or representative of mRNA-1273 showed no histopathological findings in male reproductive organs.[40] In the absence of meaningful exposure, pathological findings, or mechanistic concern, both FDA and ICH guidance supports reliance on the existing nonclinical safety package and does not require a standalone male fertility mating study.

VII. FDA-Authorized cGMP Deviations During the EUA Do Not Later Taint Licensure or Misbranding

Finally, the Petition argues that compliance with Current Good Manufacturing Practices (cGMP) "ensures accurate and truthful disclosure in the labeling of BLA biological products. Absent adherence to such procedures, biologics are mislabeled and misbranded and are therefore subject to recall and BLA licensure revocation." But the vaccines are manufactured in full compliance with applicable cGMPs and were similarly manufactured in compliance with cGMP requirements during the EUA period. For example, consistent with the FDA's EUA Conditions of Authorization for SPIKEVAX, manufacturing had to be conducted in line with GMPs,[41] and GMP documentation was submitted to the FDA for batch-level awareness and quarterly oversight.[42] Moderna complied with these requirements for GMP manufacturing. In addition, CBER conduced a pre-licensure inspection of a Moderna facility in October 2021 and classified as "no action needed" (NAI), meaning that the facility was deemed to be in an acceptable state of compliance with cGMPs and the FDA did not require any additional action.[43]

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[39] Susan M.G. Goody et al., *Biodistribution of mRNA Vaccines in Rats: Enrichment in Injection Site and Lymph Tissues and Rapid Clearance Without Tissue Persistence*, at 5, bioRxiv (posted Jan. 25, 2026), https://www.biorxiv.org/content/10.64898/2026.01.23.701408v1.full.pdf.

[40] *See* Spikevax SBRA at 14; European Medicines Agency, *Assessment Report: Spikevax*, EMA/896245/2022 at 104-109 (2022), https://www.ema.europa.eu/en/documents/variation-report/spikevax-previously-covid-19-vaccine-moderna-h-c-005791-ii-0075-g-epar-assessment-report-variation_en.pdf; Swissmedic, *Swiss Public Assessment Report*, at 13 (Dec. 3, 2021), https://www.swissmedic.ch/dam/swissmedic/en/dokumente/zulassung/swisspar/68267-spikevax-01-swisspar-20211203.pdf.download.pdf/20211203_SwissPAR-Spikevax.pdf; FDA, *mNEXSPIKE Summary Basis for Regulatory Action*, at 15-16 (May 30, 2025), https://www.fda.gov/media/187164/download.

[41] *See* Letter from Denise M. Hinton, Chief Scientist, FDA, to ModernaTX, Inc., §§ III.I & III.H (Dec. 18, 2020) (granting EUA for SPIKEVAX and imposing various conditions, including that "[a]ll manufacturing facilities will comply with Current Good Manufacturing Practice requirements" and that "[n]o changes will be implemented to the description of the product, manufacturing process, facilities, or equipment without notification to and concurrence by the [FDA]"), https://www.amlc.army.mil/Portals/73/Documents/Moderna%20COVID-19%20Vaccine%20EUA%20Letter%20of%20Authorization.pdf?ver=io4XV_A4ECFIuOSAF9tcFw%3D%3D.

[42] *See id.* §§ III.J & III.K.

[43] *See* Spikevax SBRA at 12. Elsewhere, the FDA confirmed that, as to "[t]he facilities for manufacture and testing of" the Spikevax drug substance, "[a]ll sites are cGMP compliant and have US FDA establishment licenses." FDA, *CMC Review Memorandum*, at 1 (Jan. 28, 2022), https://pink.citeline.com/-/media/supporting-documents/pink-sheet/2022/05/cmc-review-memo-january-28-2022--spikevax.pdf.

The text of the FD&C Act makes clear (as the Petition itself notes) that, during a "public health emergency," the FDA may authorize "deviations" from cGMP "with respect to an eligible product." 21 U.S.C. § 360bbb-3a(c)(1). The statute further provides that "an eligible product shall ***not*** be considered an unapproved product" and "shall ***not*** be deemed adulterated or misbranded under this chapter" when such deviations are "authorized." *Id.* § 360bbb-3a(c)(2) (emphases added); *see* Pet. at 8. cGMP compliance is evaluated during the licensure process and continuously monitored throughout the lifecycle of an approved biological product. Prior emergency conditions do not preclude full regulatory approval. Furthermore, while the FDA may permit certain "deviations" from cGMP under emergency circumstances, this does not diminish the thorough and rigorous evaluation applied to COVID-19 vaccines, particularly in light of the critical public health threat during the pandemic. Moreover, misbranding requires false or misleading labeling, not merely historical manufacturing evolution or resolved deviations. *See* 21 U.S.C. § 352(a). And the Petition does not dispute that the vaccines are currently manufactured in full compliance with applicable cGMPs.

VIII. Conclusion

For those reasons and others, the FDA should deny the Citizen Petition.

Respectfully Submitted,

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